

Closing the Quality Gap in Michigan: *A Prescription for Mental Health Care*

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EXECUTIVE SUMMARY

The publication of this action plan—the work of a distinguished panel of 25 mental health experts who served as the project steering committee—is the first phase of a multiyear effort to improve the quality of mental health care in Michigan by encouraging physicians to adopt best-practice or evidence-based practice (EBP) in the prescription and monitoring of drugs for people with major depression, bipolar disorder, and schizophrenia. The steering committee's charge was to select the guidelines/algorithms best suited for Michigan and create a research-based plan aimed at encouraging their use.

Reliable and rapidly accumulating research demonstrates that the mental health care Americans receive is not always grounded in science or generally recognized best practices. Further, the lag between the discovery of new treatments and their routine incorporation into patient care is often unacceptably long. The best practice- and evidence-based tools advocated here—guidelines and algorithms—overcome both problems by summarizing treatment options in a way that reflects the state of scientific research or the expert opinion of practitioners in the field.

Funding for this project was provided by the Ethel and James Flinn Foundation of Detroit, which contracted with Public Sector Consultants Inc. of Lansing to manage the project.

Guideline/Algorithm Selection

After a careful review of available options, the steering committee recommends that the Texas Implementation of Medication Algorithms (TIMA) guidelines be appropriately modified for use in Michigan. The TIMA guidelines are scientifically sound, field-tested, and regularly updated. Equally important, they are part of a larger program of care that includes evaluation and measurement and the education and support of patients and families.

Principles

Research sponsored by and made available to the Steering Committee indicates that the action plan would be successful to the degree that it embodies the following principles:

- The guidelines/algorithms must be easy to use and part of a broader education and disease management approach.
- Differences in knowledge and needs among psychiatrists, primary care physicians (PCPs), and consumers must be part of the plan.
- The plan should be rolled out over time, with pilot programs to enlist opinion leaders and early adopters.

Elements of the Plan

The action plan itself offers both general recommendations and specific tactics associated with seven different strategic areas. The two general recommendations are:

- **Pilot Programs.** *The steering committee and its leadership successor team should implement the EBP action plan by supporting and sponsoring three to six pilot programs at locations around Michigan over the next three years. The pilot programs, which would be designed to implement and test the efficacy of the EBP guidelines and algorithms, would be based upon the strategies and tactics described below. To the degree possible, all three conditions*

(major depression, bipolar disorder, and schizophrenia) would be included in each pilot, which would also cover public and private systems of care and accommodate the differing needs of primary care physicians and psychiatrists. The committee notes that state hospitals, university consortia, and private mental health practices that are university affiliated would be logical pilot program candidates.

■ **Leadership Team.** *To maintain the continuity and momentum of this effort and facilitate the establishment and ongoing operations of pilot programs there should be established in Michigan a leadership team with the following components:*

- 1. A “committee of the whole” composed of current steering committee members that will meet once or twice annually to review progress in the implementation of the report, suggest mid-course corrections, and serve as “ambassadors” for the project within Michigan.*
- 2. An “executive committee,” composed of volunteers from the steering committee and including both public- and private-sector participation that will provide oversight and assistance in a number of areas, especially in the critical area of funding. This group would meet more regularly, perhaps every other month.*
- 3. A “project coordination group” charged with staffing the project and doing the day-to-day work of implementation—including meeting with potential funders, developing requests for proposals (RFPs), evaluating proposals for local pilot programs, and coordinating the activities of the pilot programs that are established.*

The two recommendations create a framework within which this EBP project can proceed in Michigan and reflect the committee’s belief that EBP principles are best advanced by means of local pilot programs guided by state-level leadership. A table outlining the roles and responsibilities of the leadership team and the pilot programs is included in the report as Appendix A.

The following strategies and tactics indicate the work the pilot programs must accomplish.

Strategies for the Packaging and Distribution of Guidelines and Algorithms

Tactic 1: *The leadership team should oversee the reformatting and disseminating to the pilot programs of Michigan-specific guidelines and algorithms based upon the Texas (i.e., TIMA) model.*

Tactic 2: *The reformatted guidelines/algorithms should be available in both short and long versions and disseminated to accommodate differing needs and uses.*

Tactic 3: *The guidelines/algorithms should be tailored specifically for use with information technology, the Internet, local networks, and PDAs.*

Tactic 4: *Existing disease management tool kits available for treatment of major depression, bipolar disorder, and schizophrenia should be collected and analyzed, and, if necessary, new tool kits should be developed for use in the pilot programs.*

Tactic 5: *The newly formatted Michigan algorithms should be updated regularly.*

Strategies for Physician Education

Tactic 1: *The leadership team and pilots should develop strong, consistent messages as to explain the value of guidelines and algorithms. These should be focused on critical issues such as expected outcomes and physician autonomy and, whenever possible, be accompanied by stakeholder endorsements.*

Tactic 2: *As part of a commitment to being “centers of excellence,” one or more state medical schools should adopt and teach guidelines/algorithms as part of the medical school curriculum and in residency training programs.*

Tactic 3: *The leadership team and pilot programs should explore ways of offering Continuing Medical Education (CME) credit for conferences, training programs, and regional sessions devoted to evidence-based mental health care and the use of guidelines and algorithms.*

Tactic 4: *The leadership team and pilot programs should work together to develop site-specific physician training programs for each pilot program.*

Strategies for Consumer Education

Tactic 1: *The leadership team and pilot programs should develop materials and methods for improving patient-physician communication on the nature, importance, value, and use of guidelines and algorithms during individual treatment sessions—that is, on a “one-to-one” basis.*

Tactic 2: *Pilot programs and the leadership team should collaborate on a broader program of consumer education and awareness through the use of public service announcements, and, most especially, by employing existing advocacy groups as messengers to their constituents.*

Tactic 3: *The leadership team should evaluate the need to conduct further research into consumer needs and preferences as well as the possibility of offering consumer education tailored to specific subgroups or settings—for example, CMH settings.*

Strategies for Ongoing Physician Support

Tactic 1: *The leadership team and pilot programs should devise mechanisms to support and assist clinicians in the treatment of specific cases and patients.*

Tactic 2: *The leadership team and individual pilots should mutually develop support mechanisms to help with administration and logistics of the pilot itself.*

Tactic 3: *The leadership team should work with payers to develop prescriber profiles and make them available to prescribers and researchers, while remaining sensitive to privacy issues. As part of this process, the group should encourage as much as possible movement toward universal use of electronic medical records.*

Strategies to Develop Incentives for Change

Tactic 1: *The leadership team and pilots should develop nonfinancial incentives for the adoption of guidelines and algorithms.*

Tactic 2: *The leadership team should offer CME credit as an incentive as well as an educational opportunity.*

Tactic 3: The leadership team should approach payers to secure their buy-in for: (1) paying or creating rewards for guideline/algorithm adherence and (2) increasing reimbursement to improve the quality of care and reporting.

Tactic 4: The leadership team should work with the Michigan Department of Community Health to ensure that contracts with providers reflect EBP principles.

Strategies for Evaluation and Measurement

Tactic 1: The leadership team, working with representatives from the pilot programs, should develop multidimensional evaluation and measurement techniques that assess adherence to and variation from guidelines, effectiveness of guidelines, consumer and physician satisfaction, cost, and variations among prescribers.

Tactic 2: The leadership team and the local pilot programs should work together to establish registries of persons with the conditions of interest (depression, bipolar disorder, and schizophrenia), while remaining sensitive to privacy issues.

Strategies for Stakeholder Buy-in

Tactic 1: The leadership team should assist pilot programs in developing EBP buy-in at each site through informational outreach efforts.

Tactic 2: The leadership team should identify a suitable contractor to coordinate marketing efforts to consumer advocacy groups and other groups with an interest in mental health care.

Tactic 3: The leadership team should encourage current steering committee members to serve as active ambassadors for EBP, the use of guidelines and algorithms in mental health care, and the pilot program process.

Tactic 4: The leadership team should serve as a liaison to private foundation and corporate funders, within Michigan and nationally, and develop strategies for engaging their support for the project.

INTRODUCTION

This action plan, or “blueprint,” is the first phase of a multiyear effort to improve the quality of mental health care in Michigan by encouraging the fuller incorporation of best-practice or evidence-based principles into the delivery of health care. The plan’s focus is the use of medication guidelines or algorithms in the treatment of three conditions: major depression, bipolar disorder, and schizophrenia. Project funding was provided by the Ethel and James Flinn Foundation of Detroit, which contracted the services of Public Sector Consultants Inc. of Lansing to manage the project. Founded in 1976, the Flinn Foundation supports research into the treatment of mental illness.

The plan is the work of the distinguished panel of 25 experts who served as the project steering committee. This group of practitioners, payers, consumer advocates, state and community mental-health officials, and academic researchers met over a period of 18 months to:

- Select from a number of available options the guidelines/algorithms best suited for use in Michigan

- Identify barriers to their adoption in the field
- Create a research-based action plan aimed at more fully integrating the use of medication guidelines and algorithms into mental health care, thereby bridging the gap between what we know through research and the care clinicians offer in practice

The steering committee operated on a consensus basis and the resulting action plan is, therefore, the product of its strongest areas of agreement. A full record of the committee's activities including agendas, PowerPoint presentations, and summaries is available in Appendices B–H. Steering committee members are listed in the table below.

Steering Committee Members	
Patrick Barrie , Deputy Director Health Programs Administration Michigan Department of Community Health	Jed Magen , DO, MS, Acting Chair Department of Psychiatry Michigan State University
John Baugh , MD, Medical Director St. Clair County Community Mental Health	Michael Massanari , MD, MS, Director Center for Health Care Effectiveness Research Wayne State University School of Medicine
Richard C. Berchou , PharmD Assistant Professor Wayne State University Psychiatric Center	Karen K. Milner , MD, Director Psychiatric Emergency Services University of Michigan
Hubert A. Carbone , MD Director of Psychiatric/Medical Services, Michigan Department of Community Health	Barry Mintzes , PhD Psychologist Lansing Psychological Associates PC
Tom Carli , MD, Medical Director Medical Management Center/Disease Management Programs University of Michigan Health Plans	Michele Reid , MD, Medical Director Detroit-Wayne County Community Mental Health
Wayne Creelman , MD, Medical Director Pine Rest Christian Mental Health Services	Mark Reinstein , PhD, President and CEO Mental Health Association in Michigan
Calmeze H. Dudley , MD, Medical Director Mental Health Services Blue Cross Blue Shield of Michigan	Robert Sheehan , MSW, MBA, Executive Director Clinton-Eaton-Ingham Community Mental Health
Michael F. Engel , DO, President Michigan Psychiatric Society	Manuel Tancer , MD, Interim Chair Department of Psychiatry and Behavioral Neurosciences Wayne State University
Michael Fauman , MD, PhD, Medical Director Magellan Behavioral of Michigan Inc.	Philip E. Veenhuis , MD, MPH (retired)
Jonathan G. A. Henry , MD, Medical Director CEI Community Mental Health Board	Daniel J. Wilhelm , MD, Pediatrician Children's Healthcare (Port Huron)
Hubert Huebl , MD, President National Alliance for the Mentally Ill (Michigan Chapter)	Kathleen Williams , President American Psychiatric Nurses Association (Michigan Chapter)
Robb Imonen , DO, Psychiatrist Marquette General Health System	Michael L. Zarr , MD, MBA, Vice President, Medical Director ValueOptions, Detroit Service Center
Kevin B. Kerber , MD, Director Adult Ambulatory Services University of Michigan	Thomas C. Zelnik , MD, Chairman Department of Psychiatry St. Joseph Mercy Health System

While the specific focus here is psychopharmacological treatment of mental illness, it is understood that no adequate treatment plan can be developed in the absence of accurate diagnosis and assessment and a comprehensive array of effective rehabilitation services. Further, the project steering committee recognizes that the document cannot be read in isolation but comes, in fact, at a time when there are other important and far-ranging discussions taking place

about the future of mental health care in Michigan. In particular, the report of the Governor's Mental Health Commission will also be made public in the fall of 2004. The steering committee's hope is that this document, like the report of the Mental Health Commission, will contribute to a rich and important dialogue about how best to offer care in the first decades of the new century.

“BEST” AND “EVIDENCE-BASED” PRACTICES

No doubt many Americans were surprised earlier this year when a major study by the RAND Corporation demonstrated that patients get substandard health care about half the time, even if they live near a major teaching hospital.¹ For medical researchers, however, the study merely confirms evidence that has been accumulating for some time. The care patients receive in practice is often not as good as it could be. This is the case for mental health care as well as general medical care.

Evidence-based practice has been defined as “the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients.”² It is not a substitute for clinical judgment or what is commonly called “the art of medicine.” Indeed, both clinical expertise and patient values will always play an important role in determining a course of treatment.

In the sense in which it is used here, the phrase “evidence based” is consistent with the concept of “best practices.” The acronym “EBP,” which is used throughout, is employed broadly to refer to both concepts. Practices that are evidence based reflect the current state of knowledge. They are not gospel but, rather, a useful first step in treating an individual patient at a specific point in time. The federal Agency for Healthcare Research and Quality (AHRQ) classifies “evidence” according to strength or certainty. From highest degree of evidence to lowest, here are the classifications:

- Meta-analysis of multiple well-designed controlled studies
- Well-designed randomized controlled trials
- Well-designed nonrandomized controlled trials
- Observational studies with controls (retrospective studies, interrupted time-series studies, case-control studies, cohort studies with controls)
- Observational studies without controls (cohort studies without controls and case series)

Best practices may result from any of these five categories of evidence.

American health care certainly ranks among the best in the world, and many citizens naturally assume that the care they receive is firmly grounded in science. Yet, a substantial body of recent

¹ As reported by Lawrence K. Altman, “Study Finds Widespread Problem of Inadequate Health Care,” *New York Times* (May 5, 2004). RAND's “First National Report Card on Quality of Health Care in America” included interviews with 13,000 individual adults in 12 metropolitan areas, including Lansing. Depression was one of the conditions in the project's quality assessment tool. For more information consult “RAND Health” on the website: www.rand.org.

² D. L. Sackett, S. E. Strauss, W. S. Richardson, et al., *Evidence-Based Medicine: How to Practice and Teach EBM*, 2d ed. (New York: Churchill Livingstone, 2000). As quoted in Gregory E. Gray, *Concise Guide to Evidence-Based Psychiatry* (Washington, D.C.: American Psychiatric Publishing, 2004), 3.

research demonstrates that this is frequently not the case. As the Institute of Medicine recently notes:

Quality problems are everywhere, affecting many patients. Between the health care we have and the care we could have lies not just a gap, but a chasm.³

The same Institute of Medicine report cited evidence that the lag between the discovery of new treatments and their routine incorporation into patient care was unacceptably long—15 to 20 years in some cases.

What is true in health care generally is also true in mental health care and psychiatry. For instance, a 1999 Surgeon General's report—the first ever on mental health—notes an imperative need to develop “innovative strategies” to bridge the gap “between what is known from research and what is practiced.”⁴ More recently still, the President's New Freedom Commission on Mental Health noted that the mental health care system “needs dramatic reform because it is incapable of efficiently delivering and financing effective treatments, such as medications, psychotherapies, and other services, that have taken decades to develop.” In view of this, it is not surprising that the implementation of evidence-based practice in mental health care is a high priority in most states.⁵

One of the clearest signals that mental health and other kinds of medical care are not optimal is the documented wide variation that occurs in treatment. If practice were firmly evidence-based, one would expect far less variation than has been observed. The variation in care that has been observed in medical care nationally has also been observed in Michigan. For example, Blue Cross/Blue Shield of Michigan's *Dartmouth Atlas of Health Care in Michigan* shows considerable small area variation in the frequency with which SSRI medications are prescribed.

Practices that are not based upon science, or at least expert consensus, are often based instead upon tradition, convenience, clinician preferences, and even payer policies. This has costs. Patients may receive inappropriate, unnecessarily costly, or even harmful care. Even when no overt harm is done, an opportunity is lost to provide patients with the care they need and expect on a timely basis.

Two general types of information problems contribute to patients receiving less than optimal care:

- The simple inability of individual practitioners to stay abreast of new developments
- The over-reliance of practitioners upon unreliable sources of information

The best practice- and evidence-based tools we advocate here—guidelines and algorithms—overcome both of these problems by reliably summarizing treatment options in a way that reflects the state of scientific research or the expert opinion of practitioners in the field. Yet, the steering committee is also acutely aware that the dissemination of practice guidelines alone will

³ Institute of Medicine, *Crossing the Quality Chasm: A New Health System for the 21st Century* (Washington, D.C.: National Academy Press, 2001), 1.

⁴ United States Department of Health and Human Services, *Mental Health: A Report of the U.S. Surgeon General – Executive Summary* (Washington, D.C.: HHS, 1999), 20–21.

⁵ Presentation to the Steering Committee by Vijay Ganju, Center for Mental Health Quality and Accountability, National Association of State Mental Health Program Directors (NASMHPD), June 4, 2003.

have limited beneficial effect upon clinical practice. As the document suggests, best- and evidence-based care practices will only bring about productive change if they are part of a broader program of clinical support, education, and research.

GUIDELINES/ALGORITHM SELECTION

The question of what guidelines and/or algorithms should be recommended for use in Michigan was addressed by means of separate working groups devoted to the three conditions (major depression, bipolar disorder, and schizophrenia). The groups approached the question independently of one another and examined a number of guidelines and algorithms including the American Psychiatric Association guidelines, the Harvard algorithms, and the Texas Implementation of Medication Algorithms (TIMA), to name some of the better known examples. Each group decided that the TIMA guidelines, with appropriate modifications, would be the most useful in Michigan. Their reasons can be summarized as follows:

- The TIMA algorithms are well grounded in science and comport well with the best available evidence.
- The TIMA algorithms are not stand-alone documents, but are, rather, part of a larger program of care that includes evaluation and measurement and the education and support of patients and families.
- The TIMA algorithms have been field-tested and evaluated in Texas with largely encouraging results.
- The TIMA algorithms are regularly updated, something that would make the necessary updating process in Michigan far easier to accomplish.

The latest version of the algorithms recommended for Michigan, called the Michigan Implementation of Medication Algorithm (MIMA), is available in Appendices I–K.⁶

COMMITTEE-SPONSORED RESEARCH

Having identified algorithms that could be used in Michigan, the steering committee then identified both barriers to and promoters of their adoption. It did this in two ways: (1) a steering committee member, Dr. Michael Massanari, Director of the Center for Healthcare Effectiveness Research at Wayne State University, provided an overview on the conclusions of research into how change in practice occurs among physicians; and (2) the committee oversaw and guided a survey of prescribers in Michigan designed to produce information on their knowledge of and attitudes toward best and evidence-based practice in mental health care.

Literature Review: Implementation Barriers and Promoters

The literature reviewed by Dr. Massanari supports the following conclusions:

- Guidelines should be implemented under carefully designed protocols and linked to a concurrent evaluation process designed to measure adherence to guidelines and the impact on outcomes of care. Evaluation should include feedback from users regarding the format and usefulness of Michigan treatment guidelines.

⁶ The original TIMA algorithms upon which it is based are available at: www.mhmr.tx.us/centraloffice/medicaldirector/TIMA.

- Design of implementation protocols should be based on a detailed clinical process analysis that includes input from process engineers and practitioners with the objective of developing a “user-friendly tool kit” that will facilitate implementation.
- Implementation protocols should be multifaceted and include:
 - Education of providers and consumers
 - Making available a tool kit to support providers
 - Administrative support for implementation
 - Feedback of results of evaluation to providers
 - Access to technical support for implementation
- Additional factors to consider in promoting adoption and implementation of guidelines:
 - Mechanisms for dialogue between physician champions and practitioners who are reluctant adopters
 - Information technologies to facilitate adoption and implementation
 - External incentives to promote adoption and implementation through contracts and public rewards
 - Incorporation of case-managers into the care process

Survey of Prescribers

Staff worked with committee members and with representatives of the prescribing community to create and field a survey instrument.⁷ Some of the key findings include:

- Prescribers place a great deal of emphasis upon requiring proof that evidence-based practices actually improve patient outcomes.
- Respondents are influenced most by expert opinion, scientific evidence, and the views of colleagues.
- Peer-reviewed journals, workshops, and information provided by professional organizations are the most useful avenues of communication.
- Any plan to attack the systemic barriers to EBP needs to accommodate the differing experiences and needs of primary care physicians and psychiatrists.
- Guidelines or algorithms will be useful to the degree that they are evidence based and easy to use.

Because of concerns about the low rate of response, the quality of the contact lists, and a lack of randomness in response, the steering committee views the survey results with caution, while noting that they have a certain face validity because they comport well with the conclusions of research offered by Dr. Massanari. Further information on the survey instrument, protocols, and frequencies is available in Appendix L.

⁷ The researchers worked with groups like the Michigan State Medical Society to develop a master list of some 6,000 possible respondents to whom the survey instrument was distributed. Approximately 530 prescribers (9 percent) responded.

STRATEGIES

The survey and the literature review produced consistent and compatible results, allowing the steering committee to formulate a series of linked strategies for encouraging the greater use of medication guidelines and algorithms.

- **Strategies for packaging and presenting guidelines and algorithms.** The guidelines/algorithms must be fully customized for use in Michigan and disseminated in a way that is useable and attractive.
- **Strategies for physician and consumer education.** Physicians, patients, and families have to fully understand the guidelines/algorithms, how to use them properly, what their limitations are, and how they relate to other therapies.
- **Strategies for ongoing physician support.** There must be a structured mechanism for providing physicians with information, updates, and logistical support as well as immediate (i.e., “bedside”) assistance with difficult or complex cases.
- **Strategies to create incentives for guideline adoption.** Research suggests that certain direct financial, indirect financial, and nonfinancial incentives will hasten and promote guideline/algorithm adoption.
- **Strategies for the evaluation and measurement of guideline/algorithm use.** To provide information to physicians and other stakeholders, a multifaceted evaluation approach will be required that is firmly grounded in practice and focused upon both outcome and process measurements.
- **Strategies for stakeholder buy-in.** For the EBP project to succeed there must be buy-in from stakeholders—practitioners, patients, advocacy groups, payers, and academic researchers on both the broad state and local level.

The steering committee also discussed the specific tactics that would be appropriate to each strategy area. If the strategies describe the “*what*” of an EBP action plan, the tactics provide the “*how*.” A discussion of the strategies and tactics, endorsed by the steering committee makes up the bulk of this report.

PRINCIPLES

The survey and literature review also revealed the importance of a number of cross-cutting principles that should guide and inform the strategies and tactics:

- Guidelines/algorithms must be easy to use and valuable.
- Guidelines/algorithms by themselves are not enough; they must be part of a broader education and disease management approach.
- Differences in knowledge and needs among psychiatrists, primary care physicians (PCPs), and consumers must be part of the action plan.
- The action plan should be rolled out over time, with pilot programs to enlist opinion leaders and early adopters.

The final point warrants special attention because it identifies the framework within which the action plan can be operationalized in Michigan.

GENERAL RECOMMENDATIONS

Two general recommendations suggest a framework within which this EBP project can proceed in Michigan. They reflect the committee's belief that EBP principles are best advanced by means of local pilot programs undertaken in coordination with an ad hoc state-level leadership team. Information gleaned from these efforts should be used to improve the pilots and disseminated more broadly to the practitioner community at large.

Recommendation: Pilot Programs

The steering committee and its leadership successor team should implement the EBP action plan by supporting and sponsoring three to six pilot programs at locations around Michigan over the next three years. The pilot programs, which would be designed to implement and test the efficacy of the EBP guidelines and algorithms, would be based upon the strategies and tactics described below. To the degree possible, all three conditions (major depression, bipolar disorder, and schizophrenia) would be included in each pilot, which would also cover public and private systems of care and accommodate the differing needs of primary care physicians and psychiatrists. The committee notes that state hospitals, university consortia, and private mental health practices that are university affiliated would be logical pilot program candidates.

Rationale and Description

Any attempt to impose EBP on the entire system of mental health care in Michigan would be unrealistic and ultimately doomed to failure for a number of reasons:

- The value of guidelines and algorithms is not universally understood among prescribers and those who are aware of them do not necessarily use or agree with them.
- The contextual issues—defined as the managerial and financial constraints under which care is offered—at best do not offer incentives for better care and at worst discourage it.
- By their nature, individual practitioners will not accept change at the same rate; some will be much more likely to adopt guidelines and algorithms than others, at least in the short term.

The effort to encourage the greater use of evidenced based medicine is essentially an attempt to diffuse a complex innovation (EBP) through a complex social system (the health care system). Common sense and diffusion theory suggest that such a complex innovation is unlikely to be rapidly adopted by a majority of practitioners.⁸ Far more likely is the possibility that pioneering practitioners—innovators and early adopters—can be persuaded to change. Only if the innovation is successful—if, that is, it produces measurable, positive results—will it be widely adopted.

The best way to accommodate this dynamic of change is to encourage and support the use of guidelines/algorithms among the innovative and early adopting “champions” who are most likely to use them. If success can be demonstrated at that level, the likelihood of still broader adoption will increase dramatically. Well-designed pilot programs that incorporate the strategies enumerated above—that is, which are intelligently packaged and marketed and contain educational materials, physician support, incentives, and evaluation—are the best way to do this. In this manner the “EBP” innovations can be diffused appropriately from a group of innovators

⁸For an excellent discussion of the application of diffusion theory to health care change see D. M. Berwick, “Disseminating Innovations in Health Care,” *JAMA* 289 (April 16, 2003): 1969–75.

and early adopters to early and late majorities in the field. To facilitate the exchange of information, each pilot program should have a designated contact person.

The effort cannot be coercive, but must be built upon willing participation at the local level. Furthermore, while some level of consistency across pilot programs is imperative, they need not be identical copies of one another. Each pilot program will use the MIMA algorithms and adopt the general strategies described below. On the local, tactical level, however, there can be room for flexibility and innovation at the discretion of local leaders. For that reason it is important that the local users of MIMA and the EBP approach be regularly consulted and stay involved in the unfolding process, possibly by means of an advisory “users group.”

Recommendation: Leadership Team

To maintain the continuity and momentum of this effort and facilitate the establishment and ongoing operations of pilot programs there should be established in Michigan a leadership team with the following components:

- 1. A “committee of the whole” composed of current steering committee members that will meet once or twice annually to review progress in the implementation of the report, suggest mid-course corrections, and serve as “ambassadors” for the project within Michigan.*
- 2. An “executive committee,” composed of volunteers from the steering committee and including both public- and private-sector participation that will provide oversight and assistance in a number of areas, especially in the critical area of funding. This group would meet more regularly, perhaps every other month.*
- 3. A “project coordination group” charged with staffing the project and doing the day-to-day work of implementation—including meeting with potential funders, developing requests for proposals (RFPs), evaluating proposals for local pilot programs, and coordinating the activities of the pilot programs that are established.*

Rationale and Description

Pilot programs cannot be undertaken without significant financial resources, nor should they be undertaken absent coordination at the state level. Both considerations argue strongly for the establishment of an ongoing “leadership” structure utilizing the expertise and skills of current steering committee members. The role of the executive committee and project coordination group would be particularly key here in the coordination of fundraising and the development of pilot programs by selecting pilot programs, developing requests for proposals (RFPs), evaluating proposals, and completing certain tasks best done at the state level (for example, the modification and updating of the MIMA algorithms).

The relationship between the newly established leadership team and the local pilot programs should be flexible, innovative, and nonbureaucratic. Lessons learned on the local level would be used for local improvements but also disseminated to the other pilots via the state-level leadership team. Individual pilot programs might well serve as contractors to produce information and tools for use by all the pilots. In other words, the pilot programs will carry out most of the work of the project (collecting and analyzing data, identifying best practices, advising the leadership team, and others).

The most logical step would be for leadership positions to be filled from the ranks of the current members of the steering committee, whose duties, in addition to those outlined below, would be to serve as in-house advocates for the action plan at the September conference. Above all else it is understood that the action plan is a dynamic, not static, document; the plan will necessarily change as new evidence becomes available.

The leadership team would have the following responsibilities:

- Overseeing the preparation, printing, dissemination, and, ultimately, the updating of guidelines and algorithms
- Preparing RFPs and evaluating subsequent proposals
- Overseeing the implementation of the pilot programs and deciding what program features must be standard from pilot to pilot
- Providing expert assistance for data collection and evaluation design
- Identifying and hiring contractors who provide ongoing physician support
- Identifying, approaching, and advising potential funders
- Serving as the visible, public presence of the EBP project

All these responsibilities would be discharged with the intention of improving the chances of success for the local pilot programs. The utilization of strong and knowledgeable project coordination will be essential to the success of all implementations efforts.

RECOMMENDATIONS: STRATEGIES AND TACTICS

The following recommendations are organized according to the strategies identified above and their attendant tactics. That is, there are strategies for:

- Packaging and presenting the guidelines/algorithms themselves
- Providing physician and consumer education
- Providing ongoing physician support
- Creating incentives for changes in medical practice
- Evaluating and measuring success in implementing guidelines algorithms and the effects of doing so
- Achieving further buy-in on the part of key stakeholders

Taken together, these offer a blueprint for the types of activities that will be undertaken by the local pilots and the state leadership team. The strategies are listed separately here for the purposes of discussion and completeness. In reality, the leadership and pilot groups could very well combine them—for example, by using Web technology to respond to inquiries by both physicians and consumers. Evaluation and measurement within each pilot program will serve a dual function: (1) allow each pilot to make ongoing, mid-course corrections and (2) provide information to other pilots and to the field.

Strategies for the Packaging and Distribution of Guidelines and Algorithms

To be maximally effective, guidelines and algorithms must be adapted for practice in Michigan, easy to understand and/or use for all stakeholders, and distributed through different media and

channels, and must come from an objective and authoritative source. This implies both that the guidelines must be customized for use in Michigan and that they be formatted for different practice settings, audiences, and uses.

Tactic 1: *The leadership team should oversee the reformatting and disseminating to the pilot programs of Michigan-specific guidelines and algorithms based upon the Texas (i.e., TIMA) model.*

Rationale and Description

The Texas algorithms that the steering committee identified as most appropriate and useful for use in Michigan need to be further customized for use here. References to Texas-specific materials, procedures, and organizations have been removed and replaced with Michigan-specific references. Furthermore, a strong emphasis on diagnoses must be a part of the guideline package since a correct initial diagnosis is indispensable to proper treatment.

Roles and Responsibilities

- The state leadership team will oversee the reformatting process by identifying potential contractors, evaluating proposals, and disseminating the resulting product to pilot projects.
- The pilot programs will use common guidelines and algorithms.

Tactic 2: *The reformatted guidelines/algorithms must be available in both short and long versions and disseminated to accommodate differing needs and uses.*

Rationale and Description

The same basic material can be formatted to meet the needs of two very different audiences. Primary care physicians (PCPs) may well need short, easy-to-use algorithms and guidelines, especially for initiating proper treatment of depression. Other physicians, including those in public settings and specialty care, may well need more in-depth material for complex or difficult-to-treat cases. Wall charts, flyers, CDs, personal digital assistants (PDAs), laminated cards, and Web technology are all communication channels that might be used to convey information on symptoms and treatment options.

Roles and Responsibilities

- The leadership team will identify qualified contractors and otherwise oversee the creation of both long and short versions of the guidelines and algorithms and provide them to the pilot programs.
- The pilot programs will use both versions in accordance with local need.

Tactic 3: *The leadership team and pilots will conduct the research necessary to package the guideline and algorithm material specifically for use with information technology, the Internet, local networks, and PDAs.*

Rationale and Description

Electronic technology is the wave of the present and future. As the survey of Michigan prescribers showed, many respondents now use Web technology in the office. While research on PDA use is lacking, it is presumed to be substantial. Web-based technology can provide information via either a computer or a PDA to physicians and staff. Further, electronic

technology can be an efficient and easy way to update guideline and algorithm information for large numbers of users. It is important to stress, however, that in order for this technology to be engineered intelligently, additional investigations must be made as to the way practitioners use it.

Roles and Responsibilities

- The leadership team will sponsor research and assist in the translation of guideline and algorithm material into a form suitable for use with information technology.
- The pilot programs will provide input into the engineering of the system and will use information technology in practice.

Tactic 4: Existing disease management tool kits available for treatment of major depression, bipolar disorder, and schizophrenia should be collected and analyzed to determine their suitability for further use and dissemination. If necessary, new tool kits should be developed for use in the pilot programs.

Rationale and Discussion

Several payer groups—among them Blue Cross/Blue Shield of Michigan and Magellan—have developed “tool kits” for the treatment of certain mental illnesses. The kits contain features—for example, disease screening instruments—that can be useful in the identification and management of illness. In the interest of efficiency, these payer groups should be approached to see if all or part of existing kits could be employed in the pilot programs. If necessary, new kits, or new kit elements, should be developed.

Roles and Responsibilities

- The leadership team should approach payers such as BCBSM and Magellan and others to seek the right to evaluate and use existing materials. If new materials need to be developed the group will assist in the identification and engagement of a contractor.
- The local pilots should use existing or newly developed tool kits as appropriate.

Tactic 5: The newly formatted Michigan algorithms must be updated on a regular basis.

Rationale and Description

By its very nature, evidence-based medicine is linked to new research developments and the availability of new medications. It is therefore imperative that the guidelines and algorithms be updated regularly. Experts in the area—for example, university research programs or practitioner groups like the American Psychiatric Association, the Michigan Psychiatric Society, and the Michigan State Medical Society may be available to assist with the updating, the merits of several approaches to updating should be considered:

1. Updating every 1 to 2 years through the convening of an ad hoc group of experts
2. Collecting and reviewing data *continuously* in a quality improvement process designed to rapidly alter practice
3. Updating different sections of the guidelines/algorithms regularly on a rotating basis

Roles and Responsibilities

- The leadership team will assist in the identification and engagement of a contractor or contractors.
- The pilot programs will use the updated guidelines.

Strategies for Physician Education

Physicians, both psychiatrists and those in primary care, will require additional information about the virtues of guidelines and algorithms, how best to run a local pilot program, and how to incorporate EBP principles into practice.

***Tactic 1:** The leadership team and pilots should develop strong, consistent messages as part of programs to explain why physicians should use guidelines and algorithms. These should be focused on critical issues such as expected outcomes and physician autonomy and, whenever possible, be accompanied by stakeholder endorsements.*

Rationale and Discussion

The compelling reasons for adopting EBP principles and guidelines/algorithms in mental health prescribing are not fully understood in the field. The survey of prescribers showed that the majority of psychiatrists were aware of algorithms and guidelines but did not necessarily use them. Primary care physicians, however, tended not to know about mental health guidelines and algorithms and used them in even smaller numbers. The fact that guidelines and algorithms can improve care and reduce errors needs to be stressed.

Roles and Responsibilities

- The leadership team will evaluate proposals from outside contractors (e.g., groups like the Michigan State Medical Society [MSMS] or the Michigan Psychiatric Society [MPS]) to develop consistent messages on guidelines and algorithms and conduct training.
- The individual pilot programs will ensure that physicians who are a part of their efforts receive this information or training.

***Tactic 2:** As part of a commitment to being “centers of excellence,” one or more state medical schools should adopt and teach guidelines/algorithms as part of the medical school curriculum and in residency training programs.*

Rationale and Discussion

In the long term, EBP principles and guidelines/algorithms will be widely adopted only if they are used in the training of future generations of physicians. Although medical school curricula are unlikely to change quickly, the greater use of guidelines/algorithms should begin now with an understanding that fuller adoption will take time to accomplish. Members of the steering committee believe that with proper encouragement and assistance one or more of the state’s medical schools could do so for mental health care. Further, a commitment to guideline and algorithm use could establish the participating medical school as a “center of excellence”—i.e., a place where better care is offered because it is clearly and explicitly evidence based.

The value of EBP has also been recognized and endorsed by the Accreditation Council for Graduate Medical Education for use in residency training programs. However, Michigan training programs in psychiatry have not generally interpreted this to require teaching the use

of guidelines and algorithms, though in other specialties, cardiology, for example, their use is more common.

Roles and Responsibilities

- The leadership team should approach the state's medical schools to explore in detail the possibility of their becoming centers of excellence committed to the teaching and use of algorithms and guidelines in mental health care.
- A medical school should be a part of at least one pilot program.
- A hospital-based training program should be a part of at least one pilot program.

Tactic 3: *The leadership team and pilot programs should explore ways of offering Continuing Medical Education (CME) credit for conferences, training programs, and regional sessions devoted to evidence-based mental health care and the use of guidelines and algorithms.*

Rationale and Discussion

The continuing education of physicians currently in practice complements the education of physicians in medical schools. Offering CME credit would serve as both an educational opportunity for physicians and as an incentive for change.

Roles and Responsibilities

- The leadership team should approach CME-granting organizations to ensure that EBP programs are available.
- Pilot programs should require or strongly encourage attendance at these sessions by their participating physicians.

Tactic 4: *The leadership team and pilot programs should work together to develop site-specific training programs for each pilot program.*

Rationale and Discussion

There is more to EBP than information on drug treatment options. The use of guidelines and algorithms is part of a broader approach that includes information on pharmacology, screening tools, monitoring and tracking, evaluation and measurement, physician/patient communication, and the education of patients and family members. While all of the pilot programs should have common features and elements, they by no means need to be identical. Tailoring the core program strategies to site-specific requirements will be necessary.

Roles and Responsibilities

- The leadership team will oversee the creation of a site-specific training program through proposal evaluation and selection of a training organization.
- The pilot programs will incorporate site-specific training for physicians, administrators, and other personnel.

Strategies for Consumer Education

The tactics in this subsection flow from the idea that care will also improve to the degree that consumers and their families are involved in care, understand EBP, and actively seek practitioners who offer it. Consumer education may take place in three contexts: (1) one-to-one encounters between physicians and individual patients; (2) population-based efforts whose aim is

to assist consumers in understanding and recognizing various conditions; and (3) specific treatment settings, for example, CMHs.

***Tactic 1:** The leadership team and pilot programs should develop materials and methods for improving patient-physician communication on the nature, importance, value, and use of guidelines and algorithms during individual treatment sessions—that is, on a “one-to-one” basis. The “medical decision making” CDs used by BCBSM to aid patients suffering from diseases such as breast and prostate cancer may be a useful model.*

Rationale and Discussion

If the long-term goal is to more fully integrate guidelines and algorithms into standards of care, consumers are a powerful agent of change. Furthermore, consumers have a right to fully understand and participate in medical decisions that affect care.

Roles and Responsibilities

- The leadership team will invite potential contractors to propose an integrated program of messages and materials to improve communication between physicians and consumers.
- Pilot programs will have an integrated consumer education program as part of their activities.

***Tactic 2:** Pilot programs and the leadership team will collaborate on a broader program of consumer education and awareness through the use of public service announcements, and, most especially, by employing existing advocacy groups as messengers to their constituents.*

Rationale and Discussion

This tactic is designed to augment the communication between physicians and patients through direct marketing to consumers. Where the previous tactic dealt with the quality of communication in a clinical setting, this tactic focuses on other channels of communication. Using public service announcements and “free media” provided by advocacy groups are among the communication channels that should be explored. A broader public awareness campaign has been used to great effect in the case of bipolar disorder among children.

Roles and Responsibilities

- The leadership team will identify contractors to develop messages and disseminate them to consumers outside of clinical settings.
- The pilot programs will design their programs in a way that is congruent with the message imparted by the public awareness campaign.

***Tactic 3:** The leadership team should evaluate the need to conduct further research into consumer needs and preferences as well as the possibility of offering consumer education tailored to specific subgroups or settings—for example, CMH settings.*

Rationale and Discussion

In the short term, there is ample material available with which to begin an education outreach effort to consumers, on either a one-to-one or a broader population level. In the longer term, the effort to encourage EBP may benefit from an effort to learn more about the knowledge, attitudes, and preferences of consumers. The steering committee notes that a series of focus groups with consumers in different areas of Michigan could be especially valuable. The

possibility that consumer education materials should be designed for specific treatment settings should also be considered.

Roles and Responsibilities

- The leadership team will formally address the need for additional research and/or the development of educational materials for subgroups and settings.
- The pilot programs will assist in the research as needed and use or disseminate additional educational materials if appropriate.

Strategies for Ongoing Physician Support

This tactic area focuses on physician support that cannot be covered during an initial training period. It recognizes that a successful pilot program will require ongoing support on a number of levels, including assistance with specific patients and cases, assistance with the administration and logistics of the program, and “real time” information on prescribing patterns. The support of organized health care systems on each of these levels is especially important.

***Tactic 1:** The leadership team and pilot programs should devise mechanisms to support and assist clinicians in the treatment of specific cases and patients.*

Rationale and Discussion

Clinicians in specialty care will need assistance with difficult or unusual cases. Primary care physicians would benefit from more general assistance with all three conditions. Assistance may be either immediate (i.e., sought while the patient is in the office) or of the sort that can be sought at regular intervals in the course of treatment (i.e., “virtual rounds”). Academic researchers, specialty societies, or health plans would be logical candidates to develop and provide ongoing support. The M-line program offered by the University of Michigan is one such example. As part of its service to the community, the university underwrites the cost of a “call in” consultation with the physicians it employs.

Roles and Responsibilities

- The leadership team will evaluate proposals and/or hire credentialed contractors to create and implement the support program.
- The pilot programs will ensure that their clinicians use the established support networks as needed.

***Tactic 2:** The leadership team and individual pilots will mutually develop support mechanisms to help with administration and logistics of the pilot itself.*

Rationale and Discussion

As has been shown in Texas and amply confirmed in additional research, successful use of EBP principles is more than the use of guidelines and algorithms. Success also involves new ways of communicating, new ways of screening and monitoring patients, and a new way of monitoring. Physicians would be hard pressed to undertake comprehensive change without support.

Roles and Responsibilities

- The leadership team will evaluate proposals and ensure that contractors are available to assist when problems and unforeseen events inevitably create challenges for new program.
- The pilot programs will help in the development of support mechanisms and use them as necessary in the ongoing administration of the pilot.

***Tactic 3:** The leadership team will work with payers to develop prescriber profiles and make them available to prescribers and researchers, while remaining sensitive to privacy issues. As part of this process, the group should encourage as much as possible movement toward universal use of electronic medical records.*

Rationale and Discussion

Having prescribing profiles available serves two purposes: (1) it can help clinicians see their own prescribing activities in a broader perspective and (2) it provides important data for the evaluation and measurement of practice changes due to EBP. Profiles will allow the individual practitioner to see how his/her prescribing patterns compare with those of others. Because they shed light on variations in practice, profiles are an important part of the evaluation mechanism. In this sense, adherence to or departure from guidelines/algorithms are not examined directly. Rather, variations are identified, triggering a further investigation as to the cause. The greater use of electronic medical records, already endorsed by the federal government, would greatly facilitate the creation and analysis of profiles.

Roles and Responsibilities

- The leadership team will approach provider systems and independent practice associations to determine how prescriber profiles can be developed.
- The pilot programs will encourage participating prescribers to review their profiles regularly and to analyze fully the reasons for any perceived variance.

Strategies to Develop Incentives for Change

Research suggests that a number of direct financial, indirect financial, and nonfinancial incentives will produce improvements in practice—ranging from reimbursement for legitimate expenses to enhanced status among peers and consumers.

***Tactic 1:** The leadership team and pilots should develop nonfinancial incentives for the adoption of guidelines and algorithms.*

Rationale and Discussion

The nonfinancial incentives for change can be considerable. Quite apart from any financial compensation, practitioners are inspired by the prospect of offering better care and being recognized for doing so. There are other examples—the development of national cancer centers, for example—where practitioners willingly join a broader movement and group because of the advantages that accrue from being perceived to offer the best care possible. Participation in the EBP program could be signaled in a number of ways—perhaps through wall plaques or decals or listings on a website.

Roles and Responsibilities

- The leadership team will examine the question of how best to describe and market participation in the pilot program, perhaps through the development of a “Michigan EBP in Mental Health Care Network” or some similarly named program.
- The pilot programs will use plaques or other forms of notification to explicitly identify themselves as being participants in an effort to improve quality.

***Tactic 2:** The leadership team should offer CME credit as an incentive as well as an educational opportunity.*

Rationale and Discussion

Continuing Medical Education Credit can be a valuable vehicle for education (see above) and, since practitioners are required by law to upgrade skills and education as a condition of re-licensing, a significant incentive as well.

Roles and Responsibilities

- The leadership team will approach CME-granting organizations to ensure that EBP programs are available, focused specifically upon medication EBP in mental health care.
- Pilot programs will encourage physician attendance at these sessions.

***Tactic 3:** The leadership team should approach payers to secure their buy-in for: (1) paying or creating rewards for guideline/algorithm adherence and (2) increasing reimbursement to improve the quality of care and reporting. This buy-in should build upon existing efforts by the Greater Detroit Area Health Council, Center for Medicare and Medicaid Services, Michigan Quality Forum, and Michigan Quality Improvement Consortium to standardize quality indicators and rewards.*

Rationale and Discussion

Prescriber activities are influenced by the incentive structure in which they take place. Practitioners are more likely to adhere to guidelines and algorithms if there is a financial incentive to do so. Further, some disease management tactics—for example, using a social worker or case manager to ensure that prescriptions are filled—unquestionably cost money. Changing the incentive structure for practitioners so that they are rewarded and reimbursed for a desired behavior requires payer buy-in.

Roles and Responsibilities

- The leadership team will approach employers, health plans, CMHs, and MDCH to explore the possibility of creating rewards for guideline/algorithm adherence and reimbursement for expenses incurred that improve care.
- The pilot programs will adhere to the guidelines and undertake other activities that improve care in the expectation that they will be rewarded or reimbursed.

***Tactic 4:** The leadership team will work with MDCH to ensure that contracts with providers reflect EBP principles.*

Rationale and Discussion

The Michigan Department of Community Health (MDCH) is a major payer, in fact, the dominant payer in cases involving schizophrenia and bipolar disorder. As such, it has contracts—with community mental health service programs, prepaid inpatient health plans, and Medicaid health plans—worth many millions of dollars, which could be used to leverage guideline/algorithm use. A policy decision by MDCH to support the goals of the action plan could be given teeth through department contracts.

Roles and Responsibilities

- The leadership committee should approach MDCH to develop a plan for encouraging guideline and algorithm use, at least within one of the pilot programs.
- One or more pilot programs could be used as a venue for testing the utility of this approach.

Strategies for Evaluation and Measurement

Evaluation and measurement strategies will provide an important informational base and will, over time, link the pilot programs to the long-term use of guidelines and algorithms to treat mental illness in Michigan. An evaluation of individual pilot programs as well as a “master” evaluation of all pilots will be necessary.

***Tactic 1:** The leadership team, working with representatives from the pilot programs, should develop multidimensional evaluation and measurement techniques that assess:*

- *Adherence to and variation from guidelines, as well as the reasons for variation*
- *Effectiveness of guidelines*
- *Consumer and physician satisfaction*
- *The cost of implementing guidelines in practice*
- *Changes in observable variation among prescribers*

Rationale and Discussion

The information needs of the project will be many and varied. It would be useful to know, for example, the extent to which practitioners adhere to guidelines, how satisfied they and consumers are with the pilot program, what the program costs were, and how successful the program was in improving outcomes or reducing practice variations. Equally important, the evaluation would provide the basis for continuous pilot program improvement.

A full array of evaluation and measurement techniques would be needed to answer these questions, including the analysis of medical records and claims data and surveys of practitioners and consumers. Assessment tools must be uniform across the pilots so that they can be meaningfully compared.

Roles and Responsibilities

- The leadership team should set the evaluation and measurement agenda by identifying suitable program evaluation contractors, if there are not evaluators already affiliated with the pilots.
- The pilot programs should make the data collection and analysis an integral part of their local program.

Tactic 2: The leadership team and the local pilot programs should work together to establish registries of persons with the conditions of interest (depression, bipolar disorder, and schizophrenia) within the local settings, while remaining appropriately sensitive to privacy issues.

Rationale and Discussion

Developing registries of persons with the diseases or conditions of interest is an indispensable first step, and the foundation of any measurement scheme. Unless practitioners are able to readily identify all of their patients who suffer from depression, bipolar disorder, or schizophrenia, it is difficult to measure or evaluate such things as adherence to guidelines, patient satisfaction, outcomes or variations in practice. In the development of registries, privacy protections newly enacted into law must be recognized and respected.

Roles and Responsibilities

- The leadership team should work with payers to create registries within each of the pilot programs.
- The pilot programs should collect information to establish the initial registry in support of subsequent data collection activities.

Strategies for Stakeholder Buy-in

Initially, stakeholders are all those that the EBP project will affect or influence—physicians, consumers, families, payers, and employers. Initially buy-in will be essential to the local pilots, but it will be necessary eventually to seek buy-in on a broader basis. Over time, stakeholder groups will expand to include not only patients, but also their support networks and other mental health professionals such as psychologists as well.

Tactic 1: The leadership team should assist pilot programs in developing EBP buy-in at each site through informational outreach efforts.

Rationale and Discussion

Buy-in from the larger stakeholder community is essential, particularly if the object is to diffuse EBP more broadly within the mental health care system. Yet, one cannot simply take buy-in for granted. It has to be intelligently sought through a number of specific tactics. Using regular information outreach mechanisms such as “e-mail grams” is one way of bringing supporters on the local, pilot level into agreement.

Roles and Responsibilities

- The leadership team will coordinate efforts to achieve stakeholder buy-in statewide and provide information and techniques that can be used in local pilots.
- The local pilots will implement and employ the buy-in tactics locally.

Tactic 2: The leadership team should identify a suitable contractor to coordinate marketing efforts to consumer advocacy groups and other groups with an interest in mental health care.

Rationale and Discussion

A research-based public relations strategy would be at the center of efforts to achieve greater stakeholder buy-in at both the individual pilot and state level. Efforts should be made to

identify key stakeholder groups and their leaders and provide them with timely information on the pilot programs. This may well require contracting the services of a professional public relations firm with demonstrated expertise with medical care issues.

Roles and Responsibilities

- The leadership team should assist in the identification of a contractor to coordinate an ongoing stakeholder buy-in effort.
- The local pilots should share information on their activities and be the focus of buy-in efforts locally.

***Tactic 3:** The leadership team will encourage current steering committee members to serve as active ambassadors for EBP, the use of guidelines and algorithms in mental health care, and the pilot program process.*

Rationale and Discussion

Effectively promoting change requires knowledgeable and committed change agents. Current steering committee members, who have standing within the medical and consumer communities and a demonstrated interest in EBP issues, would be excellent ambassadors to stakeholder groups. Since the steering committee itself is highly representative, its members will have the contacts and credibility necessary to fulfill this role effectively.

Roles and Responsibilities

- The leadership team will coordinate the activities of the steering committee members, ensuring that they have a comprehensive, coherent, and factually sound message with which to approach other stakeholders.
- The pilot programs will serve as demonstration projects.

***Tactic 4:** The leadership team will serve as a liaison to private foundation and corporate funders, within Michigan and nationally, and develop strategies for engaging their support for the project.*

Rationale and Discussion

Unless adequate funding for the action plan and its elements is secured, many elements of the action plan cannot be implemented. Funders—defined as private foundations, payer and employer groups, corporate giving programs, and perhaps even state and federal government—need to be viewed as a key constituency whose buy-in is needed and actively sought. Funders need to be made aware of the pilot programs, the rationale behind them, and how they will be structured and evaluated. In some cases, it may be necessary as well to “tailor” funding requests to specific funders—for instance, local community foundations may help segments of the local pilots.

Roles and Responsibilities

- The leadership team should take responsibility for securing funder support.
- The pilot programs will be responsible for providing in-kind, matching, or purely local funding whenever possible.

Appendix A:

Evidence-Based Practice Project

Roles and Responsibilities

Strategy	Leadership Team	Pilot Programs
1. Packaging and distribution of guidelines and algorithms	<ul style="list-style-type: none"> Oversee reformatting process Oversee creation of long and short versions of guidelines/algorithms (G/A) Sponsor research and assist in translation of G/A material in a form suitable for information technology (IT) Approach payers for right to evaluate and use existing materials Assist in identification and engagement of contractor—ongoing updates 	<ul style="list-style-type: none"> Use common guidelines and algorithms Use both versions in accord with need Provide input into engineering of system and use of IT Use existing or newly developed tool kits Use updated G/A
2. Physician Education	<ul style="list-style-type: none"> Evaluate proposals from contractors to develop consistent messages on G/A and conduct training Approach medical schools to teach and use G/A Approach CME-granting organizations to ensure EBP options are available Oversee creation of site specific training through selection of training organizations 	<ul style="list-style-type: none"> Ensure physicians receive information and training Include medical school and hospital based programs Require or encourage physicians to attend programs Incorporate site-specific training
3. Consumer Education	<ul style="list-style-type: none"> Invite contractors to propose integrated messages and materials Identify contractors to develop messages and disseminate to consumers Evaluate need to conduct further research into consumer needs and audience-specific consumer education 	<ul style="list-style-type: none"> Have integrated consumer education program as part of activities Design programs in a way that is congruent with messages Assist in research and use and disseminate materials
4. Ongoing Physician Support	<ul style="list-style-type: none"> Evaluate proposals for hiring contractors to create and implement support program Ensure that contractors are available to assist when problems create challenges Approach provider system and practice associations to determine how prescriber profile is developed 	<ul style="list-style-type: none"> Ensure clinicians use established support networks Help develop support mechanisms and use as necessary Encourage prescribers to review profile and analyze reasons for variance

Strategy	Leadership Team	Pilot Programs
5. Incentives for Change	<ul style="list-style-type: none"> Examine question of how best to describe and market participation in pilot programs Approach CME organizations to ensure EBP programs are available and focused on medication EBP Approach employers, health plans, CMHs, and MDCH to explore possibility of creating rewards for G/A adherence Approach MDCH to develop plan for G/A use within at least one pilot 	<ul style="list-style-type: none"> Use plaques and other forms of notification to explicitly identify themselves as participants Encourage physician attendance at sessions Adhere to guidelines in expectation of rewards
6. Evaluation and Measurement	<ul style="list-style-type: none"> With representatives from pilots, develop evaluation techniques to assess <ul style="list-style-type: none"> adherence effectiveness satisfaction cost changes in variation Set evaluation agenda by identifying contractors Work with payers to create registries within pilots 	<ul style="list-style-type: none"> Make data collection and analysis a part of program Collect information to establish registry in support of data collection
7. Stakeholder Buy-In	<ul style="list-style-type: none"> Coordinate efforts to achieve stakeholder buy-in statewide Assist in identifying contractor to coordinate buy-in effort Coordinate activities of steering committee members in approaching other stakeholders Take responsibility for securing funder support 	<ul style="list-style-type: none"> Implement and employ buy-in tactics locally Share information on activities and be focus of local buy-in Serve as demonstration projects Provide in-kind, matching, or local funding when possible

Appendix B:

Record of Meeting 1

Flinn Project Steering Committee, Meeting 1

June 4, 2003

9:00 AM to 1:00 PM

Radisson Hotel Lansing

111 Grand Avenue North

Lansing, Michigan 48933

AGENDA

- 9:00 AM Welcome and Project Background
- *Leonard Smith*, Flinn Family Foundation
 - *Craig Ruff*, Project Team
- 9:05 AM Project Overview
- *Tom Carli*, Project Team
- 9:20 AM Implementation of EBP: A National Perspective
- *Vijay Ganju*, NASMHPD Research Institute
- 10:00 AM Critical Issues in Improving Care
- *Tom Carli*
- 10:30 AM Break
- 10:45 AM Discussion: Members' Perspectives on Information, EBP, and Guidelines
- *Peter Pratt*, Project Team
- 11:30 AM Discussion: How Do You Want to Work?
- *Peter Pratt*
- 12:30 PM Demonstration: Project Website
- *Elisabeth Weston*, Project Team
- 12:45 PM Planning: Future Meeting Dates
- *Elisabeth Weston*

PRESENTATION HANDOUTS

Flinn Foundation EBP Project Steering Committee Meeting


June 4, 2003


PSC
PUBLIC SECTOR
CONSULTANTS


Project Background


- Flinn Family Foundation's work in mental health
- Genesis and purpose of this project
- Project coordinator (PSC)
- Funder's perspective
- Other philanthropic partners


PSC
PUBLIC SECTOR
CONSULTANTS


	<h2>Public Sector Consultants</h2>
	<ul style="list-style-type: none"> ■ Expertise in public policy and facilitation ■ Bringing diverse stakeholders to consensus


	<h2>PSC: Relevant Project Examples</h2>
	<ul style="list-style-type: none"> ■ Michigan Medicaid Dialogue ■ University Investment Commission ■ Ready to Succeed Partnership ■ GDAHC Regional Health Planning ■ Land Use Council ■ Flinn Family Foundation Reports on Mental Health in Michigan


	<h2 data-bbox="483 352 971 405">Project Overview: Goal</h2> <ul data-bbox="516 485 1242 741" style="list-style-type: none"> ■ Complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder
	

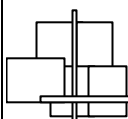
	<h2 data-bbox="483 1224 1019 1276">Project Overview: Tactics</h2> <ul data-bbox="516 1356 1242 1612" style="list-style-type: none"> ■ Consensus on guidelines/algorithms ■ Identification of barriers to adoption in the field ■ An action plan to address barriers—how do we change <i>practice</i> given what we know?
	

	<h2>Project Overview: Committee Role</h2>
	<ul style="list-style-type: none"> ■ Action-oriented steering committee (SC) ■ Limited number of meetings ■ Committee-driven process

	<h2>June 4th Meeting Overview</h2>
	<ul style="list-style-type: none"> ■ Dr. Vijay Ganju's presentation ■ Critical issues in improving care ■ Facilitated discussion of SC members' lessons learned ■ Facilitated discussion of how SC wants to work toward an action plan ■ Website demonstration ■ Next meetings

	Preliminary Project Schedule																													
	<p>■ Subject to SC modification and approval</p> <table border="1"> <tr> <td>Tue., Aug. 5, 2003</td><td>SC Meeting</td><td>11:00AM–3:00PM</td><td>Novi</td></tr> <tr> <td>Fri., Oct. 10, 2003</td><td>SC Meeting</td><td>11:00AM–3:00PM</td><td>Lansing</td></tr> <tr> <td>Thu., Dec. 4, 2003</td><td>SC Meeting</td><td>11:00AM–3:00PM</td><td>Novi</td></tr> <tr> <td>Thu., Feb. 5, 2004</td><td>SC Meeting</td><td>11:00AM–3:00PM</td><td>Lansing</td></tr> <tr> <td>Thu., Apr. 1, 2004</td><td>SC Meeting</td><td>11:00AM–3:00PM</td><td>Novi</td></tr> <tr> <td>Thu., Jun. 3, 2004</td><td>SC Meeting</td><td>11:00AM–3:00PM</td><td>Lansing</td></tr> <tr> <td>Thu., Sep. 23, 2004</td><td>Conference</td><td>8:00AM–5:00PM</td><td>Novi</td></tr> </table>			Tue., Aug. 5, 2003	SC Meeting	11:00AM–3:00PM	Novi	Fri., Oct. 10, 2003	SC Meeting	11:00AM–3:00PM	Lansing	Thu., Dec. 4, 2003	SC Meeting	11:00AM–3:00PM	Novi	Thu., Feb. 5, 2004	SC Meeting	11:00AM–3:00PM	Lansing	Thu., Apr. 1, 2004	SC Meeting	11:00AM–3:00PM	Novi	Thu., Jun. 3, 2004	SC Meeting	11:00AM–3:00PM	Lansing	Thu., Sep. 23, 2004	Conference	8:00AM–5:00PM
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	Presentation by Dr. Vijay Ganju		
			



Implementation of Evidence-Based Practices: A National Perspective

Vijay Ganju

**Director, Center for Mental Health Quality & Accountability
NASMHPD Research Institute, Inc.**

703.739.9333 ext. 132

vijay.ganju@nri-inc.org

**Presentation to the Flinn Foundation Project
Steering Committee**

Lansing, MI

June 4, 2003



PRESIDENT'S NEW FREEDOM COMMISSION ON MENTAL HEALTH

GOAL 5: ACCESS TO EFFECTIVE CARE BASED ON BEST EMERGING SCIENCE

- **Children and adults with mental health disorders will have ready access to the best treatments, services, and supports leading to recovery and cure. Accelerate research to enhance prevention of, recovery from, and ultimate discovery of cures for mental illness**
- **Strategic plan to improve recruitment, retention, diversity and skills of the workforce**



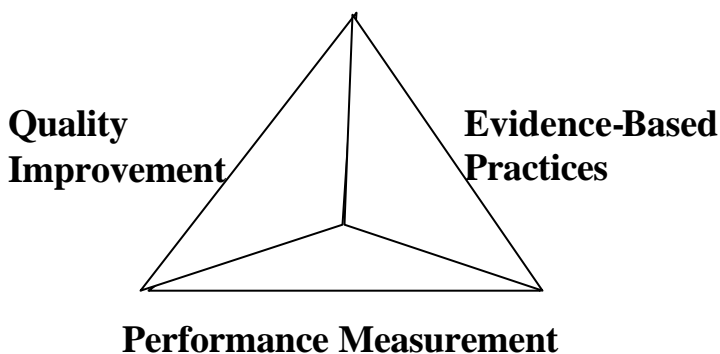
The Context

- Budget shortfalls
- Public perception of mental health services
- Unclear outcomes and “pay-offs”
- Broad-based initiatives related to quality and accountability in general health



The Quality Pyramid

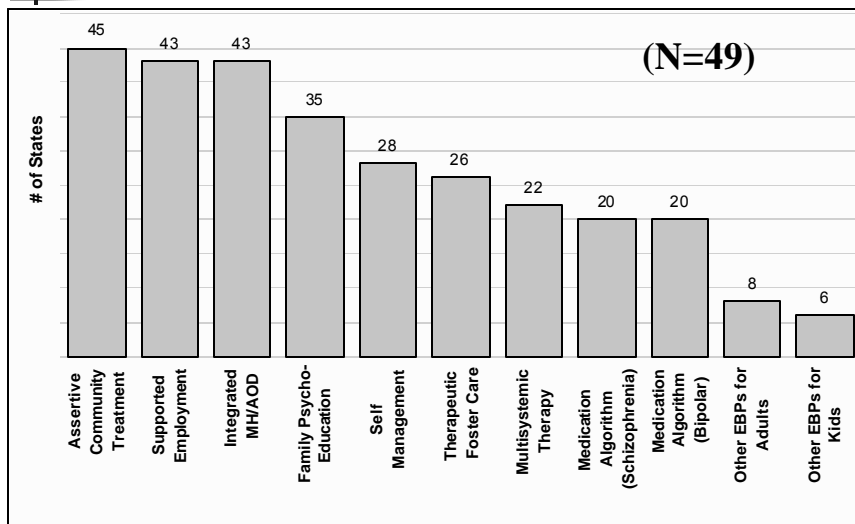
SYSTEM OUTCOMES



Evidence-Based Services

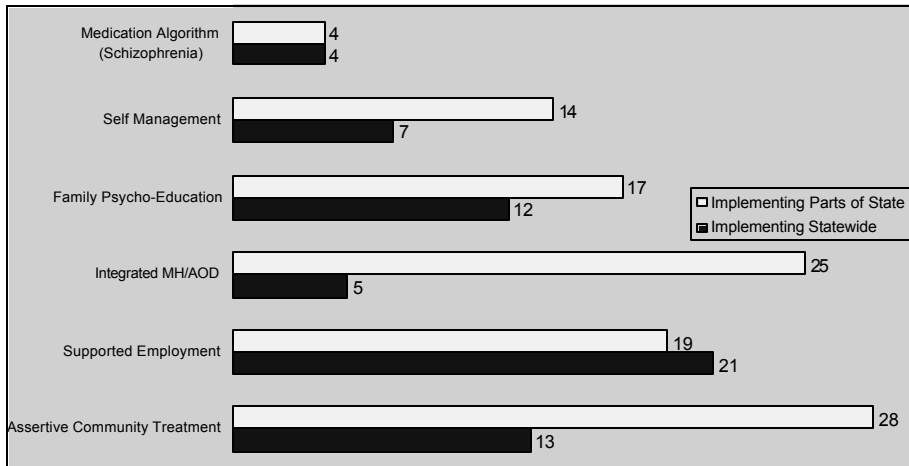
- One mechanism to achieve quality and accountability
- The Big Plus: Effectiveness is proven and inherent in evidence-based practices
- The Big Gap: Surgeon General's Report finding of the gap between knowledge and practice
- The Big Opportunity: Opportunities for system reform embedded in implementation of evidence-based practices

Number of States Implementing EBP: FY 2001



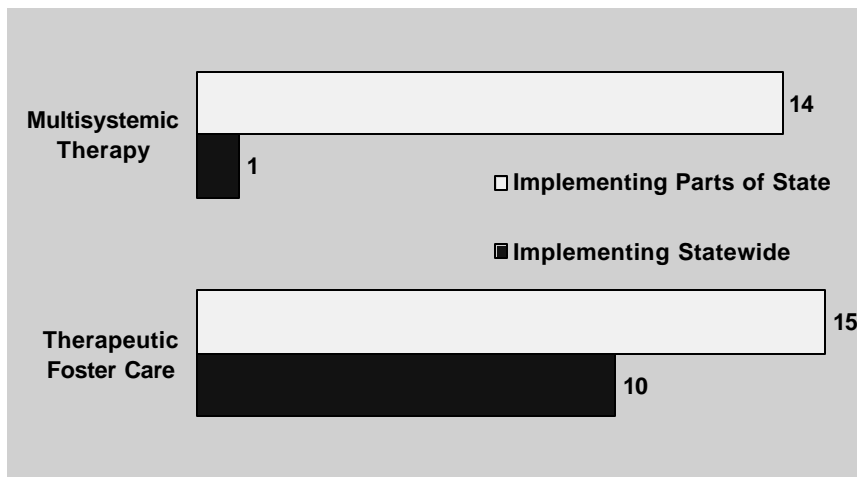
Implementation of Evidence-Based Practices For Adults

(N = 49)



Implementation of Evidence-Based Practices For Children

(N = 49)





Assessment of Fidelity

ACT	58%
Supported Employment	52%
Medication Algorithm	83%
Family Psychoed.	38%
Integrated MH/SA	67%
Self management	38%



State Mental Health Agency Initiatives

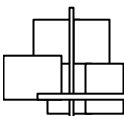
- **Individual state initiatives**
- **Toolkit project**
- **EBP Consortium of States**



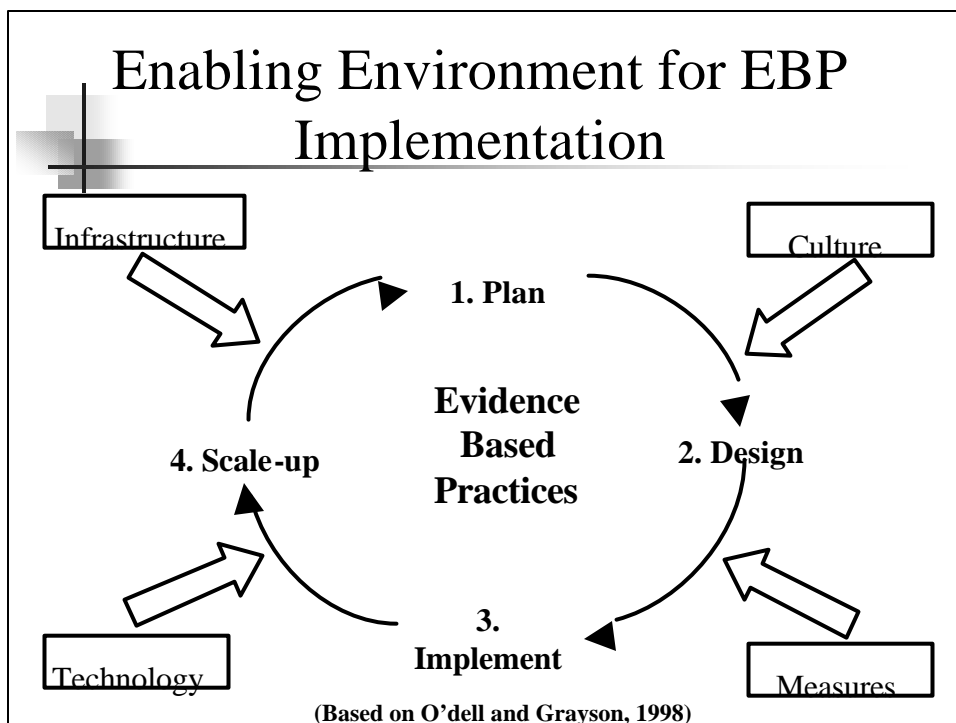
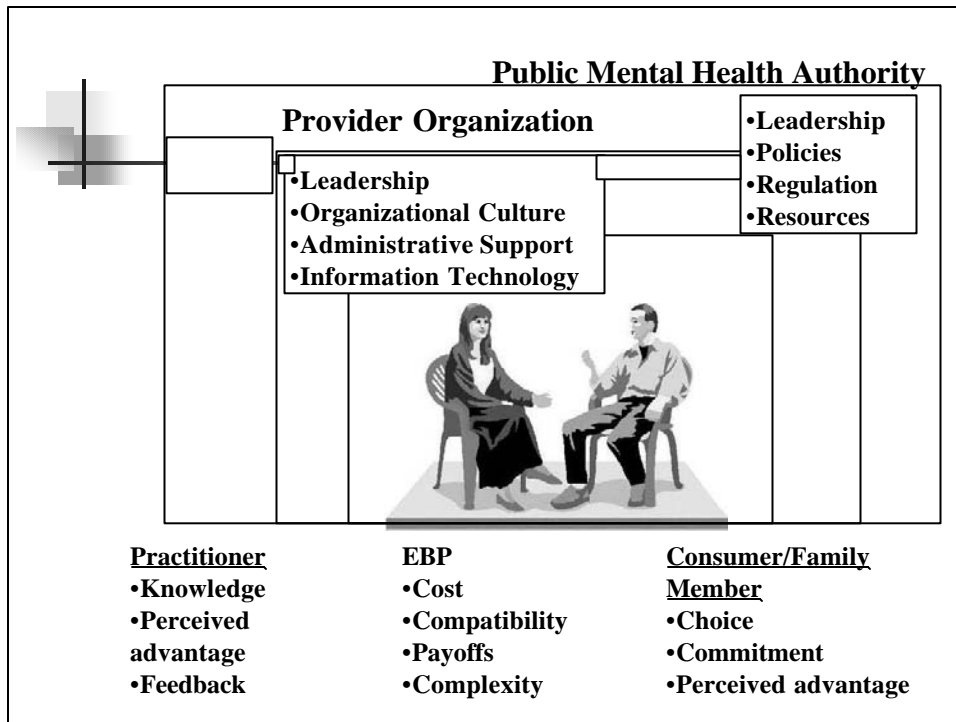
Individual State Initiatives

Examples:

- Texas
- Ohio
- New York
- South Carolina
- California
- Hawaii



**EBP Consortium expanded
to the 50 states and the
District of Columbia**





Evidence-Based Practices for Adults with Serious Mental Illness Toolkit Project

- **Six evidence-based services in project**
 - **Medications**
 - **Illness self-management**
 - **Assertive community treatment**
 - **Family psychoeducation**
 - **Supported employment**
 - **Integrated substance abuse/mental illness services**



Different Toolkits for Different Audiences

- **For each evidence-based practice, there are toolkits for different audiences**
 - **State Mental Health Authority**
 - **Provider organization**
 - **Clinician/provider**
 - **Consumer**
 - **Family member**



The EBP Process

- **Phase One**
 - **Development of “Implementation Resource Kits” (toolkits)**
- **Phase Two**
 - **Provide consultation and training**
 - **Evaluate the effectiveness**
 - **Improve the toolkits and the consultation and training based on feedback**



Implementation Resource Kit Process

- **The Phase I**
 - **Author Groups**
 - **Consensus Panels**
 - **Review Panels**
 - **Publication**



Implementation Resource Kit (toolkit) Development

- **All “toolkits” include:**
 - **Information for consumers and family member and all stakeholders**
 - **Workbooks for practitioners/clinicians**
 - **Implementation tips for provider organizations and MH authorities**
 - **Introductory and practitioner videotapes**



Pilot States for Phase Two

- | | |
|------------------------|-----------------------------------|
| ■ A.C.T. | ■ I.M.R. |
| ■ New York | ■ Vermont |
| ■ Indiana | ■ New York |
| ■ I.D.D.T. | ■ New Hampshire |
| ■ Ohio | ■ Ohio |
| ■ Indiana | ■ S.E. |
| ■ Kansas | ■ Oregon |
| ■ F.P.E. | ■ Kansas |
| ■ Vermont | ■ Maryland |
| ■ Maryland | ■ Med.M.A.P |
| ■ New Hampshire | ■ Veteran’s Administration |




Is implementation of EBPs a high priority for your State?

Yes – Currently	86.5%
Yes – Not currently, but as a long term objective	11.5%
No	2%

DRAFT RESULTS

N=52



What are the most important needs that must be met for your state to move forward with an EBP agenda (Or advance its current agenda?)

- **Funding mechanisms/incentives**
- **Infrastructure, Development/Integration**
- **Training of providers, consumers and family members**
- **Consensus Building / Buy-In**
- **Human Resource Development**
- **Outcome Measures and Fidelity Measures**
- **Technical Assistance**

DRAFT RESULTS

To address these needs, which of the following areas (which were previously identified by Commissioners as high priority areas) would you rate as helping you the most through technical assistance or collaboration with other states?

- | | |
|--|-----|
| ■ Planning/budgeting models for EBPs | 23% |
| ■ Consensus-building with stakeholders, funders, other agencies, etc | 18% |
| ■ Program implementation models for rural areas | 16% |
| ■ Fidelity measurement/monitoring | 13% |
| ■ Children's EBPs | 8% |
| ■ Readiness assessment | 8% |

DRAFT RESULTS

N=52

Steps for Moving Toward Statewide EBP Implementation

- **Awareness of EBPs**
 - Consumers and family members
 - Providers, clinicians
 - Management and program leaders
 - Legislators, funders
- **Consensus-Building**
 - Plan of action
- **Demonstration Projects**
- **Support / Infrastructure**
 - Training
 - Information systems / data reports
 - Contracts
 - Licensure / standards
 - Quality improvement
 - Monitoring / feedback
- **Expansion + Sustaining EBPs**



Challenges

- Definition of “evidence”
- Stakeholder buy-in
- Introduction of EBPs in time of budgetary restraint
- Sustained statewide effort over time
- Remote and rural areas
- Mental health services outside purview of state mental health authority



Consumer and Family Member Concerns

- **Shift from consumer and family member program initiatives**
- **Recovery orientation**
- **Consumer power, partnerships with consumers**
- **Life vs. services**
- **Techniques vs. experiences and relationships**



Practitioner Concerns

- **Research relevance**
- **Training support**
- **Professional autonomy**
- **EBP implementation support**



Administrator Concerns

- **Start-up investment**
- **Services displacement/replacement**
- **Consensus-building**
- **Systemic alignment/support**
- **Training capacity/models**



Polymaker Concerns

- **Funding alignment and incentives e.g. Medicaid**
- **Non-EBP Services**
- **Payoffs from investment**
- **Quality vs. access**



Center for Mental Health Quality and Accountability Initiatives - 2002

- ◆ **Adult Science-to-Services EBP Conference**
- ◆ **NRI/NTAC Children's EBP Workgroup**
- ◆ **State-level Evaluation of National EBP Demonstration Project**
- ◆ **Dissemination of Fidelity Measures**
- ◆ **Survey of State Needs and Priorities Related to EBP Implementation**
- ◆ **Web-site development**
- ◆ **Collaborating with individual state initiatives**
- ◆ **Development of EBP related Performance Measures**
- ◆ **Cultural Competence and EBPs**




Center for Mental Health Quality and Accountability Initiatives - 2003


- ◆ **Web-Site**
- ◆ **Surveys of States**
- ◆ **Children's Evidence-based Practices Conference**
- ◆ **Planning and Budgeting Models for EBPs**
- ◆ **Collaborations with Individual States**
- ◆ **Report on State-level Evaluation of National EBP Demonstration Project**
- ◆ **“Toolkit” project – “Lessons Learned”**
- ◆ **“Toolkit” project – Technical Assistance**



Related Federal Initiatives

- **NIMH/SAMHSA EBP Planning Grants**
- **SAMHSA's National Registry for Effective Practices (NREP) Initiative**
- **HRSA's Federal Qualified Health Centers**
- **SAMHSA's Science-to-Service Initiative**
- **President's New Freedom Commission**

	<h2 data-bbox="480 352 1166 405">Critical Issues in Improving Care</h2> <ul data-bbox="516 485 1239 720" style="list-style-type: none"> ■ How do we know there is a “gap”? ■ How do we determine evidence based best practices and guidelines? ■ What does the literature on changing physician behaviors teach us?
	

	<h2 data-bbox="480 1165 1114 1270">President’s New Freedom Commission on Mental Health</h2> <ul data-bbox="516 1354 1239 1795" style="list-style-type: none"> ■ “Dear Mr. President: Our review for this interim report leads us to the united belief that America’s mental health service delivery system is in shambles. We have found that the system needs dramatic reform because it is incapable of efficiently delivering and financing effective treatments, such as medications, psychotherapies, and other services, that have taken decades to develop.”
	

President's New Freedom Commission on Mental Health

- “As a result, too many Americans suffer needless disability, and millions of dollars are spent unproductively in a dysfunctional service system that cannot deliver the treatments that work so well.”



Crossing the Quality Chasm

- “Evidence-based practice is the integration of best research evidence with clinical expertise and patient values.”
- “The lag between the discovery of more efficacious forms of treatment and their incorporation into routine patient care is unnecessarily long, in the range of about 15 to 20 years.”



Committee on Quality of Health Care in America, Institute of Medicine. 2001. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, D.C.: National Academy Press.

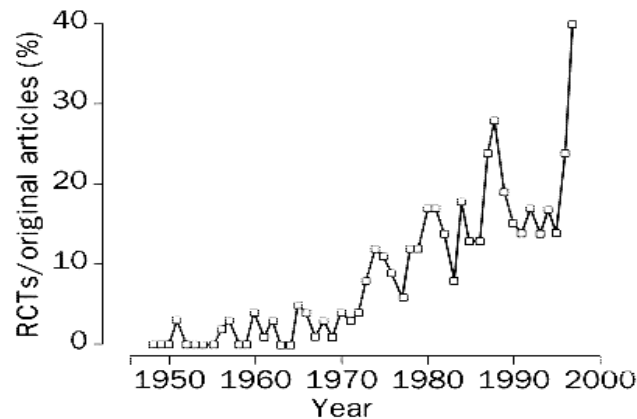
	<h2 style="text-align: center;">Crossing the Quality Chasm (cont.)</h2> <ul style="list-style-type: none"> ■ “Developing and disseminating practice guidelines alone has minimal effect on clinical practice. But a growing body of evidence indicates that guidelines implemented with patient-specific feedback and/or computer-generated reminders lead to significant improvements.” ■ “Carefully designed, evidence-based care processes, supported by automated clinical information and decision support systems, offer the greatest promise of achieving the best outcomes from care for chronic conditions.”
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	<h2 style="text-align: center;">Crossing the Quality Chasm (cont.)</h2> <ul style="list-style-type: none"> ■ Organizations will need to successfully negotiate major challenges: <ol style="list-style-type: none"> 1. Redesign care processes to serve more effectively the needs of the chronically ill for coordinated, seamless care across settings and clinicians and over time 2. Make effective use of information technology 3. Manage the growing knowledge base 4. Coordinate care across patient conditions, services, and settings over time 5. Continually advance the effectiveness of teams
--	--

	<h2 data-bbox="480 352 1227 401">Best Practices in Coordinated Care</h2> <ul data-bbox="516 478 1255 821" style="list-style-type: none"> ■ “Current health care often fails to meet the needs of chronically ill people. Treatment regimens for chronic illness often do not conform to evidence-based guidelines. Care is frequently rushed and overly dependent on patient-initiated follow-up. Providers typically devote little time to assessing function, providing instruction in behavior change or self-care, or addressing emotional or social distress.” <p data-bbox="347 877 423 940">PSC PUBLIC SECTOR CONSULTANTS</p> <p data-bbox="557 877 1219 919">A. Chen et al., Best Practices in Coordinated Care, HCFA demonstration program by Mathematica Policy Research, Inc. March 22, 2000.</p>
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	<h2 data-bbox="480 1163 1227 1272">Best Practices in Coordinated Care (cont.)</h2> <ul data-bbox="516 1350 1255 1793" style="list-style-type: none"> ■ “Care is fragmented, with little communication across settings and providers. A small proportion of chronically ill persons also incurs the large majority of health care costs. Furthermore, many unplanned hospitalizations of chronically ill persons appear to be preventable. Thus, preventive interventions targeted to this group might yield sizable overall savings in health care.” <p data-bbox="347 1751 423 1814">PSC PUBLIC SECTOR CONSULTANTS</p>
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RCTs as Percentage of Original Articles in *Lancet*, 1948–1997



Lancet 1998; 351:9103

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PUBLIC SECTOR
CONSULTANTS

Disseminating Innovations in Health Care

- Perceptions of the innovation
 - Perceived benefit of the change
 - Compatibility with values, beliefs, past history, current needs
 - Complexity of the proposed innovation
- "...simple innovations spread faster than complicated ones."

Donald M. Berwick, MD, MPP. "Disseminating Innovations in Health Care." *Journal of the American Medical Association*. April 16, 2003.

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Disseminating Innovations in Health Care (cont.)

- Characteristics of potential “adopters”
 - Innovators (2.5%)
 - Early adopters (13%)
 - Early majority (34%)
 - Late majority (34%)
 - “Laggards” (16%)
- Organizational and contextual supports or barriers

Berwick’s “Rules”

- Find sound innovations
- Find and support innovators
- Invest in early adopters
- Make early adopter activity observable
- Trust and enable reinvention
- Create slack for change (time and money)
- Lead by example

Effect of Clinical Guidelines on Medical Practice

Probability of Being Effective	Development Strategy	Dissemination Strategy	Implementation Strategy
<i>High</i>	Internal	Specific educational intervention	Patient-specific reminder at time of visit
<i>Above average</i>	Intermediate	Continuing education	Patient-specific feedback
<i>Below average</i>	External, local	Mailing targeted groups	General feedback
<i>Low</i>	External, national	Publications in journal	General reminder

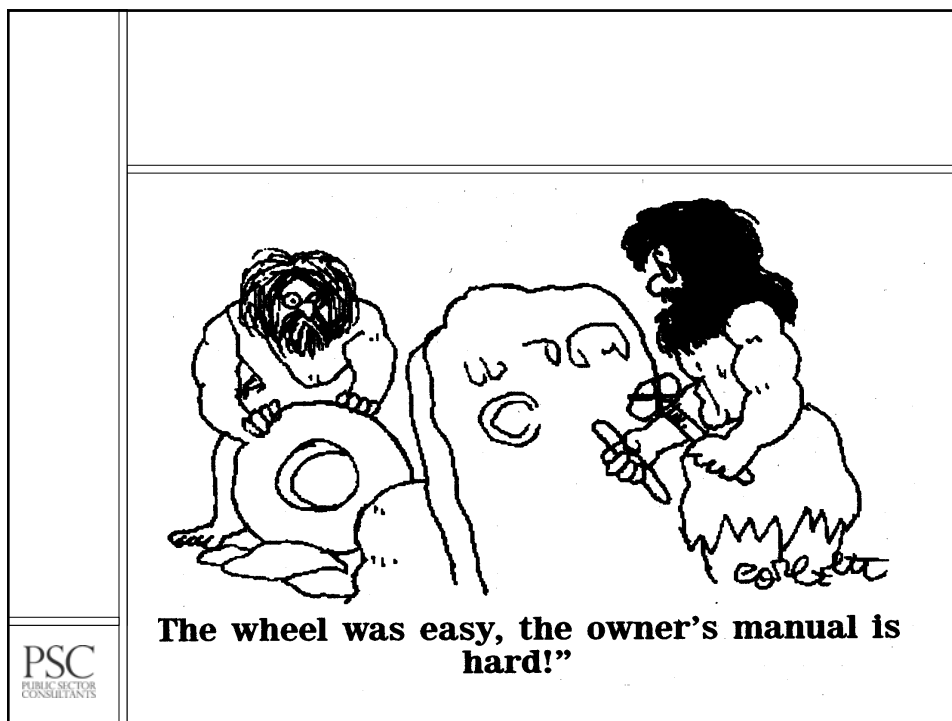
J. Grimshaw. "Effect of Clinical Guidelines on Medical Practice: A Systematic Review of Rigorous Evaluations." *Lancet* 342 (Nov. 1991).

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Evidence for "Gap" in Michigan

- Lessons from other diseases
 - GAP study
- MBCBS Dartmouth Atlas and small area variation
- Quality Compass
- Other data sources?

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Discussion: SC Views, Part I

- What readily available information will help the SC with its work?
 - Medicaid spending on psychotropics as percentage of total Rx spending?
 - Private payers' spending on psychotropics as percentage?
 - Trends in utilization, cost of antidepressants/antipsychotics?
 - Prevalence of serious mental illness?
 - Regional variations in care?
 - Gaps between what is known and what is done?

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	<h2 data-bbox="483 352 1097 405">Discussion: SC Views, Part II</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1247 611">■ What lessons have you learned from working with guidelines and algorithms that will help us in our work? <ul style="list-style-type: none"> <li data-bbox="565 636 786 667">● What worked? <li data-bbox="565 695 837 726">● What didn't work? <li data-bbox="516 753 1162 879">■ In your experience, which guidelines/algorithms do you think are best? Why?
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	<h2 data-bbox="483 1224 1032 1276">Discussion: Work Process</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1101 1388">■ How do we want to work together? <li data-bbox="516 1415 1230 1499">■ Next meeting: How do we address guidelines and/or algorithms? <ul style="list-style-type: none"> <li data-bbox="565 1524 1230 1598">● Staff compiles selected guidelines, SC agrees to one or several <li data-bbox="565 1625 938 1656">● SC modifies existing ones
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Discussion: Work Process (cont.)

- Algorithms vs. guidelines
- Subcommittees needed to examine guidelines and/or algorithms?
- Relative amount of time on
 - Guidelines?
 - Barriers?
 - Strategies to overcome barriers?

Preliminary Project Schedule

- Subject to SC modification and approval

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	<h2 data-bbox="480 352 813 405">Project Website</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 911 520">■ www.pscinc.com/flinn <li data-bbox="516 537 1185 615">■ Central communication point as project evolves <ul style="list-style-type: none"> <li data-bbox="565 632 812 667">● Collecting ideas <li data-bbox="565 678 951 714">● Disseminating information <li data-bbox="565 724 1146 760">● SC and project team contact information <li data-bbox="516 772 1084 808">■ Username and password required <li data-bbox="516 825 1114 861">■ May be augmented to suit SC needs
	

	<h2 data-bbox="480 1224 714 1276">Next Steps</h2>
	

Ethel and James Flinn Family Foundation Evidence Based Practice (EBP) Project

Steering Committee Meeting
June 4, 2003, 9 AM –1 PM
Radisson Hotel, Lansing

SUMMARY OF MEETING

Leonard Smith welcomed the group on behalf of the project funder, the Ethel and James Flinn Family Foundation of Detroit. Craig Ruff of Public Sector Consultants (PSC) introduced the project staff: Peter Pratt and Elisabeth Weston of PSC and affiliated consultants Dr. Tom Carli of the University of Michigan and Paul Smyth. Also present was Vijay Ganju of the National Association of State Mental Health Program Directors (NASMHPD) Research Institute, who offered an overview of EBP developments nationwide.

The initial discussion reiterated the goals, strategy, and general approach of the project:

1. The project *goal* is to complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder.
2. The project *tactics* will include the building of committee consensus on the best guidelines and/or algorithms for each condition, identifying barriers to the adoption of those guidelines in the field, and developing an action plan aimed at changing practice.
3. The general *approach* is action-oriented, committee-driven, with a limited number of meetings.

The key discussions focused upon what information the steering committee needs to do its work, its general understanding of EBP and guidelines (as well as potential barriers), and how it would like to work in the future.

Information Needs

The steering committee discussed information needs at length and reached a fundamental conclusion: *While additional research would be useful for a number of reasons, it is not essential to the committee's moving forward.* The aim of the project is to change practice not conduct research.

The steering committee did, however, identify information that it viewed as useful, including:

- The need for more information on “polypharmacy”
- An analysis of current prescribing patterns (“who is doing the prescribing”)
- Better information on the link between diagnosis and prescribing
- The perspective of consumers on cost, ease of compliance, and side effects

- Prevalence data with information on treatment rates and “spikes” in prescribing with no proven efficacy (example, Stratarra for ADHD)
- Data from several sources (HEDIS, the BCBSM Dartmouth AAtlas, a Washtenaw County CMH study, and an MSU study of Ford Motor Company employees) that might shed additional light on the current state of practice in Michigan
- Information on private-payer spending on psychotropics and antidepressants
- Information on the effect of insurer policies and formularies on quality of care
- Information on how many citizens in Michigan lack prescription coverage, either because their policy does not include it or because they lack health coverage altogether

Guidelines/Algorithms

Committee members made the following observations about guidelines and algorithms:

- The question of measurement needs to be considered; otherwise, how will the group know if guidelines/algorithms are helping? Absent a baseline, how can one show that quality of care is improved by guidelines? How can one tell if the guidelines are being followed? Several steering committee members added that the difficulty of measurement should not impede this effort, as there is much promise in the adoption of good guidelines/algorithms.
- A number of published guidelines do not correspond with the real world practice of psychiatry. For instance, they often assume a new diagnosis when psychiatrists most often see people with a long history of being treated by others.
- There is an inherent tension between “dumbing down” in the interest of simplicity and comprehensive guidelines that are too complex for normal use. Given their differing training and experience, primary care physicians and psychiatrists may need different guidelines/algorithms. Algorithms (as opposed to guidelines) may work better when there is considerable uncertainty—as in the case of residents in training. But there may be some danger in this if it leads to less than optimal care.
- Devising guidelines for the many different clinical settings will be a challenge. TMAP was public program. Can its guidelines be transferred as readily to the private sector?
- Physician and patients may well have differing opinions on the acceptability of guidelines. How does one reconcile this? Many patients experiment with new drugs out of desperation—the standard treatments either do not work or else have unacceptable side effects.
- Guidelines improve the level of care only if practitioners know how to use them correctly. A big issue will be dealing with exceptions—the patients for whom nothing seems to work. It has to be clear when it is appropriate for practitioners to depart from guidelines.

Barriers and Strategies

The committee offered the following initial insights on the nature of barriers and potential strategies for overcoming them:

- Guidelines by themselves are inoffensive—just a compendium of research—but the detail and structure of algorithms might make them more controversial because doctors dislike being told what to do. At MDCH, policies on the appropriate use of new medications were developed by physicians who also did the training. Face-to-face meetings with supporting materials seem to work.
- There is a need to develop information on how guidelines/algorithms affect direct and indirect costs. Quality of care and system efficiency can be potent selling points to skeptics.
- Physician education—both in medical school and CME—is “huge.” It would be very useful to get the issue of guidelines addressed in the state’s residency programs
- There is a need to address the use of guidelines in different settings. Perhaps guidelines for four or five models of psychiatric practice can be developed.
- Getting consumers and users to accept guidelines developed by others will be a challenge. There needs to be a strategy for involving them in the formulation of guidelines.
- Inherent in EBP is the assumption that the diagnosis is correct. But it is clearly wrong to assume this in every case. Primary care physicians and psychiatrists may well reach a different diagnosis for the same patient.
- Guidelines are always a work in progress and have to be updated regularly.
- Guidelines not only have to be developed—they have to be taught. Part of this is helping doctors understand which patients will fall outside guidelines.
- It is important to intervene at the point of service. Easy access to credentialed volunteers (as is done in Texas) is one possibility. Information technology and electronic medical records with prompts are other possibilities.
- It would be useful to know a good deal more about how practitioners in general react to guidelines. Perhaps more could be found out about their attitudes through a Web-based survey.

It was agreed that the next meeting would be devoted to the further discussion of guidelines the committee might choose to endorse, with subsequent meetings being devoted to the question of barriers. In preparation for the next meeting the committee and staff committed to the following work:

- All committee members are invited to send in copies of guidelines they use or recommend by June 13. Staff will place these in PDF form on the project website.
- Subcommittees of the steering committee will meet (or hold conference calls) to identify guidelines associated with the various conditions and recommend several to the full committee for endorsement. Subcommittee assignments are as follows:
 - **Depression:** Kevin Kerber, Cal Dudley, Barry Mintzes, Michael Fauman, Michele Reid, Tom Zelnick
 - **Schizophrenia:** Rob Immonen, Karen Milner, Richard Berchou, Jonathan Henry, Michael Zarr
 - **Bipolar:** Jed Magen, John Baugh

- PSC staff will conduct a structured comparative analysis of the guidelines received from the subcommittees and individual members using a tool developed by the National Guidelines Clearinghouse of the U.S. Agency for Health Care Research and Quality (AHRQ's)

As a final point of discussion the committee noted a need to publicize its activities through organizational newsletters and contacts with state and national organizations.

The second meeting of the Flinn EBP Steering Committee was tentatively scheduled for Tuesday, August 5, from 11 AM to 3 PM in Novi.

Appendix C:

Record of Meeting 2

Flinn Project Steering Committee, Meeting 2

August 5, 2003

11:00 AM to 3:00 PM

Doubletree Hotel

27000 Sheraton Drive

Novi, Michigan 48377

AGENDA

- 11:00 AM Welcome and Project Background
 - *Tom Carli*, Project Team
- 11:15 AM Depression Subcommittee Recommendations
 - *Cal Dudley*
- 12:00 PM Break
- 12:30 PM Bipolar Subcommittee Recommendations
 - *Jed Magen*
- 1:15 PM Schizophrenia Subcommittee Recommendations
 - *Rick Berchou*
- 2:00 PM Discussion: Survey of Michigan Practitioners
 - *Peter Pratt*, Project Team

PRESENTATION HANDOUTS

Flinn Foundation EBP Project Steering Committee Meeting


August 5, 2003


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Project Overview: Goal

- Complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder


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	<h2 data-bbox="483 352 1019 405">Project Overview: Tactics</h2> <ul data-bbox="516 485 1239 783" style="list-style-type: none"> <li data-bbox="516 485 1089 569">■ Achieve consensus on guidelines/ algorithms <li data-bbox="516 594 1174 636">■ Identify barriers to adoption in the field <li data-bbox="516 661 1239 783">■ Address barriers through action plan—how do we change <i>practice</i> given what we know?
	


	<h2 data-bbox="483 1224 1211 1276">Project Overview: Committee Role</h2> <ul data-bbox="516 1356 1192 1524" style="list-style-type: none"> <li data-bbox="516 1356 1192 1398">■ Action-oriented steering committee (SC) <li data-bbox="516 1423 1000 1465">■ Limited number of meetings <li data-bbox="516 1491 967 1524">■ Committee-driven process
	


	<h2 data-bbox="479 352 1063 405">August 5 Meeting Overview</h2> <ul style="list-style-type: none"> <li data-bbox="511 447 1104 531">■ Depression, Bipolar, Schizophrenia Subcommittee Reports <ul style="list-style-type: none"> <li data-bbox="560 552 844 583">● Recommendations <li data-bbox="560 611 730 642">● Discussion <li data-bbox="511 672 1023 756">■ Begin discussion of barriers to implementation <li data-bbox="511 783 1234 814">■ Next steps: survey of Michigan practitioners <div data-bbox="345 884 423 940">  </div>
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	<h2 data-bbox="479 1224 1039 1276">Depression Subcommittee</h2> <ul style="list-style-type: none"> <li data-bbox="511 1360 812 1392">■ Calmeze Dudley <li data-bbox="511 1413 812 1444">■ Michael Fauman <li data-bbox="511 1465 755 1497">■ Kevin Kerber <li data-bbox="511 1518 763 1549">■ Barry Mintzes <li data-bbox="511 1570 755 1602">■ Michele Reid <li data-bbox="511 1623 787 1654">■ Mark Reinstein <li data-bbox="511 1675 787 1707">■ Thomas Zelnik <div data-bbox="345 1755 423 1812">  </div>
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	<h2 data-bbox="483 352 1040 405">Depression Subcommittee</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1240 569">■ Recommendation: adopt Texas medication guideline/algorithm for depression <li data-bbox="516 583 1240 842">■ Basis for decision <ul style="list-style-type: none"> <li data-bbox="565 632 1154 667">● Clinically sound; sufficient evidence base <li data-bbox="565 678 1240 714">● Inclusive enough to work, simple enough to use <li data-bbox="565 724 1187 800">● Could be used in primary (early stages) and specialty care settings <li data-bbox="565 810 837 842">● Updated regularly <div data-bbox="347 884 423 940">  </div>
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	<h2 data-bbox="483 1224 1040 1276">Depression Subcommittee</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1240 1650">■ Important issues <ul style="list-style-type: none"> <li data-bbox="565 1404 1240 1520">● Implementation should include training/ education and resources for clinical use in both primary and specialty settings <li data-bbox="565 1530 1224 1604">● Algorithm should be formatted to demonstrate “timeline” nature of treatment <li data-bbox="565 1614 1224 1650">● Web-based technology may be part of solution <li data-bbox="516 1661 899 1696">■ Committee discussion <div data-bbox="347 1759 423 1816">  </div>
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	<h2>Bipolar Subcommittee</h2>
	<ul style="list-style-type: none"> ■ John Baugh ■ Jed Magen ■ Manuel Tancer


	<h2>Bipolar Subcommittee</h2>
	<ul style="list-style-type: none"> ■ Recommendation: adopt Texas medication guideline/algorithm for bipolar disorder ■ Basis for decision <ul style="list-style-type: none"> ● High degree of evidence ● Implementation in Texas and Ohio demonstrates ease of adoption ● Updated regularly


	<h2>Bipolar Subcommittee</h2>
	<ul style="list-style-type: none"> ■ Important issues <ul style="list-style-type: none"> ● Guidelines and algorithms are only as good as the diagnosis; assessment quality must be factored in ● Comorbidity issues must be addressed ● Psychotherapies, social skills training, and other therapies are a necessary and critical part of treatment for patients with bipolar disorder ● Training should be part of implementation ● Outcomes should be measured and compared ■ Committee discussion

	<h2>Schizophrenia Subcommittee</h2>
	<ul style="list-style-type: none"> ■ Richard Berchou ■ Jonathan Henry ■ Robb Imonen ■ Karen Milner ■ Michael Zarr

	<h2>Schizophrenia Subcommittee</h2>
	<ul style="list-style-type: none"> ■ Recommendation: adopt the APA schizophrenia treatment guidelines, Texas and Harvard medication algorithms for schizophrenia ■ Basis for decision <ul style="list-style-type: none"> ● Disease cannot be treated by medication alone ● APA guidelines provide credibility to most practitioners ● Texas, Harvard provide ample evidence ● Texas algorithm has been adopted elsewhere

	<h2>Schizophrenia Subcommittee</h2>
	<ul style="list-style-type: none"> ■ Important issues <ul style="list-style-type: none"> ● Medication is only part of treatment solution ● Diagnosis/assessment quality is important ● Medication costs will likely be an issue ● Expected outcomes should be stated ■ Committee discussion

	<h2 data-bbox="480 352 1003 405">Listening to Practitioners</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1057 527">■ Web-based survey of physicians <li data-bbox="516 537 1138 621">■ Invitation to comment on guidelines/algorithms, barriers to use <li data-bbox="516 632 971 674">■ Psychiatrists, PCPs, others? <li data-bbox="516 684 1219 768">■ Primary contacts through specialty societies—letter directing them to website <li data-bbox="516 779 1187 863">■ Secondary contacts through health plan newsletters, other sources?
	

	<h2 data-bbox="480 1224 724 1276">The Survey</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1138 1440">■ Multiple-choice with 1–2 open-ended questions <li data-bbox="516 1451 1162 1493">■ Issues we need to cover: SC discussion <ul style="list-style-type: none"> <li data-bbox="565 1503 1252 1587">● What would make it most likely for you to adopt guidelines/algorithms? <li data-bbox="565 1587 1252 1734">● What are the biggest obstacles to quality pharmacological treatment of your patients with depression, schizophrenia, and bipolar disorder?
	

Survey Timetable

- SC members send staff more comments and questions (Aug. 6–15)
- Staff drafts survey instrument (Aug. 18–29)
- SC members react to draft (Sep. 2–12)
- Final survey approved at October 6 meeting
- Survey fielded in October
- Results discussed at December 4 meeting

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Preliminary Project Schedule

- Subject to SC modification and approval

Tue., Aug. 5, 2003	SC Meeting	11:00AM–3:00PM	Novi
Mon., Oct. 6, 2003	SC Meeting	11:00AM–3:00PM	Lansing
Thu., Dec. 4, 2003	SC Meeting	11:00AM–3:00PM	Novi
Thu., Feb. 5, 2004	SC Meeting	11:00AM–3:00PM	Lansing
Mon., Apr. 5, 2004	SC Meeting	11:00AM–3:00PM	Novi
Thu., Jun. 3, 2004	SC Meeting	11:00AM–3:00PM	Lansing
Thu., Sep. 23, 2004	Conference	8:00AM–5:00PM	Novi

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Ethel and James Flinn Family Foundation Evidence Based Practice (EBP) Project

Steering Committee Meeting
August 5, 2003, 11:00 AM –3:00 PM
Doubletree Hotel, Novi

SUMMARY OF MEETING

The project steering committee met for the second time on August 5 at the Doubletree Hotel in Novi. All members were present except Wayne Creelman, Kevin Kerber, Karen Milner, Barry Mintzes, Bob Sheehan, Manuel Tancer, Dan Wilhelm, and Tom Zelnik.

The purpose of the meeting was to hear and discuss the reports of the Major Depression, Bipolar Disorder, and Schizophrenia Subcommittees, to begin discussion of barriers to implementation, and to discuss the upcoming survey of Michigan practitioners.

The project team opened the meeting with special thanks to the subcommittees. The value of the “brain trust” approach is confirmed. The subcommittees completed a great deal of high-quality work in a short time and achieved a high degree of consensus on how best to proceed.

The team also reiterated the goal, tactics, and general approach to activities:

- The *goal* is to complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the pharmacological treatment of major depression, schizophrenia, and bipolar disorder.
- The *tactics* include achieving consensus on guidelines/algorithms, identifying barriers to their adoption in the field, and addressing barriers and changing practice through an action plan.
- The *general approach* is action-oriented and committee-driven with a limited number of meetings.

Each of the three subcommittees then made a presentation to the full committee, with each recommending adoption of the Texas Implementation of Medication Algorithm (TIMA) model as the group moves forward.

Depression Subcommittee

Committee members: Calmeze Dudley, Michael Fauman, Kevin Kerber, Barry Mintzes, Michele Reid, Mark Reinstein, Thomas Zelnik

The Depression Subcommittee recommended adoption of TIMA because it is clinically sound, both inclusive and simple, adaptable to both primary and specialty care settings, and updated regularly. In making this recommendation the subcommittee noted that the algorithm should be reformatted to demonstrate both the “timeline” and “staging” dimensions of treatment. Examples of how TIMA could be reformatted to include these dimensions were provided. The subcommittee made several further points:

- Implementation should include training and education for clinical use in both primary and specialty care settings.
- Web-based technology may well figure strongly in all phases of the project.
- While the recommendations focus on individual practitioners and on psychopharmacological therapy per the subcommittee charge, the importance of organizational interventions and other therapies should not be discounted.
- TIMA is not evidence-based in the classical sense but, rather, based upon expert consensus.

Follow-up discussion by the full Steering Committee focused on the following points:

- The ease and adaptability of algorithms/guidelines may be especially critical in the case of depression because approximately 70 percent of depression patients are first treated by primary care physicians.
- The issue of “branding” is of concern. If the TIMA algorithm is altered for use in Michigan can it still be publicized as TIMA? (The group’s feeling was that it could be).
- The relation of primary to specialty care was explored. Some asked whether it would not be better to have more patients seeing specialty care physicians initially. Others felt that this would be impractical and that primary care physicians are a necessary entry point to the system.
- While TIMA addresses the adult population well, there was concern that the geriatric and youth populations might not be equally well served.
- The specificity of psychopharmacological recommendations is a major issue. Should the Steering Committee recommend classes of drugs or specific brand names?
- There was a feeling that all recommended algorithms/guidelines need to address co-occurring disorders.
- The targeting of individual audiences was discussed. For some practitioners, the simpler the algorithm the better. Others will want more information. Further, there are different learning styles. Some may prefer flowcharts and timelines but for others a simple outline may be enough.

Bipolar Subcommittee

Committee members: John Baugh, Jed Magen, and Manuel Tancer

The Bipolar Subcommittee also recommended that the Steering Committee adopt the TIMA model, citing the fact that it is based upon a high degree of evidence, has been successfully demonstrated in Texas and Ohio, and is updated regularly. Subcommittee members stressed the importance of issues related to comorbidity, training, and other therapies while making two other essential points:

- Guidelines and algorithms are only as good as the initial diagnosis.
- The implementation of any guideline or algorithm must also entail the measurement and comparison of outcomes.

The follow-up discussion by the Steering Committee focused upon the following points:

- The importance of monitoring symptoms and response to treatment after the diagnosis.
- Potential problems with the adoption of TIMA in its current form. It was observed that the TIMA guidelines contain strong statements about problems caused by managed care. While there was some sympathy expressed for the commentary, the general sense of the group was that it not be used for now in a committee-recommended guideline.
- The TIMA algorithms for bipolar conditions and depression are in different formats. It was agreed that the final versions would have to be reworked to make them consistent.

Schizophrenia Subcommittee

Subcommittee Members: Richard Berchou, Jonathan Henry, Robb Imonen, Karen Milner and Michael Zarr

The Schizophrenia Subcommittee recommended use of TIMA, but, in addition, recommended that the Steering Committee adopt the APA guidelines and the Harvard algorithm in support. The Texas algorithm would be the basic standard of treatment. The APA guidelines would be available if greater information was required; the Harvard algorithm would assist with unusually complicated cases. The Texas algorithm was recommended because its evidentiary base is sound and because it has been used elsewhere. The Harvard algorithm has a particularly strong evidentiary base; and the APA guidelines provide credibility to most practitioners.

The Schizophrenia Subcommittee also stressed that medication is only part of the solution, that diagnosis and assessment are critical, and that there needs to be a special emphasis on outcomes. The subcommittee placed special emphasis as well on the issue of the cost of medication.

The ensuing Steering Committee discussion elicited the following points:

- The recommendation of the Schizophrenia Subcommittee departs from those offered by the Depression and Bipolar Subcommittees. Is this justified or unduly confusing? There are difficulties and inconsistencies with any guideline or algorithm. Wouldn't these just be magnified with three, especially for primary care physicians?
- Subcommittee members explained that the Texas algorithm was intended as the base orientation but the inclusion of the APA guidelines and the Harvard algorithms accommodates those who learn differently, as well as those who need additional information.
- It was pointed out that Web technology could easily accommodate this approach because the base Texas algorithm could be linked to both the Harvard and the APA documents.

At the conclusion of the subcommittee reports, the Steering Committee agreed to move forward using TIMA for all three conditions, while holding in reserve for further research and discussion the important issues that various members raised.

Survey

The final discussion centered on what sorts of questions should be included in the upcoming survey of the field. Committee members offered suggestions on how to elicit information on barriers to implementation and strategies for communicating with practitioners. Public Sector Consultants will develop a draft survey instrument to share with the Steering Committee at its next meeting.

The next meeting of the Steering Committee was moved two weeks back from its tentatively scheduled date. It will now be held Monday, October 20, at the Radisson Hotel in Lansing from 11:00 AM to 3:00 PM.

Appendix D:

Record of Meeting 3

Flinn Project Steering Committee, Meeting 3

October 20, 2003

11:00 AM to 2:00 PM

Radisson Hotel Lansing

111 Grand Avenue North

Lansing, Michigan 48933

AGENDA

- | | |
|----------|---|
| 11:00 AM | Welcome and Introductions <ul style="list-style-type: none">• <i>Tom Carli</i>, Project Team |
| 11:15 AM | Practitioner Survey <ul style="list-style-type: none">• <i>Elisabeth Weston</i>, Project Team |
| 12:00 PM | Guideline/Algorithm Update <ul style="list-style-type: none">• <i>Elisabeth Weston</i> |
| 12:30 PM | Lunch |
| 1:00 PM | Focus Group Discussion <ul style="list-style-type: none">• <i>Peter Pratt</i>, Project Team |
| 1:30 PM | Fall 2004 Conference Discussion <ul style="list-style-type: none">• <i>Elisabeth Weston</i> |
| 1:45 PM | Next Steps <ul style="list-style-type: none">• <i>Peter Pratt</i> |
| 2:00 PM | Adjournment |

PRESENTATION HANDOUTS

Flinn Foundation EBP Project Steering Committee Meeting


October 20, 2003


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Meeting Overview


- Practitioner Survey
- Guideline/Algorithm Update
- Focus Group Discussion
- Fall 2004 Conference Discussion
- Next Steps


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	<h2 data-bbox="480 352 883 405">Practitioner Survey</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1154 520">■ Final review of survey and cover letter <li data-bbox="516 537 1036 573">■ Brief discussion of mailing lists <li data-bbox="516 590 1198 814">■ Timeline: <ul style="list-style-type: none"> <li data-bbox="565 642 867 678">● Mail on November 3 <li data-bbox="565 688 1130 724">● Collect responses through November 21 <li data-bbox="565 735 971 770">● Score through December 12 <li data-bbox="565 781 1198 814">● Analyze data, prepare report for mid-January <div data-bbox="347 884 423 940">  </div>
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	<h2 data-bbox="480 1224 1045 1276">Guideline/Algorithm Status</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1235 1440">■ JAMA article on lithium: changes to bipolar guideline? <li data-bbox="516 1465 1235 1661">■ Formatting and updating issues <ul style="list-style-type: none"> <li data-bbox="565 1528 1235 1564">● Introduction and overview need to be rewritten <li data-bbox="565 1585 1235 1661">● Plan for making updates needs to be addressed (in action plan) <div data-bbox="347 1755 423 1812">  </div>
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	<h2>Focus Group Discussion</h2>
	<ul style="list-style-type: none"> ■ Why? <ul style="list-style-type: none"> ● To enrich information from the survey ● To get deeper into the “why follow guidelines” question—qualitative ■ What? Depends on survey results ■ When? After survey results have been analyzed ■ Who? Consumers, physicians, purchasers, others? ■ Where?

	<h2>Fall 2004 Conference Discussion</h2>
	<ul style="list-style-type: none"> ■ Overview of the “gap” ■ TMAP and guidelines overview ■ What do we know about changing physician behaviors? ■ Project report ■ Michigan guidelines ■ Action plan—formulating an agenda for change

	<h2 data-bbox="480 352 1156 401">Fall 2004 Conference Decisions</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1091 525">■ Location: Lansing or SE Michigan? <li data-bbox="516 537 964 577">■ Date: September 23, 2004? <li data-bbox="516 590 821 630">■ SC member roles <ul style="list-style-type: none"> <li data-bbox="565 642 862 682">● Speakers/presenters <li data-bbox="565 686 813 726">● PR ambassadors
	

	<h2 data-bbox="480 1224 714 1272">Next Steps</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1040 1396">■ December or January meeting? <li data-bbox="516 1409 1219 1491">■ Presentation on guideline implementation by Mike Massanari <li data-bbox="516 1503 1219 1680">■ Use information from survey/focus groups to continue discussion of barriers, dissemination, and implementation of guidelines and algorithms
	

Preliminary Project Schedule

■ Subject to SC modification and approval

Mon., Oct. 20, 2003	SC Meeting	11:00AM-2:00PM	Lansing
Thu., Dec. 4, 2003	SC Meeting	11:00AM-3:00PM	Novi
Thu., Feb. 5, 2004	SC Meeting	11:00AM-3:00PM	Lansing
Mon., Apr. 5, 2004	SC Meeting	11:00AM-3:00PM	Novi
Thu., Jun. 3, 2004	SC Meeting	11:00AM-3:00PM	Lansing
Thu., Sep. 23, 2004	Conference	8:00AM-5:00PM	Novi

Ethel and James Flinn Family Foundation Evidence Based Practice (EBP) Project

Steering Committee Meeting
October 20, 2003, 11:00 AM–2:00 PM
Radisson Hotel, Lansing

SUMMARY OF MEETING

The steering committee met for the third time on October 20 at the Radisson Hotel in Lansing. All committee members were present except Hubert Huebl, Kathleen Williams, and Michael Zarr.

The purpose the October 20 meeting was to review the draft practitioner survey, receive updated information on algorithms and guidelines, discuss focus groups (the next phase of primary research), and begin discussions of the fall 2004 conference.

Practitioner Survey

The steering committee reviewed the latest iteration of the practitioner survey instrument. The version of the survey distributed at the October 20 meeting had itself been revised substantially in keeping with previous comments and suggestions from steering committee members. The issue was revisited so that committee members could have a final opportunity to review the document before it was used in the field.

Steering committee members commented at some length upon various aspects of the survey—the groups and individuals to whom it would be mailed, the mechanics of follow-up and reminder efforts, and, of course, the language and structure of the instrument itself. The most substantive discussions focused upon this last issue. As a result of the discussion, the steering committee and staff agreed to significant changes:

- The instrument would be streamlined and simplified to eliminate redundancy and confusion in one series of questions.
- The document would be revised so as to achieve greater consistency in the types of scales used.

Steering committee members stressed again that the chief purposes of the survey were to estimate the extent to which clinicians currently use guidelines and algorithms and to realistically assess the barriers that would confront efforts to encourage their wider use. The steering committee also stressed that the findings of the survey, and, indeed, all committee-sponsored research, should be interpreted and examined in the light of previously available research on evidence-based practice.

Staff agreed to distribute a revised final version of the survey instrument to the steering committee via e-mail, allowing a very brief period for additional comment.

Algorithms and Guidelines

The group tentatively agreed that the title for the recommended Michigan algorithms would be Michigan Implementation of Medication Algorithms (MIMA). Project staff then reviewed with committee members some of the difficulties that had been encountered in making the algorithms for the three conditions (depression, schizophrenia, and bipolar disorder) conform to a standard format. In particular, it had proved difficult to make flowcharts work well for algorithms other than that used for depression. The algorithms for schizophrenia and bipolar condition proved to be more complex and to have a greater number of decision points; they were thus much less amenable to being presented in a flowchart. Staff will continue to work on this and other formatting and “standardization” issues.

Spurred in part by a *Journal of the American Medical Association (JAMA)* article on lithium treatment for bipolar disorder, the steering committee discussed at some length the question of updating guidelines over time. Committee members expressed their belief that unless the recommended algorithms and guidelines were updated regularly they would quickly become useless. Several members noted that one reason the Texas/TIMA model was attractive was because regular updates were scheduled. It was further agreed that the steering committee itself could not do the updating. Doing so is not part of the committee’s charge and, in any event, it lacks available funds and time. Although updating is not a steering committee responsibility, it was agreed that the final action plan released to the public should report with a great deal of specificity on how the recommended guidelines would be updated and what resources would be needed.

Focus Groups

The steering committee began its initial discussion of the second piece of primary research contemplated for this project—the use of focus groups. Staff emphasized that the focus groups will have two major purposes:

- To assess the views and concerns of stakeholders (e.g., consumers) who would not have been contacted in a practitioner prescribing survey
- To allow the steering committee to more fully explore and evaluate some of the findings of the survey—that is, to “drill deeper” for information on specific findings or issues of interest

It was emphasized that the focus group research and the survey research are linked and will reinforce one another.

During the discussion, committee members placed particular emphasis on the role of consumers. The chances for action plan success will be improved if consumers understand and support its recommendations. There was, however, considerable committee sentiment in favor of holding focus groups in different regions of the state and including other groups, most notably purchasers of care and representatives of both primary- and specialty-care physicians. It was agreed that focus groups would be held in at least three regions of Michigan and include participants from the following groups:

- Consumers only

- Public and private purchasers only
- Clinicians (with the proviso that focus groups for primary care physicians and mental health specialists be held separately)

Staff will devise a timetable for the focus group effort, draft focus group questions and protocols, identify regional sites, and initiate the contacts necessary to recruit participants. The steering committee will be updated on progress and have an opportunity to address the focus group issue again at a subsequent meeting.

Final Conference

The final portion of the October 20 meeting was spent on an initial discussion of the concluding conference to be held in fall 2004. In making its presentation, staff stressed that, although the conference is approximately a year away, planning cannot begin too soon. A suitable venue has to be selected, speakers have to be arranged, and potential invitees have to be given ample time for scheduling.

The committee considered various questions including the nature of the invitation list, a roster of possible speakers, and the development of a public relations strategy to accompany the unveiling of the action plan. It was agreed that the conference should not be open to the general public but should be aimed at persons who can make a difference—leaders or “early adopters” in the mental health care field. John Rush, Michael Hogan, and Robert Drake were among those mentioned prominently as possible speakers. The steering committee also discussed the establishment of a speaker’s bureau or structured “road show” presentations that could be included as part of a public relations strategy.

The most important question the group addressed, however, was whether the purpose of conference would be a rollout of a finalized action plan, or, alternatively, the presentation of a substantially complete draft with the understanding that it could be subject to further revision and refinement as a result of the conference. The steering committee generally agreed that the latter approach would be better. The steering committee will draft a substantially complete action plan—that is, a document that identifies the most desirable algorithm and guidelines and specifies how they will be updated and implemented. The document will be duly attentive to the perspectives of all stakeholders as well as costs to the mental health care system generally. The draft action plan, however, certainly could be revised by the steering committee in light of comments received at the conference.

Staff will begin planning the conference and bring recommendations and/or options regarding the conference date, venue, invitation list, speakers, and public relations strategy back for steering committee review and action at a later date.

Next Meeting

The committee discussed whether it would be better to hold its next meeting as previously scheduled (on December 4) or to postpone it until January so that the preliminary results of the survey could be discussed. The latter was agreed upon, and the committee set the next meeting date of January 12, in Novi.

Appendix E:

Report of Meeting 4

Flinn Project Steering Committee, Meeting 4

January 12, 2004

11:00 AM – 3:00 PM

Doubletree Hotel

27000 Sheraton Drive

Novi, Michigan 48377

AGENDA

- 11:00 AM Welcome and Background/Introductions
- *Tom Carli*, Project Team
- 11:15 AM Work Plan for Remainder of Project
- *Peter Pratt*, Project Team
- 11:30 AM Presentation: Practitioner Survey Results
- *Melissa Riba*, Project Team
- 12:15 PM Break
- 12:30 PM Presentation: Obstacles to and Opportunities for Guideline/Algorithm Adoption (ref. articles sent by mail)
- *Mike Massanari*
- 1:00 PM Discussion: Obstacles, Barriers, and Solutions to Guideline/Algorithm Adoption in Michigan
- *Tom Carli*
- 2:00 PM Discussion: Determining the Value of Focus Groups for this Project
- *Tom Carli*
- 2:30 PM Discussion: Conference (September 2004)
- *Elisabeth Weston*, Project Team
- 3:00 PM Adjournment

PRESENTATION HANDOUTS

Flinn Foundation EBP Project Steering Committee Meeting

January 12, 2004




Agenda


11:00	Welcome and Background/Introductions	Tom Carli
11:15	Work Plan for Remainder of Project	Peter Pratt
11:30	Presentation: Practitioner Survey Results	Melissa Riba
12:15	Break (working lunch)	
12:30	Presentation: Obstacles to and Opportunities for Guideline/Algorithm Adoption	Mike Massanari
1:00	Discussion: Obstacles, Barriers, and Solutions to Guideline/Algorithm Adoption in Michigan	Tom Carli
2:00	Discussion: Determining the Value of Focus Groups for this Project	Tom Carli
2:30	Discussion: Conference (September 2004)	Elisabeth Weston
3:00	Adjournment	



<div data-bbox="249 795 328 855" data-label="Page-Header"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2 data-bbox="382 262 868 311">Project Overview: Goal</h2>
	<ul data-bbox="419 394 1139 653" style="list-style-type: none"> ■ Complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder

<div data-bbox="249 1678 328 1738" data-label="Page-Header"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2 data-bbox="382 1143 919 1192">Project Overview: Tactics</h2>
	<ul data-bbox="419 1275 1139 1576" style="list-style-type: none"> ■ Achieve consensus on guidelines/algorithms ■ Identify barriers to adoption in the field ■ Address barriers through action plan—how do we change <i>practice</i> given what we know?

	<h2>Project Overview: Committee Role</h2>
	<ul style="list-style-type: none"> ■ Action-oriented steering committee (SC) ■ Limited number of meetings ■ Committee-driven process


	<h2>January 12 Meeting Overview</h2>
	<ul style="list-style-type: none"> ■ Overview of remaining work plan ■ Presentation: survey results ■ Presentation: factors that promote and impede guideline implementation ■ Discussion: obstacles, barriers, solutions ■ Discussion: focus groups ■ Discussion: conference (September 2004)


<div data-bbox="249 795 327 853" data-label="Page-Header"> <p>PSC PUBLIC SECTOR CONSULTANTS</p> </div>	<h2 data-bbox="382 262 1089 311">Work Plan for Completing Project</h2>
	<ul style="list-style-type: none"> ■ February 5 meeting: action plan strategy development <ul style="list-style-type: none"> ● Implementation barriers, best practices, and opportunities ● Strategies to overcome barriers ● Action steps <ul style="list-style-type: none"> ○ Resources needed ○ Responsible parties ○ Timeline


<div data-bbox="249 1678 327 1736" data-label="Page-Header"> <p>PSC PUBLIC SECTOR CONSULTANTS</p> </div>	<h2 data-bbox="382 1143 1089 1192">Work Plan for Completing Project</h2>
	<ul style="list-style-type: none"> ■ February–April <ul style="list-style-type: none"> ● Perform assigned duties toward completing work plan ● Finalize plans for conference; first mailing to prospective attendees ■ April 5 meeting: finish work plan ■ April–June: PSC drafts final report ■ June 3 meeting: review and finalize report


<div data-bbox="249 797 328 859"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2 data-bbox="382 266 1088 314">Work Plan for Completing Project</h2>
	<ul style="list-style-type: none"> <li data-bbox="419 396 1071 521">■ Possible August meeting: review and finalize plan for conference and public outreach <li data-bbox="419 537 872 575">■ September 23: Conference


<div data-bbox="249 1678 328 1740"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2 data-bbox="382 1145 702 1193">Survey Results</h2>
	<ul style="list-style-type: none"> <li data-bbox="419 1275 662 1313">■ Methodology <li data-bbox="419 1329 801 1367">■ Profile of respondents <li data-bbox="419 1383 771 1421">■ Information sources <li data-bbox="419 1437 1082 1514">■ Limitations on prescribing psychotropic meds <li data-bbox="419 1530 1115 1568">■ Familiarity with algorithms and guidelines <li data-bbox="419 1584 711 1622">■ Use and barriers <li data-bbox="419 1638 1090 1676">■ Bottom line: guideline adoption and use


	<h2>Methodology</h2>
	<ul style="list-style-type: none"> ■ Two formats: paper and Internet ■ Mailing lists of Michigan practitioners from <ul style="list-style-type: none"> ● Michigan Psychiatric Society ● American Medical Association ● Michigan State Medical Society ● Michigan Osteopathic Association ■ 6,208 surveys sent (mailed twice) ■ Response rate: approximately 9% (N=531)

	<h2>Profile of Respondents (Q1–6)</h2>
	<ul style="list-style-type: none"> ■ 40% psychiatrists / 60% PCPs <ul style="list-style-type: none"> ● Psychiatrists (214): 84% treat adults, 16% treat children ● PCPs (277): 51% general or family practice practitioners ■ Half of respondents can transmit and receive patient information electronically ■ Most have access to the Internet and use it from their place of work ■ Psychiatrists more often than PCPs have patients with major depression, bipolar disorder, or schizophrenia ■ Major depression is the most seen diagnosis and is more prescribed

	<h2>Information Sources (Q7 and Q8)</h2>
	<ul style="list-style-type: none"> ■ Peers and interactions with peers are most important sources of information ■ Peer reviewed journals are easiest source to access, followed by non-peer reviewed journals and pharmaceutical representatives ■ Peer reviewed journals also top pick for usefulness ■ Workshops, colleagues, and professional organizations are most useful ways of keeping abreast but not easy to access ■ No great difference in responses of psychiatrists and PCPs

	<h2>Limitations on Prescribing (Q9)</h2>
	<ul style="list-style-type: none"> ■ More PCPs perceive/experience restrictions or limitations in their ability to prescribe ■ This is especially true for private health plans and Medicaid

	<h2>Algorithm/Guideline Familiarity (Q10)</h2>
	<ul style="list-style-type: none"> ■ Psychiatrists <ul style="list-style-type: none"> ● 59%t “somewhat/very familiar” with APA guidelines ● 38% “somewhat/very familiar” with TMAP ■ PCPs <ul style="list-style-type: none"> ● 8% “somewhat/very familiar” with APA guidelines ● Practically no one is familiar with TMAP (<2%) ● Most familiar with private health plan guidelines (11%)

	<h2>Use and Barriers (Q11–14)</h2>
	<ul style="list-style-type: none"> ■ Little difference in the use of <i>any</i> guideline <ul style="list-style-type: none"> ● 48% of psychiatrists report using or relying on <i>any</i> guideline and algorithm ● 42% of PCPs report using <i>any</i> guideline or algorithm ■ Drop-off in use among psychiatrists <ul style="list-style-type: none"> ● 59% familiar with APA guidelines; only 24% “often or always” use them in treatment ● 38% familiar with TMAP; 10% “often or always” use it ■ Nearly all PCPs who are familiar with guidelines also use them <ul style="list-style-type: none"> ● 8% are familiar with APA guidelines and report often or always using the those guidelines

Facilitating Factors (Q13)

- Both groups use algorithms and guidelines for the same reasons:
 - Significant evidence that they improve patient outcomes
 - Easy to understand and use
 - Influence of colleagues
 - Recommendations by professional group
 - Recommendations from experts in the field

Barriers (Q14): Psychiatrists

- Top five reasons for not using algorithms/guidelines
 - Patients need individualized treatment
 - Already do what guidelines recommend
 - Lack of training in how to use them
 - Patient preferences
 - Lack of evidence that they improve patient outcomes

Barriers (Q14): PCPs

- Top five reasons for not using algorithms/guidelines
 - Patients need individualized treatment
 - Lack of training in how to use them
 - Formulary restrictions
 - Not easy to use when they are seeing patients
 - Adds too much time

Bottom Line: What Will it Take? (Q15)

- Top factor for both groups: more evidence that guidelines make a difference in patient outcomes

Preliminary Analysis: Big Picture

■ “Messengers”

- All respondents are similar in the information sources they have access to and find useful
- They value expert opinion, evidence, and the ability to interact in various ways with colleagues
- Peer reviewed journals cited as accessible and useful to all. Other venues, such as workshops and professional organizations are rated as useful, but are not as accessible as other sources, e.g., pharmaceutical representatives

Preliminary Analysis: Big Picture

■ *Systemic barriers encountered by the two groups of practitioners may be different*

- Any plan that tackles systemic barriers needs to address how and why these groups differ and how they may experience the system of mental health care differently
- While the venues for education, training, and dissemination can be similar for both groups, the plan may need to diverge when it comes to tackling barriers to implementation

Preliminary Analysis: Big Picture

■ *Facilitating use*

- Evidence
- Make it easy to use

Survey Results


■ Initial discussion

Presentation: Mike Massanari

- Factors that promote and impede guidelines implementation

Discussion

- Obstacles, barriers, solutions
- Include preliminary analysis of Michigan practitioner survey

	<h2>Focus Groups</h2>
	<ul style="list-style-type: none"> ■ Recap of previous discussion on value of focus groups for this project ■ Discussion of what, if anything, could be gained by having them

	<h2>September Conference</h2>
	<ul style="list-style-type: none"> ■ Invitation only ■ Speakers ■ Reaction to draft action plan ■ Online comment before and after conference ■ SC meeting afterward to finalize report

Next Steps

- February 5 committee meeting (Lansing)
 - Formulate action plan
 - Finalize conference planning
- February–April: work on action plan
- April 5 meeting (Novi): finish work plan
- April–June: PSC drafts final report
- June 3 meeting (Lansing): review and finalize report

Ethel and James Flinn Family Foundation Evidence Based Practice (EBP) Project

Steering Committee Meeting
January 12, 2004, 11:00 AM–3:00 PM
Doubletree Hotel, Novi

SUMMARY OF MEETING

Research

Barriers to Implementation

In his review of the literature, Mike Massanari characterizes barriers to algorithm and guideline implementation as being either *intrinsic* or *extrinsic*.

Intrinsic barriers include:

- Knowledge barriers due to lack of familiarity or awareness
- Attitudinal barriers due to:
 - Specific or general disagreements with guidelines
 - Lack of outcome expectancy
 - Lack of self efficacy
 - Lack of motivation

Extrinsic barriers include:

- Patient factors, especially patient preference
- Guidelines factors, including format issues and substantive inconsistencies from guideline to guideline
- Environmental factors (lack of time, lack of resources, lack of reimbursement, etc.)

The survey (including the qualitative portions) supported these findings and added useful, Michigan-specific detail:

- Both psychiatrists and primary care physicians cite the need for individualized patient treatment and lack of training as reasons for not using guidelines.
- Psychiatrists also cite the fact that they already do what guidelines recommend, patient preferences, and lack of outcome expectancy as barriers.
- Primary care physicians identify formulary restrictions, difficulty in use, and time constraints as barriers.
- The perceived existence of multiple, competing guidelines and algorithms may hinder broader implementation.
- At least some practitioners in Michigan are extremely skeptical about what they call “cookbook medicine.”

- Guidelines or algorithms are not always useful in difficult situations involving co-morbidity or co-occurring disorders and different drug regimens.

Promoters of Implementation

Massanari identifies significant *extrinsic environmental promoters* of guideline/algorithm implementation, including:

- External incentives (e.g., public recognition)
- Information technology

Further, he identifies a number of factors that improve physician performance generally:

- Shared goals
- Substantial administrative support
- Strong physician leadership
- High-quality feedback data.

The survey suggests that in Michigan:

- There is considerable interest in guidelines and algorithms provided that they are practical and easy to use.
- Psychiatrists and primary care physicians agree that ease of use along with recommendations from colleagues, professional groups, and experts in the field would promote algorithm and guideline use.
- Psychiatrists and primary care physicians agree that better evidence that algorithms and guidelines improve outcomes would be the single biggest promoter.

Additional Findings and Considerations

The two presentations included a number of other points that are useful as background and context:

- Commonly used guidelines and education are likely to be ineffective absent other, supporting interventions.
- Implementing guidelines will require a substantial change in investment of resources.
- In Texas, at least, follow-up studies demonstrated that the use of algorithms achieved only limited success.
- Half the Michigan survey respondents can transmit and receive patient information electronically; most respondents have access to the Internet and use it from their place of work.
- Major depression is the most seen diagnosis and the one for which most prescriptions are written.
- Psychiatrists play a significant role in treating all three conditions; primary care physicians have a very significant role in the treatment of depression and a lesser (though still important) role to play in the treatment of bipolar disorder and schizophrenia.

- Psychiatrists and primary care physicians vary very little with regard to how they seek information. Peers and interactions with peers are the most important sources of information. Peer reviewed journals are viewed as both useful and accessible. Workshops, colleagues, and professional organizations are viewed as useful but harder to access.

The qualitative sections of the survey suggest attention to the following concerns as well:

- There is an interest in guidelines for children and adolescent depression if any are available.
- There is a concern that this project involves only drug therapy.
- There is a concern over the relationship of algorithm and guideline use and exposure to malpractice liability.
- There is a concern that the current system, whose features include patient autonomy and physician independence, may be very difficult to change.

Committee Comments

Members of the Steering Committee made the following observations in response to the two presentations:

- We may need specific examples (“vignettes”) of patients with different arrays of symptoms and circumstances that doctors can respond to when they are using the guidelines/algorithms.
- For many uses we need to simplify the TIMA/MIMA guidelines considerably, perhaps boiling them down to 8–10 points.
- We must identify who doctors really listen to (“mavens,” “clinical influential”) and get them on our team (outreach to early adopters).
- We should focus on inappropriate prescribers; to do so would require institutional pressure (this is the opposite of starting with early adopters).
- We should craft a pilot that asks doctors to test the guidelines to see if they produce better outcomes. BCBSM did something like this with the GAP (Guidelines in Application) project for care after heart attacks. Payer funded the data collection by an add-on to DRG payment.
- We should agree on simple, narrow outcome measures to test the value of guidelines and/or algorithms.
- We need to stress the importance of the initial diagnosis. Getting the patient in the right diagnosis at the right level is critical.
- We need to stress that while improving outcomes is important, the role algorithms and guidelines play in reducing adverse outcomes is also important.
- We must be realistic in stating goals—changes in medical practice can take a very long time.

Recommendations

At this juncture we have on the table specific recommendations by Mike Massanari and Tom Zelnick. At the last meeting, Tom Carli offered a summary of Steering Committee

recommendations. As we move forward, it is important to recall our earlier agreement that recommendations in the action plan should be accompanied by:

- Supporting rationale
- Indications of who is responsible for future action
- Indications of resource needs
- Provisions for monitoring, evaluation, and feedback
- Timetables

Mike Massanari recommends the development of a “multi-faceted implementation protocol” that includes:

- Education of physicians and consumers
- Development (with the help of “process engineers”) of a “user friendly” tool kit for providers
- Administrative support for implementation
- Evaluation and feedback to providers
- Access to technical support

Further, he suggests the importance of information technology, external incentives, case managers, and a mechanism for dialogue between physician champions and practitioners.

Tom Zelnick addresses the fact that psychiatrists and primary care physicians have different requirements and that there is a paramount need for a research component—not just to test the assumption that guidelines and algorithms improve outcomes, but also to test the extent to which key practitioners comply with certain key process benchmarks. His major points:

- Primary care practitioners, in particular, have a need for an “easy-to-implement, credible, *algorithm* for treatment of depression.”
- Psychiatrists and psychiatric subspecialists would benefit more from “more sophisticated but still user-friendly” *guidelines* for the treatment of all three conditions.
- There would be great value in monitoring certain agreed-upon and valid *process measures* to identify “outliers” in both primary and specialty care.
- Any algorithms, guidelines, or process measures the Steering Committee might endorse should be validated through pilot programs across the state.

In a summation that appeared acceptable to the Steering Committee, Tom Carli suggested that the group had reached agreement on the following points:

- We want to implement guidelines that practitioners will use and find valuable.
- Guidelines by themselves are inadequate; they need to be supplemented in a number of ways.
- Packaging/presenting guidelines must be simple and easy to read (laminated card, etc.) with more complex background information available for those who want it.

There should be a rollout of education opportunities on the guidelines (through targeted groups of physicians, workshops, CME, med school/residency training).

- We should look at health care organization care processes to reinforce guideline use (IT support, administrative leadership).
- Financial incentives to use guidelines should be considered, even if only in a pilot (see bullet above).
- Patient education is important (materials, workshops).
- Accountability, evaluation, and measurement should be built into the plan.

Our next step is to consider how these initial suggestions and recommendations can be translated into a proposed outline of the action plan.

Appendix F:

Record of Meeting 5

Flinn Project Steering Committee, Meeting 5

February 5, 2004

11:00 AM – 3:00 PM

Holiday Inn South

6820 S. Cedar Street

Lansing, Michigan 48911

AGENDA

- 11:00 AM Welcome, review of charge, overview of today's meeting
- Tom Carli, Project Team
- 11:15 AM Presentation: MIMA guidelines and algorithms (short and long formats)
- Tom Carli
- 11:45 AM Review of barriers to and promoters of guideline implementation
- Tom Carli
- 12:00 PM Break (working lunch)
- 12:30 PM Review consensus approach from January meeting (guiding principles and topics for action plan)
- Tom Carli
- 1:00 PM Full group discussion of principles
- 1:15 PM Small group discussion: action plan strategies
- 2:00 PM Report out; full discussion of strategies
- 2:30 PM Finalize conference details
- Elisabeth Weston
- 3:00 PM Adjourn

PRESENTATION HANDOUTS

Flinn Foundation EBP Project Steering Committee Meeting

February 5, 2004




Agenda


11:00	Welcome, Review, and Overview	Tom Carli
11:15	Presentation: MIMA Guidelines/Algorithms	Tom Carli
11:45	Review of Implementation Barriers, Promoters	Tom Carli
12:00	Break (working lunch)	
12:30	Review of Principles and Topics for Action Plan	Tom Carli
1:00	Discussion: Action Plan Principles	
1:15	Small Groups: Strategy Development	
2:00	Report Out: Discuss Strategies	
2:30	Finalize Conference Details	Elisabeth Weston
3:00	Adjourn	





<div data-bbox="249 795 328 855" data-label="Page-Header"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2 data-bbox="382 262 868 311">Project Overview: Goal</h2>
	<ul data-bbox="419 394 1139 653" style="list-style-type: none"> ■ Complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder

<div data-bbox="249 1678 328 1738" data-label="Page-Header"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2 data-bbox="382 1143 919 1192">Project Overview: Tactics</h2>
	<ul data-bbox="419 1275 1139 1576" style="list-style-type: none"> ■ Achieve consensus on guidelines/algorithms ■ Identify barriers to adoption in the field ■ Address barriers through action plan—how do we change <i>practice</i> given what we know?

	<h2>Project Overview: Committee Role</h2>
	<ul style="list-style-type: none"> ■ Action-oriented steering committee (SC) ■ Limited number of meetings ■ Committee-driven process

	<h2>February 5 Meeting Overview</h2>
	<ul style="list-style-type: none"> ■ Action plan strategy development <ul style="list-style-type: none"> ● Review guideline/algorithm format ● Implementation barriers, best practices, and opportunities ● Strategies to overcome barriers ● Action steps <ul style="list-style-type: none"> ○ Responsible parties ○ Timeline ■ Finalize conference plans

	<h2>Work Plan for Completing Project</h2>
	<ul style="list-style-type: none"> ■ February–April <ul style="list-style-type: none"> ● Perform assigned duties toward completing work plan ● Finalize plans for conference; first mailing to prospective attendees ■ April 5 meeting: finish work plan ■ April–June: PSC drafts final report ■ June 3 meeting: review and finalize report ■ Possible August meeting: review, finalize plan for conference and public outreach ■ September 23: Conference

	<h2>MIMA Guidelines/Algorithms</h2>
	<ul style="list-style-type: none"> ■ Review of MIMA guidelines <ul style="list-style-type: none"> ● Standard format ● Short and long versions ■ Remaining issues <ul style="list-style-type: none"> ● Missing sections (overview, introduction, etc.)

Implementation Barriers, Promoters

- Intrinsic barriers
 - Knowledge
 - Attitude
- Extrinsic barriers
 - Patient factors
 - Guideline factors
 - Environmental factors
- Extrinsic promoters
 - External incentives
 - Information technology

Recommendation Principles


- Guidelines and algorithms must be easy to use and valuable
- Guidelines by themselves are not enough
- Differences in knowledge and needs among psychiatrists, PCPs, and consumers must be part of the plan
- Action plan should be rolled out over time, with pilots to enlist opinion leaders and early adopters


<div data-bbox="249 797 328 857"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2>Topics for Action Plan</h2>
	<ul style="list-style-type: none"> ■ Stakeholder buy-in <ul style="list-style-type: none"> ● Consumer groups ● Physician groups ● Health insurers/plans ● Purchasers ● Michigan Mental Health Commission

<div data-bbox="249 1678 328 1738"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2>Topics for Action Plan</h2>
	<ul style="list-style-type: none"> ■ Ongoing support <ul style="list-style-type: none"> ● Administrative support (information technology, leadership from health care organizations) ● Technical support (who and where physicians and consumers can go with questions)


<div data-bbox="249 797 328 857"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2>Topics for Action Plan</h2>
	<ul style="list-style-type: none"> ■ Packaging and presenting guidelines and algorithms <ul style="list-style-type: none"> ● Tool kit ● Laminated cards ● More complex background information for those who want it


<div data-bbox="249 1678 328 1738"> PSC PUBLIC SECTOR CONSULTANTS </div>	<h2>Topics for Action Plan</h2>
	<ul style="list-style-type: none"> ■ Physician and consumer education <ul style="list-style-type: none"> ● CME, residency training, and medical school for physicians ● Forums, workshops, and materials for consumers


	<h2>Topics for Action Plan</h2>
	<ul style="list-style-type: none"> ■ Financial incentives ■ Evaluation and measurement of guideline and algorithm use <ul style="list-style-type: none"> ● Do the guidelines improve care?

	<h2>Discussion of Principles</h2>
	<ul style="list-style-type: none"> ■ Review principles <ul style="list-style-type: none"> ● Guidelines and algorithms must be easy to use and valuable ● Guidelines by themselves are not enough ● Differences in knowledge and needs among psychiatrists, PCPs, and consumers must be part of the plan ● Action plan should be rolled out over time, with pilots to enlist opinion leaders and early adopters ■ Additions, deletions, modifications?

	<h2>Strategy Development (Small Groups)</h2>
	<ul style="list-style-type: none"> ■ Barrie, Huebl, Reid, Sheehan, Wilhelm, Zelnik <ul style="list-style-type: none"> ● Stakeholder buy-in ● On-going support ■ Berchou, Engel, Milner, Reinstein, Zarr <ul style="list-style-type: none"> ● Packaging, presentation ● Physician, consumer education ■ Carbone, Dudley, Fauman, Henry, Massanari, Veenhuis <ul style="list-style-type: none"> ● Financial incentives ● Evaluation, measurement

	<h2>Strategy Development (Small Groups)</h2>
	<ul style="list-style-type: none"> ■ What strategies will make a difference? ■ Which individuals or organizations are in the best position to take the lead on this strategy?

	<h2>Small Groups Report Out</h2>
	<ul style="list-style-type: none"> ■ One member of each group report group's strategies ■ Discussion and refinement of strategies ■ PSC will synthesize, summarize

	<h2>September 23 Conference/Summit</h2>
	<ul style="list-style-type: none"> ■ Lansing, half-day, possible teleconference or web simulcast ■ Invitation only ■ Speakers ■ Reaction to draft action plan ■ Online comment before and after conference ■ SC meeting afterward to finalize report

Next Steps

- April 5 meeting (Novi): finish work plan
 - Develop for each strategy:
 - o Major action steps
 - o Responsible parties
 - o Monitoring
 - o Timelines
- April–June: PSC drafts final report
- June 3 meeting (Lansing): review and finalize report

Ethel and James Flinn Family Foundation Evidence Based Practice (EBP) Project

Steering Committee Meeting
February 5, 2004, 11:00 AM–3:00 PM
Holiday Inn South, Lansing

SUMMARY OF MEETING

The chief purpose of the February 5th Steering Committee meeting was to develop strategies for the final action plan. However, the group also discussed various other topics, including the Michigan Implementation of Medication Algorithms (MIMA) Guidelines/Algorithms, barriers and promoters of implementation, and the September conference. The Steering Committee also felt obliged to take note of two recent EBP-related stories that had been featured prominently in the media:

- A feature story in the Business section of the February 1, 2004, *New York Times* (attached) discussing the controversy that had arisen over the role pharmaceutical companies may have played in the development and dissemination of the Texas medication guidelines. The story also indicated that a soon-to-be-published study by a Patient Outcomes Research Team (PORT) funded by the National Institute of Mental Health conflicted with the Texas guidelines for treatment of schizophrenia.
- Extensive coverage of FDA hearings on the claim that SSRI drugs may cause suicidal ideation and actual suicide among children and adolescents. The hearings, which culminated in stronger warnings being issued by the FDA, followed an earlier decision by health officials in Great Britain to recommend against the use of some SSRI drugs by depressed minors.

With regard to the Texas guidelines, the committee felt that they were scientifically sound and developed in good faith. Some pharmaceutical company money was used for their development, but the greater share came from other sources, including private foundations. Of greater concern to the Steering Committee was the fact that the same companies continued to underwrite speaking engagements for Texas officials around the country. Members of the Steering Committee felt that since the Texas guidelines are sound, and since the Flinn project is not itself influenced by pharmaceutical companies, there was little cause for concern. The Steering Committee does, however, wish to review the PORT guidelines if possible.

With regard to the FDA hearings, the Steering Committee noted that the adverse effects of SSRI use among minors are small and only observable across a large population. Some concern was expressed that previously unpublished studies might indicate even stronger effects. The Steering Committee felt, however, that the issue is not of immediate relevance to its work because the Texas guidelines that are being adapted for use in Michigan were not designed for the treatment of minors and will not be marketed that way.

MICHIGAN IMPLEMENTATION OF MEDICATION ALGORITHMS (MIMA)

Staff reported that its efforts to translate the TIMA guidelines into MIMA guidelines appropriate for use in Michigan had encountered difficulties. The TIMA guidelines contain references to such things as forms and state-sponsored consultants that do not yet exist in Michigan. The three Steering Committee subgroups that had earlier recommended the use of the Texas Guidelines/Algorithms will reconvene to suggest how the operative portions of MIMA can be kept intact for the treatment of depression, bipolar disorder, and schizophrenia while eliminating the Texas-specific references.

EMERGING STRATEGIES

After a brief review of implementation barriers and promoters, the Steering Committee reviewed at greater length staff-proposed topics and principles for action plan development. It was agreed that four basic principles should inform guideline development:

- Guidelines and algorithms must be easy to use and valuable.
- Guidelines by themselves are not enough.
- Differences in knowledge and needs among psychiatrists, PCPs, and consumers must be part of the plan.
- The action plan should be rolled out over time, with pilots to enlist opinion leaders and early adopters.

It was also agreed that the Steering Committee would develop action plan items within six broad topic areas:

- Stakeholder buy-in
- Ongoing support
- Packaging and presenting guidelines and algorithms
- Physician and consumer education
- Financial incentives
- Evaluation and measurement of guidelines and algorithm use

The members of the Steering Committee then broke into small groups to begin the process of developing strategy recommendations, incorporated below.

Staff will use the results of the group reports and the subsequent discussion to prepare materials for the April 5th meeting when recommendations will be considered further.

Strategies for Stakeholder Buy-in and Ongoing Support

Group Members: Patrick Barrie, Hubert Huebl, Michelle Reid, Dan Wilhelm, and Tom Zelnick

The group decided to collapse the two issues, believing that if one identified key stakeholders and their needs and natural contacts, one would automatically understand what sort of ongoing support each would need and be able to contribute. Furthermore, the

group felt that “stakeholders” should be used to identify and contact other organizational partners—the Michigan Depression and Bipolar Support Alliance and the Michigan Association of Community Mental Health Boards, to name two examples.

The group specified the steps that needed to be taken and began inventorying what Steering Committee members and other groups could contribute. Proposed action steps include:

- Identifying stakeholders and potential organizational partners and stratifying them according to their ability to help with marketing (“getting the word out”) and with educational efforts, including pilot programs
- Contacting stakeholders/partners to arrange articles in newsletters, presentations at meetings and conferences, and face-to-face contacts
- Convening key stakeholders before the September 23d conference to present the action plan and solicit input (“tweaking”)
- Disseminating information on the Flinn EBP website
- Using steering committee members to identify other key stakeholders with whom they have personal or professional relationships
- Ensuring that there is a version of the educational materials for patients’ family members to use when they go to the doctor
- Identifying various possible donors (e.g., foundations and pharmaceutical companies) who can help defray the costs of printing, training, mailing, etc.
- Holding a roundtable of Steering Committee members to determine how each can best contribute

The group also made two major points of emphasis:

- There is a need to stress that various nonmedication treatments are available to augment prescription drug treatment.
- Any research or pilot programs need to contain a “feedback loop,” following the centers of excellence concept.

The group made an initial attempt to describe the natural affiliations or contacts each member of the Steering Committee would have. The general theory is that a focused use of Steering Committee contacts is the single best way to ensure broad project buy-in and, ultimately, success.

Committee Member	Organizational Contacts
Patrick Barrie	State Hospitals, CFP
Hubert Carbone	MDCH
Michele Reid (Detroit-Wayne)	CMH Medical Director
John Baugh (St. Clair)	Contractors
Jonathon Henry (Ingham, Eaton, Clinton)	
Mark Reinstein	Mental Health Association, government policymakers, members of public
Hubert Huebl	NAMI, family members and consumers, interface with providers
Tom Carli, Jed Magen, Manuel Tancer	Medical school, residency training, nurse practitioners and physicians assistants
Cal Dudley	BCBSM subscribers, providers, and purchasers
Michael Fauman	Magellan subscribers, providers, and purchasers
Wayne Creelman	Care Choices, subscribers, providers, and purchasers
Dan Wilhelm	Michigan State Medical Society (members and publications), Medical Services Administration, FHSC, and MHP
Tom Zelnik	Trinity Health System, independent practice associations
Tom Carli	IPAs, UM Family and Group Practice
Michael Zarr	Health Alliance Plan, Value Options
Michael Engel et al	Michigan Psychiatric Society

The list is suggestive not exhaustive and does not include the contacts of all Steering Committee members. In addition, the work group listed a number of potential organizational partners, including:

- Legislative leadership
- Medical Services Administration
- Michigan Association of Community Mental Health Boards
- Michigan Association of Health Plans
- Michigan Hospital Association
- Michigan Osteopathic Association
- Other payers (HMO's, PPO's)
- Quality Management Organizations (MQIC, GDAHC)

Possible funders include:

- Center for Health Care Strategies
- Centers for Medicaid and Medicare Services
- HRSA
- Kellogg, Skillman, Prechter and R. W. Johnson foundations
- NIMA
- Pharmaceutical companies
- SAMHSA

Strategies for Packaging and Presenting Guidelines and Algorithms

Group Members: Richard Berchou, Cal Dudley, Jed Magen, Mark Reinstein, Mike Zarr.

The packaging, distribution, and presentation of guidelines and algorithms should be viewed as discrete *processes* (not products) that change in response to end-user needs and feedback—much the way that guidelines and algorithms change in response to new studies and developments.

- Develop materials for both physician audiences (PCP, specialty care).
 - It may or may not be delivered as a single package (depending on distribution strategy), but there should be obvious materials for each group.
 - Materials should contain both short (quick reference) and long (detailed explanation) versions so clinician can choose according to need, comfort level.
- Consult with packaging and distribution experts for developing something that can compete for provider's attention.
 - Packaging experts should conduct focus groups of end-users (care providers and patients) to obtain initial and on-going feedback.
 - Distribution experts should also conduct focus groups of end-users and develop a plan that incorporates medical professional societies as a distribution channel. Provider organizations such as MDCH and BCBSM may also be considered as distributors.
- As a general principal, integrate technology in the packaging and distribution of guidelines and algorithms, as a general principle.
 - The practical, systemic use of guidelines and algorithms must anticipate the future of health care administration and delivery, such as electronic medical records (EMR).
 - Consider alliances with General Electric and other providers of health care electronics.

Strategies for Physician and Consumer Education

Group Members: Richard Berchou, Cal Dudley, Jed Magen, Mark Reinstein, Mike Zarr.

Physician Education

- Address the practicing physician's questions, "Why should I change my current practices?" and "What is the motivation of those who are promulgating these guidelines and algorithms?"
 - Demonstrate the reduction of outcome variation that results from systemwide use of guidelines and algorithms.
 - Demonstrate the time and cost savings associated with the implementation of comprehensive guidelines that serve as one-stop guides.
- Education efforts must be directed toward physicians at every level through which they are influenced.

- “Top-end” organizations that have the greatest impact on physician practices must buy in to and/or adopt the guideline/algorithm implementation. Such organizations include major payers such as health plans and state government.
 - Membership organizations and medical societies can play a role by endorsing the guidelines and algorithms.
- Physician education and awareness must be sought through flexible methods that allow for input and feedback, such as pilot programs for voluntary early adopters.

Consumer Education

Although prescribers are the primary target audience for awareness-raising efforts, consumers must also be educated because they play an increasingly influential role in their doctors’ prescribing practices.

- Encourage clinicians to educate consumers about the use of guidelines and algorithms at the time of treatment.
- Enlist support of the use of guidelines and algorithms from both primary consumers and groups representing their families and support networks.
- Include information about the guidelines and algorithms in relevant state government publications and programs (MDCH website, MDCH consumer handbook, clubhouses, etc.).
- Distribute information at meetings of consumer groups (regularly scheduled or convened specifically for this purpose).

Strategies for Financial Incentives

Group Members: Hugh Carbone, Mike Engel, Mike Fauman, John Henry, Mike Massanari, Phil Veenhuis.

Financial incentives were not rated highly in the provider survey. The group discussed various ways to structure financial incentives for adherence to guidelines and algorithms. It then discussed other, less direct financial incentives as well as non-financial incentives.

Strategies for **structuring financial incentives** that were discussed:

- Use of pay-for-performance models that have proven successful elsewhere
- Implementation of quality incentives (demonstrable quality improvement) through adherence to guidelines and algorithms
- Making a business case for quality by emphasizing the value that comes from quality improvement and adoption of the guidelines
- For direct financial incentives, create a process that ensures “pass-through” to the providers who use the guidelines; cut out the “middleman”

Nondirect financial incentives included:

- CME credit for using the guidelines
- Cost savings (e.g., lower malpractice insurance rates)

- Create a process to demonstrate good outcomes (although there was concern as to how the outcomes would be defined)

Other incentives:

- Create a system that acknowledges participation in the EBP project (e.g., providers who use the guidelines or are participating in any pilot have a decal they can display to acknowledge their use of the guidelines)
- Promote the intrinsic value of adopting and using the guidelines (providing the best care to patients, being an early adopter/innovator)

Throughout this discussion, the group emphasized the multiple entities that need to be considered in the structuring of any incentive process—individual providers, group practices, purchasers (e.g., the State of Michigan, Ford, General Motors), payers (e.g. the Blues), and malpractice insurance providers. Providing direct financial incentives to individual practitioners and group practices may have some impact.

Another thread of the discussion concerning strategies for creating or providing financial incentives is how it links to evaluation and measurement of the process and outcomes of implementing guideline use. The undercurrent of this discussion was the need to demonstrate that using the guidelines “works”—although how exactly this is done would need to be dealt with in depth and with much greater precision. Incentives were seen as a part of encouraging participation in a pilot study and roll out of the guidelines, as well as creating a means to demonstrate improvements in quality of care, performance, cost savings, and issues with malpractice insurance.

Strategies for Evaluation and Measurement

The group focused on the question of *how* to evaluate and measure the use of guidelines. This then led into a discussion of what a potential pilot study could look like. Embedded in this discussion are strategies for how to evaluate and measure use and its impact.

Overall concerns about evaluating and measuring the use of guidelines raised by the group include:

- How do we measure outcomes? What indicators do we choose or create? This must be done carefully. Most specifically, the group returned to the question of what it means to “use the guidelines.” They pointed to the need to document and define “use” as a part of any pilot study.
- Be clear about which measures are process versus outcome measures. In the short term it will be easier to measure adherence to guidelines (process) than outcomes of care.
- Leverage technology to provide efficient, user-friendly data collection. For example, Web-based data collection from providers could be conducted. However, this would only be feasible if the participating providers had high-speed Internet connections to speed the exchange of data.
- Make evaluation as unobtrusive and least burdensome to participants as possible. If the collection of data makes additional work or adds to the burden on providers (or their staff), it is unlikely they will choose to participate.

- Patients and their families must be included in evaluation. For example, it was suggested that patients could fill out a brief, on-line survey immediately after their visit to assess their perceptions of their care.
- The pilot study must have on-going rather than retrospective data collection.
- Participation in the pilot study should be tied into the incentives and the role of incentives should be included as a point of evaluation. In other words, the evaluation should help determine what incentives may provide “tipping points” to adoption of the guidelines and in what settings. For some providers, the promise of upgrading the technological capacity of his/her office might be important, for other it might be a per patient incentive, etc.

The group then discussed what a potential pilot program could look like:

- **Select 100 clinicians for the pilot study.** This can be done a number of ways. The group discussed identifying the early adopters of guidelines or those willing to participate (self-selected). The recruitment could occur through the assistance of the various professional organizations (MPS, MOS, ACP-MI, MSMS).
- **Leverage best technology practices to facilitate data collection and provide incentive to participate.** Partner with Comcast to provide or update high-speed cable connections to the 100 clinicians in the pilot study. Comcast would provide this free or at reduced cost in exchange for being recognized for their public service, etc. If clinicians already have the necessary technology, offer alternatives that would increase their technological capacity in some other way.
- **Create user-friendly templates for Web-based data collection.** Clinicians could fill out forms quickly and easily. Patients could be directed to fill out a quick survey or form about their visit. The important thing here is ease of use.
- **Data collection is on-going.** By setting up the evaluation and measurement as intrinsic to the pilot study, data collection becomes a part of the roll-out. Evaluation and measurement will address two objectives: (1) Feedback regarding the usefulness of the guideline (e.g. comprehensibility, applicability, etc.) can be used by producers to edit and improve the format of the guidelines/algorithms; (2) Feedback regarding adherence and outcomes can be used by clinicians and managers to improve care delivery processes. This would allow for timely adjustments as the roll-out proceeded, rather than waiting a long period of time to evaluate how the roll-out is going.

SEPTEMBER 23 CONFERENCE/SUMMIT

Staff outlined for Steering Committee members the elements of the September Conference as it is now being planned:

- The conference will be a half-day affair held in Lansing, with possible teleconference or Web simulcast.
- Attendance will be by invitation only and will feature high-profile speakers.
- A key purpose of the conference will be to solicit reactions to the action plan.
- There will be opportunities for online comment both before and after the conference.

- The Steering Committee will meet after September 23 to formally finalize the report.

The Steering Committee agreed to proceed on this basis, and members further agreed to provide the names of three or four individuals that they would like to see invited.

Appendix G:

Record of Meeting 6

Flinn Project Steering Committee, Meeting 6

April 5, 2004

11:00 AM – 3:00 PM

Doubletree Hotel

27000 Sheraton Drive

Novi, Michigan 48377

AGENDA

- 11:00 AM Call to order; review of charge/goals/tactics; overview of today's meeting
- Working meeting of whole committee
 - Review
 - what action plan *is* (agenda for change of prescribing practices; set of recommendations that a funder could issue—collectively or individually—as RFP for pilot project)
 - what action plan *is not* (global communiqué on how EB prescribing for these disorders must be delivered)
 - Reaction to/refinement of action plan topic areas, keeping principles in mind:
 - Guidelines and algorithms must be easy to use and valuable
 - Guidelines by themselves are not enough
 - Differences in knowledge and needs among psychiatrists, PCPs, and consumers must be part of the plan
 - The action plan should be rolled out over time, with pilots to enlist opinion leaders and early adopters
- 11:15 AM **Topic 1:** Packaging and presenting guidelines/algorithms
- 11:45 AM **Topic 2:** Physician and consumer education
- 12:00 PM Lunch
- 12:30 PM **Topic 3:** Ongoing support
- administrative support (information technology, leadership from health care organizations)
 - technical support (who and where physicians and consumers can go with questions)
- 1:00 PM **Topic 4:** Financial incentives
- 1:30 PM **Topic 5:** Evaluation and measurement of guideline and algorithm use (do the guidelines improve care?)
- 2:00 PM **Topic 6:** Stakeholder buy-in
- 2:30 PM Updates
- September 23rd Conference: update
 - Speakers
 - Invitation list
 - SC expectations?
 - MH commission: update (Michele Reid)
 - FDA Ruling on SSRI's (Tom Carli)
- 3:00 PM Next meeting information; Adjournment

PRESENTATION MATERIALS

Flinn Foundation EBP Project Steering Committee Meeting


April 5, 2004


PSC
PUBLIC SECTOR
CONSULTANTS


Agenda


11:00	Call to Order, Review, and Overview	Carli
11:15	Tactics: Packaging/Presenting Gs/As	Carli/Pratt
11:45	Tactics: Physician/Consumer Education	Carli/Pratt
12:00	Break (working lunch)	
12:30	Tactics: Ongoing Support	Carli/Pratt
1:00	Tactics: Financial Incentives	Carli/Pratt
1:30	Tactics: Evaluation and Measurement	Carli/Pratt
2:00	Tactics: Stakeholder Buy-in	Carli/Pratt
2:30	Updates: Conference, MH Commission; SSRI Ruling	Weston/Reid /Carli
3:00	Adjourn	


PSC
PUBLIC SECTOR
CONSULTANTS


	<h2 data-bbox="480 352 967 405">Project Overview: Goal</h2> <ul data-bbox="516 485 1240 741" style="list-style-type: none"> ■ Complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder
	


	<h2 data-bbox="480 1224 1016 1276">Project Overview: Tactics</h2> <ul data-bbox="516 1356 1235 1654" style="list-style-type: none"> ■ Achieve consensus on guidelines/algorithms ■ Identify barriers to adoption in the field ■ Address barriers through action plan—how do we change <i>practice</i> given what we know?
	


	<h2>Project Overview: Committee Role</h2>
	<ul style="list-style-type: none"> ■ Action-oriented steering committee (SC) ■ Limited number of meetings ■ Committee-driven process


	<h2>April 5 Overview: Tactic Development</h2>
	<ul style="list-style-type: none"> ■ Review guiding principles for action plan ■ Review strategies (“what”) for action plan ■ Brainstorm tactics (“how”) for action plan ■ Develop for each strategy: <ul style="list-style-type: none"> ● Major action steps ● Responsible parties ● Monitoring ● Timelines


	<h2>Guiding Principles</h2>
	<ul style="list-style-type: none"> ■ Guidelines and algorithms must be easy to use and valuable ■ Guidelines by themselves are not enough ■ Differences in knowledge and needs among psychiatrists, PCPs, and consumers must be part of the plan ■ Action plan should be rolled out over time, with pilots to enlist opinion leaders and early adopters

	<h2>Strategies for Action Plan</h2>
	<ol style="list-style-type: none"> 1. Packaging and presenting guidelines and algorithms 2. Physician and consumer education 3. Ongoing support 4. Financial incentives 5. Evaluation and measurement of guideline and algorithm use 6. Stakeholder buy-in

	<h2>Packaging/Presenting</h2>
	<ul style="list-style-type: none"> ■ Strategy #1: Develop materials for PCPs, physicians in specialty care, therapists, social workers, families, and consumers <ul style="list-style-type: none"> ● Tactics discussion


	<h2>Packaging/Presenting</h2>
	<ul style="list-style-type: none"> ■ Strategy #2: Consult with packaging and distribution experts with a view to creating products that compete well for provider's attention and are widely distributed to users <ul style="list-style-type: none"> ● Tactics discussion


	<h2>Packaging/Presenting</h2>
	<ul style="list-style-type: none">■ Strategy #3: Integrate technology into the packaging and distribution of guidelines and algorithms as fully as possible<ul style="list-style-type: none">● Tactics discussion


	<h2>Packaging/Presenting</h2>
	<ul style="list-style-type: none">■ Strategy #4: Establish a process for the regular updating of algorithms and guidelines<ul style="list-style-type: none">● Tactics discussion


	<h2 data-bbox="480 352 943 407">Packaging/Presenting</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1222 701"> ■ Strategy #5: Link the guidelines/algorithms to a disease management module in presenting the product to primary care physicians <ul style="list-style-type: none"> <li data-bbox="565 667 837 701"> ● Tactics discussion
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	<h2 data-bbox="480 1224 911 1278">Physician Education</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1222 1665"> ■ Strategy #1: Develop information that specifically addresses physician questions such as “Why should I change my current practices?” and “What is the motivation of those who are promulgating these algorithms?” <ul style="list-style-type: none"> <li data-bbox="565 1629 837 1665"> ● Tactics discussion
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	<h2 data-bbox="480 352 911 405">Physician Education</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1203 653"> ■ Strategy #2: Develop education efforts for physicians at every level through which they are influenced <ul style="list-style-type: none"> <li data-bbox="565 625 837 653"> ● Tactics discussion
	

	<h2 data-bbox="480 1222 927 1274">Consumer Education</h2> <ul style="list-style-type: none"> <li data-bbox="516 1354 1230 1570"> ■ Strategy #1: Develop information specifically targeted to consumers because they plan an increasingly influential role in their doctors' prescribing practices <ul style="list-style-type: none"> <li data-bbox="565 1543 837 1570"> ● Tactics discussion
	

	<h2 data-bbox="483 352 841 405">Ongoing Support</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1247 747"> ■ Strategy #1: Develop some kind of ‘prescribing profile’ for physicians by which they could review their use of medications, which could further be refined to reflect the cost of the medicines they are prescribing <ul style="list-style-type: none"> <li data-bbox="565 716 837 747"> ● Tactics discussion <div data-bbox="345 884 423 940">  </div>
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	<h2 data-bbox="483 1224 898 1276">Financial Incentives</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1122 1482"> ■ Strategy #1: Develop <u>direct</u> financial incentives for physician use of EBP <ul style="list-style-type: none"> <li data-bbox="565 1451 837 1482"> ● Tactics discussion <div data-bbox="345 1755 423 1812">  </div>
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	<h2>Financial Incentives</h2>
	<ul style="list-style-type: none">■ Strategy #2: Develop <u>indirect</u> financial incentives for physician use of EBP<ul style="list-style-type: none">● Tactics discussion


	<h2>Financial Incentives</h2>
	<ul style="list-style-type: none">■ Strategy #3: Develop other, non-financial incentives<ul style="list-style-type: none">● Tactics discussion


	<h2 data-bbox="480 352 1101 403">Evaluation and Measurement</h2> <ul style="list-style-type: none"> <li data-bbox="516 483 1198 701"> ■ Strategy #1: Select clinicians for a pilot study aimed at evaluating and improving the algorithm tool itself as well as the quality of care <ul style="list-style-type: none"> <li data-bbox="565 667 837 701"> ● Tactics discussion
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	<h2 data-bbox="480 1222 1101 1272">Evaluation and Measurement</h2> <ul style="list-style-type: none"> <li data-bbox="516 1352 1243 1617"> ■ Strategy #2: Develop some kind of ‘prescribing profile’ for physicians by which they could review their use of medications, which could further be refined to reflect the cost of the medicines they are prescribing <ul style="list-style-type: none"> <li data-bbox="565 1583 837 1617"> ● Tactics discussion
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	Stakeholder Buy-in
	<ul style="list-style-type: none"> ■ Strategy #1: Use the natural contacts of the steering committee to build familiarity with and commitment to the EBP concept and leverage additional commitments <ul style="list-style-type: none"> ● Tactics discussion
	

	Stakeholder Buy-in
	<ul style="list-style-type: none"> ■ Strategy #2: Identify key primary care physicians in the state, looking for their acceptance and help in expanding the project to physicians <ul style="list-style-type: none"> ● Tactics discussion
	

	<h2 data-bbox="480 352 1208 407">September 23 Conference Update</h2> <ul style="list-style-type: none"> <li data-bbox="516 485 935 611"> ■ Invitation list progress <ul style="list-style-type: none"> <li data-bbox="565 533 935 564">● Names from SC members <li data-bbox="565 579 850 611">● MH commissioners
	

	<h2 data-bbox="480 1222 1192 1276">Update on MH Commission Work</h2> <ul style="list-style-type: none"> <li data-bbox="516 1354 1224 1440"> ■ Description of how this project might be identified to commission as “best practice”
	

	<h2 data-bbox="480 352 1081 407">Update on FDA SSRI Ruling</h2> <ul data-bbox="516 478 1156 567" style="list-style-type: none"> ■ March 22 public health advisory (blue handout)
	

	<h2 data-bbox="480 1224 714 1278">Next Steps</h2> <ul data-bbox="516 1350 1148 1547" style="list-style-type: none"> ■ April–June: PSC drafts final report ■ June 3 meeting (Lansing): review and finalize report ■ August meeting?
	

Ethel and James Flinn Family Foundation Evidence Based Practice (EBP) Project

Steering Committee Meeting
April 5, 2004, 11:00 AM–3:00 PM
Doubletree Hotel, Novi

Present: Richard Berchou, Michael Fauman, Hubert Huebl, Kevin Kerber, Jed Magen, Michael Massanari, Barry Mintzes, Michelle Reid, Mark Reinstein, Manuel Tancer, Philip Veenhuis, Daniel Wilhelm, Michael Zarr

MEETING SUMMARY

The purpose of the April 5 meeting was to specify tactics for the six action plan strategies developed at previous meetings. The strategies provide the “what” of the action plan; the tactics explain the “how.” The discussion of tactics is especially important because there is only one more meeting scheduled before the September conference. Members were urged to look ahead and consider what sort of concrete, fundable proposals they would like to see emerge from the EBP project.

As part of the initial discussion, considerable interest was expressed in encouraging the Michigan Surgeon General to be more directly involved in mental health issues. The interest of that office thus far has been largely in physical health. The importance of customizing the Texas algorithm for use in Michigan was also stressed. TIMA was part of a total disease management package that does not quite fit with everything that is going on in Michigan.

Tactics for Packaging/Presenting Guidelines and Algorithms

The discussion of “packaging and presenting” guidelines and algorithms focused on identifying the audience, specific suggestions for packaging, and identifying useable, previously created materials. Specific suggestions include:

- Fliers, laminated cards, office signs, CDs, and even “slide rules” (a mechanism for matching symptoms and pharmacological treatment options) should all be considered.
- Materials should be developed for “quick reference,” with longer, more detailed information available for complex cases. The former may be more appropriate for physicians in primary care; the latter for specialists.
- Certain toolboxes (e.g., the one Blue Cross/Blue Shield has developed for depression) could be examined for useful materials, including screening devices to help with the critical question of diagnosis.
- Information technology, including the Internet, websites, and handheld devices, should be considered as a way to convey information. IT materials not only have to be created but also maintained.

It was stressed that the packaging question really cannot be seen in isolation from other parts of the project. Even if guidelines and algorithms are packaged attractively, they

have to be targeted to practitioners willing to use them, not disseminated immediately to the field at large. In this sense the discussion confirmed the pilot project approach. It makes sense to “start small” with willing participants.

Tactics for Physician and Consumer Education

Physician Education

A good deal of the discussion focused on the need for greater use of algorithms and/or guidelines in medical school curricula and clinical teaching settings. There was a broad consensus that EBP will take off if it is stressed at medical schools and will be significantly impeded if it is not. The Accreditation Council for Graduate Medical Education (ACGME) has stressed the importance of EBP skills. Thus far the emphasis on EBP has not focused in any significant way on guidelines and algorithms. Specific tactics include:

- Develop a strong message explaining why physicians should use EBP. Its potential for improving care and reducing mistakes must be stressed; the fear that EBP amounts to “cookbook” medicine must be specifically addressed.
- Work with one or more of the state’s medical schools to incorporate EBP and guidelines/algorithms more directly into their offerings, perhaps by designating them as centers of excellence.
- Hold site-specific training programs for pilot programs that address, in addition to the message, questions of implementation as well as establishment of infrastructure (medical records, monitoring, tracking, etc.).

Consumer Education

Involving consumers is necessary both because it is important that they understand developments that affect care, but also because getting patients and their families involved is a powerful means of advancing the use of EBP. Two main tactical suggestions were offered:

- Develop materials and methods for improving physician-patient communication on the value of algorithms.
- Develop a broader public EBP awareness campaign using existing consumer group networks and MDCH channels of communication, as well, perhaps, as Internet technology and media campaigns.

With regard to the second tactic, public endorsements from respected groups would carry weight. Great care, however, must be taken in developing the message, which must be clear and forceful and yet not suggest that current practice is flawed.

Tactics for Ongoing Physician Support

Ongoing support might be offered to physicians for the treatment of specific cases, for the administration and logistics of the program, and for ongoing practice improvements. Three concrete suggestions emerged from the discussion:

- Develop support for physician decision making either immediately (i.e., when the patient is in the office) or at regular intervals during treatment. Having experts available for consultation is important; perhaps case managers would help as well. The M-line approach offered by the University of Michigan is one possibility.
- Develop administrative and technical support for clinicians who are attempting to adopt algorithms and guidelines, i.e., help setting up the whole disease management program, not just information on what medicine to prescribe.
- Develop “prescribing profiles” that allow individual clinicians to chart their own prescribing patterns against those of a comparable group of practitioners.

Tactics to Create Incentives for Change

Direct financial, indirect financial, and nonfinancial incentives were all discussed. Specific suggestions include:

- Work with CME credit-granting organizations to ensure that an interest in EBP and guidelines/algorithm use is rewarded and recognized.
- Ensure that a demonstrated interest in EBP leads to recognition and status—perhaps through “quality assurance” signs or plaques.
- Seek major payer buy-in to create incentives for guideline/algorithm adherence.
- Create reimbursement schemes when adherence to guidelines/algorithms imposes extra cost burdens (e.g., when a social worker is used to follow up on the filling of prescriptions).
- Work with MDCH to ensure that state contracts with providers reflect EBP principles.

The issue of rewarding guideline/algorithm use elicited considerable discussion. The flexibility inherent in both guidelines and algorithms can create difficulties in determining whether they have been followed. It was agreed, however, that it should be possible to identify certain easily described indicators that would provide important measures of adherence.

Tactics for Evaluation and Measurement

Evaluation and measurement are key because they provide the informational base that ultimately will link the pilot programs to the broader practice community. Two major suggestions emerged:

- Develop multidimensional evaluation and measurement techniques that assess adherence to guidelines, effectiveness of guidelines, consumer and physician satisfaction, cost of implementing guidelines in practice, and changes in variation among prescribers.
- Develop registries as a way to identify populations of interest within a pilot setting.

Tactics to Foster Stakeholder Buy-in

Stakeholders are all those that the EBP project will affect or influence—physicians, consumers and families, payers, and employers. Initially, buy-in will be essential to the

local pilots, but eventually it will be necessary to seek buy-in on a broader basis. Specific suggestions include:

- Use many of the same communication channels used for education—newsletters, presentations at conferences, CDs, a website, or even “mailgrams” of the sort used by the University of Michigan with its practitioners.
- Devise strategies to engage funders as key stakeholders.
- Use the current members of the steering committee as a source of contacts and as “ambassadors” for the project and EBP principles.

It was also noted that one of the purposes of the September conference was to generate buy-in.

Additional Considerations

In the concluding discussion, several additional important points were made:

- An opportunity exists to merge the activities of the EBP project with the subsequent recommendations of Governor Granholm’s Mental Health Commission. This possibility should be pursued.
- Some manner of “leadership” or “oversight” committee will most likely be required to help administer and guide the EBP pilot programs. The committee would both assist funders and oversee the completion of state-level work that would benefit each of the pilot programs.
- The group must stay fully abreast of issues related to possible links between SSRI antidepressant use and suicidal or violent tendencies.

The upcoming meeting on June 3 is the last regularly scheduled meeting for the group. During April and May staff will draft an action plan for the steering committee’s review. That and issues concerning the September conference will be the focus of discussion in June. If substantial work is needed on the draft, or if areas of disagreement remain, another meeting prior to the conference may be required.

Appendix H:

Record of Meeting 7

Flinn Project Steering Committee, Meeting 7

June 3, 2004

11:00 AM to 3:00 PM

Radisson Hotel Lansing

111 Grand Avenue North

Lansing, Michigan 48933

AGENDA

- 11:00 AM Call to order, overview, updates, initial thoughts
- 11:20 AM Discussion: introduction, general recommendations
- 12:00 PM Break (working lunch)
- 12:30 PM Discussion: packaging strategies
- 12:50 PM Discussion: education strategies
- 1:10 PM Discussion: ongoing support strategies
- 1:30 PM Discussion: incentives strategies
- 1:50 PM Discussion: evaluation strategies
- 2:10 PM Discussion: buy-in strategies
- 2:30 PM Implementation process
- 2:45 PM Moving forward: report sign-off and distribution; conference
- 3:00 PM Adjourn

Flinn Foundation EBP Project Steering Committee Meeting


June 3, 2004




Agenda

11:00	Call to order, overview, updates, initial thoughts
11:20	Discussion: introduction, general recommendations
12:00	Break (working lunch)
12:30	Discussion: packaging strategies
12:50	Discussion: education strategies
1:10	Discussion: ongoing support strategies
1:30	Discussion: incentives strategies
1:50	Discussion: evaluation strategies
2:10	Discussion: buy-in strategies
2:30	Implementation process
2:45	Moving forward: report sign-off and distribution; conference
3:00	Adjourn




	<h2 data-bbox="480 352 967 405">Project Overview: Goal</h2> <ul data-bbox="516 485 1240 741" style="list-style-type: none"> ■ Complete an action plan for dissemination and adoption of committee-endorsed guidelines and/or algorithms for the psychopharmacological treatment of major depression, schizophrenia, and bipolar disorder
	


	<h2 data-bbox="480 1224 1018 1276">Project Overview: Tactics</h2> <ul data-bbox="516 1356 1235 1654" style="list-style-type: none"> ■ Achieve consensus on guidelines/algorithms ■ Identify barriers to adoption in the field ■ Address barriers through action plan—how do we change <i>practice</i> given what we know?
	


<div data-bbox="344 879 423 940" data-label="Page-Header"> <p>PSC PUBLIC SECTOR CONSULTANTS</p> </div>	<h2>Project Overview: Committee Role</h2>
	<ul style="list-style-type: none"> ■ Action-oriented steering committee (SC) ■ Limited number of meetings ■ Committee-driven process


<div data-bbox="344 1751 423 1812" data-label="Page-Header"> <p>PSC PUBLIC SECTOR CONSULTANTS</p> </div>	<h2>Updates</h2>
	<ul style="list-style-type: none"> ■ Mental health commission, potential EBP role ■ MDCH activities ■ Other?


	<h2>June 3 Overview: Action Plan Review</h2>
	<ul style="list-style-type: none"> ■ Discuss background, general recommendations ■ Discuss each section of strategies and tactics ■ Feedback from Flinn Foundation on possible implementation process ■ Remaining steps <ul style="list-style-type: none"> ● Final report sign-off ● Report distribution ● September 23 conference


	<h2>Introduction, recommendations <i>(pp 1–7)</i></h2>
	<ul style="list-style-type: none"> ■ Case for EBP ■ Guidelines/algorithm selection ■ Committee-sponsored research ■ Strategies, principles ■ General recommendations <ul style="list-style-type: none"> ● Pilot programs ● State leadership group


	<h2 data-bbox="480 352 1097 407">Packaging/Presenting <i>(pp 8–10)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1170 520">■ Tactic 1: Finalize, customize guidelines <li data-bbox="516 537 1203 573">■ Tactic 2: Format guidelines appropriately <li data-bbox="516 590 1187 625">■ Tactic 3: Research packaging and IT use <li data-bbox="516 642 1097 678">■ Tactic 4: Evaluate existing tool kits <li data-bbox="516 695 984 730">■ Tactic 5: Update guidelines
	


	<h2 data-bbox="480 1224 1081 1278">Physician Education <i>(pp 10–12)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1118 1392">■ Tactic 1: Develop themes, messages <li data-bbox="516 1409 1159 1486">■ Tactic 2: Enlist curricular support from medical schools <li data-bbox="516 1503 1170 1539">■ Tactic 3: Investigate CME opportunities <li data-bbox="516 1556 1118 1591">■ Tactic 4: Develop training programs
	


	<h2 data-bbox="483 352 1096 405">Consumer Education <i>(pp 12–13)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1193 611">■ Tactic 1: Develop materials to improve patient/physician communication about guidelines <li data-bbox="516 625 1234 709">■ Tactic 2: Develop consumer education and awareness program
	

	<h2 data-bbox="483 1224 1011 1276">Ongoing Support <i>(pp 13–14)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1105 1440">■ Tactic 1: Develop clinician support mechanisms <li data-bbox="516 1455 1130 1539">■ Tactic 2: Develop administrative and logistic support mechanisms <li data-bbox="516 1554 1125 1596">■ Tactic 3: Develop prescriber profiles
	

	<h2 data-bbox="483 352 1114 405">Incentives for Change <i>(pp 14–16)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1208 569">■ Tactic 1: Develop nonfinancial incentives for guideline use <li data-bbox="516 579 956 617">■ Tactic 2: Offer CME credit <li data-bbox="516 632 1219 716">■ Tactic 3: Enlist payer support for guideline use incentives <li data-bbox="516 730 1235 814">■ Tactic 4: Enlist MDCH support for guideline use incentives
	

	<h2 data-bbox="483 1224 1268 1276">Evaluation and Measurement <i>(pp 16–17)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1200 1440">■ Tactic 1: Develop multidimensional evaluation and measurement techniques <li data-bbox="516 1455 1162 1539">■ Tactic 2: Establish registries of relevant populations
	

	<h2 data-bbox="483 352 1052 405">Stakeholder Buy-in <i>(pp 17–19)</i></h2> <ul style="list-style-type: none"> <li data-bbox="516 485 1149 562">■ Tactic 1: Enlist broad support through outreach <li data-bbox="516 583 1190 661">■ Tactic 2: Coordinate marketing efforts of stakeholder groups <li data-bbox="516 682 1117 760">■ Tactic 3: Encourage and support SC member “ambassadors” <li data-bbox="516 781 1190 858">■ Tactic 4: Develop strategies for engaging foundation and corporate funders
	

	<h2 data-bbox="483 1224 992 1276">Implementation Process</h2> <ul style="list-style-type: none"> <li data-bbox="516 1356 1060 1396">■ Roles of leadership group, pilots <li data-bbox="516 1409 967 1449">■ Project coordination team
	

	<h2>Next Steps</h2>
	<ul style="list-style-type: none"> ■ Sign-off on final report ■ Distribution of final report ■ September 23 conference

Appendix I:
Michigan Implementation of Medication Algorithms (MIMA)
Guidelines for Treating Schizophrenia
MIMA Physician Procedural Manual

Michigan Implementation of Medication Algorithms (MIMA)

Guidelines for Treating Schizophrenia

MIMA Physician Procedural Manual

2004

This manual is adapted from Alexander L. Miller, Catherine S. Hall, M. Lynn Crismon, and John A. Chiles, *Texas Implementation of Medication Algorithms (TIMA) Procedural Manual, Schizophrenia Module* (January 8, 2003), available on the TIMA website: <http://www.mhmr.state.tx.us/centraloffice/medicaldirector/timasczman.pdf>.

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Notice

These guidelines reflect the state of knowledge, current at the time of publication, on effective and appropriate care, as well as clinical consensus judgments when knowledge is lacking. The inevitable changes in the state of scientific information and technology mandate that periodic review, updating, and revisions will be needed. These guidelines (algorithms) do not apply to all patients, and each must be adapted and tailored to each individual patient. Proper use, adaptation, modifications, or decisions to disregard these or other guidelines, in whole or in part, are entirely the responsibility of the clinician who uses the guidelines. The authors bear no responsibility for the use of these guidelines by third parties.

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Overview of MIMA

The Michigan Implementation of Medication Algorithms (MIMA) presented here are part of a broader action plan aimed at encouraging greater use of evidence-based practice (EBP) in mental health care in Michigan. As the name suggests, these medication algorithms for major depression, bipolar disorder, and schizophrenia were adapted from the Texas Implementation of Medication Algorithms (TIMA) project, implemented in that state over the past five years.

Funding for the Michigan EBP project was provided by the Ethel and James Flinn Foundation of Detroit, in partnership with Public Sector Consultants Inc. of Lansing. The project goal, simply stated, was to develop an action plan that would bridge the gap between what is known and what is done in psychiatry, between scientific evidence and actual practice.

Both the MIMA and the action plan of which the algorithms are a part were developed by the project Steering Committee, a diverse group of Michigan mental health experts with demonstrated expertise in EBP. Subcommittees of the Steering Committee reviewed various publicly available algorithms and guidelines and ultimately endorsed those used in Texas on the grounds that they were scientifically sound, had been field-tested and evaluated, were regularly updated, and were part of a broader disease management program.

The disease management component warrants special emphasis. The MIMA should not be viewed in isolation but as part of a program that includes clinical and technical support for physicians and patients, patient/family education, uniform documentation of patient outcomes, and a quality management program. The various components of this multifaceted program will be pilot-tested and evaluated in several Michigan locales over the next few years, with the results informing follow-up EBP programs in the future.

The Michigan EBP project, like other similar projects across the country, was devised in response to accumulating evidence that there is a significant gap between the state of knowledge and the treatment of patients in clinical practice. In many fields of medicine, psychiatry included, practice lags years behind research findings. Research also demonstrates that there are wide variations in practice even within a single state. It is therefore reasonable to conclude that the practices of at least some clinicians vary substantially from what is known to be effective.

Part of the problem is “information overload.” It is impossible for any psychiatrist to keep up with all the developments in his or her field. Another aspect of the problem is the uncritical acceptance of information from sources such as friends and colleagues, flawed studies, or pharmaceutical companies.

EBP has been criticized as a cost-cutting approach that undermines the “art” of medicine. The express intent of the MIMA, however, is actually the reverse. The MIMA in no way trivialize the clinician’s role, but rather formalize what has long been the ideal of practice: the use of science to inform the art of medicine. Clinical expertise continues to play an important role in the MIMA by allowing the clinician to rapidly integrate

research evidence and/or the practice judgments of the broader medical community in making decisions about patient care. Rather than being “cookbook medicine,” the MIMA empower clinicians to make their own decisions about patient care, guided by the best available evidence to support those decisions.

Introduction to Algorithm Implementation

Algorithms go beyond guidelines in providing an explicit framework for clinical decision making. Algorithms do not dictate decisions, but rather provide an approach to clinical decision making that should yield similar answers in similar situations. The MIMA are not just general recommendations for medication treatment, they are also a systematic guide to the treatment of individual patients, which includes a number of critical factors: initial medication and dosage, dosage changes, methods and frequency of assessment, and minimum and maximum treatment periods.

Further, algorithms can be divided into *strategies* and *tactics*. Strategies are the various acceptable treatment regimen options for the care of an individual condition. Tactics address how optimally to implement a chosen regimen, and include such considerations as dose, monitoring, and how best to help an inadequately responding patient. Tactics also address the degree of symptom and functional improvement. As was the case with the TIMA, the MIMA presume that the aim of treatment is remission or the maximum possible improvement in cases where remission is not possible.

The MIMA approach is informed by the experience of Texas, which demonstrated that the successful implementation of algorithms is a human and social, as well as a technical, consideration. Assuring implementation of a treatment algorithm within a health care organization is a complex endeavor, requiring, in addition to research evidence, integrated changes in health care system design, patient and family education, and evaluation. Recommendations for just such a comprehensive, multifaceted approach are detailed in the Michigan EBP action plan.

Implementation of treatment algorithms is an evolutionary process, and change within systems does not occur without significant planning, goodwill, and effort. Yet the payoff in improved patient care is potentially enormous. Through an explicit process of algorithm implementation, evaluation, and revision, incremental improvements in many areas can result in major improvements in the overall quality of care.

At-a-Glance

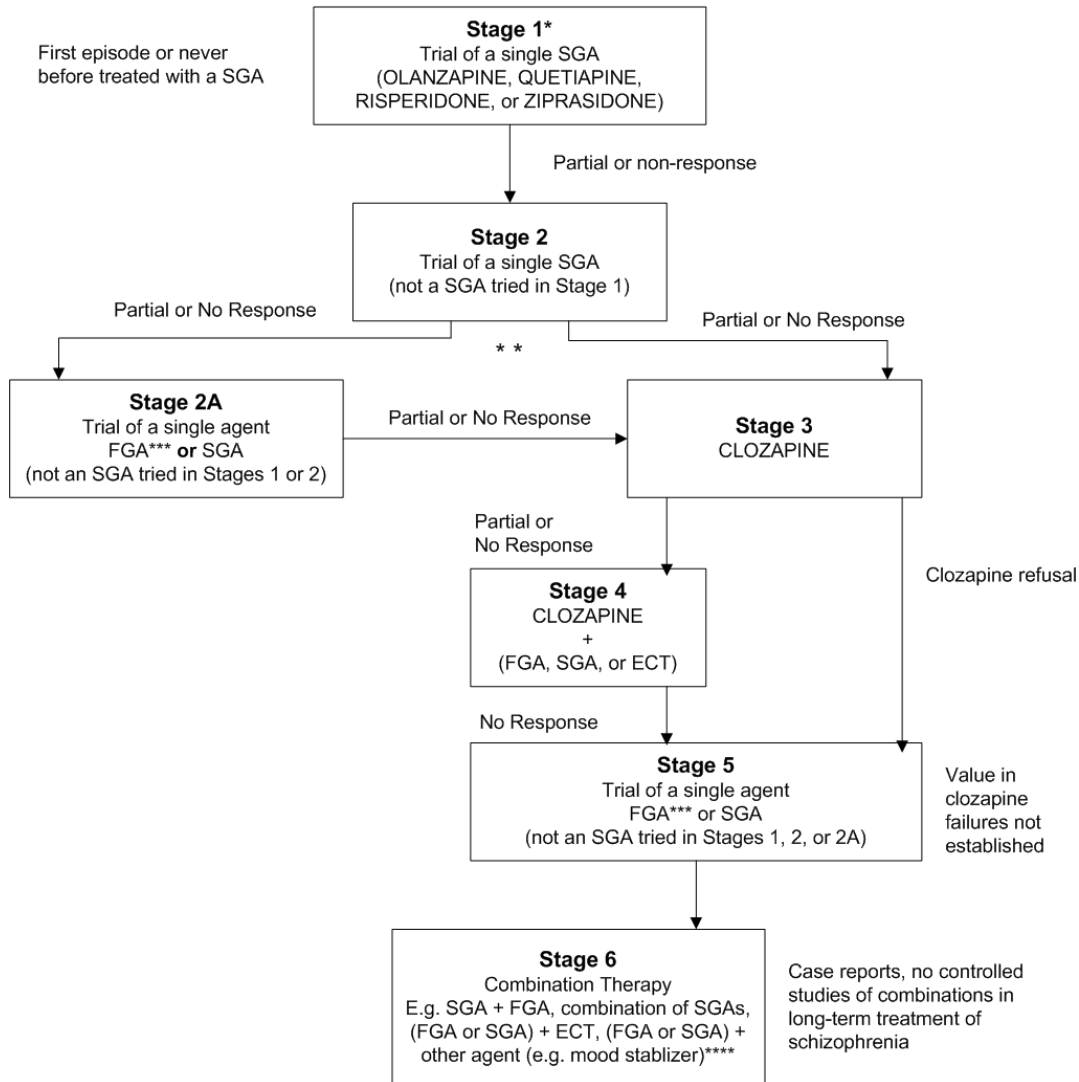
Schizophrenia Medication Algorithm

- Optimal implementation of the algorithm calls for a team approach.
- At each visit where medications are evaluated, decisions will be based on objective as well as subjective assessments of patient response.
 - Physicians will assess core symptom severity, other symptoms (anxiety, mood ability, etc.), and side effects.
 - Patients will provide a global self-report of symptoms and side effects.
 - Nonphysician personnel will administer brief positive and negative symptom rating scales and convey results to the psychiatrist who will make the ultimate treatment decision.
- Persistent positive or negative symptoms, unacceptable side effects, or the need for multiple side effect medications indicate that a medication change may be necessary. See the Evaluation of Patient Response section for discussion of using brief positive and negative symptom rating-scale scores.
- As much as possible, patients should receive an adequate trial of each antipsychotic.
 - Patients need at least four weeks of therapeutic doses of an antipsychotic (excluding clozapine) before they can be classified as “nonresponders” to the medication. Clozapine requires more time, up to three months.
 - Assessing the full effects of an antipsychotic can take 12 weeks or longer.
 - During acute relapses, multiweek trials of agents are difficult to sustain. However, failure to respond to an antipsychotic in 1–2 weeks should not eliminate it from future consideration as a possibly effective agent. Another trial may be worthwhile under more elective circumstances.
- No algorithm addresses all clinical situations that will arise in the medication management of schizophrenia.
- Choice of antipsychotic (AP) should be guided by considering the clinical characteristics of the patient and the efficacy and side effect profiles of the medication.

EXHIBIT 1

Algorithm for the Treatment of Schizophrenia

Any stage(s) can be skipped depending on the clinical picture or history of antipsychotic failures.



*If patient is nonadherent to medication, the clinician may use haloperidol decanoate or fluphenazine decanoate at any stage, but should carefully assess for unrecognized side effects and consider a different oral AP if side effects could be contributing to nonadherence.

** See text for discussion. Current expert opinion favors choice of clozapine.

***Assuming no history of failure on FGA.

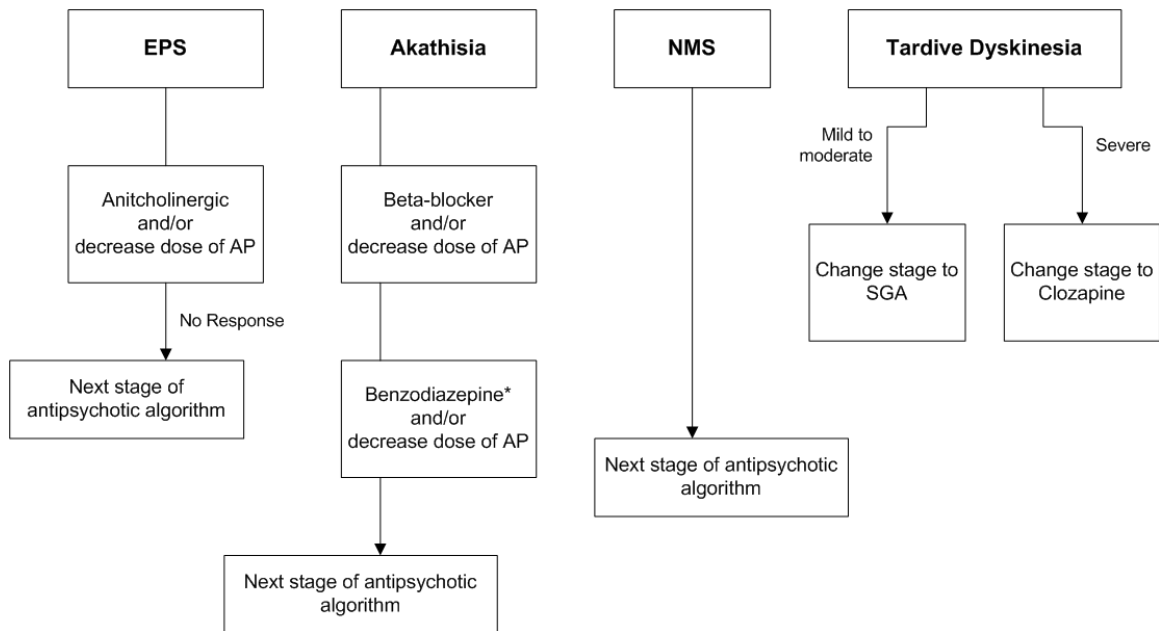
****Whenever a second medication is added to an antipsychotic (other than clozapine) for the purpose of improving psychotic symptoms, the patient is considered to be in Stage 6. See Description of Tactics and Critical Decision Points section for more explanation.

FGA = First generation AP

SGA = Second generation AP

EXHIBIT 2

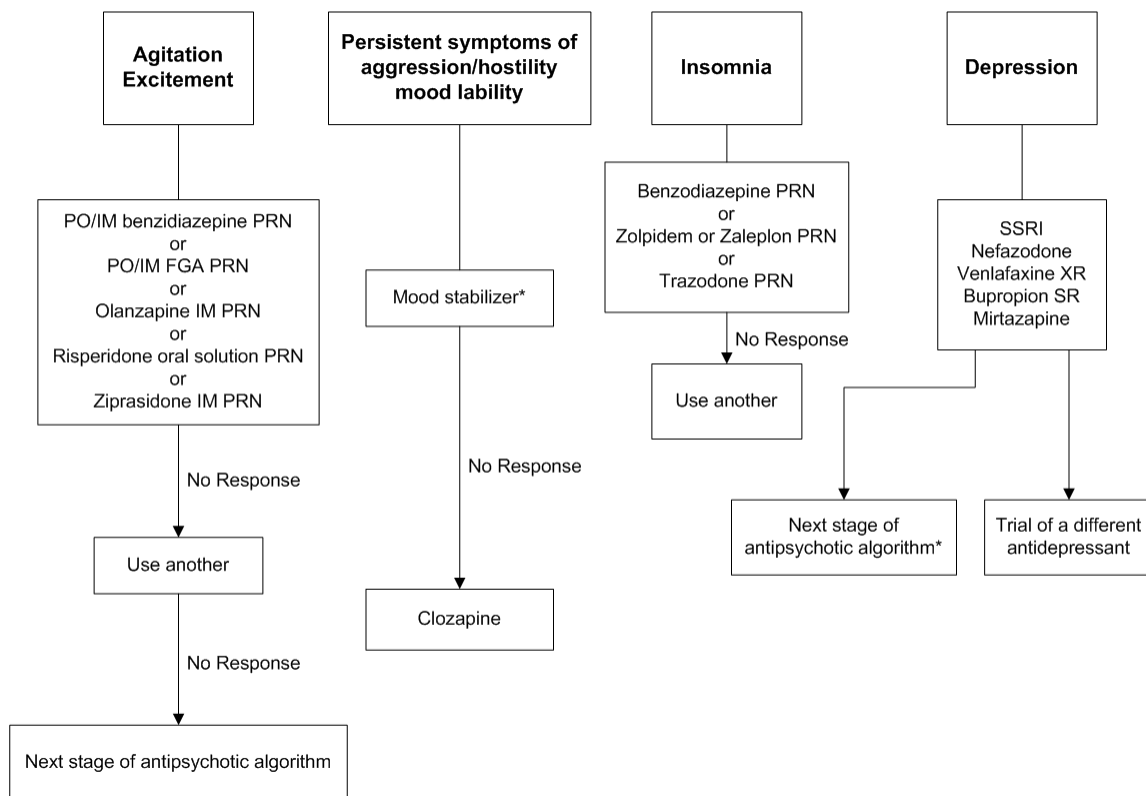
Side Effects Algorithms



*Avoid combinations of FGA, anticholinergic, and benzodiazepine.

EXHIBIT 3

Coexisting Symptoms Algorithms



*See Persistent Symptoms of Aggression/Hostility/Mood Lability in Medications and Dosing section.

**Consider clozapine in patients with persistent suicidal behaviors or ideation.

Description of the Stages of the Antipsychotic Algorithm

This section of the manual explains the rationale behind the sequence of stages in the schizophrenia algorithm and highlights some of the changes made at the Schizophrenia Algorithm Update Conference in January 2002.

The antipsychotic algorithm for schizophrenia distinguishes between acute and maintenance treatment. First generation antipsychotics (FGAs),¹ while not recommended at Stage 1 as first-line treatments, may be used short term to help control symptoms of agitation and excitement (see Coexisting Symptoms Algorithms [on page 8](#)). The FGAs are not first-line treatments because, compared to the second generation antipsychotics (SGAs),² they cause more bothersome side effects, have greater potential for producing tardive dyskinesia, are equal or worse for negative symptoms, are less likely to improve cognitive deficits, and are no more effective for positive symptoms (a).³ SGAs do have side effects that can be medically serious, but they differ enough from one another in this regard that clinicians can monitor for these side effects and, if necessary, choose another SGA with a different side effect profile.

An important outcome of the update conference was the decision to add ziprasidone (Geodon®) to the list of first-line medications for the treatment of schizophrenia. Ziprasidone was submitted to the FDA in 1997 but was not approved until February 2001 because of concerns over its potential to prolong the QT interval. At the time of the update conference, 150,000 patients had received ziprasidone since its approval by the FDA, and data analysis revealed no increased incidence of sudden death, a marker for fatal arrhythmias. Because it appears that ziprasidone's risk of sudden death and cardiac events is no greater than that of the other agents used as first-line therapy, the experts decided to include ziprasidone as a first-line medication in the antipsychotic algorithm. The case of ziprasidone illustrates the algorithm's policy of requiring widespread utilization of new medications in a variety of clinical settings before their inclusion in the algorithm. As future medications acquire FDA approval, clinicians may use them before they are staged in the algorithm as long as the clinical situation warrants their use and the clinician documents on the clinical record form the rationale for using the new medication.

Although no large-scale research studies have adequately addressed the issue, 90 percent or more of psychiatrists polled at algorithm training sessions indicate that, based on their clinical experience, if a patient fails or only partially responds to one SGA, a trial of another SGA is warranted. For this reason, if a patient does not demonstrate a full

¹ Chlorpromazine, perphenazine, haloperidol, etc.

² Clozapine, olanzapine, risperidone, quetiapine, ziprasidone.

³ The symbols a, b, and c, in parentheses following statements, indicate the authors' assessment of the level of evidence for the statements: (a) denotes recommendations arising from strong empirical trials using randomization and blinding, (b) indicates open label trials, cohort studies, and epidemiologic studies, (c) indicates recommendations based on a few case reports and/or consensus among the consensus panel (Woolf 1992).

response to an adequate trial of a SGA in Stage 1, the patient should receive a different SGA in Stage 2. (See section on Description of Tactics and Critical Decision Points, [page 13](#), for discussion of what constitutes an adequate trial for each agent.) Once a patient has failed to respond or only partially responded to adequate trials of two SGAs, many experts believe that this establishes treatment resistance and that clozapine is the next logical step (Stage 3). Others believe that a trial of a third SGA or, in patients who have never received a trial of a conventional antipsychotic, an FGA may be worthwhile (Stage 2A). While current expert opinion favors using clozapine after Stage 2, the branch point in the diagram after Stage 2 indicates that a trial of a third SGA or an FGA is also a reasonable treatment alternative. If the patient fails to respond or only partially responds to an adequate trial of the Stage 2A medication, the physician should institute a trial of clozapine (Stage 3).

Approximately 50 percent of patients treated with clozapine do not respond adequately to the medication. Since clozapine is the “last best hope” for patients with treatment refractory schizophrenia, adding another antipsychotic or electroconvulsive therapy (ECT) to clozapine in patients who do not adequately respond to monotherapy makes sense and is probably the clinician’s best option at this point. One randomized controlled trial (Shiloh et al. 1997) and a number of open label studies support clozapine in combination with a second antipsychotic in patients in whom clozapine monotherapy has yielded unsatisfactory results. For more information on combining ECT with clozapine, see “Electroconvulsive Therapy in Schizophrenia” in the Medications and Dosing section. The definition of adequacy of response to clozapine is discussed in Response, Partial Response, and No Response in the Evaluation of Patient Response section.

After Stage 4 (clozapine plus a second antipsychotic or ECT), there is a paucity of evidence to guide the selection of antipsychotic treatments for nonresponders or clozapine refusers. The general view of the consensus conference attendees was that it is preferable to exhaust reasonable antipsychotic monotherapy alternatives before progressing to combinations of antipsychotics. Stage 5 reflects the expert consensus that if a patient who has failed or refused clozapine has not exhausted all second generation monotherapy options, a trial of monotherapy with a different SGA should be attempted before the patient is started on combination therapy. In addition to the fact that little research evidence supports their use, combination therapies present adherence, safety, tolerability, and financial concerns. Complex medication regimes lead to poorer adherence than simple ones. Combinations also increase the likelihood of risky drug-drug interactions and of unexpected side effects and tolerability problems.

STAGING CONVENTIONS

“Stage 99” is reserved for those patients who insist on returning to the FGA they were taking prior to entry into the algorithm. “Stage 0” indicates a patient that was never entered into the algorithm and has never received an SGA.

Patients who are noncompliant and require a depot preparation are coded as Stage 1-D, 2-D, 2A-D on the clinical record form, the number reflecting which stage they were in at the time noncompliance became an issue, and the “D” indicating that a depot is now being used. The descriptor “R” is reserved for patients who return to an earlier stage.

Therefore, if a patient returns to Stage 2 after an inadequate response in Stage 2A, it would be designated as Stage 2-R.

As mentioned in the notice that appears at the beginning of this manual, these guidelines reflect the state of knowledge at the time of publication. As new studies elucidate different aspects of the medication management of schizophrenia, the algorithm will be periodically revised and updated.

Description of Tactics and Critical Decision Points

Each stage of the antipsychotic algorithm represents a trial of a different antipsychotic, and the medication options that clinicians and patients have to choose from are the algorithm's "strategies." While medications are the algorithm's "strategies," specific recommendations concerning medication use (dose titration, measurement of treatment response, trial duration, etc.) are the algorithm's "tactics." It is in these details of medication management that clinicians most often deviate from expert recommendations. This section of the manual and the following, Evaluation of Patient Response, provide instructions concerning the tactics of medication use.

The critical decision point (CDP) is a point in the course of the medication trial when the clinician decides whether to continue the present medication regimen, adjust the medication dose, or move on to another medication (the next stage of the algorithm). At each CDP, the clinician will use the clinical rating scales to assess the patient's level of response to the antipsychotic. The clinician will then make a therapeutic decision based on the results of the clinical rating scales, patient global self-report, ratings of other symptoms, etc. The response criteria and process measures (tools used to assess patient response) are discussed in the Evaluation of Patient Response section.

EXHIBIT 4

Critical Decision Points (CDPs) for Antipsychotic Algorithm, Stages 1, 2, 2A, 4, 5, and 6

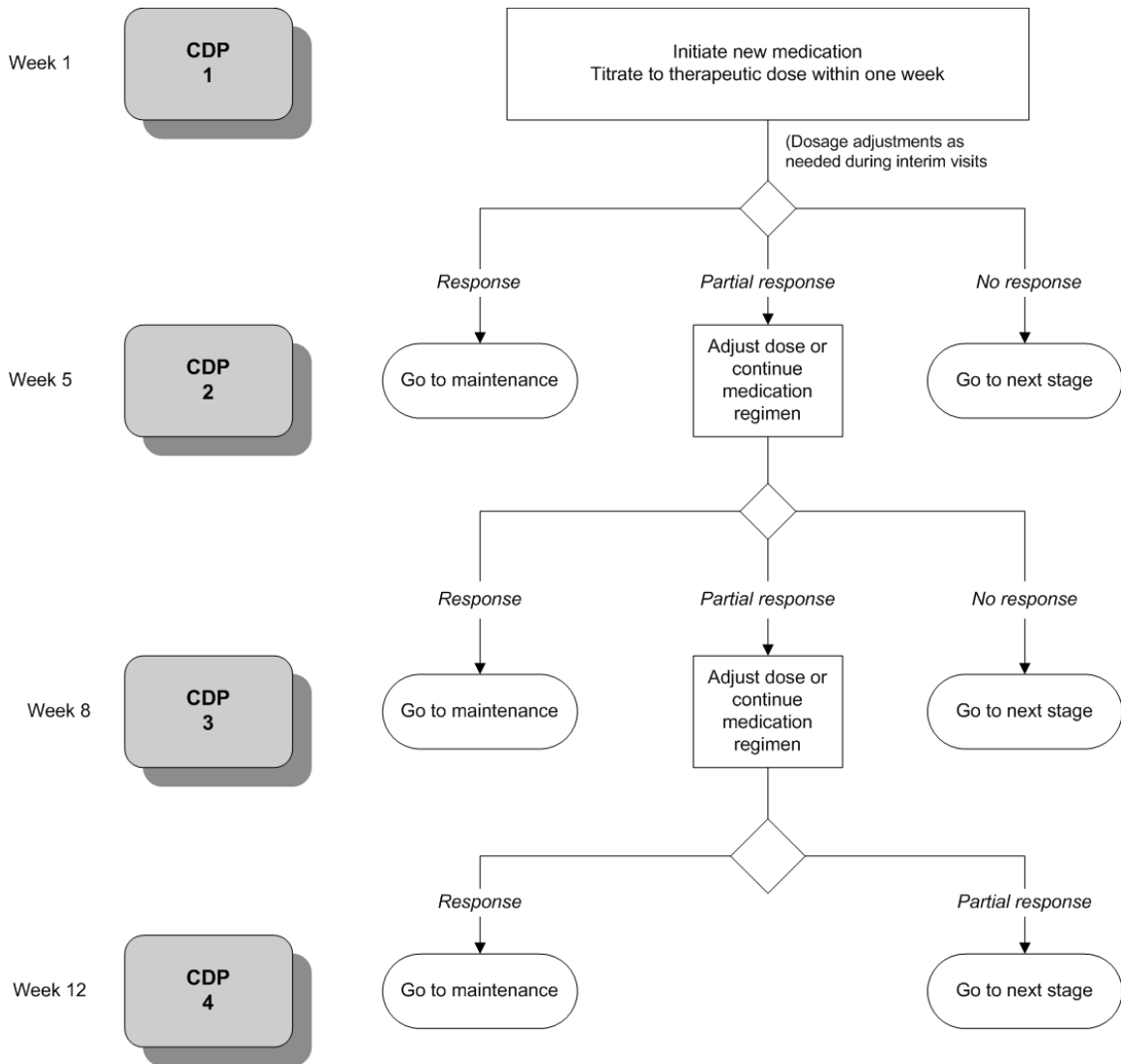
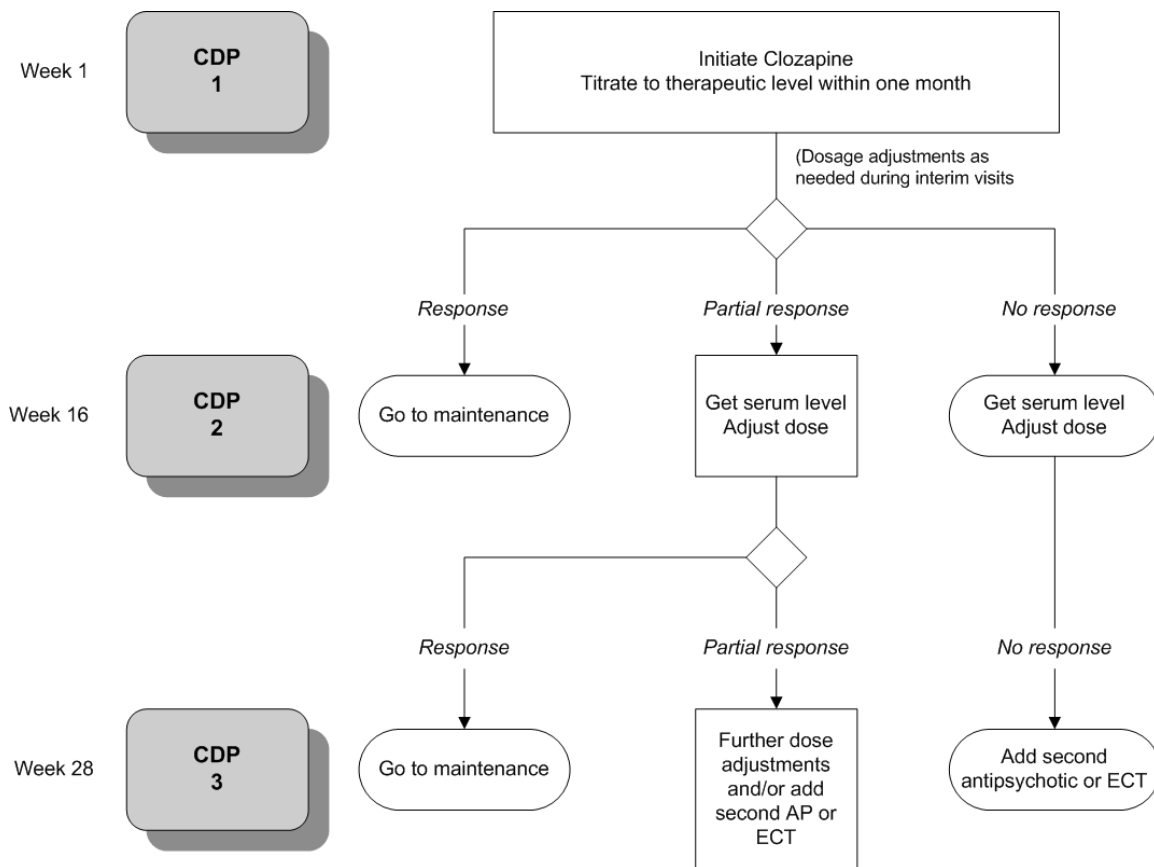


EXHIBIT 5

Critical Decision Points for Antipsychotic Algorithm, Stage 3, Clozapine



SCHEDULE OF CDPS FOR STAGES 1, 2, 2A, 4, 5, AND 6

As stated above, the CDP is a point in the course of medication therapy at which the physician decides whether to continue the present medication regimen, adjust the medication dose, or move on to the next stage of the algorithm. The CDPs are at the same times in treatment stages 1, 2, 2A, 4, 5, and 6.

CDP 1, Week 1

CDP 1 occurs at week 1. This is the point at which the patient enters the algorithm or changes stages in the algorithm. For new patients, decisions need to be made as to what stage of the algorithm the patient will enter and which medication will be prescribed. If the patient enters at Stage 1, the clinician will prescribe olanzapine, quetiapine, risperidone, or ziprasidone.

If the patient has had poor results in the past with any of these antipsychotics, the practitioner should determine if an adequate trial duration at an adequate dose was used before eliminating the possibility of trying that drug again. If any of these drugs can be

used, the physician decides which is preferable. As allowed by the clinical situation, the patient, and when possible, the family should have input into this decision.

The medication should be titrated to a therapeutic dose during the first week, and the patient should be seen weekly for four more visits, if feasible, to evaluate drug tolerability and the need for dosage adjustments. During this five-week medication initiation and dose titration period, it is important to have contact with the patient as frequently as possible to monitor for symptom improvement, possible symptom worsening, and emergent side effects; to encourage medication adherence; and to provide patient/family reassurance. Early intervention may allow management of side effects or symptom worsening, thus possibly preventing hospitalization. If weekly office visits are not possible, nurses or other providers can check on the patient by phone. As symptoms improve, patients can be seen less often for medication visits but should still be seen at least every 2–3 weeks. As stabilization occurs, patient visit frequency can be gradually decreased until eventually a stabilized patient may only need to be seen once every three months.

CDP 2, Week 5

The second critical decision point occurs at about week 5, after titration and after the patient has been on therapeutic doses of medication for four weeks. At this point, the clinical rating scales and other assessment tools are evaluated to determine whether the patient has

- responded adequately enough to continue on the same maintenance dose, or
- had only a partial response requiring dosage adjustment, or
- had a complete lack of response, which indicates moving to the next stage of the algorithm. (Studies suggest that patients who show no response after four weeks of therapeutic doses of medication are not likely to respond after more time on the drug [Marder et al. 2002].)

CDP 2 should be in the time frame of approximately four weeks on a therapeutic dose. Shorter or longer time periods warrant a comment that explains the clinical reasoning.

An issue that may arise at any time is nonadherence. This may require switching to a depot preparation of haloperidol or fluphenazine (or a depot SGA when available). The use of depot drugs requires a trial of at least 8 to 12 weeks and a determination of full response, partial response, or nonresponse. The issue of nonadherence is also discussed in the Medications and Dosing section below.

CDP 3, Week 8

The third CDP occurs at about week 8. Nonresponders and partial responders who are no better at CDP 3 than at CDP 2 should move to the next stage. Partial responders who improve between CDP 2 and CDP 3 may continue another four weeks to CDP 4. The time window for CDP 3 is 7–9 weeks. Shorter or longer periods require a note of explanation. Serum levels of haloperidol and fluphenazine can be useful in deciding if Stage 2A or Stage 5 patients on these medications need dose adjustments.

CDP 4, Week 12

By the twelfth week, failure to achieve an adequate therapeutic response to the medication indicates the need to move on to the next stage (a). The same CDPs repeat for trials of a FGA or any SGA other than clozapine.

FURTHER DISCUSSION OF STAGES 4, 5, AND 6

Stage 4

Since there is no antipsychotic shown to be effective for partial or nonresponders to clozapine, it is worthwhile to try to improve response to clozapine with the addition of another antipsychotic or ECT. These are widely used but understudied tactics.

Although the literature is sparse, the best-supported combination strategies appear to involve adding an FGA, an SGA, or ECT. Patients who, despite an adequate trial of clozapine, still have persistent positive symptoms may benefit from the addition of modest doses of a higher potency typical antipsychotic such as loxitane (Mowerman and Siris 1996) or pimozide (Friedman et al. 1997). (Clinicians should bear in mind pimozide's association with QTc interval prolongation and risk of torsade de pointes.) It should be noted, however, that addition of a typical antipsychotic to clozapine may result in extrapyramidal symptoms (EPS) and potentially decrease some of the benefits of using clozapine (Kapur et al. 2001). A recent report indicates that adding risperidone to clozapine was helpful for ten out of twelve outpatients who were clozapine partial responders (b) (Henderson and Goff 1996). There are several reports of using ECT for patients who are persistently psychotic on clozapine. The combination of ECT and clozapine in these patients produced improvement in a majority of patients with poor or partial responses to clozapine (b). See Electroconvulsive Therapy in Schizophrenia in the Medications and Dosing section.

While mood stabilizers may help patients with schizophrenia with concomitant symptoms of mood instability and/or impulsivity, there is scant evidence to support their role as adjuncts in patients whose positive symptoms only partially respond to clozapine. If clinicians do use mood stabilizers for this purpose, they should carefully monitor the target symptoms and, if no improvement is noted, discontinue the adjunctive mood stabilizer. With regard to staging, if the mood stabilizer is being added to clozapine in an attempt to ameliorate symptoms of psychosis, the patient is in Stage 6. This is because there is virtually no evidence that mood stabilizers enhance the antipsychotic effects of clozapine. Therefore the combination of clozapine plus a mood stabilizer for psychotic symptoms falls in the category of unproven combination treatments. Addition of an anticonvulsant, such as divalproex, to clozapine for another purpose, such as seizure prevention, would not be Stage 6, since only the clozapine is being used as an antipsychotic. If the mood stabilizer is added to clozapine in an attempt to target nonpsychotic symptoms (hostility, mood lability, etc.), the patient is in Stage 3 and the algorithm for coexisting persistent symptoms of aggression, hostility, and mood lability is followed.

The CDPs in this stage of the algorithm reflect the time to response for the medication that is added to clozapine therapy. The augmenting agent should be titrated to a

therapeutic dose in one week with CDPs at weeks 5, 8, and 12. The CDPs for Stage 4 are included above with those for stages 1, 2, 2A, 5, and 6. Due to financial and safety issues (drug interactions, additive side effects) involved in using multiple medications, it is crucial that clinicians use both the clinical rating scales and subjective information (patient self-report, global impressions) to assess the impact of the additional agent and discontinue it if it is not helping the patient.

Stage 5

As mentioned in the Description of Stages of the Antipsychotic Algorithm section, there is practically no evidence to guide antipsychotic selection in patients who either do not respond to or refuse to take clozapine. Stage 5 reflects the expert consensus that if a patient who has failed to respond to or refused clozapine has not exhausted all second generation monotherapy options, a trial of monotherapy with an untried SGA should be attempted before the patient is started on combination therapy. (If there is no history of failure on a FGA, an untried FGA would be another treatment option.) In switching from clozapine to another antipsychotic, the clozapine dose should be tapered down slowly while the new antipsychotic is titrated to a therapeutic dose. If the patient's clinical status worsens during this process, consideration should be given to reinstituting the prior clozapine dose. The CDPs for Stage 5 are included above with those for stages 1, 2, 2A, 4, and 6.

Stage 6

Patients in Stage 6 have persistent psychotic symptoms that warrant the addition of a second agent. (Patients whose nonpsychotic target symptoms [e.g., agitation] require the temporary addition of a second agent would remain in their current algorithm stage and follow one of the coexisting symptoms algorithms.) Long-term combination therapy should be considered a “last resort” for those patients who have exhausted all reasonable monotherapy options. As with combination therapy with clozapine (Stage 4), the CDPs reflect the time to response for the second (or the “added”) agent. Due to safety and financial concerns, it is imperative that clinicians use both the clinical rating scales and subjective information to assess the effect of the second medication. If the patient's clinical status has not improved after a 12-week trial of the “added” agent, the second agent should not be continued.

SCHEDULE OF CDPS FOR STAGE 3

There are three critical decision points when using clozapine.

CDP 1

CDP 1 is the point at which the patient has failed at least two antipsychotic trials (by history or trial). At this point clozapine would be started and the dosage titrated to therapeutic levels over one month. For the next three months the patient should be clinically evaluated at least monthly and dosage adjustments made.

CDP 2

CDP 2 for Stage 3 occurs at 16 weeks or after one-month titration and three months at therapeutic doses (minimum of 300 mg/day) (a). If the patient has responded to

clozapine, begin maintenance treatment. If the patient has had a partial response or no response, obtain a serum level and adjust the dose to achieve a serum level above 350 ng/ml.

CDP 3

CDP 3 for Stage 3 occurs at week 28, or after six months of clozapine at therapeutic doses. If the patient has had a partial response, a dosage increase and/or the addition of a second antipsychotic or ECT is indicated. If there has been no response, proceed to Stage 4.

It can be difficult to differentiate between an absolute lack of response versus a partial response to clozapine. It is not uncommon for a clinician to realize that a “nonresponder” was actually a “partial responder” after a patient’s condition deteriorates dramatically while clozapine is being tapered and discontinued. However, the clinician must also keep in mind that the rate of the medication taper, not the absence of the drug, may be causing the reemergence of psychotic symptoms. (Clozapine should be tapered down over at least three months; decreasing the dose too rapidly has been associated with a reemergence of florid psychosis.)

Evaluation of Patient Response

Generally speaking, symptoms respond to antipsychotics in somewhat different time frames. Agitation, sleep, and appetite often respond during the first 1–2 weeks, whereas personal hygiene and basic interpersonal socialization may be slower to respond (2–3 weeks), and psychotic symptoms can gradually decrease over 2–6 weeks or longer. Residual symptoms may continue to improve at 6–12 weeks. Chronic patients may show slower responses of all symptoms (c).

The MIMA response criteria are shown below (see Exhibit 6). Descriptions of the process measures used to evaluate patient response begin on [page xx](#).

EXHIBIT 6 MIMA Patient Response Criteria

STAGE 1	Positive symptom score ≤ 6
STAGE 2	Positive symptom score ≤ 6
STAGE 2A	Positive symptom score ≤ 6
STAGE 3	> 20% decrease in positive symptoms
STAGE 4	> 20% decrease in positive symptoms
STAGE 5	> 20% decrease in positive symptoms
STAGE 6	> 20% decrease in positive symptoms

Negative symptoms are no longer included in the response criteria as little evidence exists on which to base realistic goals for negative symptom improvement. Compared to the older agents, the newer medications are thought to be “better” for negative symptoms, but this superiority may be explained by the newer agents’ reduced propensity to cause EPS (which can lead to secondary negative symptoms). Several factors (depression, environmental deprivation, positive symptoms) can contribute to negative symptoms and medications may have little effect on *core* negative symptoms.

This in no way implies that negative symptoms are not important and do not need to be measured. On the contrary, recent findings indicate that negative and cognitive symptoms have more of an impact on patients’ functional status than the positive symptoms of schizophrenia. At each medication visit, clinicians should perform the Positive Symptoms Rating Scale (PSRS), Brief Negative Symptom Assessment (BNSA), and assessments of “other symptoms” such as mood lability, anxiety, agitation, etc. and incorporate all findings into the clinical decision-making process.

RESPONSE

The goal of stages 1–2A of the antipsychotic algorithm is to achieve control of positive symptoms so that their effects on patient functioning are diminished. Most deterioration in functioning occurs during the first years of the illness; therefore, it is important to aggressively treat symptoms in recent-onset patients.

Control of positive symptoms means that the total score on the four positive symptoms items is six or below. This means that no item can be above mild in severity and that if one item is mild in severity the others must be normal. As mentioned above, the algorithm does not specify a goal for negative symptom response, but it does recommend an approach to their treatment. While evaluating negative symptoms, the clinician should consider the patient's prior history and potential for change. As a guiding principle, the better the premorbid history, the more aggressive one should be in treating negative symptoms, and the worse the history, the less likely that dramatic negative symptom responses will occur (c).

In stages 3–6 of the algorithm, absence of significant positive symptoms may be an unrealistic goal. Therefore, the criteria for response are relative rather than absolute. At least a 20 percent reduction from prior positive symptom levels would justify continuation of the same treatment. Addition of an augmenting agent can be tried in either Stage 4 or Stage 6 in attempt to gain further improvement.

For patients who enter the algorithm at stages 1–2A, these responses can be compared with those in stages 3–6 to decide if there is at least a 20 percent improvement. If not, it is reasonable to return to the best of the earlier antipsychotics if the response in the later stages seems inadequate. For patients who enter the algorithm at Stage 3 or later and are not responding to therapy, and for whom no objective ratings have been done, the clinician is encouraged to try stages 1–2A medications if the history of response to first or second generation antipsychotics is not definitively negative.

It is expected that about half of patients tried on clozapine will not respond (a). The new algorithm recommends combination therapy for nonresponders because, once the patient is on clozapine, it is worth the effort of adding a second agent before going to treatments that have no proven value in clozapine nonresponders. After clozapine discontinuation, it is sometimes found that apparent clozapine “nonresponders” were actually partial responders, a fact that further supports combination therapy in clozapine nonresponders.

PARTIAL RESPONSE

A partial response at any stage of the algorithm is a basis for continuing the patient in that stage, up to the maximum recommended amount of time for that stage. At CDPs there is the option of changing the antipsychotic dose for partial responders. This is not a requirement, however. For many patients, further duration of treatment may be all that is needed (a). There are, unfortunately, no empirical guidelines for deciding when this is the case. As a general rule, prior time to achieve a response in a particular patient is helpful in judging when that patient is likely to respond to the current treatment.

In stages 1–2A, less than a 20 percent reduction in positive symptoms after at least three weeks on the highest recommended dose would mean that the patient is a nonresponder, not a partial responder. If patient and clinician agree that there has been noticeable improvement, however, a partial response may have occurred that is not evident in the PSRS. In this case, continuation of treatment in the same stage is justified, up to the maximum duration recommended.

In summary, a partial responder in stages 1–2A has less than 20 percent improvement in positive symptoms, but his/her absolute positive symptom scores exceeds 6. In stages 3–6, partial response is a clinical judgment that the patient whose symptoms have improved by less than 20 percent is “better.” It is not clinically meaningful to try to use scale score changes of less than 20 percent to distinguish between partial responders and nonresponders.

NO RESPONSE

At any stage, before concluding that a patient is a nonresponder to an antipsychotic, the clinician should consider causes of nonresponse that would indicate a course of action other than changing to a new antipsychotic. Included in this list are:

1. Medication nonadherence (If due to side effects, try another SGA. If not due to side effects, consider a depot preparation.)
2. Incorrect diagnosis
3. Substance abuse (Check urine, if in doubt and patient consents.)
4. “Covert” side effects (If patient feels “lousy” on medication but does not have typical side effects, consider trial of a different antipsychotic.)
5. Psychosocial stressors (Ask about changes in home, work, finances, etc.)
6. Undiagnosed or uncorrected general medical problem such as diabetes (Get routine labs—CBC, thyroid function tests, chem profile.)

Process Measures

This section of the manual discusses methods used to evaluate patient response to medication therapy. It covers both physician and provider administered assessments.

PHYSICIAN-ADMINISTERED ASSESSMENTS

The physician can rate the patient at each visit using the scale of 0 = no symptoms to 10 = extreme (see page 26). The areas assessed are core symptom severity, other symptoms, and overall side effect severity.

Provider-Administered Assessments

The following assessments should be completed before the physician sees the patient. The individual performing the following ratings can be a nurse, social worker, or any other mental health professional trained in the administration of the assessments. The administration manual for the clinical rating scales (PSRS, BNSA) is provided in Appendix A. Below is a brief description of each of the three provider-administered assessments.

The Four-Item Positive Symptoms Rating Scale (PSRS)

The four-item PSRS may be administered at each visit. The ratings for the four-item PSRS and the BNSA are on the same score sheet. For the four-item PSRS, the items are ranked on a scale of: N/A = not assessed, 1 = not present, 2 = very mild, 3 = mild, 4 = moderate, 5 = moderately severe, 6 = severe, 7 = extremely severe.

The four-item PSRS assesses positive symptoms of schizophrenia (suspiciousness, unusual thought content, hallucinations, and conceptual disorganization). These items are from the BPRS (Overall and Gorham 1962) and the expanded version of the BPRS (Lukoff et al. 1993), both of which have been shown to be valid and reliable. Item selection was based, in part, on a factor analysis of the expanded BPRS conducted by Ventura and colleagues in 1995. Included are suggested questions intended to guide the interviewer in obtaining the information required for making the ratings. The interview takes five minutes or less.

The Brief Negative Symptom Assessment (BNSA)

The BNSA may be administered at each visit. The ratings for the four-item PSRS and the BNSA are on the same worksheet (see page XX). For the BNSA, the items are ranked on a scale of 1 through 6. The BNSA is a four-item instrument used to assess a subset of DSM-IV negative symptoms (alogia, amotivation, flat affect, and asociality). The items are based on items from the Negative Symptom Assessment developed by Alphas et al. (1989) and the Scale for the Assessment of Negative Symptoms (SANS) developed by Andreason (1981). The BNSA provides quick assessment of distinct negative symptoms, takes less than five minutes to administer, and is based largely on observation.

Patient Global Ratings (Self-Report) of Symptom Severity and Side Effects

These ratings should apply to the symptoms and side effects the patient has experienced during the past week, and are rated on a scale of 0–10, with 0 indicating none and 10 indicating severe.

Symptom Severity—The provider should ask the patient to make a global rating of symptoms he/she has experienced in the past week where:

- 0 = no symptoms
- 5 = moderate symptoms
- 10 = very severe symptoms

“Which rating best describes any symptoms you might have had in the past *week*?”

Side Effects—The provider should ask the patient to make a global rating of side effects he/she has experienced in the past week where:

- 0 = no side effects
- 5 = moderate side effects
- 10 = very severe side effects

“Which rating best describes any medication side effects you might have had in the past *week*?”

Medications and Dosing

DOSING

The FDA approved product labeling contains dose range information for all marketed antipsychotic medications. These recommendations are based largely upon the results of randomized controlled trials. Evidence that some patients may obtain an enhanced response at doses above the range recommended in the labeling may be found in the medical literature. In the case of risperidone, clinical experience has shown that higher doses (> 6 mg) lead to greater extrapyramidal side effects, and average daily doses have actually decreased over time.

For olanzapine and risperidone, PET data examining D₂ and 5HT_{2A} binding in relatively small numbers of patients support the usual dosage range for the average patient.

Studies with first generation antipsychotics indicate that time on drug is often more important than dose escalation above usual doses, and that patients' symptoms on a given antipsychotic may improve with continued drug exposure, with or without a dosage increase. Similar studies with second generation antipsychotics are not yet in the literature.

In a partially, but inadequately responding patient, it may be reasonable to increase the dose above the usual dose range, if the patient has received an adequate trial (8–12 weeks) at higher doses within the usual dosage range. In such cases, the higher dose trial should be time limited (e.g., 4–6 weeks) unless there is evidence of significant clinical benefit. Clinical rating scales should be used to document whether the symptom improvement is greater than that achieved with usual doses. Patients not receiving additional benefit at higher doses within the designated time period should typically be switched to a trial with an alternate agent.

Based on current usage patterns, it is anticipated that:

- The average daily dose of **risperidone** is about 4–5 mg/day. Risperidone doses are usually adjusted in 1–2 mg increments every 3–7 days. Risperidone doses can be taken once daily.
- The average daily dose of **olanzapine** is about 15 mg/day. Olanzapine doses are usually adjusted in 5 mg increments every seven days. The recommended starting dose of olanzapine is 10 mg/day. Higher doses of olanzapine (20 mg) may lead to faster response in positive symptoms (b), but the patient may then do well on a lower maintenance dose once stabilized (c). Olanzapine is usually taken at bedtime.
- **Quetiapine** dosing should be individualized, in the range of 300 mg to 800 mg per day. The starting dose is 25 mg BID, which is titrated up to at least 300 mg (150 mg BID) over 3–7 days. The rate of titration should be adjusted according to side effects. Early postural hypotension and sedation are usually mild and improve with time. The maximum recommended dose is 800 mg/day. Quetiapine has a very low incidence of EPS. When cross-tapering quetiapine and another agent, it is often possible to titrate the quetiapine dose to 300 mg/day before beginning to decrease the old antipsychotic. Some clinicians choose to give most of the quetiapine dose at bedtime, to take

advantage of its sedative properties. This dosing strategy seems reasonable but has not been systematically evaluated.

- **Ziprasidone's** package insert recommends an initial dose of 40 mg/day (20 mg BID). However, many clinicians start the medication at 80 mg/day (40 mg BID) and titrate up to the 120 mg/day target dose over a 3–7 day period. (Doses up to 160 mg/day may be necessary in some patients.) While some patients experience sedation when they start taking ziprasidone, others may transiently feel “activated” or even somewhat agitated. This latter group of patients may benefit from co-prescription of a low-dose benzodiazepine (e.g., clonazepam or lorazepam) during the initial weeks of ziprasidone therapy. The presence of food can increase ziprasidone's absorption up to twofold.
- The recommended first dose of **clozapine** is 12.5 mg (half a 25 mg tablet) on day one. If this dose does not produce symptomatic postural hypotension, progress to 25 mg HS for three days. Further increases at the rate of 25 mg every three days are usually well tolerated. Clozapine should be given in divided doses, with about 1/3 of the dose in the morning and 2/3 at bedtime. Above 100 mg/day, dose increases can be by 50 mg every three days until a daily total dose of at least 300 mg is reached. Subsequent dose increases should be guided by clinical response. The risk of seizures rises from 1 percent at 300 mg/day to 5 percent or more at 900 mg/day.

Clozapine serum levels are recommended before increasing doses above 600 mg/day. There is no clear threshold, but a reasonable current recommendation is to increase the dose further if the patient is not responding and if the serum level is below 350 ng/ml. Serum clozapine levels should be obtained before the morning dose, approximately twelve hours after the prior dose, and after at least five days on the same daily dose.

EXHIBIT 7

Second Generation Antipsychotic (SGA) Dosage Guidelines

SGA	Starting dose	Titration	Range	Max. dose	Schedule
Clozapine	12.5 mg/day (half a 25 mg tab) Starting day 3, dose increased every 3 days	Day 2: 25 mg HS Day 3: 25 mg BID Day 6: 25 mg AM, 50 mg HS Day 9: 50 mg BID Day 12: 75 mg BID Day 15: 100 mg BID Day 18: 125 mg BID Day 21: 150 mg BID Day 24: 100 mg AM, 200 mg HS	300–900 mg/day (serum level for doses > 600 mg/day)	900 mg/day	BID Eventual maintenance dose schedule is: BID (1/3 in AM, 2/3 in PM)
Olanzapine	5–10 mg/day	5 mg/week	10–20 mg/day	40 mg/day ^a	HS
Quetiapine	25 mg BID	50 mg/day	300–800 mg/day	800 mg/day	BID
Risperidone	1–2 mg/day	1 mg/2–3 days	2–6 mg/day	16 mg/day ^b	HS or AM
Ziprasidone	40–80 mg/day	20–40 mg/2–3 days	80–60 mg/day	160 mg/day	BID The presence of food can increase ziprasidone's absorption up to twofold

^aSome data indicate that olanzapine doses > 20 mg may benefit patients who only partially respond to an adequate trial of olanzapine 20 mg. (Volavka et al. 2002; Lindenmayer et al. 2001)

^bThe risk of EPS is significantly increased by using doses > 6 mg daily.

EXHIBIT 8

First Generation Antipsychotic (FGA) Dosage Guidelines

Drug	Starting dose	Dose range	Usual max. dose
Chlorpromazine	50–100 mg/day	300–1000 mg/day	1000 mg/day
Fluphenazine	5 mg/day	5–20 mg/day	20 mg/day
Fluphenazine D	12.5–25 mg IM/2–3 weeks	6.25–50 mg IM/2–4 weeks	100 mg IM/4 weeks
Haloperidol	2–5 mg/day	2–20 mg/day	20 mg/day
Haloperidol D	25–50mg IM/2 weeks	50–200 mg/2–4 weeks	300 mg/3–4 weeks
Loxapine	20 mg/day	50–150 mg/day	150 mg/day
Molindone	20 mg/day	50–150 mg/day	150 mg/day
Perphenazine	4–8 mg/day	16–64 mg/day	64 mg/day
Thiothixene	5–10 mg/day	15–50 mg/day	50 mg/day
Trifluoperazine	2 mg BID	5–40 mg/day	40 mg/day

DECISION TO CHANGE ANTIPSYCHOTIC

The decision to change antipsychotic medications can be based on symptomatology or side effects.

1. In general, persistent positive symptoms that are more than mild in intensity should lead to a medication change, unless there is good clinical evidence that further improvement with a medication change is unlikely (a).
2. Patients with persistent negative symptoms should be evaluated for depression and medication side effects as contributing factors (a).
3. The clinician should then decide if it is better to add a treatment (e.g., antidepressant or anticholinergic) or change to another antipsychotic. It is better not to do two things at once (e.g., change antipsychotic and add an antidepressant) (c).
4. The threshold for deciding to change antipsychotics because of side effects should be low, given the favorable side effect profiles of new antipsychotics (a).
5. Some side effects are treatable with adjunctive medication. If this tactic is unsuccessful or clinically inadvisable, move the patient on to the next stage of the algorithm.
6. Some side effects tend to decrease over time (sedation, postural hypotension, for example), and it is worth allowing 4–6 weeks for these adaptations to occur if the patient is benefiting from the medication and the side effects are not intolerable or dangerous.
7. Patients on multiple medications for side effects are candidates for switching to a different antipsychotic if there are other choices that are less likely to produce these side effects and if the side effect medications themselves produce side effects.
8. In addition to typical EPS and akathisia, consider patients' complaints about the medication making them feel physically or mentally uncomfortable (e.g., dysphoric or zombie-like) as possible reasons for changing antipsychotics (b).
9. In the case of treatment-resistant patients on clozapine, it is worth spending considerable effort helping patients cope with side effects, since it is unlikely that they will do better on a different antipsychotic (b).

USE OF FIRST GENERATION ANTIPSYCHOTICS

As discussed in the Description of Stages of the Algorithm section above, FGAs are not recommended as first-line agents because, in general, they are no more effective than the SGAs and have a greater propensity to cause EPS and tardive dyskinesia. There may be times, however, when an FGA is the most appropriate choice for a patient. The following clinical situations may warrant the long-term use of an FGA:

1. Individuals who are currently responding well to an FGA and have no EPS, akathisia, or tardive dyskinesia.
2. Individuals who have a history of responding better to FGAs than to SGAs.
3. Individuals who are candidates for depot therapy (this will likely change as second generation depot antipsychotics become available).

NONADHERENCE

Because medication nonadherence is frequently a result of bothersome side effects (a), clinicians should consider a trial of another first-line SGA before beginning a depot preparation. However, there are instances when the physician can reasonably conclude that the patient is unlikely to comply with another oral medication and that it is not worth trying an alternate SGA (c). In this case, the basis for the conclusion should be documented and the patient put on a depot antipsychotic. These patients can be switched back to a first-line oral antipsychotic at any time if the physician believes that the likelihood of medication compliance has substantially increased (e.g., the patient has gained insight into his/her illness and the need for treatment) and there are current (e.g., EPS) or potential (e.g., TD) problems with the depot treatment. As noted above, criteria for use of depot antipsychotics may change with the advent of depot second generation antipsychotics.

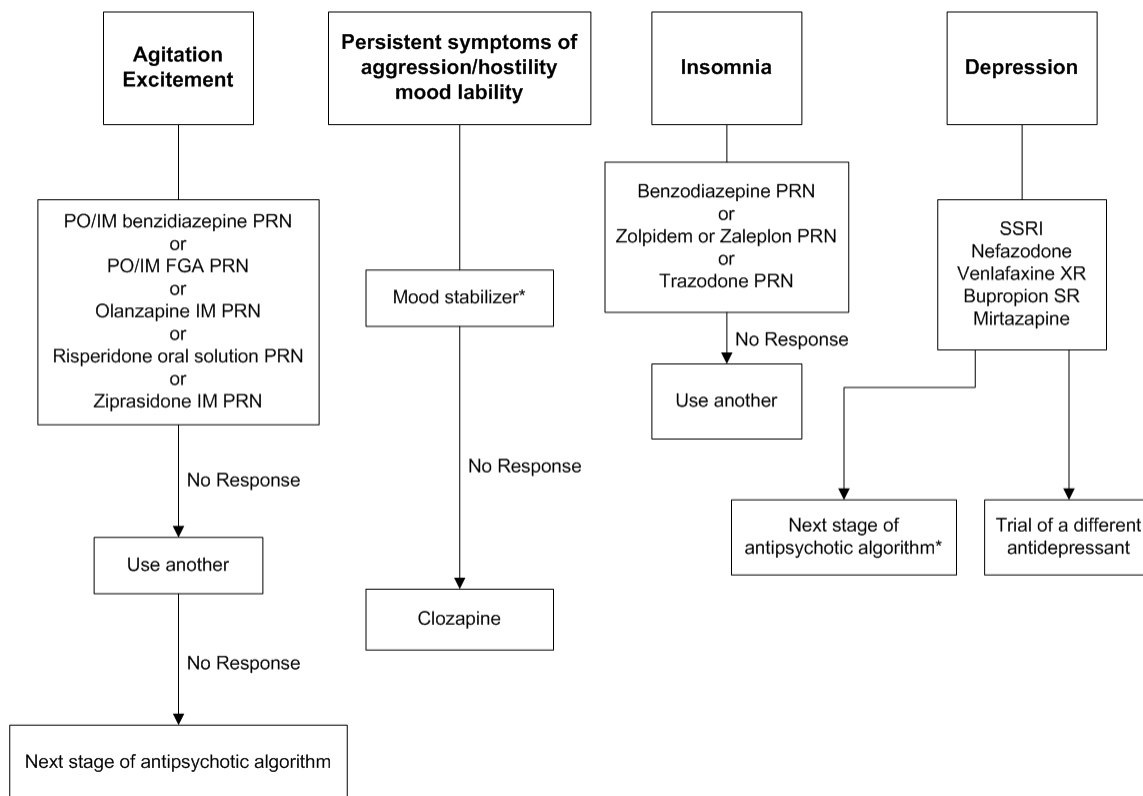
ELECTROCONVULSIVE THERAPY IN SCHIZOPHRENIA

Electroconvulsive therapy (ECT) is a controversial treatment that has been understudied in schizophrenia for the past three decades. Almost all studies have shown beneficial effects of ECT for persistent psychotic states (b), but most of these preceded clozapine and newer second-generation antipsychotics. There are a number of case studies showing improvement when ECT was administered to clozapine-resistant patients kept on clozapine (c). Because of these data, ECT is listed as a choice in stages 4 and 6, in combination with clozapine or another antipsychotic. Lack of ECT availability may be an insurmountable hurdle in some locations, but clinicians who have access to ECT are encouraged to consider it for treatment-resistant patients who fail or refuse clozapine. It is a common clinical impression that when ECT is used for schizophrenia, more treatments are needed (ten or more) and electrode placement should be bilateral (c). There are no controlled studies of ECT for schizophrenia in which number of treatments, duration of treatments, and electrode placement have been systematically evaluated.

MEDICATIONS FOR COEXISTING SYMPTOMS

As used in this algorithm, the term “coexisting symptoms” refers to the nonpsychotic symptoms that frequently accompany an exacerbation of schizophrenia or schizoaffective disorder (excitement, agitation, insomnia) or that frequently complicate the course of these illnesses (depression). The treatments for these symptoms are generally time limited and symptom oriented, in contrast to the maintenance and illness-oriented role of antipsychotics. The algorithms for coexisting symptoms appear below and on [page 8](#). Medications used to manage side effects are discussed in the section of the manual entitled Management of Side Effects on [page 40](#).

EXHIBIT 9 Coexisting Symptoms Algorithms



*Consider clozapine in patients with persistent suicidal behaviors or ideation.

Agitation and Excitement

Agitation and excitement are often the symptoms that lead to recognition of and hospitalization for exacerbations of schizophrenia. Historically, antipsychotics have been used both for these symptoms and for the psychosis, but a number of clinicians report that the SGAs seem less effective for the agitation and excitement of an acute exacerbation. For this reason, the algorithm for these symptoms is separate from the algorithm for psychosis and allows for PRN use of FGAs, benzodiazepines, olanzapine IM, risperidone oral solution or ziprasidone IM. It is important to stress that these PRN treatments should be time limited and discontinued as soon as clinically feasible. In the case of the FGAs this is because of increased risk of EPS, dysphoria, and tardive dyskinesia. In the case of benzodiazepines, the desirability of limiting amount and duration of PRN use relates to the development of tolerance over 2–3 weeks of steady use. On an outpatient basis, benzodiazepines should be used with caution in patients with a recent history of alcohol or drug abuse. Clinician choice of medication for agitation and excitement should be individualized to the needs and circumstances of the patient, guided by past history of response. Outpatients are likely to be more familiar with self-administering benzodiazepines on a PRN basis and may need education on PRN use of one antipsychotic while taking another regularly. Outpatients with a history of EPS should be started on an anticholinergic concurrent with starting a PRN FGA. Olanzapine IM,

risperidone oral solution, and ziprasidone IM act more rapidly than their oral counterparts and their use may be warranted in cases where the patient cannot tolerate or does not respond to FGAs and/or benzodiazepines. The concentration of risperidone oral solution is 1 mg/mL.

If a short course of an adjunctive FGA is being used for agitation, this should not affect the patient's staging in the algorithm. If the combination therapy continues beyond three to four weeks, however, it is no longer considered adjunctive (i.e., the patient is in Stage 6 of the algorithm).

EXHIBIT 10

Medications for Agitation and Excitement

Drug	Starting dose	Range (daily dose)
Lorazepam (Ativan)	0.5–1 mg TID	1–8 mg
Clonazepam (Klonopin)	0.25–0.5 mg BID	0.5–4 mg

Persistent Symptoms of Aggression/Hostility/Mood Lability

While benzodiazepines and FGAs may be used PRN to treat the agitation and excitement of an acute exacerbation of schizophrenia, mood stabilizers may help patients whose schizophrenia is complicated by persistent symptoms of aggression, hostility, and mood lability. In the event that a mood stabilizer is added to clozapine, the clinician should keep in mind that seizures are a risk with clozapine, especially at higher doses, so valproic acid may be safer than lithium. Combination therapy with clozapine and carbamazepine is contraindicated secondary to each agent's bone marrow suppressing effects. Carbamazepine also lowers antipsychotic serum levels secondary to its capacity to induce several different CYP 450 isoenzymes. Due to quetiapine's low bioavailability, carbamazepine's effects on quetiapine are of particular clinical significance. The clinician should periodically assess whether the addition of the mood stabilizer has resulted in a decreased frequency of aggressive, hostile, and/or mood episodes. If there is no discernible change in the clinical picture, the clinician should discontinue the adjuvant mood stabilizer and consider switching the patient to clozapine for persistent symptoms of aggression/hostility.

Insomnia

Insomnia as an acute symptom of psychosis differs in its treatment from the chronic difficulty falling asleep which is common among patients with schizophrenia who have poor sleep hygiene (daytime naps, caffeinated beverages in the evening, etc.). Some treatments for the acute insomnia associated with an exacerbation of psychosis include benzodiazepines, zolpidem (Ambien), zaleplon (Sonata), and trazodone (priapism risk in males). As with the acute interventions for agitation and excitement, PRNSs for insomnia should be time limited in their use.

EXHIBIT 11
Medications for Insomnia

Drug	Starting dose	Range (daily dose)
Zolpidem (Ambien)	10 mg HS	5–10 mg
Zaleplon (Sonata)	10 mg HS*	5–10 mg
Trazodone (Desyrel)	25 mg HS	12.5–100 mg

*May be administered in the middle of the night to reestablish sleep with no next-day hangover.

Depression

Both depression and suicide are common in schizophrenia. Almost half of patients with schizophrenia have major depression at some point in their illness and about 10 percent die by suicide. Medication treatments for depression in schizophrenia are not different from those used in major depressive disorder. For reasons of safety and tolerability, the selective serotonin reuptake inhibitors (SSRIs), bupropion SR, nefazodone, venlafaxine XR, and mirtazapine are recommended as first line treatments for depression in schizophrenia.

If a patient's depressive symptoms do not respond to a trial of one of the aforementioned antidepressants, the clinician should consider whether the patient has been diagnosed correctly, has an undiagnosed medical condition that could precipitate depression, or has been abusing illicit substances. If none of these is the case, there is little evidence to guide the clinician's decision with regard to changing the antipsychotic or trying a different antidepressant. However, a large multinational study showed an advantage for clozapine relative to olanzapine in reducing suicidal behaviors in patients with schizophrenia at increased risk for suicide.

Since some antidepressants can, by themselves, cause akathisia, this side effect should be watched for and not misattributed to the concurrent antipsychotic treatment. (For more information on antidepressant side effects, see the MIMA Guidelines for Treating Major Depressive Disorder). It is worth remembering that failure to respond to one SSRI does not necessarily predict failure on other SSRIs. Duration of treatment should be the same as for any episode of major depression (6–12 months), though this issue has not been well studied in schizophrenia. Recommended doses of antidepressants are listed below (see Exhibit 12).

EXHIBIT 12

Recommended Doses of Antidepressants

Type/Class	Medication	Usual target dose to achieve in weeks 1–3	Usual maximum recommended dose	Recommended administration schedule
SSRI	Citalopram	20 mg/day	60 mg/day	QAM
	Fluoxetine	20 mg/day	40–80 mg/day	QAM
	Paroxetine	20–30 mg/day	40–60 mg/day	QAM
	Sertraline	50–100 mg/day	150–200 mg/day	QAM
Others	Bupropion SR	200–300 mg/day	400 mg/day	BID ≤ 200 mg/dose
	Bupropion	225–300 mg/day	450 mg/day	BID–TID ≤ 150 mg/dose
	Mirtazapine	30 mg/day	60 mg/day	QHS
	Nefazodone	200–400 mg/day	600 mg/day	BID
	Venlafaxine	150–225 mg/day	375 mg/day	BID
	Venlafaxine XR	75–225 mg/day	375 mg/day	QD

DRUG INTERACTIONS

In addition to prior history of response to antidepressant treatment, the selection of an antidepressant agent should take into account potential drug-drug interactions. Of particular concern with regard to drug toxicity are the inhibitory effects of some antidepressants on clozapine metabolism, leading to increased serum levels and risk of seizures. Fluvoxamine (Luvox) can cause large increases in clozapine serum levels and should be avoided. Some other SSRIs and nefazodone may also cause clinically significant increases in clozapine serum levels and should be used carefully in clozapine treated patients. Clozapine serum levels should be monitored after adding one of the above antidepressants to clozapine. Because bupropion itself has an inherent risk of seizures, a pharmacodynamic interaction exists with clozapine. Therefore, the combination of clozapine and bupropion should be avoided.

In order to avoid troublesome drug interactions, Exhibit 13, Antidepressant/Antipsychotic Interactions, should be consulted whenever an antidepressant is added to an antipsychotic or whenever either component of an antidepressant-antipsychotic combination is being changed. **Note:** Venlafaxine (Effexor) increases haloperidol levels, but not by Cytochrome P450 interaction.

EXHIBIT 13

Antidepressant/Antipsychotic Interactions

Inhibitor (Inhibits substrate)	Substrate (Drug metabolized by pathway)		
	1A2	2D6	3A3/4
Bupropion (Wellbutrin)		Phenothiazines (some) Clozapine* Olanzapine*	
Citalopram (Celexa)		Phenothiazines Clozapine* Olanzapine*	
Fluoxetine (Prozac)		PHENOTHIAZINES THIORIDAZINE Clozapine* Olanzapine*	Clozapine Quetiapine
Fluvoxamine (Luvox)	CLOZAPINE THIORIDAZINE** HALOPERIDOL OLANZAPINE THIOTHIXENE		Clozapine Quetiapine
Nefazodone (Serzone)			QUETIAPINE Clozapine
Paroxetine (Paxil)		PHENOTHIAZINES THIORIDAZINE Clozapine* Olanzapine*	
Sertraline (Zoloft)		Phenothiazines Clozapine* Olanzapine*	Clozapine Quetiapine

Regular type = small changes in levels (low probability of clinically significant interaction)

Bold type = moderate changes in levels (moderate probability of clinically significant interaction)

BOLD CAPS = very large changes in levels (high probability of clinically significant interaction)

* = Minor pathway

** Fluvoxamine has been shown to inhibit the metabolism of thioridazine but it is unclear whether the interaction occurs at CYP 1A2 and/or CYP 2C19 (Carrillo et al. 1999).

Risperidone is metabolized through CYP 2D6 to 9-OH-risperidone. Both risperidone and its metabolite are equally potent, however, and the sum of the two remains the same with CYP 2D6 inhibition, usually resulting in no change in clinical effect and no need for reduction of the risperidone dose. There are currently no known inducers of CYP 2D6 (DeVane and Nemeroff 2000).

Quetiapine is a cytochrome P450 3A3/4 substrate and, because of the medication's low bioavailability, clinicians need to be aware of drug interactions that occur through this pathway. It may be necessary to increase the quetiapine dose above 800 mg per day when

quetiapine is used with 3A3/4 inducers such as carbamazepine, phenytoin, phenobarbital, etc.

Ziprasidone is metabolized in the liver, primarily through the aldehyde oxidase enzyme system. These enzymes metabolize approximately two-thirds of ziprasidone and are not known to be significantly inhibited or induced by other medications. Less than one-third of ziprasidone's metabolism is attributable to the cytochrome P450 enzyme system, therefore there should be few problems with pharmacokinetic interactions with ziprasidone. The package insert warns against combining ziprasidone with medications that significantly prolong the QT interval. The drugs to be avoided are listed in the most current package insert and include mesoridazine, thioridazine, chlorpromazine, droperidol, pimozide, quinidine, dofetilide, sotalol, moxifloxacin, and sparfloxacin (not a complete list). The package insert also warns about avoiding the use of ziprasidone in conditions in which there may be QT interval prolongation, such as hypokalemia and hypomagnesemia (Weiden et al. 2002). For more information on ziprasidone, see the Management of Side Effects section, [page 40](#).

Smoking is a potent inducer of hepatic isoenzymes, especially 1A2, and may decrease the serum levels of multiple different antipsychotics. This should be considered when patients move from a smoke-free environment to an environment where they may resume smoking.

Information on drug interactions is subject to rapid change, based upon new research findings and clinical experiences. Clinicians are encouraged to consult current references for current drug interactions information. A useful, frequently updated website for this information is maintained by Dr. David Flockhart at Indiana University (<http://medicine.iupui.edu/flockhart>).

Management of Side Effects

SIDE EFFECTS ALGORITHMS

Many of our medication efforts in the treatment of schizophrenia and related disorders are targeted toward counteracting the side effects of antipsychotic therapy. Although medications are recommended below (see Exhibit 2) to treat antipsychotic side effects, using a medication to treat a side effect can result in additional adverse effects. In these cases, consideration should be given to changing stages—particularly if the patient’s symptoms of illness are not optimally controlled.

Extrapyramidal Symptoms (EPS)

The anticholinergics remain the treatment of choice for acute dystonias and pseudoparkinsonism but have their own set of bothersome side effects (dry mouth, constipation, mild cognitive impairments, etc.). Doses are given in Exhibit 15 below. Intramuscular administration is necessary for prompt relief of emergent symptoms (oculogyric crisis, lingual dystonia, opisthotonus). Failure of the anticholinergic to treat EPS or intolerance of the anticholinergic side effects are both indications for moving to the next stage of the antipsychotic algorithm. The exception would be progression to an FGA from an SGA, since it is likely that EPS will be more problematic. In patients with pseudoparkinsonism, clinicians should also consider reducing the antipsychotic dose or changing stages.

EXHIBIT 14
Anti-EPS Dosing

Anti-EPS	Starting dose	Range (daily dose)
Benztropine (Cogentin)	1 mg BID	2–6 mg
Trihexyphenidyl (Artane)	2 mg BID	4–12 mg

Akathisia

Although akathisia is a form of EPS, it is dealt with separately from the other EPS because it differs in its optimal treatment. The first-line treatment for akathisia is a beta-blocker and, as with pseudoparkinsonism, the clinician should also consider reducing the antipsychotic dose. Though the data on relative frequency of various EPS with SGAs are sparse, a common clinical observation is that one may see akathisia in patients who experience no other EPS. Moreover, these patients may not complain of restlessness, even though they exhibit it (so-called pseudoakathisia). Thus, clinicians should be especially alert to observing restlessness in patients on SGAs. Again, beta-blockers are the first-line treatment. If they fail, or only partially relieve symptoms, benzodiazepines may be a reasonable alternative. Beta-blockers and benzodiazepines can be used in combination for akathisia caused by an SGA, but it is usually preferable to try another SGA rather than having the patient on a three-drug regimen.

In patients taking FGAs who are already on an anticholinergic for EPS, failure of a beta-blocker to relieve akathisia is an indication to change to an SGA rather than trying the alternative of a benzodiazepine for akathisia. This recommendation is based on the premise that the profile of physical and cognitive side effects from the three-drug combination of a FGA, an anticholinergic, and a benzodiazepine will almost certainly be more problematic than the side effects from one of the SGAs.

EXHIBIT 15

Antiakathisia Dosing

Antiakathisia	Starting dose	Range (daily dose)
Propranolol (Inderal)	10 mg QID	20–160 mg

Metoprolol 200–300 mg, nadolol 40–80 mg, pindolol 5 mg, and betaxolol 5–20 mg have all shown efficacy in the treatment of akathisia. (Fleischhacker et al. 1990).

Pulse/blood pressure monitoring may be necessary when using higher doses of beta-blockers.

Neuroleptic Malignant Syndrome

Neuroleptic malignant syndrome (NMS) is frequently undetected in its early stages. Since immediate cessation of the patient's current antipsychotic is the first step and may be all that is needed, early diagnosis is important. Muscular rigidity, change in mental status, hyperthermia, and autonomic instability are the four cardinal symptoms of NMS. Elevated WBC and CPK levels are also frequently seen. Progression of symptoms is a medical emergency requiring supportive medical measures. NMS has been reported with all antipsychotics, so that there is no clear choice for which one to start once the acute episode is resolved. If the patient has been on an FGA, changing to an SGA is reasonable. Re-starting the same antipsychotic is typically not recommended, but there are no studies reporting differential likelihood of NMS across drug classes for such patients. Patients with a history of NMS should be educated about the need to stay well hydrated and avoid strenuous physical activity when outside during hot weather.

Tardive Dyskinesia

It is now generally accepted that the SGAs are less likely to cause tardive dyskinesia (TD) than the FGAs. As mentioned previously, this is one of the reasons why the algorithm does not recommend the older antipsychotics as first-line therapy in the treatment of schizophrenia. Recent studies suggest that changing patients from FGAs to SGAs will lower their risk of developing TD (Tollefson 1997; Jeste 1999).

Clozapine has demonstrated an extremely low (if not absent) risk of TD and is therefore the treatment of choice for the patient with severe TD who needs to be on an antipsychotic. Patients with mild to moderate TD who are still on an FGA should be switched to an SGA because there is some evidence to suggest that the movements may improve when patients are switched to the newer medications.

COMPARING SIDE EFFECTS OF THE DIFFERENT AGENTS

The side effect profiles of the antipsychotics vary from agent to agent. These differences emphasize the importance of using the clinical characteristics of the patient to guide the choice of antipsychotic.

EXHIBIT 16
Comparison of Antipsychotic Adverse Effects

Drug	EPS	TD	Orthostatic hypotension	Prolactin	Sedation	Weight gain	Anti-cholinergic
Clozapine (Clozaril)	+ / –	–	+++	+ / –	++++	++++	++++
Risperidone (Risperdal)	+ / + +	+	+	+++	+	++	+
Olanzapine (Zyprexa)	+	+	+	+ / –	++	+++	++
Quetiapine (Seroquel)	+ / –	+ / –	++	+ / –	++	++	+
Ziprasidone (Geodon)	+	+	+	+	+	+ / –	–
Haloperidol (Haldol)	++++	++++	+	+++	+	+	+
Chlorpromazine (Thorazine)	+++	+++	++++	++	++++	++	+++

– none + mild +/- mild to none ++ moderate +++ moderately severe ++++ severe

In recent years, there has been growing concern about the potential of the newer antipsychotic medications to cause serious medical problems including weight gain, diabetes, hyperlipidemias, cardiac arrhythmias, hyperprolactinemia, and cataracts. Currently, there are no evidence-based guidelines that address which lab tests and/or procedures need to be done to monitor each antipsychotic agent (or how frequently these tests should be performed). The range of expert recommendations is wide. In their marketing, antipsychotic manufacturers tend to emphasize the risks of their competitors' agents, leading to an attitude of wariness and uncertainty on the part of many clinicians. Some mental health agencies have already developed new monitoring guidelines for their clinicians to follow. Until an evidence-based expert consensus on monitoring recommendations is available, clinicians who prescribe in the absence of such guidelines should exercise their own best judgment, recognizing that the costs and inconvenience of increased monitoring must be balanced against the need to ensure patient safety and the wish to avoid liability for harmful side effects.

USE OF PSYCHOTROPIC AGENTS IN PREGNANCY AND LACTATION

Exhibit 17 outlines the effects of medications during various stages of gestation along with descriptions of the potential toxicities of these psychotropic agents.

EXHIBIT 17

Use of Psychotropic Agents in Pregnancy and Lactation

Medication	Trimester			Category*	Summary
	1st	2d	3d		
Tricyclic antidepressants	±	+	+	D	Possible association between 1st trimester and limb malformation by some case reports but further studies showed no association. Perinatal syndromes: antidepressant withdrawal with jitteriness and irritability.
Desipramine				C	
Clomipramine				C	
Serotonin selective agents	±	+	+	B/C**	Fluoxetine has been the most studied. No higher rates of major congenital malformation in those who took fluoxetine in the 1st trimester than the general population.
Other antidepressants	±	+	+	C	Teratogenicity was not revealed in animals even at much higher doses than that used in humans.
Bupropion				B	
Lithium	Ø	+	±	D	Associated with cardiac anomalies when used in 1st trimester. Prematurity associated with use in 2d and 3d trimester. Watch for maternal lithium toxicity after delivery due to volume change—need to decrease dose by half before delivery. Lithium levels may be increased in neonates—risk of “floppy baby” and hypothyroidism
Valproic acid	Ø	Ø	Ø	D	Associated with neural tube defects/1–5% risk of spina bifida
Carbamazepine	±	±	±	D	0.5–1% risk of spina bifida
Other anticonvulsants	±	±	±	C	Gabapentin, lamotrigine, and topiramate were not teratogenic in animal studies but some malformations were observed.
Typical antipsychotics	±	±	±	C	Most common malformations reported include cardiac, genital, skeletal (3.5%). Use of high potency agents is recommended. Avoid low potency agents due to decrease BP and uteroplacental blood flow. Use in 3d trimester associated with neonatal associated extrapyramidal effects such as agitation, tremor, poor sucking, swallowing, primitive reflexes, and hypertonicity/DC drugs 5–10 days prior to delivery to allow fetal drug level to decrease.
Haloperidol					
Chlorpromazine					
Fluphenazine					
Loxapine					
Mesoridazine					
Thioridazine					
Thiothixene					
Atypical antipsychotics	±	±	±	C	Little information on atypical antipsychotics
Clozapine				B	
Anticholinergics	±				Main association is suggested cardiovascular effects. Possible association with minor malformations.
Benzotropine		±	±	C	
Trihexiphenidyl		±	±	C	
Diphenhydramine		+	+	B	
Propranolol	±	+	±	C	Has been used to treat pregnancy-induced hypertension and does not appear to be associated with malformations. Neonatal adverse effects have included hyperbilirubinemia, bradycardia, respiratory depression, and low birth weights.
Benzodiazepines	Ø	±	±	D	Increased risk of cleft palate in 1st trimester, especially diazepam and alprazolam. 3rd trimester exposure leads to tremors, hypertonicity, failure to feed, cyanosis and apnea. Best avoided but if needed use lorazepam (PRN only).
Buspirone	±	±	±	B	Little information available

*Based on *Drugs in Pregnancy and Lactation*, 5th ed.

Ø Use is not recommended

± May be used (least risk)

± May be used if no other alternative available

**Package insert and *Drugs in Pregnancy and Lactation*, 5th ed., differ.

EXHIBIT 18

FDA Categories

Pregnancy	Category definition
Category A	Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester and no evidence of a risk in later trimesters. The possibility of fetal harm appears remote.
Category B	Studies in animals have not demonstrated a fetal risk but there are no controlled studies in pregnant women or animal-reproduction studies have shown adverse effect that was not confirmed in controlled studies in women in the first trimester.
Category C	Studies in animals have revealed adverse effects on the fetus and there are no controlled studies in women or studies in animals and women are not available. Drugs should be given only if the benefit justifies the potential risk to the fetus.
Category D	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk.
Category X	Studies in animal or women have demonstrated fetal abnormalities or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

ANTIPSYCHOTIC AGENTS IN PREGNANCY

- A number of studies have shown no increase in malformations after first trimester exposure to first generation antipsychotic drugs.
- Two studies found an increase in nonspecific congenital anomalies after exposure to phenothiazines during early pregnancy.
- Available data show no effect of in utero FGA exposure on IQ in humans.
- A mild, transient neonatal withdrawal syndrome of hypertonia, tremor, and poor motor maturity can result after antipsychotic use in late pregnancy.
- Withdrawal dyskinesia, which may include irritability, abnormal hand and trunk posturing, tongue thrusting, and a shrill cry, is a rare reaction to FGA exposure. These symptoms resolve spontaneously over several months with normal subsequent motor development.
- Anticholinergic side effects can be seen in the fetus, neonate, or the pregnant woman.
- Very little information is available concerning the use of atypical antipsychotics during pregnancy.
- Atypical antipsychotics that are prolactin-sparing make implementation of effective contraceptive counseling for seriously ill patients more urgent.
- Glucose intolerance is a problem in pregnancy and the risk may increase with the use of antipsychotics; especially olanzapine and clozapine.
- There are increased risks in pregnancy with the use of clozapine: glucose intolerance in the mother and possible fetal macrosomia, increased anticholinergic type side

effects (constipation) in the mother, increased fatigue and sedation, hypotensive risk in the mother, and neonatal risk for agranulocytosis.

Guidelines for Using Antipsychotic Agents During Pregnancy

- Agents of choice are haloperidol and trifluoperazine, due to being relatively well studied and having the fewest pregnancy-associated side effects. Atypicals are a possibility, but there are limited data.
- Avoid use during first trimester if possible.
- Use only when benefit clearly outweighs the risk.
- For withdrawal dyskinesias in the newborn, diphenhydramine elixir can alleviate symptoms.
- It is recommended that pregnant women on antipsychotics be given calcium supplementation, which has been shown to reduce EPS, but no other prophylaxis for EPS is indicated.
- Avoid long-acting (depot) preparations of the high-potency group in order to limit the duration of any possible toxic effect in the neonate.

Strategies for Switching Antipsychotics

Even though switching patients between antipsychotics is an extremely common event, there are only a few systematic studies of the process. Comparisons of abrupt versus cross-tapered switching from other antipsychotics to ziprasidone or to aripiprazole found no differences in outcome, regardless of approach (b). Yet, most clinicians favor a crossover strategy that extends over weeks to months, citing instances from their personal experiences of gross decompensations, apparently triggered by too sudden switches. Thus, clinical consensus seems at variance with the modest amount of available evidence. One reason for this discrepancy may be that the switch studies were carried out under controlled conditions, with frequent clinic visits, in contrast to most naturalistic situations.

Some literature-based observations provide helpful guidance to circumstances that favor cross-titration and gradual tapering. Factors considered to favor a more gradual approach include clinical instability, stable response to clozapine, and high doses of “old” agent (b). Abrupt discontinuation of antipsychotics can be associated with withdrawal symptoms such as nausea, sweating and muscle aches, increased motor symptoms, and relapse of psychotic symptoms (b). In switching from a regimen in which anticholinergic treatment was required to an antipsychotic less likely to produce EPS, extending the anticholinergic for at least a few days beyond the last dose of the discontinued antipsychotic is recommended (b). It has been suggested that substitution of agents with overlapping neuropharmacological profiles (e.g., similar relative potency in 5HT₂ blockade) may lessen withdrawal type symptoms in the switching process (c).

As a practical matter, many antipsychotics can produce distressing side effects if initiated in full therapeutic doses and should be titrated up at rates determined by the urgency of the clinical circumstances and by their tolerability to the patient. Under these conditions, if the patient is at all responsive to the medication that is being discontinued, it makes sense to taper the old medication in such a way as to try to keep the total dose of antipsychotic in the therapeutic range.

A final consideration in switching is the likelihood that the patient will be able to follow a set of complex directions. Given the substantial body of data showing high rates of poor adherence to medication regimens in most chronic illnesses, it seems likely that complicated switching strategies will often not be done as recommended, unless the treatment team provides explicit directions and aids. Thus, written instructions that detail each day’s medications during the crossover are useful. For some patients, compartmented medication containers labeled by day of the week can be filled in the office/clinic with the doses of each medication that are to be taken each day.

MEDICATION DISCONTINUATION

A trial period off antipsychotics may be reasonable for some patients early in the course of illness. This, an individualized decision, depends on a number of factors that do not lend themselves to an algorithmic approach. Although research shows increased relapse rates among patients in discontinuation studies, only minimal guidance is provided regarding this treatment decision in patients who responded well to antipsychotics early

in the course of their illness and have maintained a complete remission for a prolonged time period (e.g., more than two years) (c). Thus, the schizophrenia algorithm contains no guidelines for antipsychotic medication discontinuation, which is anticipated to be a rare event in the typical mental health clinic patient population.

MEDICATION MAINTENANCE

The evidence overwhelmingly favors the conclusion that, for most patients, maintenance antipsychotic medication is a key aspect of successful treatment, in preference to discontinuation or intermittent treatment (a). Less clear is what the maintenance dose of antipsychotic medication should be for any individual patient. A common clinical aphorism is that the maintenance dose should be the lowest that will keep the patient relatively symptom free. However, very low doses of maintenance medication are clearly less effective for a proportion of patients than doses in the usual range. Moreover, schizophrenia is an illness of natural exacerbations and remissions. Doses that are just sufficient during periods when the illness is quiescent are likely to be inadequate during periods when an exacerbation threatens. That is to say, the optimal maintenance dose is likely to be somewhat higher than the dose that prevents symptoms under the best of circumstances. On the other hand, too high a maintenance dose elevates side effect risks without therapeutic gain.

TOOLS FOR ALGORITHM IMPLEMENTATION AND ADHERENCE

Patient Algorithm

An individual patient's medication history obtained from patient interview and chart review can be recorded on the personal algorithm form (see Appendix B), and, when kept up-to-date, will provide a quick reference for determining a patient's placement in the algorithm. The most recent start date in an algorithm box should correspond to the current medication. In addition, progress may be numerically tracked with the highest number written in the box indicating the current stage, but it is still recommended that start dates be included to assist in determining length of previous medication trials.

For patients who have had trials of second generation antipsychotics prior to enrollment in the algorithm, "PTE" (prior to enrollment) can be written in the appropriate box accompanied by the date, if known.

Modifications for Inpatient Use

The algorithm recommends that clinicians see patients every week when a new medication is started, approximately every three weeks while the patient is adjusting to the medication, and no less often than every three months once the patient is stable. These recommendations are more applicable to the outpatient than the inpatient setting where, in some facilities, clinicians see their patients every day. **As a general rule, inpatient physicians should fill out a clinical record form for each patient on a weekly basis.** The authors recognize that, compared to outpatients, acutely ill inpatients may require higher antipsychotic doses. After the patient's condition has stabilized, the clinician should attempt to lower the antipsychotic dose (see Medication Maintenance section on [page 46](#)). In-patients may also require more adjunctive medications than their outpatient counterparts. Algorithm staging, however, should be based on the maintenance antipsychotic. For example, if a first break patient is taking olanzapine but receiving injections of haloperidol PRN, he or she would be in Stage 1 of the algorithm based on the olanzapine prescription, as long as the use of the adjunct does not exceed a 3–4 week period.

Admission to a psychiatric unit is almost always due to acute circumstances such as imminent danger to self or others, grave disablement, and/or a marked exacerbation of symptoms. The necessity of an inpatient admission signals that a change in treatment should be considered and each admission should trigger a thorough evaluation of algorithm staging. Rarely, a patient is admitted for his or her “first break,” and these patients will be started in Stage 1. Far more often, the patient has an extensive medication history and the admitting clinician assumes that the current medication is not working and advances the patient to the next stage of the algorithm. Before changing a stage, however, the clinician should evaluate the following four factors:

1. Has the patient been taking the medication? Nonadherence is a major issue in most chronic diseases. Medication does nothing if not taken and, in order to produce maximum benefits, must be taken as directed. Explore this with the patient. Re-starting the current medication may be the best treatment.
2. Is substance abuse a problem? Drug abuse can cause acute and chronic psychiatric symptoms, which often remit (albeit slowly) when the abuse stops. Always evaluate for symptoms of withdrawal and, if present, help the patient through the withdrawal period before staging the patient in the algorithm. Keep in mind that patients may resort to drugs of abuse to alleviate medication side effects, especially neurological ones.
3. Is the patient experiencing symptoms of depression, anxiety, and/or insomnia? Patients with schizophrenia frequently have coexisting symptoms. Refer to the coexisting symptoms algorithms ([page 8](#)) before changing the primary antipsychotic.
4. Is the patient dealing with psychosocial stresses like housing problems, family difficulties, and/or employment uncertainties? If so, the treatment team needs to do what it can to help the patient resolve the problem(s) and a change in

medication may not be beneficial. However, a medication change is probably warranted if the clinician determines that increased symptomatology was one of the major causes of the patient's psychosocial problem(s).

COORDINATING TRANSITIONS BETWEEN INPATIENT AND OUTPATIENT SETTINGS

The transition between inpatient and outpatient care is often unsuccessful. Most inpatient clinicians have dealt with the frustration of discharging a patient only to see him or her return to the hospital within a few weeks as a result of not receiving outpatient follow-up and/or not filling prescriptions. Managed care's insistence on brief stays further aggravates the problem by forcing clinicians to discharge patients before they are truly stabilized. By the same token, outpatient clinicians must constantly revise their treatment plans when the originally formulated plan is not followed by the inpatient physician. The following may improve transitions between the two treatment settings:

1. **Document the treatment plan.** It is imperative that all clinicians document the rationale behind treatment decisions and outline the expected treatment plan. Inpatient clinicians may want to start notes to their outpatient colleagues with "transfer" rather than "discharge" (I am 'transferring' the acute care of this patient...) because the former term implies a continuation of care while the latter suggests a disruption. This plan must be sent to the outpatient clinician before the first outpatient visit.
2. **Follow-up.** Ensure that the patient has an outpatient clinic appointment within one week after discharge and that the patient leaves the hospital with enough medication to last until the first follow-up appointment. The discharge planning process requires communication and coordination between the inpatient and outpatient treatment teams. Physicians and other staff working in both arenas should get to know each other and brainstorm about ways to improve coordination between the two settings. A staff member from the outpatient clinic should attend inpatient treatment team meetings and be actively involved in the discharge planning process. Organized quarterly meetings between key inpatient and outpatient staff members can also be useful in identifying and solving problems involved with transition in care issues.

Appendix A:

Administration Manual

*Four-Item Positive Symptom Rating Scale (PSRS),**

and

*Brief Negative Symptom Assessment (BNSA)***

*The four-item PSRS was adapted from the expanded version of the BPRS developed by: J. Ventura, D. Lukoff, K. H. Nuechterlein, R. P. Liberman, M. F. Green, and A. Shaner, Manual for the expanded Brief Psychiatric Rating Scale, *International Journal of Methods Psychiatry Research* 3 (1993): 227–44.

**The Brief Negative Symptom Assessment was adapted from the Negative Symptom Assessment and the Scale for the Assessment of Negative Symptoms developed respectively by: Alphas and Summerfelt, *The Negative Symptom Assessment: A new instrument to assess negative symptoms of schizophrenia*, *Psychopharmacology Bulletin* 25, no. 2 (1989): 159–63; N. Andreasen, Modified scale for the assessment of negative symptoms, *NIMH treatment strategies in schizophrenia study*, Public Health Administration, U.S. Department of Health and Human Services, 1984. ADM (9/85): 9–102.

In the past 7 days . . .

FOUR-ITEM POSITIVE SYMPTOM RATING SCALE

Scale Items and Anchor Points

1. **SUSPICIOUSNESS:** Expressed or apparent belief that other persons have acted maliciously or with discriminatory intent. Include persecution by supernatural or other nonhuman agencies (e.g., the devil). Note: Ratings of “3” or above should also be rated under Unusual Thought Content.

Do you ever feel uncomfortable in public? Does it seem as though others are watching you?

Are you concerned about anyone's intentions toward you?

Is anyone going out of their way to give you a hard time, or trying to hurt you? Do you feel in any danger?

If patient reports any persecutory ideas/delusions, ask the following:

How often have you been concerned that [use patient's description]? Have you told anyone about these experiences?

1—Not Present

2—Very Mild

Seems on guard. Reluctant to respond to some “personal” questions. Reports being overly self-conscious in public.

3—Mild

Describes incidents in which others have harmed or wanted to harm him/her that sound plausible. Patient feels as if others are watching, laughing, or criticizing him/her in public, but this occurs only occasionally or rarely. Little or no preoccupation.

4—Moderate

Says others are talking about him/her maliciously, have negative intentions, or may harm him/her. Beyond the likelihood of plausibility, but not delusional. Incidents of suspected persecution occur occasionally (less than once per week) with some preoccupation.

5—Moderately Severe

Same as 4, but incidents occur frequently, such as more than once per week. Patient is moderately preoccupied with ideas of persecution OR patient reports persecutory delusions expressed with much doubt (e.g., partial delusion).

6—Severe

Delusional—speaks of Mafia plots, the FBI, or others poisoning his/her food, persecution by supernatural forces.

7—Extremely Severe

Same as 6, but the beliefs are bizarre or more preoccupying. Patient tends to disclose or act on persecutory delusions.

2. **UNUSUAL THOUGHT CONTENT:** Unusual, odd, strange or bizarre thought content. Rate the degree of unusualness, not the degree of disorganization of speech. Delusions are patently absurd, clearly false or bizarre ideas that are expressed with full conviction. Consider the patient to have full conviction if he/she has acted as though the delusional belief were true. Ideas of reference/persecution can be differentiated from delusions in that ideas are expressed with much doubt and contain more elements of reality. Include thought insertion, withdrawal and broadcast. Include grandiose, somatic and persecutory delusions even if rated elsewhere. Note: If somatic concern, guilt, suspiciousness, or grandiosity are rated “6” or “7” due to delusions, then unusual thought content must be rated a “4” or above.

Have you been receiving any special messages from people or from the way things are arranged around you? Have you seen any references to yourself on TV or in the newspapers?

Can anyone read your mind?

Do you have a unique relationship with God?

Is anything like electricity, X-rays, or radio waves affecting you?

Are thoughts put into your head that are not your own?

Have you felt that you were under the control of another person or force?

If patient reports any odd ideas/delusions, ask the following]:

How often do you think about [use patient's description]?

Have you told anyone about these experiences? How do you explain the things that have been happening [specify]?

1—Not Present

2—Very Mild

Ideas of reference (people may stare or may laugh at him), ideas of persecution (people may mistreat him). Unusual beliefs in psychic powers, spirits, UFOs, or unrealistic beliefs in one's own abilities. Not strongly held. Some doubt.

3—Mild

Same as 2, but degree of reality distortion is more severe as indicated by highly unusual ideas or greater conviction. Content may be typical of delusions (even bizarre), but without full conviction. The delusion does not seem to have fully formed, but is considered as one possible explanation for an unusual experience.

4—Moderate

Delusion present but no preoccupation or functional impairment. May be an encapsulated delusion or a firmly endorsed absurd belief about past delusional circumstances.

5—Moderately Severe

Full delusion(s) present with some preoccupation OR some areas of functioning disrupted by delusional thinking.

6—Severe

Full delusion(s) present with much preoccupation OR many areas of functioning are disrupted by delusional thinking.

7—Extremely Severe

Full delusions present with almost total preoccupation OR most areas of functioning are disrupted by delusional thinking.

3. **HALLUCINATIONS:** Reports of perceptual experiences in the absence of relevant external stimuli. When rating degree to which functioning is disrupted by hallucinations, include preoccupation with the content and experience of the hallucinations, as well as functioning disrupted by acting out on the hallucinatory content (e.g., engaging in deviant behavior due to command hallucinations). Include “thoughts aloud” (“gedankenlautwerden”) or pseudohallucinations (e.g., hears a voice inside head) if a voice quality is present.

Do you ever seem to hear your name being called?

Have you heard any sounds or people talking to you or about you when there has been nobody around? [If hears voices]: What does the voice/voices say? Did it have a voice quality?

Do you ever have visions or see things that others do not see? What about smell — odors that others do not smell?

If the patient reports hallucinations, ask the following:

Have these experiences interfered with your ability to perform your usual activities/work? How do you explain them? How often do they occur?

1—Not Present

2—Very Mild

While resting or going to sleep, sees visions, smells odors, or hears voices, sounds, or whispers in the absence of external stimulation, but no impairment in functioning.

3—Mild

While in a clear state of consciousness, hears a voice calling the subject's name, experiences nonverbal auditory hallucinations (e.g., sounds or whispers), formless visual hallucinations, or has sensory experiences in the presence of a modality relevant stimulus (e.g., visual illusions) infrequently (e.g., 1–2 times per week) and with no functional impairment.

4—Moderate

Occasional verbal, visual, gustatory, olfactory, or tactile hallucinations with no functional impairment OR nonverbal auditory hallucinations/visual illusions more than infrequently or with impairment.

5—Moderately Severe

Experiences daily hallucinations OR some areas of functioning are disrupted by hallucinations.

6—Severe

Experiences verbal or visual hallucinations several times a day OR many areas of functioning are disrupted by these hallucinations.

7—Extremely Severe

Persistent verbal or visual hallucinations throughout the day OR most areas of functioning are disrupted by these hallucinations.

4. **CONCEPTUAL DISORGANIZATION:** Degree to which speech is confused, disconnected, vague, or disorganized. Rate tangentiality, circumstantiality, sudden topic shifts, incoherence, derailment, blocking, neologisms, and other speech disorders. Do not rate content of speech.

1—Not Present

2—Very Mild

Peculiar use of words or rambling but speech is comprehensible.

3—Mild

Speech a bit hard to understand or make sense of due to tangentiality, circumstantiality, or sudden topic shifts.

4—Moderate

Speech difficult to understand due to tangentiality, circumstantiality, idiosyncratic speech, or topic shifts on many occasions OR 1–2 instances of incoherent phrases.

5—Moderately Severe

Speech difficult to understand due to circumstantiality, tangentiality, neologisms, blocking, or topic shifts most of the time OR 3–5 instances of incoherent phrases.

6—Severe

Speech is incomprehensible due to severe impairments most of the time. Many PSRS items cannot be rated by self-report alone.

7—Extremely Severe

Speech is incomprehensible throughout interview.

Sources of information (check all applicable):

- ☐ Patient
- ☐ Parents/relatives
- ☐ Mental health professionals
- ☐ Chart
- ☐ Difficult to assess due to formal thought disorder

Explain here if validity of assessment is questionable:

- ☐ Symptoms possibly drug-induced
- ☐ Underreported due to lack of rapport
- ☐ Underreported due to negative symptoms
- ☐ Patient uncooperative

Confidence in assessment:

- ☐ Rate on a scale of 1–5, where 1 = Not confident at all and 5 = Very confident.

Other: _____

BRIEF NEGATIVE SYMPTOM ASSESSMENT SCALE

Items adapted from NSA and SANS

1. **PROLONGED TIME TO RESPOND** (a measure of alogia): Observed throughout communication with the patient. After asking the patient a question, he or she pauses for inappropriately long periods before initiating a response. Delay is considered a pause if it feels as though you are waiting for a response or if you consider repeating the question because it appears that the patient has not heard you. He or she may seem “distant” and sometimes the examiner may wonder if the patient has even heard the question. Prompting usually indicates that the patient is aware of the question, but has been having difficulty in developing his/her thoughts in order to make an appropriate reply. Rate severity on the frequency of these pauses.

1—Normal

No abnormal pauses before speaking.

2—Minimal

Minimal evidence of inappropriate pauses (brief but not abnormally lengthy pauses occur) may be extreme of normal.

3—Mild

Occasional noticeable pauses before answering questions. Due to the length of the pause, you feel the need to repeat yourself once or twice during the interview.

4—Moderate

Distinct pauses occur frequently (20–40% of responses).

5—Marked

Distinct pauses occur most of the time (40–80% of responses).

6—Severe

Distinct pauses occur with almost every response (80–100% of responses).

2. **EMOTION: UNCHANGING FACIAL EXPRESSION; BLANK, EXPRESSIONLESS FACE** (a measure of flat affect): The patient's face appears wooden, mechanical, frozen. Facial musculature is generally expressionless and unchanging. The patient does not change expression, or change is less than normally expected, as the emotional content of discourse changes. Because of this, emotions may be difficult to infer. Disregard changes in facial expression due to abnormal involuntary movements, such as tics and tardive dyskinesia. The two dimensions of importance when making this rating are degree of emotional expression and spontaneity.

1—Normal

Spontaneous displays of emotion occur when expected. Normal degree of expressiveness of emotions is present.

2—Minimal

Spontaneous expressions of emotion occur when expected. However, there is a reduction in degree or intensity of the emotions expressed. May be extreme of normal.

3—Mild

Spontaneous expressions of emotion occur infrequently. When emotions are expressed there is a reduction in degree or intensity displayed.

4—Moderate

Obvious reduction in spontaneous expressions. Spontaneous expressions of emotion may occur very rarely during interaction and only when discussing topics of special interest or humor to the subject.

5—Marked

Facial expression is markedly decreased. There are no spontaneous expressions of emotion unless prompted or coaxed by the interviewer.

6—Severe

There are no expressions of emotion even when attempts are made to elicit an emotional response. The subject's face remains blank throughout the interview.

3. **REDUCED SOCIAL DRIVE** (a measure of asociality): This item assesses how much the subject desires to initiate social interactions. Desire may be measured in part by the number of actual or attempted social contacts with others. If the patient has frequent contact with someone (e.g., family member) who initiates the contact, does the patient appear to desire the contact (i.e., would he or she initiate contact if necessary)? In making this rating, probe the desire to initiate social interactions, number of social interactions, and the ability to enjoy them.

Assessed by asking the patient questions like:

How have you spent your time in the past week?

Do you live alone or with someone else?

Do you like to be around people?

Do you spend much time with others?

Do you have difficulty feeling close to others?

Who are your friends?

How often do you see them?

Did you see them this past week?

Have you called them on the phone?

When you get together, who decides what to do and where to go?

When you spend time with others, do you ask them to do something with you or do you wait until they ask you to do something?

Is anyone concerned about your happiness or well being?

1—Normal

Normal desire to initiate and normal number of contacts. Social contacts are enjoyable.

2—Minimal

Minimal reduction in either the desire to initiate social contacts or the number of social relationships. May initially seem guarded, but has the ability to establish relationships over time. Social relationships are enjoyable.

3—Mild

Reduction in desire to initiate social contacts. The patient has few social relationships and these social contacts are enjoyable.

4—Moderate

Obvious reduction in the desire to initiate social contacts. The patient has few relationships toward which he or she feels indifference. However, a number of social contacts are initiated each week.

5—Marked

Marked reduction in desire to initiate social contacts. The patient has very few relationships toward which he or she feels indifference. The patient does not initiate social contacts but may maintain a few contacts (such as with family).

6—Severe

Patient does not desire social contact. Actively avoids social interactions.

4. **GROOMING AND HYGIENE** (a measure of amotivation): Observed during interaction with the patient. The patient displays less attention to grooming and hygiene than normal. The patient presents with poorly groomed hair, disheveled clothing, etc. Do not rate grooming as poor if it is simply done in what one might consider poor taste (e.g., wild hairdo or excessive makeup). In addition to observation, one must ask the patient about regularity of bathing, brushing teeth, changing clothes, etc. This is particularly important with outpatients, as the patient may present his or her best grooming and hygiene at their clinic visit. Two dimensions to keep in mind when making this rating are current appearance and regularity of grooming behaviors.

Assess the patient by asking questions like:

How many times in the past week have you taken a shower or bath?

How often do you change your clothes?

How often do you shower and brush your teeth?

1—Normal

Patient is clean (e.g., showers every day) and dressed neatly.

2—Minimal

Minimal reduction in grooming and hygiene, may be at the extreme end of the normal range.

3—Mild

Apparently clean but untidy appearance. Clothing may be mismatched. Patient may shower less often than every other day, or may brush teeth less than every day.

4—Moderate

There is an obvious reduction in grooming and hygiene. Clothes may appear unkempt, rumpled, or the patient may look as if he or she just got out of bed. The patient may go without shower or bathing for two days at a time. The patient may go for two days without brushing their teeth.

5—Marked

There is a marked reduction in grooming and hygiene. Clothing may appear dirty, stained or very unkempt. The subject may have greasy hair or a body odor. The patient may go three days at a time without showering or three or four days without brushing their teeth.

6—Severe

Clothing is badly soiled. Patient has a foul odor. Patient may go more than four days in a row without showering or more than four days in a row without brushing his/her teeth. Poor hygiene may present a health risk.

WORKSHEET
for Four-Item Positive Symptom Rating Scale and
Brief Negative Symptom Assessment

Four-Item Positive Symptom Rating Scale

Use each item's anchor points to rate the patient.

- | | | | | | | | | | |
|-------------------------------|----|---|---|---|---|---|---|---|--------------|
| 1. Suspiciousness | NA | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
| 2. Unusual thought content | NA | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
| 3. Hallucinations | NA | 1 | 2 | 3 | 4 | 5 | 6 | 7 | |
| 4. Conceptual disorganization | NA | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Total: _____ |

* NA – not able to be assessed

Four-Item Negative Symptom Rating Scale

Use each item's anchor points to rate the patient.

- | | | | | | | | | |
|---|--|---|---|---|---|---|---|--------------|
| 1. Prolonged time to respond | | 1 | 2 | 3 | 4 | 5 | 6 | |
| 2. Emotion unchanging facial expression
blank, expressionless face | | 1 | 2 | 3 | 4 | 5 | 6 | |
| 3. Reduced social drive | | 1 | 2 | 3 | 4 | 5 | 6 | |
| 4. Poor grooming and hygiene | | 1 | 2 | 3 | 4 | 5 | 6 | Total: _____ |

Sources of information (check all applicable):

- ☐ Patient
- ☐ Parents/relatives
- ☐ Mental health professionals
- ☐ Chart
- ☐ Difficult to assess due to formal thought disorder

Explain here if validity of assessment is questionable:

- ☐ Symptoms possibly drug-induced
- ☐ Underreported due to lack of rapport
- ☐ Underreported due to negative symptoms
- ☐ Patient uncooperative

Confidence in assessment:

- ☐ 1 = Not at all - 5 = Very confident

Other: _____

The Four-item PSRS was adapted from the Expanded Version of the BPRS developed by: J. Ventura, D. Lukoff, K. H. Nuechterlein, R. P. Liberman, M. F. Green, and A. Shaner, Manual for the expanded Brief Psychiatric Rating Scale, *International Journal of Methods Psychiatry Research* 3 (1993): 227–44.

The Brief Negative Symptom Assessment was adapted from the Negative Symptom Assessment and the Scale for the Assessment of Negative Symptoms developed respectively by: Alphas and Summerfelt, *The Negative Symptom Assessment: A new instrument to assess negative symptoms of schizophrenia*, *Psychopharmacology Bulletin* 25, no. 2 (1989): 159–63; N. Andreasen, *Modified scale for the assessment of negative symptoms*. NIMH treatment strategies in schizophrenia study, Public Health Administration, U.S. Department of Health and Human Services, 1984, ADM (9/85): 9–102

In the past 7 days . . .

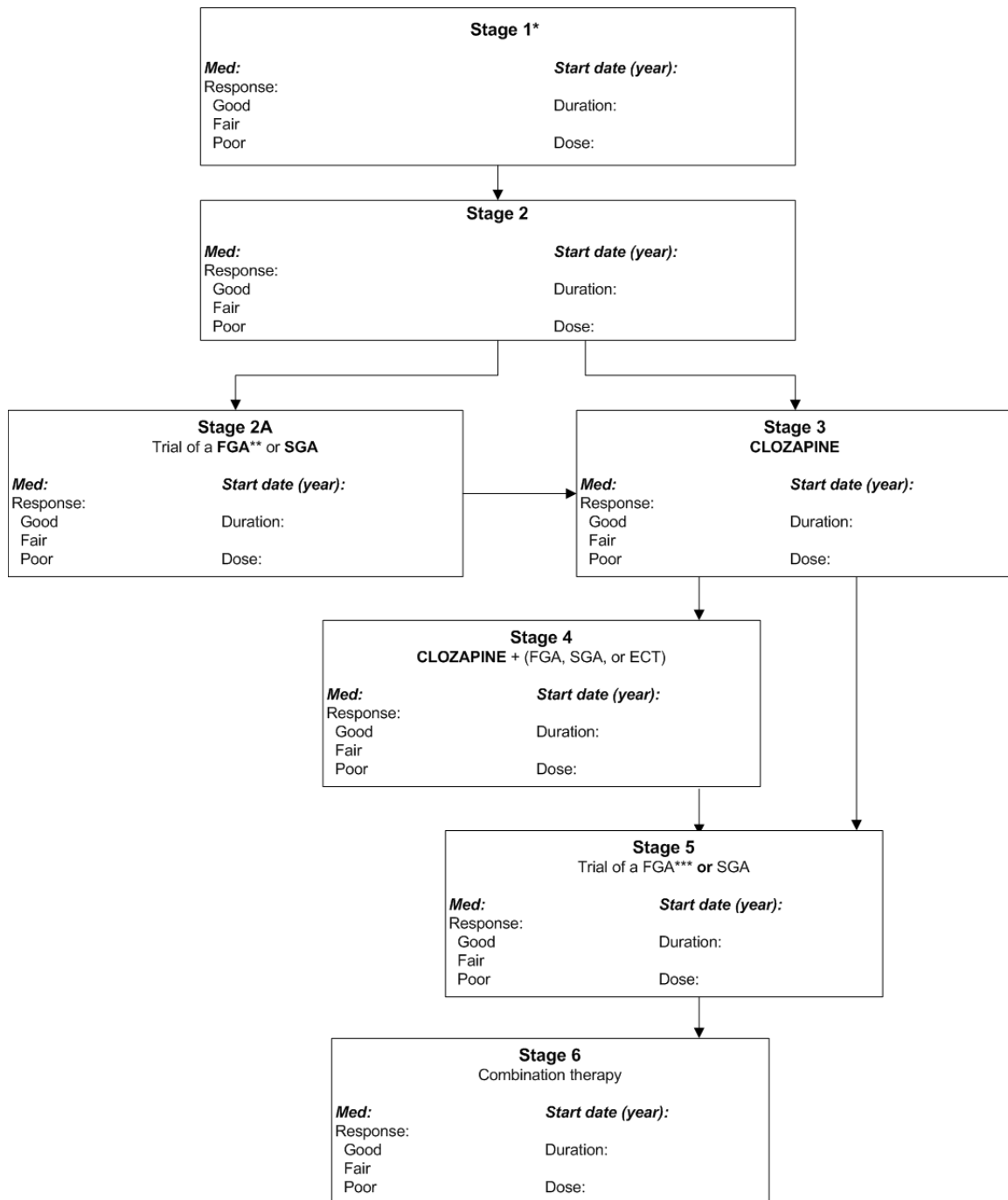
.

Appendix B:

Personal Algorithm Form

Fill in boxes using all available past and current information about antipsychotic treatments and responses

SCZ Patient Algorithm for: _____ Clinic ID # _____ Entered: _____



Appendix J:

Michigan Implementation of Medication Algorithms (MIMA)
Guidelines for Treating Major Depressive Disorder
MIMA Physician Procedural Manual

Michigan Implementation of Medication Algorithms (MIMA)

Guidelines for Treating Major Depressive Disorder

MIMA Physician Procedural Manual

2004

This manual is adapted from Madhukar H. Trivedi, Steven Shon, M. Lynn Crismon, and Tracie Kay, *Texas Implementation of Medication Algorithms (TIMA) Guidelines for Treating Major Depressive Disorder, TIMA Physician Procedural Manual, ed. 12/00* (Dallas, Texas: Depression Module Texas Medication Algorithm Project, 2000), available on the TIMA website: <http://www.mhmr.state.tx.us/centraloffice/medicaldirector/timasczman.pdf>.

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Notice

These guidelines reflect the state of knowledge, current at the time of publication, on effective and appropriate care, as well as clinical consensus judgments when knowledge is lacking. The inevitable changes in the state of scientific information and technology mandate that periodic review, updating, and revisions will be needed. These guidelines (algorithms) do not apply to all patients, and each must be adapted and tailored to each individual patient. Proper use, adaptation, modifications, or decisions to disregard these or other guidelines, in whole or in part, are entirely the responsibility of the clinician who uses the guidelines. The authors bear no responsibility for the use of these guidelines by third parties.

Address Correspondence to:

Michigan contact

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Overview of MIMA

The Michigan Implementation of Medication Algorithms (MIMA) presented here are part of a broader action plan aimed at encouraging greater use of evidence-based practice (EBP) in mental health care in Michigan. As the name suggests, these medication algorithms for major depression, bipolar disorder, and schizophrenia were adapted from the Texas Implementation of Medication Algorithms (TIMA) project, implemented in that state over the past five years.

Funding for the Michigan EBP project was provided by the Ethel and James Flinn Foundation of Detroit, in partnership with Public Sector Consultants Inc. of Lansing. The project goal, simply stated, was to develop an action plan that would bridge the gap between what is known and what is done in psychiatry, between scientific evidence and actual practice.

Both the MIMA and the action plan of which the algorithms are a part were developed by the project Steering Committee, a diverse group of Michigan mental health experts with demonstrated expertise in EBP. Subcommittees of the Steering Committee reviewed various publicly available algorithms and guidelines and ultimately endorsed those used in Texas on the grounds that they were scientifically sound, had been field-tested and evaluated, were regularly updated, and were part of a broader disease management program.

The disease management component warrants special emphasis. The MIMA should not be viewed in isolation but as part of a program that includes clinical and technical support for physicians and patients, patient/family education, uniform documentation of patient outcomes, and a quality management program. The various components of this multifaceted program will be pilot-tested and evaluated in several Michigan locales over the next few years, with the results informing follow-up EBP programs in the future.

The Michigan EBP project, like other similar projects across the country, was devised in response to accumulating evidence that there is a significant gap between the state of knowledge and the treatment of patients in clinical practice. In many fields of medicine, psychiatry included, practice lags years behind research findings. Research also demonstrates that there are wide variations in practice even within a single state. It is therefore reasonable to conclude that the practices of at least some clinicians vary substantially from what is known to be effective.

Part of the problem is “information overload.” It is impossible for any psychiatrist to keep up with all the developments in his or her field. Another aspect of the problem is the uncritical acceptance of information from sources such as friends and colleagues, flawed studies, or pharmaceutical companies.

EBP has been criticized as a cost-cutting approach that undermines the “art” of medicine. The express intent of the MIMA, however, is actually the reverse. The MIMA in no way trivialize the clinician’s role, but rather formalize what has long been the ideal of practice: the use of science to inform the art of medicine. Clinical expertise continues to play an important role in the MIMA by allowing the clinician to rapidly integrate

research evidence and/or the practice judgments of the broader medical community in making decisions about patient care. Rather than being “cookbook medicine,” the MIMA empower clinicians to make their own decisions about patient care, guided by the best available evidence to support those decisions.

Introduction to Algorithm Implementation

Algorithms go beyond guidelines in providing an explicit framework for clinical decision making. Algorithms do not dictate decisions, but rather provide an approach to clinical decision making that should yield similar answers in similar situations. The MIMA are not just general recommendations for medication treatment, they are also a systematic guide to the treatment of individual patients, which includes a number of critical factors: initial medication and dosage, dosage changes, methods and frequency of assessment, and minimum and maximum treatment periods.

Further, algorithms can be divided into *strategies* and *tactics*. Strategies are the various acceptable treatment regimen options for the care of an individual condition. Tactics address how optimally to implement a chosen regimen, and include such considerations as dose, monitoring, and how best to help an inadequately responding patient. Tactics also address the degree of symptom and functional improvement. As was the case with the TIMA, the MIMA presume that the aim of treatment is remission or the maximum possible improvement in cases where remission is not possible.

The MIMA approach is informed by the experience of Texas, which demonstrated that the successful implementation of algorithms is a human and social, as well as a technical, consideration. Assuring implementation of a treatment algorithm within a health care organization is a complex endeavor, requiring, in addition to research evidence, integrated changes in health care system design, patient and family education, and evaluation. Recommendations for just such a comprehensive, multifaceted approach are detailed in the Michigan EBP action plan.

Implementation of treatment algorithms is an evolutionary process, and change within systems does not occur without significant planning, goodwill, and effort. Yet the payoff in improved patient care is potentially enormous. Through an explicit process of algorithm implementation, evaluation, and revision, incremental improvements in many areas can result in major improvements in the overall quality of care.

At-a-Glance

Depression Medication Algorithms

Visit Frequency

Weekly contact (office visit or by phone) for the first four weeks of each stage; then every two weeks until 50 percent improvement in symptoms is maintained for at least one month; then every four weeks until 75 percent improvement is maintained for at least one month; then every three months. Support personnel may contact patients by phone if the physician is unable to see them.

Assessment Frequency

Quick Inventory of Depressive Symptomatology—Self-Report (QIDS-SR) may be used at each visit.

Duration of Acute Treatment

Until 75 percent symptom improvement is achieved for four weeks, then move to continuation phase. (See Critical Decision Points [CDP].)

Response

- No response (<25 percent improvement)
- Minimal response (25–50 percent improvement)
- Partial response (50–75 percent improvement)
- Full response/remission (75–100 percent improvement)

Criteria for Medication Change

Anything less than 75 percent improvement or full response **may** require a medication change.

Evaluations

At each visit, a physician assessment of core symptom severity, overall functional impairment, and side effect severity. Assessments, using QIDS-SR and patient global self-rating of symptom severity and side effects, should be done prior to patient contact with the physician.

Medication Switching

Discontinue or taper according to the table in **Exhibit 15** or the Guidelines for Switching Between Antidepressant Medications in Appendix F.

Medication Doses

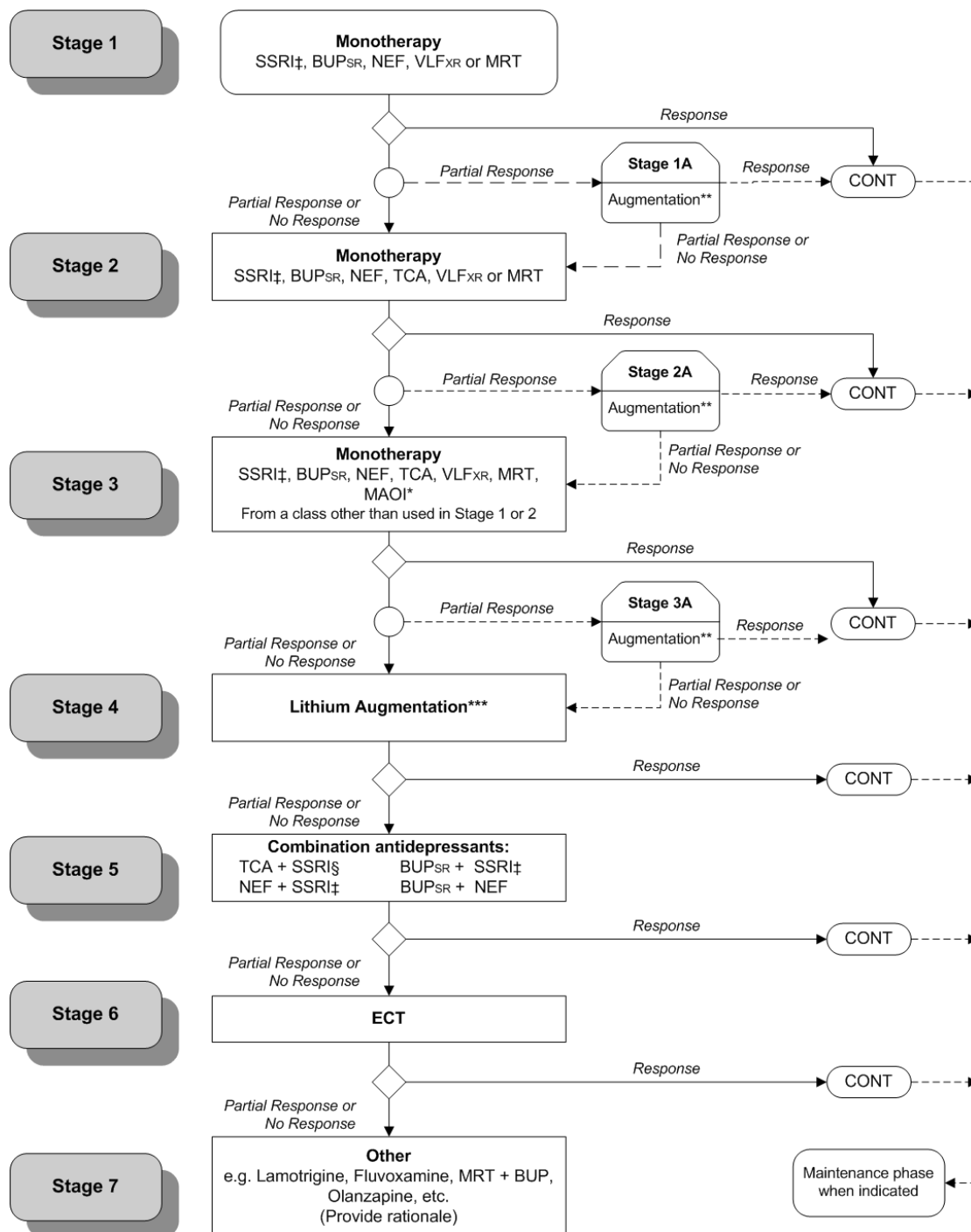
See Exhibits 6, 8, and 10 and the Guidelines in the Appendices for information on medications. Doses outside of the ranges should have a chart note indicating “change from algorithm recommended” and documentation of rationale for change.

Augmentation and Combination:

If a partial response is achieved, physicians may augment with lithium, thyroid medication (Cytomel), or buspirone to potentiate a greater response. A combination of two antidepressants, both at full doses, is suggested at Stage 5 of the algorithm.

EXHIBIT 1

Algorithm for the Treatment of Major Depression (Nonpsychotic)



*Consider TCA/VLF if not tried.

**Lithium, thyroid, buspirone.

***Skip if Li augmentation has already failed.

§ Most studied combination

‡ SSRI = Fluox, Sert, Parox, Cital.

EXHIBIT 2

Algorithm for the Treatment of Major Depression (Psychotic)

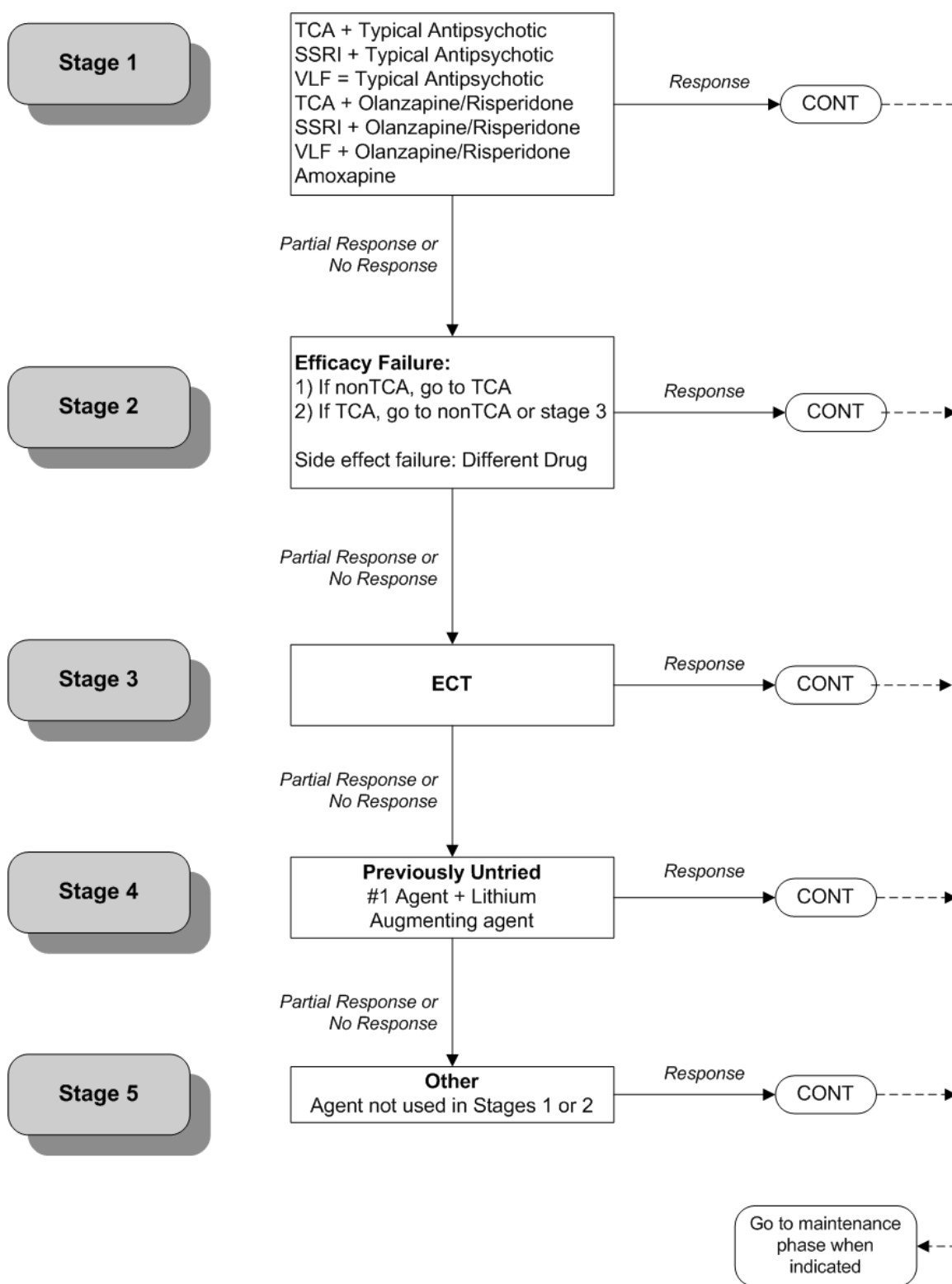
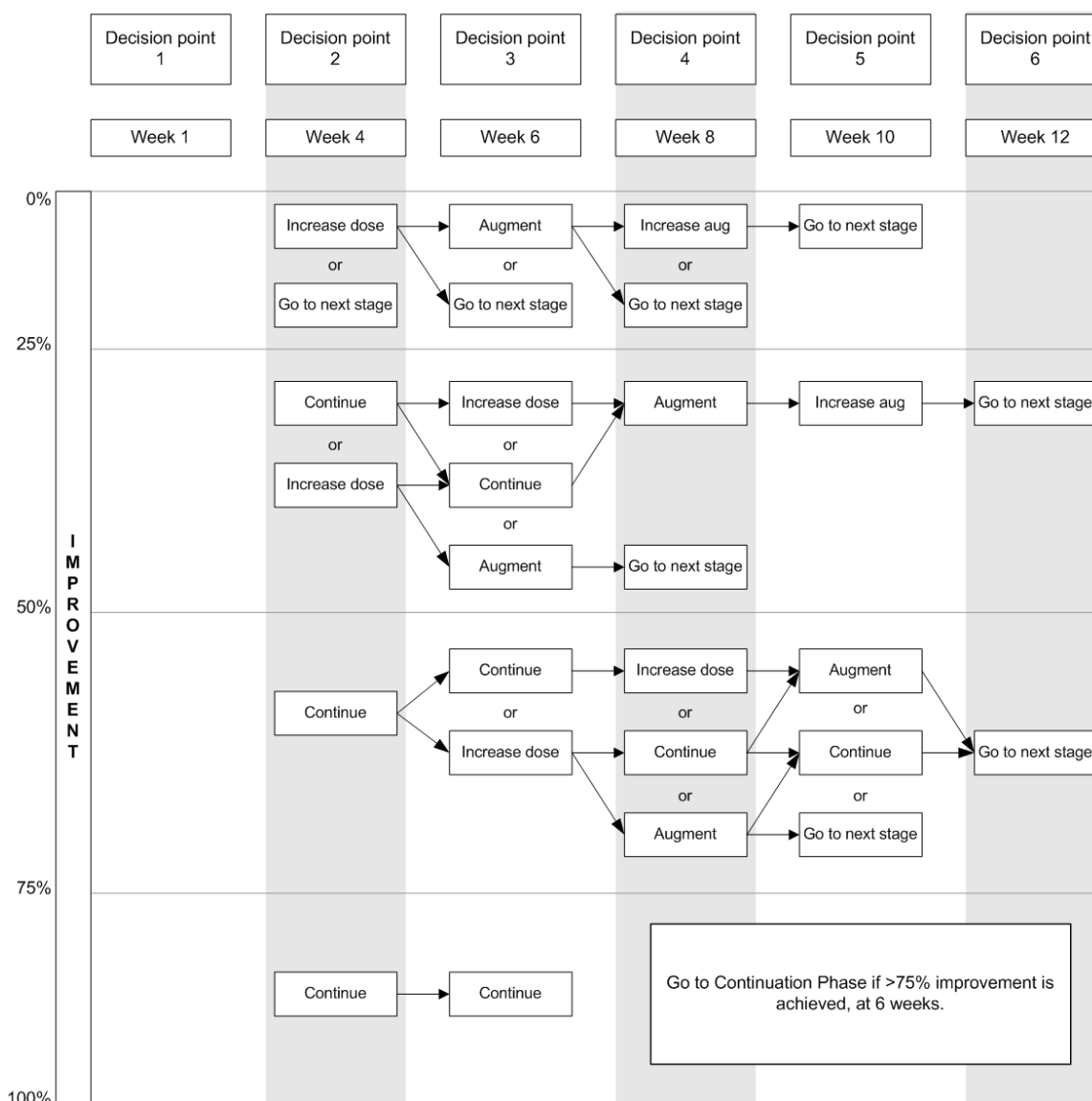


EXHIBIT 3

Critical Decision Points (CDPs) for Major Depressive Disorder: Tactics for the Treatment of Major Depression (Nonpsychotic)



TREATMENT OF DEPRESSION WITH ANTIDEPRESSANTS

- 50 percent of patients either do not receive adequate levels of antidepressants or are not treated for an adequate period of time.
- 10 to 20 percent of patients are intolerant to an initial trial of antidepressant medication.
- 25 to 30 percent of patients who complete an adequate trial do not show an acceptable response.

- The strategies for achieving remission include maximizing the dose as tolerated, switching to a different class if indicated, augmenting a partial response, or combining antidepressants when needed.

EXHIBIT 4

Strategies for Acute Phase Treatment of Major Depressive Episodes

Stage	Nonpsychotic depression	Psychotic depression
Stage 1	Monotherapy ^a SSRI, ^b Bupropion (BUP), Nefazodone (NEF), Venlafaxine (VLF), Mirtazapine (MRT) (A evidence ^c)	Antidepressant + Antipsychotic TCA + Antipsychotic (A-B evidence) ^d SSRI + Antipsychotic (B-C evidence) Amoxapine (B evidence) VLF + Antipsychotic (B-C evidence)
Stage 2	Monotherapy SSRI, BUP, NEF, VLF, Mirtazapine (MRT) OR a TCA EFFICACY FAILURE: Switch to another antidepressant. SIDE EFFECT FAILURE: Switch classes, or consider staying within the class if a contrasting SE profile is available or expected.	Antidepressant + Antipsychotic EFFICACY FAILURE: If nonTCA used in Stage 1, switch to TCA. If TCA used, try an antidepressant from a different class. SIDE EFFECT FAILURE: Switch to an agent from a different class.
Stage 3	Monotherapy SSRI, BUP, NEF, VLF, MRT, TCA or MAOI Choose a medication from a different class than used in Stage 1 or 2.	ECT If the patient refuses ECT or does not respond, go to the next stage or repeat an earlier stage with a different agent.
Stage 4	Augmentation Previously untried antidepressant + lithium, thyroid, ^e or buspirone Begin medications simultaneously.	Augmentation Previously untried treatment + lithium, thyroid, or buspirone Begin medications simultaneously.
Stage 5	Combination Therapy TCA + SSRI, SSRI + BUP, SSRI + NEF, BUP _{SR} + NEF	Other Any antidepressant + antipsychotic not tried in Stage 1 or 2
Stage 6	ECT If patient refuses ECT or does not respond, go to next stage or repeat an earlier stage with a different agent.	Other Any antidepressant + antipsychotic not tried previously
Stage 7	Other Any antidepressant or combination not previously tried	Other Any antidepressant + antipsychotic not tried previously

^a Acceptable antidepressants for Stage 1: Discuss treatment options with the patient and depending on prior treatment history, patient's clinical presentation, life style, and personal preferences, etc., assess the relative advantages of Stage 1 medications and make an initial treatment selection.

^b FDA-approved SSRIs for depression include: fluoxetine (FLU), paroxetine (PRX), sertraline (SERT), and citalopram (CIT).

^c Evidence level: A = controlled clinical trials; B = open trials and retrospective data analyses; C = clinical consensus and/or case reports.

^d Acceptable TCAs for psychotic depression include: desipramine (DMI), nortriptyline (NT), amitriptyline (AMI), clomipramine (CMI), or imipramine (IMI).

^e T₃ thyroid medication Cytomel (triiodothyronine) is suggested before T₄ Synthroid.

EXHIBIT 5

Critical Decision Points (CDPs) and Tactics for Acute Phase Treatment of Major Depression

(within each strategy stage, approaches to conducting a therapeutic trial with an antidepressant)

Critical decision point	Clinical status	Plan ^a
Week 1 (CDP 1)	Symptomatic	Initiate medication; adjust dose to lower end of therapeutic dose range or serum level.
Week 4 (CDP 2)	Full Response	Continue current dose.
	Partial Response ^b	<ul style="list-style-type: none"> Continue current dose. Consider increasing dose.
	Minimal or No response	<ul style="list-style-type: none"> Increase dose.^c Go to the next stage.
Week 6 (CDP 3)	Full Response	Go to continuation phase if full response sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	<ul style="list-style-type: none"> Maximize dose. Augment with lithium, thyroid, or buspirone.
	No response or minimal response	<ul style="list-style-type: none"> Augment with lithium or alternative augmenting agent. Go to the next stage.
Week 8 (CDP 4)	Full Response	Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	<ul style="list-style-type: none"> Augment with lithium or alternative augmenting agent. Go to the next stage.
	No response or minimal response to lithium or alternative augmentation for 2–3 weeks	Discontinue and go to the next stage.
Week 10 (CDP 5)	Full Response	Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	<ul style="list-style-type: none"> Adjust dose (antidepressant and/or augmentation dose). Go to the next stage.
	No response or minimal response	Go to the next stage.
Week 12 (CDP 6)	Full Response	Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Partial Response	Go to the next stage.

^aFor patients showing minimal or no response, total trial should not exceed 4–8 weeks. For patients with a partial response the trial may last up to 12 weeks to increase dose and implement augmentation strategy. Patients with only a partial response at any stage beyond 12 weeks should be considered for a medication change or a move to a subsequent treatment stage. In cases of treatment-resistant depression (TRD), longer trials may be necessary in later stages.

^bWith partial response, the clinician and patient assess both the absolute degree of improvement and the rate of improvement. No response is <25% improvement in overall symptoms, minimal response is 25–50% improvement in overall symptoms, partial response is 50–75% improvement in overall symptoms, full response is >75% improvement in overall symptoms.

^cIn patients with psychotic depression, dose increases may include the antidepressant, the antipsychotic, and/or the augmenting agent.

EXHIBIT 6
Antidepressant Dosing Used for Acute Phase Treatment of Depression

Type/Class	Medication	Initial target dose (level)	Maximum dose (level)	Recommended administration schedule
SSRI	Fluoxetine (Prozac)	20 mg	40–80 mg	QAM
	Paroxetine (Paxil)	20–30 mg	40–60 mg	QAM
	Sertraline (Zoloft)	50–100 mg	150–200 mg	QAM
	Citalopram (Celexa)	20 mg	60 mg	QAM
TCA	Amitriptyline	150–200 mg	300 mg	QHS
	Clomipramine	100–150 mg	250 mg	QHS
	Desipramine	150 mg (>125 ng/ml)	300 mg	QHS
	Imipramine	150 mg (IMI+DMI>200 ng/ml)	300 mg (200–400 ng/ml)	QHS
	Nortriptyline	75–100 mg (50–150 ng/ml)	150 mg (50–150 ng/ml)	QHS
Others	Amoxapine	200–300 mg	400 mg	QHS
	Bupropion SR (Wellbutrin SR)	200–300 mg	400 mg	BID≤200 mg/dose
	Bupropion (Wellbutrin)	225–300 mg	450 mg	TID≤150 mg/dose
	Mirtazapine (Remeron)	30 mg	60 mg	QHS
	Nefazodone (Serzone)	200–400 mg	600 mg	BID
	Venlafaxine (Effexor)	150–225 mg	375 mg	BID
	Venlafaxine XR (Effexor XR)	75–225 mg	225 mg	QD
MAOIs	Phenelzine	45–60 mg	90–120 mg	QD–TID
	Tranylcypromine	30–40 mg	60–80 mg	QD–TID

NOTE: Also refer to the Antidepressant Monographs in Appendix B.

EXHIBIT 7

Common Side Effects (SEs) for Antidepressant Medications

Medication	Common side effects ^a
SSRIs (Citalopram, Fluoxetine, Paroxetine, Sertraline, Fluvoxamine)	Dizziness, dry mouth, insomnia, agitation, nausea, sexual dysfunction, headache
Bupropion SR; Bupropion (immediate release)	Headache, agitation, weight loss, insomnia, nausea
Nefazodone	Dizziness, headache, nausea, somnolence, insomnia
Venlafaxine XR; Venlafaxine	Dizziness, somnolence, insomnia, decreased appetite, anxiety, headache, nausea, sexual dysfunction
TCAs (Amitriptyline, Clomipramine, Desipramine, Imipramine, Nortriptyline)	Sedation, dizziness, dry mouth, nausea, insomnia, anxiety, anticholinergic effects, tremor, constipation, blurred vision, arrhythmias
Amoxapine	Sedation, dizziness, dry mouth, nausea, anticholinergic effects, anxiety, insomnia, extrapyramidal reactions, seizures
Mirtazapine	Dizziness, diarrhea, increased appetite, drowsiness, dry mouth
MAOIs (Phenelzine, Tranylcypromine)	Restlessness, dizziness, blurred vision, diarrhea, insomnia, weakness, arrhythmias, headache, sexual dysfunction

^a For complete side effects information, consult with the official product labeling.

EXHIBIT 8

Dosing of Medications for Treatment of Associated Symptoms of Depression

Associated symptom	Medication	Usual dose range, mg/day	Schedule
Insomnia	Lorazepam	0.5–2.0 mg	QHS; taper after 7–10 days or as soon as possible
	Clonazepam	0.5–2.0 mg	
	Zolpidem	5–10 mg	
	Trazodone	25–100 mg	
Anxiety	Lorazepam ^a	0.5–4.0 mg	Q4–6h PRN throughout the day
	Alprazolam	0.75–4.0 mg	
	Clonazepam	1.5–3.0 mg	
Anxiety (if history of substance abuse or if benzodiazepines are contraindicated ^b)	Buspirone	15–60 mg	BID-TID
Severe Agitation	Lorazepam	0.5–2.0 mg	QD
	Clonazepam	0.5–2.0 mg	
	Alprazolam	0.75–4.0 mg	
	Propranolol	10–30 mg	

^a In general, treatment emergent side effects should be addressed first by dose reduction or medication switching, as pharmacological intervention may increase the risk of drug interaction and additional adverse effects, thus decreasing patient compliance.

^b Benzodiazepines are best avoided in patients with prior history of substance abuse/dependence or who are at risk for substance abuse. Nonaddicting agents such as zolpidem or buspirone may be preferred.

EXHIBIT 9

Dosing of Medications for Treatment-Emergent Side Effects

Treatment emergent side effect	Medication	Usual dose range (mg/day)	Schedule
Insomnia Due to Medication (especially SSRI, BUP, or VLF)	Lorazepam ^a	0.5–2.0 mg	QHS; taper as soon as possible
	Clonazepam	0.5–2.0 mg	
	Zolpidem	5–10 mg	
	Trazodone	25–100 mg	
EPS from Antipsychotic	Benztropine ^b	2–4 mg	QHS or BID
Sexual Dysfunction	Bupropion	75 mg	QD
	Amantadine	100–200 mg	
	Methylphenidate	10–15 mg	
	OR Consider switch to agent with low sexual side effects, such as bupropion, nefazodone, or mirtazapine		

^a In general, treatment emergent side effects should be addressed first by dose reduction or medication switching, as pharmacological intervention may increase the risk of drug interaction and additional adverse effects, thus decreasing patient compliance.

^b Benzodiazepines are best avoided in patients with prior history of substance abuse/dependence or who are at risk for substance abuse. Nonaddicting agents such as zolpidem or buspirone may be preferred.

EXHIBIT 10

Characteristics of Antidepressant-Induced Sexual Dysfunction

Antidepressant	Type of sexual dysfunction*	Incidence*
Venlafaxine	Impaired ejaculation, delayed/absent orgasm	12%
Paroxetine	Impaired ejaculation, delayed/absent orgasm	13–28% 2–10%
Fluvoxamine	Impaired ejaculation, delayed/absent orgasm	2–8%
Sertraline	Impaired ejaculation, delayed/absent orgasm	14%
Citalopram	Impaired ejaculation, delayed/absent orgasm, decreased libido	1–3%**
Fluoxetine	Impaired ejaculation, delayed/absent orgasm, decreased libido, and erectile impairment	2–11%
Mirtazapine	Decreased libido	2–6%**
Nefazodone	Decreased libido	1%**
Bupropion	Decreased libido	1–3%**
MAOIs	Impaired ejaculation, delayed/absent orgasm, erectile impairment, decreased libido	NA***
TCAs	Impaired ejaculation, delayed/absent orgasm, erectile impairment, decreased libido	NA***

*Based on AHFS drug information and R. M. Hirschfeld, *J Clin Psychiatry* 1999, 60 (suppl 14):27–30; A. J. Rothschild, *J Clin Psychiatry* 2000, 61 (suppl 11):28–36; and A. L. Montego-Gonzalez et al., *Journal of Sex & Marital Therapy* 1997, 23(3):176–94.

**No different than placebo.

***Case reports available.

NOTE: Higher incidences of sexual dysfunction have been reported in settings where patients are specifically queried about sexual problems.

TREATMENT OF PSYCHOTIC DEPRESSION

- Combination treatment with an antidepressant and antipsychotic agent has been shown to be significantly more effective than either given alone.
- Currently the majority of data in the treatment of psychotic depression has been demonstrated with tricyclic antidepressants and conventional antipsychotics, but data evaluating combinations of newer antidepressants and atypical antipsychotics is accumulating.
- The advent of atypical antipsychotics has greatly increased treatment options.
- Advantages of atypical antipsychotics include (a) lower incidence of extrapyramidal symptoms (EPS), (b) broader efficacy profile, and (c) minimal impact on prolactin concentrations with olanzapine and quetiapine.

EXHIBIT 11

Antipsychotic Dosing for Treatment of Psychotic Depression

Type/Class	Medication	Target dose (Level)	Maximum dose (level)	Recommended administration schedule
Atypicals	Olanzapine (Zyprexa)	10–15 mg	20 mg	QHS
	Risperidone (Risperdal)	2–4 mg	6 mg	BID or QD
	Quetiapine (Seroquel)	100–800 mg	800 mg	BID or TID
High potency	Haloperidol (Haldol)	2–5 mg	5–15 mg	QHS
Medium potency	Perphenazine (Trilafon)	8–16 mg	64 mg	QHS

NOTE: Also refer to the Antipsychotic Monographs in Appendix D.

EXHIBIT 12

Common Side Effects (SEs) of Antipsychotic Medications

Antipsychotic	EPS	Sedation	Tardive dyskinesia	Anticholinergic effects	Blood pressure	Sexual dysfunction	Weight gain
Clozapine (Clozaril)	+/-	++++	—	++++	+++	+	++++
Haloperidol (Haldol)	++++	+	++++	+	+	+	+
Olanzapine (Zyprexa)	+	++	+	++	+	—	+++
Risperidone (Risperdal)	++	+	+	+	+	+	++
Quetiapine (Seroquel)	+/-	++	?	+/-	++	—	++

— none + mild +/- mild to none ++ moderate +++ moderately severe ++++ severe ? unknown

TREATMENT OF DEPRESSION USING AUGMENTATION THERAPY

- In randomized controlled trials, at least 30 percent of depressed patients fail to respond to first-line antidepressant treatment, despite adequate dose, duration, and compliance.
- Up to 21 percent of patients with major depression who seek treatment have not recovered after two years.

- Augmentation of treatment can result in a more rapid response to antidepressant medication. Studies have shown that, among partial responders to serotonin reuptake inhibitors, patients demonstrate a higher recovery rate with augmented antidepressant therapy in comparison to antidepressant treatment alone, as assessed by scores on standardized depression rating scales.
- When an antidepressant medication elicits only partial response (25–75 percent), augmentation agents can potentiate an improved response, thus preventing the necessity of discontinuing the initial antidepressant.

EXHIBIT 13

Augmentation Dosing for Inadequate Response

Type/Class	Medication	Target dose (blood level)	Maximum dose (blood level)	Recommended administration schedule
Recommended Augmentation Agents	Lithium	600–1200 mg (0.4–0.6 mEq/L)	1200–1800 mg (0.8–1.0 mEq/L)	BID
	T3–Cytomel	25–50 µg	50 µg	QAM
	Buspirone	25–50 mg	45–60 mg	BID-TID
Other Augmenting Agents	Dextroamphetamine	5–30 mg	60 mg	QAM
	Methylphenidate	5–30 mg	40–60 mg	BID

NOTE: Also refer to the Monographs for Augmentation Agents in Appendix C.

EXHIBIT 14

Common Side Effects of Augmentation Agents

Medication	Side effects at therapeutic blood level
Lithium	Cognitive impairment, tremor, drowsiness, muscle weakness, nausea/vomiting, thirst, polyuria
Buspirone	Dizziness, nausea/vomiting, insomnia, dry mouth, nervousness
Cytomel	Insomnia, diarrhea, tremor, increased/decreased appetite, headache, heat intolerance, nausea

SWITCHING BETWEEN ANTIDEPRESSANT MEDICATIONS

The following principles apply to the tactics of switching antidepressant medications, depending on the reasons for switching and on the duration of exposure to the first agent.

- If the first antidepressant is being discontinued due to intolerance following a brief exposure (<7 days), it can be stopped and the second drug started.

- If the first drug is being discontinued after a longer exposure (≥ 7 days) due to symptomatic breakthrough or inadequate response, then it should be tapered and the second drug started gradually (notable exception being a switch from an MAOI).
- **Serotonin discontinuation syndrome** can occur following abrupt cessation of antidepressant therapy, particularly for those antidepressants with shorter half-lives (sertraline, paroxetine, fluvoxamine, citalopram) or no active metabolites. The syndrome is characterized by dizziness, insomnia, nervousness, nausea, and agitation. Initiating a medication taper does not always prevent its occurrence but may minimize severity.

EXHIBIT 15

Guidelines for Switching Between Antidepressant Medications

From	To	Plan
SSRI	SSRI	Discontinue SSRI 1 and begin SSRI 2; or Taper SSRI 1 and initiate SSRI 2.
SSRI	TCA Bupropion	Discontinue SSRI and begin TCA or bupropion; or taper SSRI and initiate TCA or bupropion gradually as tolerated to therapeutic dose range.
SSRI	Nefazodone Venlafaxine	Discontinue SSRI and begin nefazodone or venlafaxine; or taper SSRI and initiate nefazodone or venlafaxine gradually as tolerated to therapeutic dose range.
SSRI	MAOI	Discontinue SSRI. After a 5-week washout period for fluoxetine or a 2-week washout period for sertraline, paroxetine, or citalopram, MAOI therapy can safely be initiated.
TCA Venlafaxine Nefazodone Bupropion	TCA	Discontinue TCA 1 (or venlafaxine, nefazodone, bupropion) by taper and then initiate TCA 2; or taper TCA 1 (or venlafaxine, nefazodone, bupropion) while initiating TCA 2 gradually as tolerated to therapeutic dose range.
TCA Venlafaxine Nefazodone Bupropion	SSRI	Taper and discontinue TCA (or venlafaxine, nefazodone, bupropion) and then initiate SSRI; or taper TCA (or venlafaxine, nefazodone, bupropion) while initiating SSRI at a low dose.
TCA Venlafaxine Nefazodone Bupropion	Nefazodone Venlafaxine Bupropion	Discontinue TCA (or venlafaxine, nefazodone, bupropion) and initiate nefazodone, venlafaxine, or bupropion; or taper and discontinue TCA (or venlafaxine, nefazodone, bupropion) to initiate nefazodone, venlafaxine, or bupropion gradually as tolerated to therapeutic dose range.
TCA	MAOI	Discontinue TCA. After a 2-week washout, MAOI therapy can be safely initiated.
MAOI	MAOI Nefazodone Venlafaxine Bupropion	Discontinue MAOI 1. After a 2-week washout, therapy with MAOI 2 (or TCA, venlafaxine, nefazodone, or bupropion) can be safely initiated.

NOTE: Also refer to the Guidelines for Switching Between Antidepressant Medications in Appendix F for case examples.

COMBINING ANTIDEPRESSANTS FOR TREATMENT OF DEPRESSION

- Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in an adequate dose for a sufficient length of time.
- It is estimated that about 20 percent of depressed patients are resistant to monotherapy. Several studies have reported the efficacy of combining two antidepressants to treat patients with TRD.
- In general, because of the potential for drug interactions, antidepressant combination treatment should be used carefully, and patients monitored closely. The goal of combination antidepressant regimens is to combine medications to theoretically enhance clinical response.
- Stage 5 of the algorithm recommends combining two antidepressants. The medications should be initiated simultaneously at a low dose, then titrated upwards gradually to a therapeutically recommended dose.
- If a tricyclic antidepressant (TCA) is being used in combination treatment, plasma levels should be monitored.
- Because there is a risk of developing Serotonin Syndrome with combination antidepressant therapy, patients should be monitored for signs of confusion, disorientation, agitation, restlessness, diaphoresis, diarrhea, ataxia, and hyperreflexia.

EXHIBIT 16

Guidelines for Combining Antidepressant Medications

Combination	Plan
SSRI with TCA	Because SSRIs markedly increase blood levels of TCAs up to values exceeding therapeutically recommended ranges, serum levels of TCA should be monitored throughout treatment and adjusted accordingly.
SSRI with Bupropion SR	Monitor for agitation.
SSRI with Nefazodone	Initiate low dose of nefazodone as an addition to SSRI treatment, then gradually increase to therapeutic dose range. Monitor for increased side effects.
Other Combinations^a	
Bupropion SR with Nefazodone	Monitor side effects.
Venlafaxine with Mirtazapine	

^aNo systematic studies available as yet.

Algorithm Implementation

The purpose of treatment algorithms is to integrate available research information and clinical experience into the development of user-friendly, step-by-step “preferred practice,” medication guidelines, or medication algorithms. **Algorithms do not decrease the need for clinicians having adequate education and clinical training, nor are they intended to restrict treatment options.** Rather, they are designed to facilitate a systematic approach to recommended treatment interventions.

It is assumed that a comprehensive psychiatric evaluation, a complete general medical history, and relevant diagnostic tests are completed prior to entry into any treatment algorithm. Some patients may not be appropriate for entry into the algorithms. In addition, patients may enter the algorithms at different stages depending upon their specific clinical features and previous treatment history. For example, patients may enter Stage 2 or 3 if they have already failed to respond to an adequate trial of another antidepressant monotherapy.

Treatment algorithms are not a substitute for clinical assessment or clinical judgment. They are tools to assist clinicians in making clinical decisions to optimize therapeutic outcomes. The purpose of this document is to amplify the steps in implementing a medication algorithm in order to maximize effectiveness. We describe issues related to the strategic choices for pharmacological interventions based on the MIMA Depression Algorithm. Additionally, preferred tactical steps and critical decision points are described to enable users to best apply the strategy selected for implementation.

These algorithms focus on the pharmacotherapy and patient/family education for major depressive disorder. This does not imply that other nonpharmacological treatments including psychotherapy and rehabilitation are not indicated for the treatment of major depressive disorder (MDD). **Instead, this algorithm is restricted to a single focus: a multi-step medication approach in the treatment of patients with MDD.** Other modalities used in the treatment of mental disorders are sufficiently complex that it is felt that patient care can be best enhanced, initially, by utilizing algorithms that focus on one major aspect of treatment—in this case the use of pharmacological interventions. Additionally, patient and family education packages (**ED packages**) are also included in the overall protocol, since it is felt that proper implementation of the medication algorithm is enhanced through active participation of patients and families. Subsequent iterations may include psychological and rehabilitative services in the treatment package(s).

GENERAL MEDICAL PRINCIPLES GUIDING ALGORITHM IMPLEMENTATION:

Treatment Goals

The ultimate goal in the acute phase of treatment (1–12 weeks) is achieving symptomatic remission and full return of psychosocial functioning. The prevention of relapse and recurrence is the essential goal of the continuation and maintenance phases of treatment.

Medication Phasing

The treatment options recommended at various points in the algorithms are based upon available data from: (a) controlled clinical trials [Level A evidence]; (b) open trials and retrospective data analyses [Level B evidence]; and (c) case reports and clinical consensus [Level C evidence]. The later stages in the algorithm involve more complicated single or combined regimens, while the earlier stages involve simpler, more routine medications in terms of safety, ease of use, side effect profiles, etc.

Previous History

A patient's previous response to antidepressant treatments should always be considered when selecting the point of entry into an algorithm. If a patient responded well to a specific pharmacotherapy or other treatment intervention during a previous episode of depression, the same treatment should be used again. Similarly, if a patient failed to respond, or was unable to tolerate an adequate trial of a specific medication during a previous episode of depression, that medication is not recommended for the current or future depressive episodes.

Physician-Patient Team

An adequate discussion between the clinician and the patient regarding available treatment options and information concerning specific medications (including expected results, routine dosing strategies, possible side effects, drug interactions, as well as potential toxicity in overdose) is essential. Medication selection should be dependent on these factors. When these considerations suggest that several medications are equivalent, patient preference becomes paramount and should define the particular option selected. It has been well documented that patient participation during this process is likely to enhance compliance to the chosen treatment option.

Entering the Algorithm

Eligibility and point of entry into the algorithm for an individual patient should be determined by the physician based upon a review of relevant psychiatric factors (e.g., symptom severity, suicidality, comorbidity, etc.), medical status (e.g., concomitant medications or illnesses, age, etc.), and prior treatment history. **A rationale should be provided when a patient enters the algorithm at a later point/stage or when stages in the algorithm are skipped.**

Visit Frequency

At the beginning of each stage, weekly contact is recommended (office visit or by phone) for the first four weeks; then every other week until 50 percent improvement in symptoms is attained for at least four weeks; then once per month until 75 percent improvement has been attained for at least four weeks. After 75 percent improvement has been reached, visits may be scheduled monthly and then every three months as the patient moves into the maintenance phase of treatment. Increased visit frequency is recommended in an attempt to optimize treatment outcomes by: (a) encouraging patient adherence with treatment and (b) rapidly identifying and correcting potential problems or adverse events associated with treatment (e.g., worsening of depression, potential suicidal

ideology, etc.). Support personnel may contact patients by phone if the physician is unable to see them.

Treatment Duration

Response to a medication is enhanced by ensuring an adequate treatment trial of at least 4–8 weeks of administration at the recommended dose range. However, if a patient fails to respond to an adequate dose of a specific medication for 4–6 weeks or has an unsatisfactory or partial response by weeks 6–8, an alternative treatment plan is recommended. The duration of a treatment trial may be extended to 8–12 weeks if an augmentation strategy has been instituted in patients with a partial response.

Continuation Phase

Continuation phase treatment is recommended to prevent relapse for all patients with major depressive disorder who achieve a satisfactory clinical response, preferably symptom remission. After a full response, the medication(s) should be continued for 6–9 months at the dose effective during the acute phase. Patients should be evaluated at least once every three months during continuation treatment (preferably every 1–2 months). Interim phone calls are also recommended one week before medication refills to enhance adherence.

Maintenance Phase

Maintenance phase treatment is recommended for patients with major depressive disorder who: (a) have had at least three episodes of major depression, or (b) have experienced two episodes of major depression and have additional factors that contribute to an increased risk of recurrence (e.g., comorbid anxiety disorder or substantial residual functional impairment). Maintenance medication should be continued at full therapeutic doses and, as in the continuation phase, the regimen associated with symptom remission is recommended. The optimal duration of maintenance treatment has not been established, but depending on risk factors, is generally between one year past continuation phase and lifetime administration. Patients should be evaluated every 3–6 months during maintenance treatment.

Lack of Significant Improvement Despite Treatment

A Structured Clinical Interview for DSM-IV (SCID) or further evaluation of symptoms should be considered: (a) to confirm a diagnosis, (b) to reconfirm the diagnosis if there has been no response after three months, (c) if comorbid psychiatric conditions are present, or (d) if patient has failed on two different classes or stages of medications.

Documentation

Adequate documentation should be completed for each algorithm stage and treatment choice or critical decision point. If algorithm stages are skipped or if treatment deviates from the algorithm recommendations, the rationale behind the decision should be adequately documented.

Psychotherapy

At baseline and throughout treatment, possible psychosocial interventions, including psychotherapy, should be considered to optimize treatment. The protocol allows for the addition of psychotherapy if clinically indicated based on individual patient situations.

Treatment of Associated Symptoms and Side Effects

Adjunctive medications prescribed for the treatment of associated symptoms such as anxiety or treatment emergent side effects should be discontinued once these symptoms resolve. It should always be remembered that the prescription of additional medication also carries the risk of increased side effects. The rationale for their use should be carefully documented. The continued indication for these medications should be reassessed on a regular basis.

Critical Decision Points for the Nonpsychotic Depression Algorithm

Critical decision points (CDPs) are designed to prompt an assessment of symptoms and a determination of a need for a change in strategy or tactics. At each CDP, the physician should assess the patient for improvement and make a decision to either continue or change treatment based on improvement in symptoms or lack thereof. **Note:** Patients begin at CDP 1 at the beginning of each stage.

STAGES 1, 2, 3

Patients entered into one of these stages will be placed on a monotherapy treatment regimen. These medications are staged in the algorithm according to efficacy, side effect profile, and ease of use. Placement in the algorithm should be determined by the patient and physician based on prior history of antidepressant use, clinical presentation, and personal preferences.

Patients should return to the physician's office or be contacted by office personnel weekly (office visit or by phone) for the first four weeks of each treatment stage and then every two weeks until 50 percent improvement in symptoms is maintained for at least one month. Patients will then be evaluated monthly until 75 percent improvement is maintained for at least one month. Support personnel may contact patients by phone if the physician is unable to see them.

CDP 1, Week 1

Inclusion Criteria:

Patients entering Stages 1, 2, or 3 of the nonpsychotic algorithm should have a diagnosis of major depressive disorder of sufficient severity to merit medication treatment; they should (a) have not been on any antidepressant medication for the current episode of MDD or (b) need a medication change to another monotherapy antidepressant.

Treatment Options:

Stage 1:

- Selective serotonin reuptake inhibitors (SSRIs)—citalopram, fluoxetine, paroxetine, sertraline
- Venlafaxine XR
- Bupropion SR
- Nefazodone
- Mirtazapine

Stage 2:

- Selective serotonin reuptake inhibitors (SSRIs)—citalopram, fluoxetine, paroxetine, sertraline
- Venlafaxine XR

- Bupropion SR
- Nefazodone
- Mirtazapine
- Tricyclic Antidepressants (TCAs)—desipramine, nortriptyline, etc. **Note:** In general, secondary amines should be tried before tertiary amines.

Stage 3:

- Selective Serotonin Reuptake Inhibitors (SSRIs)—citalopram, fluoxetine, paroxetine, sertraline
- Venlafaxine XR
- Bupropion SR
- Nefazodone
- Mirtazapine
- Tricyclic Antidepressants (TCAs)—desipramine, nortriptyline, etc. **Note:** In general, secondary amines should be tried before tertiary amines.
- MAOIs

Stages 2–7 are summarized in the following tables.

EXHIBIT 17

CDP 2–6, Stages 1, 2, and 3 Nonpsychotic MDD

CDP 2, Week 4		Stages 1, 2, and 3 Nonpsychotic MDD
Symptom Improvement (SEs tolerable)		
0–50%		Gradually increase dose as tolerated for an additional 2 weeks.
50–75%		Continue current dose; or gradually increase dose as tolerated for an additional 2 weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose and address SEs, or Decrease dose and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		Return in 2 weeks.
CDP 3, Week 6		Stages 1, 2, and 3 Nonpsychotic MDD
Symptom Improvement (SEs tolerable)		
0–25%		Strongly consider augmenting (refer to the Guidelines for Augmentation Therapy in Appendix C); or go to the next stage.
25–50%		If dose was not increased at Week 4, increase dose; or if dose was increased at Week 4, augment or continue with current treatment.
50–75%		Increase dose; or consider augmentation.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose and address SEs; or decrease dose and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.

Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 4, Week 8	Stages 1, 2, and 3 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–25%	Increase augmentation; or go to the next stage.
25–50%	Augment, if not done previously; or go to the next stage.
50–75%	Maximize dose, if not done previously; or consider augmentation.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable	Go to the next stage.
Return to physician's office	If > 50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 5, Week 10	Stages 1, 2, and 3 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–25%	Go to the next stage.
25–50%	Increase augmentation.
50–75%	Increase augmentation; or Go to the next stage.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable	Go to the next stage.
Return to physician's office	If > 50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 6, Week 12	Stages 1, 2, and 3 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–75%	Go to the next stage.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable	Go to the next stage.
Return to physician's office	If > 50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

STAGE 4

Clinical trials suggest that at least 30 percent of depressed patients fail to respond to first-line antidepressant treatment, despite adequate dose, duration, and compliance. In addition, up to 21 percent of patients with major depression who seek treatment have not recovered after two years. Clinicians have developed various pharmacological strategies to treat such refractory depression, including augmentation of therapy with thyroid (T₃ - Cytomel) medication, lithium, or bupirone. Studies have shown that, among nonresponders to serotonin reuptake inhibitors, patients demonstrate a higher recovery rate with augmented antidepressant therapy in comparison to antidepressant treatment alone, as assessed by scores on standardized depression rating scales. These augmentation strategies have clearly illustrated an efficacy and clinical utility, possibly resulting in complete or near-complete recovery in up to 60 percent of cases.

CDP 1, Week 1

Inclusion Criteria

Stage 4 includes patients from Stages 1–3 who (a) did not have a full response or (b) were unable to tolerate side effects. Patients may enter at or skip to Stage 4 if their previous history or current condition suggests that Stage 4 is most clinically appropriate.

Treatment Option

An antidepressant, preferably from a different class not tried in Stages 1–3, augmented by either lithium, bupropion, or a thyroid agent. Both medications should be started at the same time, following critical decision points outlined in Exhibit 5 and the CDP Flowchart (Exhibit 3). If lithium augmentation was not used in a previous stage, consider using it here due to Level A evidence of lithium augmentation.

EXHIBIT 18 CDP 2–6, Stage 4 Nonpsychotic MDD

CDP 2, Week 4	Stage 4 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Gradually increase antidepressant dose as tolerated and continue for an additional 2 weeks and/or increase the dose of the augmenting agent. See Exhibits 6 and 13 for dosing. Note: A gradual dose increase is critical for the Stage 4 antidepressants since response is enhanced by titration within a therapeutic dose range.
50–75%	Continue current dose(s); or gradually increase the dose(s) as tolerated.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
Improved, but SEs are intolerable	Continue current dose(s) and address side effects; or decrease dose(s) and continue; or go to the next stage.
Not improved and SEs are intolerable	Go to the next stage.
Return to physician's office	Return in 2 weeks.
CDP 3, Week 6	Stage 4 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–25%	Maximize the antidepressant dose and/or augmentation dose.
25–50%	Maximize the antidepressant dose and attain lithium serum levels of 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy.
50–75%	Continue with current dose(s); or gradually increase the antidepressant dose; or if already at maximum dose of the antidepressant, increase the dose of augmentation dose (if not at maximum).
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. <i>Otherwise</i> , continue current dose.
Improved, but SEs are intolerable:	Continue current dose(s) and address side effects; or decrease dose(s) and continue, or go to the next stage.
Not improved and SEs are intolerable	Go to the next stage.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. <i>Otherwise</i> , return in 2 weeks.

CDP 4, Week 8		Stage 4 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Increase augmentation dose, if not at maximum.
50–75%		If patient is at maximal tolerable therapeutic dose, consider an alternative augmenting agent; or continue with current dose(s).
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 5, Week 10		Stage 4 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–25%		Go to the next stage.
25–50%		Increase augmentation dose.
50–75%		Maximize the antidepressant dose and increase augmentation dose to achieve a lithium steady-state serum concentration of 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy; or if the patient is receiving the maximal therapeutic lithium or alternative augmentation agent dose, go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 6, Week 12		Stage 4 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Go to the next stage.
50–75%		Maximize the antidepressant dose and maximize augmentation dose to achieve a lithium steady-state serum concentration of 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy; or if the patient is receiving the maximal therapeutic lithium or alternative augmentation agent dose, go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

STAGE 5

Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in adequate doses for sufficient lengths of time. It is estimated that about 20 percent of depressed patients are resistant to monotherapy. Several studies have reported the efficacy of combining two antidepressants to treat patients with TRD.

CDP 1, Week 1

Inclusion Criteria

Stage 5 includes patients who did not have a full response during Stage 4 or who had intolerable side effects.

Treatment Options

Antidepressant combination therapy may be considered if patients have failed to respond in previous stages. If a TCA or SSRI is being used as monotherapy, consider a TCA/SSRI combination [Level B evidence]. Both antidepressants should be initiated simultaneously. Since the SSRIs—particularly fluoxetine and paroxetine—may inhibit the metabolism of TCAs, close monitoring of TCA serum concentrations should occur during TCA/SSRI combination treatment [Level A evidence]. Because of norfluoxetine's long elimination half-life, maximum effects of fluoxetine on elevation of the TCA serum concentrations may not be observed for 4–6 weeks. If a TCA is added to an SSRI, it will not take this long, as maximal enzyme inhibition will have already occurred and time to steady state is dependent on the particular TCA used. The goal is to obtain two serial TCA levels—at least one week apart—that are essentially the same. Since evidence for the efficacy of other antidepressant combinations is derived entirely from case series, they are recommended only as additional options at this stage.

In general, because of the potential for drug interactions, antidepressant combination treatment should be used carefully, and patients monitored closely. The goal of combination antidepressant regimens is to combine medications to theoretically enhance clinical response.

Considerable care is required to obviate potential drug interactions associated with combined regimens. Exhibit 16 is provided as a guideline for the tactic of antidepressant combinations. Other treatment tactics included in Stage 5 are identical to those outlined in Stage 4.

EXHIBIT 19

CDP 2–6, Stage 5 Nonpsychotic MDD

CDP 2, Week 4	Stage 5 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Gradually increase dose(s) as tolerated for an additional 2 weeks.
50–75%	Continue current dose(s); or gradually increase dose(s) as tolerated for an additional 2 weeks.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable	Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or go to the next stage.
Not improved and SEs are intolerable	Go to the next stage.
Return to physician's office	Return in 2 weeks.

CDP 3, Week 6		Stage 5 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Go to the next stage.
50–75%		Continue current dose(s); or gradually increase dose(s) as tolerated for an additional 2 weeks; or increase to maximum therapeutic dose(s) and continue to monitor for an additional 2 weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 4, Week 8		Stage 5 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–75%		Go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue with current dose(s) and address side effects, <i>or</i> Decrease dose(s) and continue; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 5, Week 10		Stage 5 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–75%		Go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 6, Week 12		
<i>Symptom Improvement (SEs tolerable):</i>		
0–75%		Go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

STAGE 6

Electroconvulsive therapy (ECT) has been shown to be an effective treatment option for mentally ill patients who are nonresponders to antidepressant medications or intolerant of the side effects. Patient groups expected to be favorable responders to ECT are manic-

depressive and psychotic depressive patients. The antidepressive effects of ECT are immediate and comprehensive, and can elicit an improved response from medication when used in combination. Schizophrenia patients have also derived benefits from ECT therapy, when administered concurrently with antipsychotic medication.

CDP 1, Week 1

Inclusion Criteria

Stage 6 includes patients who did not have a full response during Stages 4 or 5 or who were unable to tolerate side effects. Depending on a patient's current condition or past treatment history, a patient may initially enter the algorithm at Stage 6. For example, a severely depressed patient with significant risk of suicide should be considered for initial entry at Stage 6—treatment with ECT.

Treatment Options

Stage 6 treatment is ECT. If the patient refuses ECT, or if ECT is unavailable or contraindicated, go to Stage 7.

As cognitive side effects are generally less severe compared with bilateral ECT, treatment may begin with right unilateral ECT. However, before declaring a patient resistant to ECT, a course of bilateral ECT should be considered. The electrical dose of right unilateral ECT should be at least 2.5 times the initial seizure threshold, while bilateral ECT should be dosed no more than 1.5 times the initial threshold. ECT should be terminated when patients are in full remission or fail to sustain additional improvement over 1–2 treatments. With either ECT modality, at least 6–10 ECT treatments should be attempted before declaring a patient resistant to treatment. (**Note:** Avoid ECT when the patient is taking lithium because central nervous system (CNS) lithium toxicity may ensue.)

STAGE 7

Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in adequate doses for sufficient lengths of time. It is estimated that about 20 percent of depressed patients are resistant to monotherapy. If a patient has not attained complete remission of symptoms after adequate trials of medication treatment, then it may be necessary to accept partial response (25–75 percent) as a satisfactory outcome. The duration of critical decision points (CDPs) may need to be extended in order to allow slow responders a longer period of time on their medication.

CDP 1, Week 1

Inclusion Criteria

Stage 7 includes patients who fail to fully respond during Stages 1–6 (including patients who refuse consent to ECT) or who are unable to tolerate side effects.

Treatment Options

Stage 7 includes the alternatives not used previously during earlier stages (e.g., olanzapine, lamotrigine, or one of the newer antidepressants). It also includes other antidepressant combinations (not included in Stage 5) that are more speculative than those previously discussed in earlier stages. Alternative augmenting agents such as **T₃**, buspirone, and methylphenidate are also included in Stage 7. At Stage 7, combinations of antidepressants or antidepressants plus an alternative augmenting agent are preferable to a monotherapy not previously tried. Even though stage(s) can be skipped in the algorithm, Stage 7 is most likely to be indicated for those patients who have already failed to respond to multiple earlier stages in the algorithm.

Antidepressant Switching Tactics

Because of the possibility of drug interactions, care should be taken when switching from one antidepressant to another. Please refer to Exhibit 15 and Appendix F for guidelines concerning switching from one antidepressant to another.

EXHIBIT 20 CDP 2–6, Stage 7 Nonpsychotic MDD

CDP 2, Week 4	Stage 7 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Gradually increase dose(s) as tolerated for an additional 2 weeks.
50–75%	Continue current dose(s); or gradually increase dose(s) as tolerated for an additional 2 weeks.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable	Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP 1.
Not improved and SEs are intolerable	Consider consultation.
Return to physician's office	Return in 2 weeks.
CDP 3, Week 6	Stage 7 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Consider switching to an alternative medication. If beginning a trial of an antidepressant, return to CDP 1.
50–75%	Continue current dose(s); or gradually increase dose as tolerated for an additional 2 weeks.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable	Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP 1.
Not improved and SEs are intolerable	Consider consultation.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

CDP 4, Week 8	Stage 7 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Consider consultation.
50–75%	If patient is at maximum tolerable therapeutic dose(s). Consider consultation.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable	Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP 1.
Not improved and SEs are intolerable	Consider consultation.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 5, Week 10	Stage 7 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Consider consultation.
50–75%	If patient is at maximum tolerable therapeutic dose(s). Consider consultation.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable	Continue with current dose(s) and address side effects; or decrease dose(s) and continue; or consider switching to an alternative medication. If beginning a trial of a second antidepressant, go back to CDP 1.
Not improved and SEs are intolerable	Consider consultation.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 6, Week 12	Stage 7 Nonpsychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–75%	Consider consultation.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable	Consider consultation.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

Critical Decision Points for the Psychotic Depression Algorithm

Critical decision points (CDPs) are designed to prompt an assessment of symptoms and a determination of a need for a change in strategy or tactics. At each critical decision point, the physician should assess the patient for improvement and make a decision to either continue or change treatment based on improvement in symptoms or lack thereof. **Note:** Patients begin at CDP 1 at the beginning of each stage.

STAGE 1

The advent of a new generation of antipsychotic medications has opened up more treatment options for psychiatrists in treating disorders with psychotic symptoms. The newer medications, signified as “atypical” antipsychotics, have several advantages over their predecessors and are more desirable candidates for this patient population. These include: olanzapine (Zyprexa), risperidone (Risperdal), and quetiapine (Seroquel). Notable benefits include a lower incidence of extrapyramidal symptoms, a broader efficacy profile—particularly with negative symptoms—and minimal impact on prolactin concentrations (olanzapine and quetiapine). Older antipsychotic agents have demonstrated a higher incidence of problematic side effects that hinder their use. Combination treatment with an antidepressant and an antipsychotic agent has shown to be significantly more effective than either given alone. Initial findings have demonstrated this with tricyclics and conventional antipsychotics, and data evaluating combinations of newer antidepressants and atypical antipsychotics are now accumulating.

Patients should return to the physician’s office or be contacted by office personnel weekly for the first four weeks of each treatment stage; then every other week until 50 percent improvement is maintained for at least one month; then every four weeks until 75 percent improvement is maintained for at least one month.

CDP 1, Week 1

Inclusion Criteria

The patient entered into the algorithm at Stage 1 is most likely either experiencing his/her first episode of major depression complicated by psychotic features or has previously responded to a Stage 1 regimen during a past episode.

Treatment Options

- A tricyclic antidepressant (TCA) [amitriptyline, clomipramine, desipramine, imipramine, or nortriptyline] plus an antipsychotic [Level A evidence]; or
- A serotonin selective reuptake inhibitor (SSRI) plus an antipsychotic or venlafaxine XR plus an antipsychotic, [Level B evidence]; or
- Amoxapine [Level A evidence]

Stages 2–5 are summarized in the following tables.

EXHIBIT 21

CDP 2–6, Stage 1 Psychotic MDD

CDP 2, Week 4		Stage 1 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Gradually increase dose(s) as tolerated for an additional 2 weeks.
50–75%		Continue current dose(s); or gradually increase dose(s) as tolerated for an additional 2 weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose of drug thought to be causing side effect (i.e., antidepressant or antipsychotic) and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		Return in 2 weeks.
CDP 3, Week 6		Stage 1 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–25%		Strongly consider augmenting (refer to the Monographs for Augmentation Agents in Appendix C); or go to the next stage.
25–50%		If dose(s) were not increased at Week 4, increase dose(s). If dose(s) were increased at Week 4, augment or continue with current treatment.
50–75%		Increase dose(s); or consider augmentation.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 4, Week 8		Stage 1 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–25%		Increase augmentation; or go to the next stage.
25–50%		Augment if not done previously; or go to the next stage.
50–75%		Increase dose(s); or consider augmentation.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

CDP 5, Week 10		Stage 1 Psychotic MDD
Symptom Improvement (SEs tolerable):		
0–25%		Go to the next stage.
25–50%		Increase augmentation.
50–75%		Increase augmentation; or go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 6, Week 12		Stage 1 Psychotic MDD
Symptom Improvement (SEs tolerable):		
0–25%		Go to the next stage.
25–50%		Increase augmentation.
50–75%		Go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If > 50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

STAGE 2

CDP 1, Week 1

Inclusion Criteria

Stage 2 includes patients who did not have a full response at Stage 1 or who were unable to tolerate side effects. Patients may enter the algorithm at Stage 2 if their history of response during previous depressive episodes suggests that Stage 1 is not appropriate. If the patient's clinical presentation dictates a need for more immediate clinical response (e.g., emergent suicidality) or if the patient has a history of previous response to ECT, entry at Stage 3 should be considered.

Treatment Options

- Patient did not have full response at Stage 1.
 - If the patient received a TCA during Stage 1 and did not respond, consider venlafaxine XR (increase the dose to >225 mg/QD) with an antipsychotic or proceed to Stage 3 (ECT).
 - If an SSRI was the antidepressant used in Stage 1, consider a TCA with an antipsychotic.
 - If amoxapine was the antidepressant used in Stage 1, consider a TCA with an antipsychotic.
- If the patient did not respond during Stage 1 due to intolerable side effects, select an antidepressant from a different class than the previous choice and with a contrasting

side effect profile (e.g., from a TCA to an SSRI). If a patient is unable to tolerate two different antidepressant monotherapies from distinct chemical classes, consider proceeding to Stage 3.

- The tactics for drug treatment in Stage 2 are essentially the same as those outlined in Stage 1. Patients should be initiated with doses of antidepressants at the lower end of the therapeutic range and the dose gradually increased as tolerated if response is not attained. Patients should be seen and monitored frequently during the initial month. At week four, if full response is absent, response and medication tolerability should be assessed. Further assessments at subsequent critical time points on a 2-week basis should be completed to assess for dose increase as outlined in treatment tactics (see Exhibit 5).

EXHIBIT 22

CDP 2–5, Stage 2 Psychotic MDD

CDP 2, Week 4	Stage 2 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	Increase antidepressant dose to a maximal therapeutic level and continue for two additional weeks.
50–75%	Continue current antidepressant dose; or gradually increase antidepressant dose as tolerated to a maximal therapeutic range.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current antidepressant dose.
Improved, but SEs are intolerable	Continue current antidepressant dose and address side effects; or decrease antidepressant dose and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable	Go to the next stage.
Return to physician's office	Return in 2 weeks.
CDP 3, Week 6	Stage 2 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–50%	If the antidepressant dose was maximized at week 4, go to the next stage; or if the antidepressant dose was not maximized at week 4, increase the dose to the maximum therapeutic level (monitor serum concentration for TCAs).
50–75%	Continue current antidepressant dose; or gradually increase antidepressant dose as tolerated to a maximal therapeutic range.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable	Continue current antidepressant dose and address side effects; or decrease antidepressant dose and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable	Go to the next stage.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

CDP 4, Week 8		Stage 2 Psychotic MDD
Symptom Improvement (SEs tolerable):		
0–50%		Go to the next stage.
50–75%		Continue at maximal doses for 2 additional weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 5, Week 10		Stage 2 Psychotic MDD
Symptom Improvement (SEs tolerable):		
0–75%		Go to the next stage.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

STAGE 3

Electroconvulsive therapy (ECT) has been shown to be an effective treatment option for mentally ill patients who are nonresponders to antidepressant medications or intolerant of the side effects. Patient groups expected to be favorable responders to ECT are manic-depressive and psychotic depressive patients. The antidepressive effects of ECT are immediate and comprehensive, and can elicit an improved response from medication when used in combination. Schizophrenia patients have also derived benefits from ECT therapy, when it is administered concurrently with antipsychotic medication.

Inclusion Criteria

Stage 3 includes patients who did not have a full response at Stage 2 or who were unable to tolerate side effects. Patients may enter the algorithm at Stage 3 if their current condition, associated features, or history of response during a previous depressive episode suggest that Stage 1 or 2 is not appropriate or is contraindicated. If the patient's clinical presentation warrants a more immediate clinical response (e.g., emergent suicidality) or history of previous response to ECT, entry at Stage 3 should be considered.

Treatment Options

- Stage 3 treatment is ECT.

As cognitive side effects are generally less severe compared with bilateral ECT, treatment may begin with right unilateral ECT. However, before declaring a patient resistant to ECT, a course of bilateral ECT should be considered. The electrical dose of right unilateral ECT should be at least 2.5 times the initial seizure threshold, while bilateral ECT should be dosed no more than 1.5 times the initial threshold. ECT should be terminated when patients are in full remission or fail to sustain additional improvement over 1–2 treatments. With either ECT modality, at least 6–10 ECT

treatments should be attempted before declaring a patient resistant to treatment. (**Note:** Avoid ECT when the patient is taking lithium because central nervous system (CNS) lithium toxicity may ensue.)

- In general, any antidepressant or antipsychotic medication should be discontinued before initiating ECT.
- If a patient does not give informed consent for ECT, fails to respond to ECT, or ECT is not available, proceed to Stage 4.

STAGE 4

Clinical trials suggest that at least 30 percent of depressed patients fail to respond to first-line antidepressant treatment, despite adequate dose, duration, and compliance. In addition, up to 21 percent of patients with major depression who seek treatment have not recovered after two years. Clinicians have developed various pharmacological strategies to treat such refractory depression, including augmentation of therapy with thyroid (T₃-Cytomel) medication, lithium, and buspirone. Studies have shown that, among partial responders to serotonin reuptake inhibitors, patients demonstrate a higher recovery rate with augmented antidepressant therapy in comparison to antidepressant treatment alone, as assessed by scores on standardized depression rating scales. These augmentation strategies have clearly illustrated an efficacy and clinical utility, possibly resulting in complete or near-complete recovery in up to 60 percent of cases.

CDP 1, Week 1

Inclusion Criteria

Stage 4 includes patients from Stage 3 who (a) did not have a full response or (b) were unable to tolerate side effects. Patients may enter or skip to Stage 4 if their previous history or current condition suggests that Stage 4 is most clinically appropriate.

If the patient did not have a full response to any of the combinations in Stages 1 or 2, Stage 4 should be completed prior to beginning Stage 5.

Treatment Options:

At least one attempt at lithium augmentation should be initiated (unless contraindicated) before proceeding to Stage 5. Both the antidepressant and the augmenting agent should be started simultaneously.

If the patient fails an adequate trial of lithium augmentation (or is unable to tolerate lithium), alternative augmenting agents such as T₃ or buspirone should be strongly considered.

EXHIBIT 23

CDP 2–5, Stage 4 Psychotic MDD

CDP 2, Week 4		Stage 4 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Increase antidepressant dose to a maximal therapeutic level and continue for two additional weeks.
50–75%		Continue current dose(s); or gradually increase dose(s) as tolerated to a range of 0.4–0.8 mEq/L for lithium or the maximal therapeutic dose for the selected augmentation strategy and to the therapeutic range appropriate for the antidepressant.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue for 2 additional weeks; or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		Return in 2 weeks.
CDP 3, Week 6		Stage 4 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		If the antidepressant dose was already maximized at week 4, increase the lithium dose so that serum levels between 0.8–1.2 mEq/L are attained or the maximal therapeutic dose for the selected augmentation strategy; or if the antidepressant dose was not maximized at week 4 and the patient is currently tolerating the antidepressant, the dose should be increased to the usual maximum dose (monitor serum concentration for TCAs).
50–75%		If the antidepressant dose was maximized at week 4, continue current dose(s) for an additional 2 weeks; or maximize the antidepressant dose within the therapeutic range and the lithium dose should be increased to 0.8–1.2 mEq/L or the maximal therapeutic dose for the selected augmentation strategy for an additional 2 weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose(s).
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue for 2 additional weeks; or consider switching medications if side effects are attributable to a particular medication, or go to the next stage.
Not improved and SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP 4, Week 8		Stage 4 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Go to the next stage.
50–75%		Continue at maximal doses for 2 additional weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current doses.
SEs are intolerable		Go to the next stage.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

CDP 5, Week 10	Stage 4 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–75%	Go to the next stage.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable	Go to the next stage.
Return to physician's office	If > 50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

STAGE 5

Treatment-resistant depression (TRD) is defined as depression that is resistant to two courses of monotherapy with pharmacologically different antidepressants given in an adequate dose for a sufficient length of time. It is estimated that about 20 percent of depressed patients are resistant to monotherapy. If a patient has not attained complete remission of symptoms after adequate trials of medication treatment, then it may be necessary to accept partial response (25–75 percent) as a satisfactory outcome. The duration of critical decision points (CDPs) may need to be extended in order to allow slow responders a longer period of time on their medication.

CDP 1, Week 1

Inclusion Criteria

Stage 5 includes patients who fail to fully respond during Stages 1–4 or who are unable to tolerate side effects.

Treatment Options

Stage 5 includes the alternatives not used previously during earlier stages (e.g., lamotrigine or one of the newer antidepressants). It also includes antidepressant combinations. Alternative augmenting agents such as T₃ or buspirone should be strongly considered, and methylphenidate is also included in Stage 5. **Even though stage(s) can be skipped in the algorithm, Stage 5 is most likely to be indicated for those patients who have already failed to respond to multiple earlier stages in the algorithm.**

EXHIBIT 24

CDP 2–5, Stage 5 Psychotic MDD

CDP # 2, Week 4		Stage 5 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Increase antidepressant dose to a maximal therapeutic level and continue for 2 additional weeks.
50–75%		Continue current dose(s); or gradually increase dose(s) as tolerated to a maximal therapeutic range.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue for 2 additional weeks.
Not improved and SEs are intolerable		Consider consultation.
Return to physician's office		Return in 2 weeks.
CDP # 3, Week 6		Stage 5 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		If the antidepressant dose was maximized at week 4; or If the antidepressant dose was not maximized at week 4, increase the dose to the usual maximum dose (monitor serum concentration for TCAs).
50–75%		If the antidepressant dose was maximized at week 4, continue current dose(s) for an additional 2 weeks; or maximize the antidepressant dose within the therapeutic range and continue for an additional 2 weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose(s).
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue for 2 additional weeks; or consider switching medications if side effects are attributable to a particular medication.
Not improved and SEs are intolerable		Consider consultation.
Return to physician's office		If > 50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.
CDP # 4, Week 8		Stage 5 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>		
0–50%		Consider consultation.
50–75%		Continue at maximal doses for 2 additional weeks.
75–100%		Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
Improved, but SEs are intolerable		Continue current dose(s) and address side effects; or decrease dose(s) and continue for 2 additional weeks; or consider switching medications if side effects are attributable to a particular medication.
Not improved and SEs are intolerable		Consider consultation.
Return to physician's office		If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

CDP # 5, Week 10	Stage 5 Psychotic MDD
<i>Symptom Improvement (SEs tolerable):</i>	
0–75%	Consider consultation.
75–100%	Go to Continuation if 75% improvement for at least 4 weeks. Otherwise, continue current dose.
SEs are intolerable	Consider consultation.
Return to physician's office	If >50% improvement for 1 month, return in 4 weeks. Otherwise, return in 2 weeks.

Continuation and Maintenance Phase Treatment

CONTINUATION PHASE TREATMENT

1. Patient received pharmacotherapy during acute phase

At baseline and throughout treatment, other psychosocial or nonmedication treatment modalities such as concomitant psychotherapy should be considered. After full response, the medication(s) should be continued for 6–9 months at the dose effective during the acute phase. Patients should be evaluated at least once every three months during continuation treatment (preferably every 1–2 months). For initial episodes of major depression, medication tapering and discontinuation should be considered after the continuation period is completed. If previous depressive episodes have occurred, maintenance treatment should be considered. When discontinuing the antidepressant, the dose should be tapered no more rapidly than 25 percent per week and not before 6–8 months of full remission have occurred. Tapering and discontinuation usually can be completed over a 2–3 month period. Patients should be educated concerning the signs and symptoms of recurrence of depressive symptoms. A new depressive episode is most likely to occur within the first eight months of medication discontinuation; therefore, patients should be evaluated every 2–4 months during that period. If depression recurs, prompt treatment with the medication previously effective should be initiated (i.e., initiate algorithm stage and tactic that previously resulted in remission of depressive symptoms).

No systematic studies regarding the optimal duration of antipsychotic treatment during the continuation phase have been reported. It is recommended that the acute phase antipsychotic at the same dose be maintained at least for 1–2 months and then slowly tapered over the continuation phase. The duration of antipsychotic treatment should be limited to the minimum duration indicated in order to reduce the risk of tardive dyskinesia. If a patient is receiving a tricyclic antidepressant (TCA), the serum concentration should be monitored, and the dose adjusted as necessary to maintain the level with the recommended therapeutic window (with and without the neuroleptic co-administered).

2. Patient received ECT during acute phase:

Continuation treatment with an antidepressant is recommended. It is preferable to select an antidepressant that the patient has not received or one that the patient has responded to during a previous episode of depression. However, if necessary, a previously ineffective antidepressant may be used in combination with lithium. Dosing, duration of treatment, monitoring, and medication tapering are as above.

If a patient relapses during continuation treatment with an antidepressant, continuation electroconvulsive therapy (ECT) should be considered.

MAINTENANCE PHASE TREATMENT

Patients experiencing an initial episode of major depression have at least a 50 percent chance of having a second episode, and by the third episode of major depression, there is a 90 percent chance of recurrence. Therefore, all patients having a third depressive episode and some patients experiencing a second episode should be evaluated for maintenance antidepressant treatment.

EXHIBIT 25

Indications for Maintenance Medication

Feature	Strength of indication
1. Three or more episodes of major depression	Very strongly recommended
2. Two episodes of major depressive disorder, and one or more of the following: (a) Family history of bipolar disorder (b) History of recurrence within one year after previously effective medication was discontinued (c) A family history of recurrent major depression (d) Early onset (before age 20) of the first depressive episode (e) Depressive episodes were severe, sudden, or life-threatening within the past 3 years	Strongly recommended

SOURCE: *AHCPR Guidelines for the Treatment of Depression in Primary Care* (1993), 2:111.

Maintenance medication should be continued at full therapeutic doses and, as in the continuation phase, the regimen associated with symptom remission is recommended. The optimal duration of maintenance treatment has not been established, but depending on risk factors, is generally between one year past continuation phase and lifetime administration.

Active discussions regarding the initiation and duration of maintenance treatment are an important element in the clinician-patient collaboration for this as well as other phases of pharmacological management of major depressive disorder. The patient's personal preference, as well as the risk factors for recurrence, should be considered in the decision process.

Appendix A:

DSM-IV Criteria for Major Depressive Disorder

CRITERIA FOR MAJOR DEPRESSIVE EPISODE

- A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

Note: Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations.

1. Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful). **Note:** In children and adolescents, can be irritable mood.
2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)
3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5 percent of body weight in a month), or decrease or increase in appetite nearly every day. **Note:** In children, consider failure to make expected weight gains.
4. Insomnia or hypersomnia nearly every day
5. Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)
6. Fatigue or loss of energy nearly every day
7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)
9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

- B. Symptoms do not meet criteria for a mixed episode.

- C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

- D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

- E. The symptoms are not better accounted for by bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than two months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

Diagnostic criteria for 296.2x Major Depressive Disorder, Single Episode

- A. Presence of a single major depressive episode.
- B. The major depressive episode is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.
- C. There has never been a manic episode, a mixed episode, or a hypomanic episode.
Note: this exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance- or treatment-induced or are due to the direct physiological effects of a general medical condition.

Specify (for current or most recent episode):

- Severity/Psychotic/Remission Specifiers
- Chronic
- With Catatonic Features
- With Melancholic Features
- With Atypical Features
- With Postpartum Onset

Diagnostic criteria for 296.3x Major Depressive Disorder, Recurrent

- A. Presence of two or more major depressive episodes. **Note:** to be considered separate episodes, there must be an interval of at least two consecutive months in which criteria are not met for a major depressive episode.
- B. The major depressive episodes are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.
- C. There has never been a manic episode, a mixed episode, or a hypomanic episode.
Note: this exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance- or treatment-induced or are due to the direct physiological effects of a general medical condition.

Specify (for current or most recent episode)

- Severity/Psychotic/Remission Specifiers
- Chronic
- With Catatonic Features
- With Melancholic Features
- With Atypical Features

- With Postpartum Onset

Specify:

- Longitudinal Course Specifiers (with and without interepisode recovery)
- With Seasonal Pattern

Appendix B:

Antidepressant Monographs

Note: *When using any antidepressant agent in a patient with a history of manic symptoms, caution should be taken to monitor for precipitation of a manic episode.*

Amitriptyline

Tricyclic antidepressant (TCA) that blocks reuptake of norepinephrine and serotonin into nerve endings. Peak plasma concentrations are reached within 2–12 hours. It is 90–97 percent protein bound and thus may cause drug interactions by displacing other agents from protein-binding sites. Amitriptyline and its metabolites are metabolized via multiple pathways; however amitriptyline is metabolized by the liver via CYT P450 2C9/19, with a half-life 10–50 hours. It does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, seizure disorders, and prostatic hypertrophy. Increases vasopressor effects of epinephrine and central nervous system (CNS) depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions, or hypertensive episode may occur if used with monoamine oxidase inhibitors (MAOIs); a 2-week washout is recommended before switching between TCAs and MAOIs.

Amoxapine

Tetracyclic antidepressant that blocks the reuptake of norepinephrine primarily, and serotonin weakly, into nerve endings. Its 7-hydroxy metabolite blocks dopamine receptors with potency comparable to that of haloperidol. Peak plasma concentrations are reached within 1–2 hours. It is 90 percent protein bound. It is metabolized by the liver, with a half-life of 8–30 hours, and does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders, and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions or hypertensive episode may occur if used with MAOIs; a 2-week washout is recommended before switching between TCAs and MAOIs.

Bupropion (immediate release)/bupropion SR

An antidepressant that inhibits the reuptake of dopamine and norepinephrine, with little effect on serotonin. Uses include major depression and smoking cessation. Peak plasma concentrations are reached within three hours, its half-life is 10–21 hours, and steady state is achieved in one week. It is not highly protein bound. Bupropion is metabolized through the liver via multiple isoenzymes and may be a weak inhibitor of CYT P450 2D6 activity. It is contraindicated in patients with seizure disorders or eating disorders. Use cautiously in patients with renal and hepatic disease, recent MI or cranial trauma, or any patient with factors that may increase the risk of seizures.

Citalopram

A selective serotonin reuptake inhibitor (SSRI) that is an effective inhibitor of neuronal serotonin reuptake. Absorption is fast, almost complete, and unaffected by food.

Bioavailability is 80 percent; time to peak is 2–4 hours, with a half-life of 33 hours. Citalopram is 80 percent protein bound with a low potential for displacement interactions. It is hepatically metabolized via CYT P450 2C9/19 isoenzymes and possesses very weak inhibitory effects on 1A2, 2C9, and 2D6. Should not be used with MAOIs because the combination may lead to serotonin syndrome (altered mental status, restlessness, hyperreflexia, diaphoresis, tremor).

Clomipramine

Tricyclic antidepressant that potently inhibits serotonin reuptake and increases dopamine metabolism. Uses include major depression, dysphoria, phobias, anxiety, agoraphobia and obsessive-compulsive disorder. Extensively bound to tissue and plasma proteins and thus may displace other agents from protein-binding sites. Peak plasma concentrations are reached within 2–6 hours and the half-life is 21 hours for the parent compound and 36 hours for metabolites. It is hepatically metabolized via CYT P450 2C9/19 isoenzymes but does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders, and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions, or hypertensive episode may occur if used with MAOIs.

Desipramine

Tricyclic antidepressant that blocks the reuptake of norepinephrine into nerve endings. Peak plasma concentration is reached within 3–6 hours and protein binding ranges from 73–92 percent. It is hepatically metabolized via CYT P450 2D6, with a half-life of 11–46 hours. It does not alter hepatic metabolism, however. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders, and prostatic hypertrophy. Increases vasopressor effects of epinephrine, and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions, or hypertensive episode may occur if used with MAOIs.

Fluoxetine

An SSRI that is an effective inhibitor of neuronal serotonin reuptake. Uses include major depression, obsessive-compulsive disorder, and bulimia nervosa. Peak plasma concentrations are reached within 4–8 hours. It is >90 percent protein bound and thus may displace other agents from protein-binding sites. It is hepatically metabolized by CYT P450 2C9/19, with a half-life of 4–6 days and 4–16 days for its active metabolite, norfluoxetine. Fluoxetine is a potent CYT P450 2D6 inhibitor, and norfluoxetine is a CYT P450 3A4 inhibitor. Fluoxetine may increase the half-life of diazepam, tricyclic antidepressants, nefazodone, and some antipsychotics. TCA plasma concentration monitoring is recommended when this combination is used. Should not be used with MAOIs.

Fluvoxamine

An SSRI that is an effective inhibitor of neuronal serotonin reuptake. It reaches plasma concentrations in 2–8 hours and is not highly protein bound. It is eliminated via CYT P450 1A2, with an elimination half-life of 15–26 hours. Fluvoxamine is a potent inhibitor

of CYT P450 1A2 and 2C19. An increase in the half-life of TCAs may occur; therefore, TCA plasma concentration monitoring is recommended. Like other SSRIs, fluvoxamine should not be combined with MAOIs. The current FDA indication is for the treatment of obsessive/compulsive disorder. However, since it is an SSRI, it is used investigationally for the treatment of depression.

Imipramine

Tricyclic antidepressant that blocks the reuptake of norepinephrine and serotonin into nerve endings. It reaches peak plasma concentrations in 1.5–3 hours and is highly protein bound. It is metabolized via CYT P450 1A2, with a half-life of 6–34 hours. Imipramine does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders, and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions, or hypertensive episode may occur if used with MAOIs. Do not break, crush, or chew imipramine film-coated tablets.

Mirtazapine

An antidepressant that blocks presynaptic alpha 2 inhibitory receptors and postsynaptic serotonin receptors, thereby enhancing noradrenergic and serotonergic activity. Peak plasma levels are reached within two hours, and plasma protein binding is low. Mirtazapine is likely metabolized by CYT P450 2D6, 1A2, and 3A4 but does not alter hepatic metabolism itself. The presence of food in the stomach has a minimal effect on both the rate and extent of absorption.

Nefazodone

An antidepressant that selectively inhibits serotonin reuptake in the brain. Peak concentrations are reached in 1–2 hours and it is not highly protein bound. Metabolized in the liver via CYT P450 3A4 with an elimination half-life of 2–4 hours. It is a potent inhibitor of CYT P450 3A4, and thus increases plasma concentrations of some benzodiazepines, quetiapine, carbamazepine, and cisapride. Increases the effect of CNS depressants. Possible hypertensive crisis when combined with MAOIs. Drug use and smoking can increase metabolism and decrease effects. Use cautiously in patients with cardiovascular disease or seizure disorder.

Nortriptyline

Tricyclic antidepressant that blocks the reuptake of norepinephrine and serotonin into nerve endings. Peak plasma concentration is reached in 3–12 hours, and it is highly protein bound. It is hepatically metabolized by primarily CYT P450 2D6, with a half-life of 16–88 hours. It does not alter hepatic metabolism. Contraindicated in the recovery phase of myocardial infarctions, convulsive disorders, and prostatic hypertrophy. Increases vasopressor effects of epinephrine and CNS depressant effects of alcohol, barbiturates, and benzodiazepines. Possible hyperpyretic crisis, convulsions, or hypertensive episode may occur if used with MAOIs.

Paroxetine

An SSRI that is an effective inhibitor of neuronal serotonin reuptake. Uses include major depression, obsessive-compulsive disorder, panic disorder, and social phobia. Peak plasma concentrations are achieved in 5–7 hours. Protein binding is 95 percent. Paroxetine is metabolized through the liver via CYT P450 2D6, with a half-life of 21 hours. It is a potent inhibitor of CYT P450 2D6 metabolism, thus it may increase plasma levels of TCAs and some antipsychotics. Like other SSRIs, it should not be used with MAOIs.

Phenelzine

MAOI antidepressant that increases concentrations of endogenous epinephrine, norepinephrine, serotonin, and dopamine in storage sites in the central nervous system by inhibiting MAO. Contraindicated in hypertension, elderly, congestive heart failure (CHF), severe hepatic disease, pheochromocytoma, severe renal disease, and severe cardiac disease.

Sertraline

An SSRI that is an effective inhibitor of neuronal serotonin reuptake. Uses include major depression, obsessive-compulsive disorder, panic disorder, and post-traumatic stress disorder. Sertraline plasma concentrations peak in 5–9 hours, reaching steady state in one week. Taking with food decreases the time required to reach peak plasma levels but does not affect total concentration of drug absorbed. It is 99 percent plasma protein-binding with a half-life of 27 hours. It is hepatically metabolized via CYT P450 2C9/19 and also has the ability to inhibit 2C9/19 and 2D6 activity, particularly at higher doses. May cause fatal reactions when used in combination with MAOIs.

Tranylcypromine

MAOI antidepressant that increases concentrations of endogenous epinephrine, norepinephrine, serotonin, and dopamine in storage sites in the central nervous system by inhibiting MAO. Contraindicated in hypertension, elderly, CHF, severe hepatic disease, pheochromocytoma, severe renal disease, and severe cardiac disease.

Venlafaxine/venlafaxine XR

Potent inhibitor of neuronal serotonin and norepinephrine reuptake and a weak inhibitor of dopamine reuptake. Peak plasma concentration is reached within two hours and protein binding is minimal. Extensively hepatically metabolized primarily via CYT P450 2D6 to an active metabolite with 87 percent of drug recovered in the urine. The half-life for regular release and extended release are five hours and 48 hours, respectively. May cause hyperthermia, rigidity, rapid fluctuations of vital signs, and mental status changes when used with MAOIs. Use cautiously in patients with mania, hypertension, or seizure disorder.

Appendix C:

Monographs for Augmentation Agents

Lithium

Antimanic that may alter sodium, potassium ion transport across cell membrane in nerve cells and may balance noradrenergic and serotonergic activity in the central nervous system (CNS) by acting on postsynaptic second messengers. Peak plasma concentration is reached in 1–12 hours with no protein binding. It does not undergo hepatic metabolism but rather is eliminated renally. Half-life is 14–30 hours. Therapeutic range is 0.5–1.2 mEq/L. When adjusting dose, 300 mg of lithium will generally increase lithium serum levels by 0.2–0.4 mEq/L. Sodium restriction, renal impairment, dehydration, vomiting/diarrhea, or other factors that may alter sodium levels or renal function may cause lithium toxicity. Contraindicated in hepatic disease, renal disease, brain trauma, and severe cardiac disease.

Buspirone

Antianxiety agent that acts by regulating the action of serotonin. May be used as augmentation therapy due to increased effects when used with psychotropic drugs. Peak plasma concentration is reached within one hour. It is 95 percent protein bound, with a half-life of 2–3 hours. It is hepatically metabolized via CYT P450 3A4. Use cautiously in elderly patients and patients with impaired hepatic/renal functioning. Increased ALT when combined with trazodone. Do not use with MAOIs.

Liothyronine (T₃)

Increases metabolic rates, cardiac output, oxygen consumption, body temperature, blood volume, growth, and development at the cellular level. Peak plasma concentration is reached within two hours, with a half-life of 1.5 days. Use cautiously in elderly patients and patients with angina pectoris, hypertension, ischemia, cardiac disease, pregnancy, and lactation. Increases the effects of TCAs, as well as anticoagulants and sympathomimetics. Decreases the effects of digitalis drugs, insulin, hypoglycemics, liothyronine, and estrogens.

Appendix D:

Antipsychotic Monographs

Note for all antipsychotic medications: *Once psychotic symptoms have remitted, maintain the patient on the lowest necessary dose to maintain remission for a period of three months. After three months of no psychotic symptoms, gradually taper the patient off the antipsychotic medication over a period of two weeks.*

Haloperidol

A high-potency traditional antipsychotic that blocks dopamine (D2) receptors at the mesolimbic and mesocortical areas of the brain, thus treating psychotic symptoms. Peak plasma concentration is achieved within three hours and protein binding is low. Haloperidol is hepatically metabolized via CYT P450 1A2 and 3A4, with a half-life of 15–30 hours. Contraindicated in alcohol and barbiturate withdrawal states, Parkinson's disease, angina, epilepsy, and urinary retention. Possible toxicity when combined with epinephrine.

Olanzapine

An atypical antipsychotic that may mediate antipsychotic activity by both dopamine and serotonin type 2 antagonism. Peak plasma levels are reached within five hours. It is hepatically metabolized via CYT P450 1A2 and 2D6, with a half-life of 27 hours. Use cautiously in patients with hypertension, hepatic disease, cardiac disease, and in elderly patients. Patients on olanzapine should be monitored for weight gain, glucose intolerance, and hyperlipidemia.

Perphenazine

A medium potency traditional antipsychotic that blocks dopamine (D2) receptors at the mesolimbic and mesocortical areas of the brain, thus treating psychotic symptoms. Peak plasma level is achieved in 3–5 hours and protein binding is low. It is hepatically metabolized, with a half-life of 10–20 hours.

Quetiapine

Neuroleptic antipsychotic that functions as an antagonist at dopaminergic and serotonergic receptors in the brain. It has a higher affinity for serotonergic receptors than dopamine receptors. Peak plasma level is achieved in 1–2 hours, and protein binding is considered low (83 percent). Quetiapine is hepatically metabolized by CYT P450 3A4 and possibly 2D6, with a half-life of six hours. It should be used with caution in patients taking antihypertensives and central nervous system (CNS) depressants, and baseline liver function tests and thyroid panel should be obtained.

Risperidone

Neuroleptic antipsychotic that may mediate antipsychotic activity through both dopamine type 2 and serotonin type 2 antagonism. Peak plasma concentration is reached in 1–2 hours, and protein binding is 90 percent. Risperidone is metabolized by CYT P450 2D6 to an active metabolite, 9-hydroxyrisperidone. The active metabolite is then eliminated

renally. Half-lives for the parent compound and active metabolite are three and 24 hours, respectively. Contraindicated in seizure disorders.

EXHIBIT 26

Antidepressant/Antipsychotic Interactions

INHIBITOR (Inhibits substrate)	SUBSTRATE (Drug metabolized by pathway)		
	1A2	2D6	3A3/4
Bupropion (Wellbutrin)		<i>Phenothiazines (some)</i>	
		Clozapine*	
		Olanzapine*	
Citalopram (Celexa)		Phenothiazines	
		Clozapine*	
		Olanzapine*	
Fluoxetine (Prozac)		PHENOTHIAZINES	Clozapine
		Clozapine*	Quetiapine
		Olanzapine*	
Fluvoxamine (Luvox)	CLOZAPINE		
	HALOPERIDOL		Clozapine
	OLANZAPINE		Quetiapine
Nefazodone (Serzone)			CLOZAPINE
			QUETIAPINE
Paroxetine (Paxil)		PHENOTHIAZINES	
		Clozapine*	
		Olanzapine*	
Sertraline (Zoloft)		Phenothiazines	Clozapine
		Clozapine*	Quetiapine
		Olanzapine*	

Regular type = small changes in levels (low probability of clinically significant interaction)

Bold type = moderate changes in levels (moderate probability of clinically significant interaction)

BOLD CAPS = very large changes in levels (high probability of clinically significant interaction)

*Minor pathway

Note: Venlafaxine (Effexor) increases haloperidol levels, but not by Cytochrome P450 interaction.

Appendix E:

Monographs for other agents used to manage associated symptoms or treatment-emergent side effects

Amantadine

An antiparkinsonian agent that exerts its therapeutic effect by enhancing dopaminergic activity, primarily through dopamine reuptake blockade. Peak plasma concentration is achieved in 1–4 hours, and protein binding is low. The elimination half-life ranges between 10 and 31 hours, and it is primarily excreted unchanged by the kidneys. Therefore, lower doses are recommended in patients with compromised renal function. Because amantadine causes increases in dopamine levels initially, patients may experience visual hallucinations or symptoms of delirium. Symptoms will usually subside with continued treatment; however the lowest effective dose should always be used. In addition, to minimize this effect, amantadine should not be combined with anticholinergic agents.

Alprazolam

A short-acting benzodiazepine that is approved by the Federal Drug Administration (FDA) for the treatment of Generalized Anxiety Disorder (GAD). It exerts its anxiolytic effect by enhancing gamma-aminobutyric acid (GABA) inhibition. Peak plasma level is reached in one hour, and protein binding is considered low (<90 percent). It is hepatically metabolized via CYT P450 3A4, and its half-life is 12–15 hours. It has no active metabolites, and thus drug accumulation with chronic use is minimal. As with any benzodiazepine, central nervous system (CNS) depressant effects may be increased if combined with agents that have CNS depressant properties (alcohol, barbiturates, narcotic analgesics, etc.). Tapering (25 percent reduction weekly) rather than abrupt discontinuation is recommended if a patient has been receiving benzodiazepine therapy for at least six weeks. Withdrawal symptoms to monitor for include increased anxiety, insomnia, restlessness, and agitation/irritability.

Benzotropine

An antimuscarinic, antiparkinsonian agent that acts to block acetylcholine and possibly enhance dopaminergic activity, thus correcting the proposed dopamine deficiency-cholinergic excess theory of pseudoparkinsonism. **Peak plasma level is reached in and its half-life is >24 hours.** To minimize sedation from its antihistaminic activity, bedtime administration is suggested.

Clonazepam

A benzodiazepine that is FDA approved for the treatment of seizures and panic disorder, but has clinical utility in the management of anxiety, drug-induced akathisia, catatonia, and depression. It acts by enhancing GABA activity. Peak plasma level is reached within 1–4 hours and protein binding is 85 percent. Clonazepam is metabolized via CYT P450

3A4, with no active metabolites, and has an elimination half-life of 30–40 hours. Its CNS depressant effects may be increased if combined with other agents that have CNS depressant properties. If discontinuation is necessary, tapering (25 percent reduction weekly) is recommended for patients taking clonazepam chronically for at least six weeks. Withdrawal symptoms to monitor for include increased anxiety, insomnia, restlessness, and agitation/irritability. Clonazepam is contraindicated in acute narrow angle glaucoma and significant liver disease.

Dextroamphetamine

A stimulant that is FDA approved for the treatment of ADHD and narcolepsy, but has been tried clinically for the management of depression and obesity. Peak plasma levels are reached within 1–2.5 hours, with a half-life of 10–12 hours. Adverse effects include nervousness, insomnia, anorexia, tachycardia, and changes in blood pressure. Most adverse effects can be resolved by lowering the dose. As with other stimulants, it is contraindicated in arteriosclerosis, moderate/severe hypertension, hyperthyroidism, glaucoma, diabetes mellitus, agitated states, patients with a history of drug abuse/dependence, and those on a monoamine oxidase inhibitor.

Lorazepam

A short-acting benzodiazepine that is FDA approved for the treatment of GAD. It exerts its anxiolytic effect by enhancing GABA inhibition. Peak plasma level is reached within 2–4 hours. Protein binding is considered low (<90 percent). Lorazepam undergoes conjugation only and thus is not at risk for hepatic CYT P450 drug interactions. Lorazepam has no active metabolites and therefore drug accumulation with repeated use is minimal. As with any benzodiazepine, CNS depressant effects may be increased if combined with agents that have CNS depressant properties (alcohol, barbiturates, narcotic analgesics, etc.). Tapering (25 percent reduction weekly) rather than abrupt discontinuation is recommended if a patient has been receiving benzodiazepine therapy for at least six weeks. Withdrawal symptoms to monitor for include increased anxiety, insomnia, restlessness, and agitation/irritability.

Methylphenidate

A stimulant that is FDA approved for the treatment of attention deficit hyperactivity disorder (ADHD) and narcolepsy, but has been tried clinically for alleviation of antidepressant-induced sexual dysfunction, in doses of 5–25 mg taken either daily or one hour before intercourse, and as augmentation therapy in depression, in doses of 5–30 mg daily. It is proposed that dopamine agonist activity may be responsible for its clinical benefits in sexual dysfunction. Adverse effects include nervousness, insomnia, anorexia, tachycardia, and changes in blood pressure. Most adverse effects can be resolved by lowering the dose. Should be used with caution in patients with hypertension, seizures, or electroencephalogram (EEG) abnormalities. It is contraindicated in glaucoma, Tourette's disorder, severe hypertension, hyperthyroidism, arteriosclerosis, patients with a history of drug abuse/dependence, persons with severe anxiety or agitation, and those on a monoamine oxidase inhibitor.

Propranolol

A beta-adrenergic receptor blocker that is FDA approved as an antihypertensive agent, but is clinically used for the management of moderate anxiety and agitation in doses of 10–30 mg daily. Peak plasma level is reached within 1–1.5 hours and protein binding is high. Propranolol is hepatically metabolized via CYT P450 1A2, 2D6, 2C19 and has a half-life of 3–5 hours. Primary adverse effects include bradycardia, dizziness, nausea/vomiting, fatigue, and constipation. Should be used with caution in patients with CHF, coronary artery disease, sinus node dysfunction, chronic bronchitis, or emphysema. It is contraindicated in patients with Raynaud's syndrome, asthma, and 2nd or 3rd degree heart block.

Trazodone

An antidepressant that is chemically unrelated to TCAs and SSRI antidepressants. It inhibits serotonin reuptake and decreases adrenergic sensitivity. Trazodone is also highly sedating (antihistaminic effects) and therefore is clinically used to alleviate insomnia, in doses of 25–100 mg, 30–60 minutes before bedtime. Peak plasma level is reached within two hours and protein binding ranges from 85–95 percent. It is hepatically metabolized by CYT P450 2D6 and has a half-life of 7–8 hours. Primary adverse effects are sedation, orthostatic hypotension, tachycardia, dry mouth, constipation, and blurred vision.

Zolpidem

A nonbenzodiazepine sedative-hypnotic that acts to enhance GABA inhibitory activity. Peak plasma level is reached within 0.5 hours and protein binding is high (92 percent). It is hepatically metabolized by CYT P450 3A4 and has a half-life of two hours. Unlike benzodiazepines, zolpidem has minimal effect on sleep architecture, and the development of tolerance/physical dependence is rare. In doses of 5–10 mg nightly, no significant amnesic effect is observed.

EXHIBIT 27

Fetal Effects of Psychotropic Agents

Medication	Trimester			Category*	Summary
	1st	2d	3d		
Tricyclic antidepressants	±	+	+	D	Possible association between 1st trimester and limb malformation by some case reports but further studies showed no association. Perinatal syndromes: antidepressant withdrawal with jitteriness and irritability.
Serotonin Selective Agents	±	+	+	C	Fluoxetine has been the most studied. No higher rates of major congenital malformation in those who took fluoxetine in the 1st trimester than the general population.
Other Antidepressants	±	+	+	C	
Lithium	Ø	+	±	D	Associated with cardiac anomalies when used in 1st trimester. Prematurity associated with use in 2d and 3d trimester. Watch for maternal lithium toxicity after delivery due to volume change—need to decrease dose by half before delivery. Lithium levels may be increased in neonates—risk of “floppy baby” and hypothyroidism.
Valproic acid	Ø	Ø	Ø	D	Associated with neural tube defects/1–5% risk of spina bifida.
Carbamazepine	±	±	±	C	0.5–1% risk of spina bifida
Other Anticonvulsants	±	±	±	C	Gabapentin, lamotrigine, and topiramate were not teratogenic in animal studies but some malformations were observed.
Typical antipsychotics Haloperidol Chlorpromazine Fluphenazine Loxapine Mesoridazine Thioridazine Thiothixene	±	±	±	C	Most common malformations reported include cardiac, genital, skeletal (3.5%). Use of high-potency agents is recommended. Avoid low potency agents due to decreased BP and utero-placental blood flow. Use in 3d trimester associated with neonatal-associated extrapyramidal effects such as agitation, tremor, poor sucking, swallowing, primitive reflexes, and hypertonicity/DC drugs 5–10 days prior to delivery to allow fetal drug level to decrease.
Atypical antipsychotics Clozapine	±	±	±	C B	Little information on atypical antipsychotics.
Anticholinergics Bentropine Trihexiphenidyl Diphenhydramine	±	± ± +	± ± +	C C B	Main association is suggested cardiovascular effects. Possible association with minor malformations. Benadryl is the preferred agent.
Propranolol	±	+	±	C	It has been used to treat pregnancy-induced hypertension and does not appear to be associated with malformations. Neonatal adverse effects have included hyperbilirubinemia, bradycardia, respiratory depression, and low birth weights.
Benzodiazepines	Ø	±	±	D	Increased risk of cleft palate in 1st trimester, especially diazepam & alprazolam. 3rd trimester exposure leads to tremors, hypertonicity, failure to feed, cyanosis, and apnea. Best avoided but if needed use lorazepam (PRN only).
Buspirone	±	±	±	B	Little information is available.

*Based on *Drugs in Pregnancy and Lactation*, 5th ed.

Ø Use is not recommended

+ May be used (least risk)

± May be used if no other alternative available

Appendix F:

Guidelines for Switching Between Antidepressant Medications

SWITCHING FROM A SELECTIVE SEROTONIN REUPTAKE INHIBITOR (SSRI)

1. SSRI/1 to SSRI/2:

- Discontinue SSRI/1 and then start SSRI/2
-or-
- Decrease SSRI/1 to initiate SSRI/2 to taper and discontinue SSRI/1

Case Example: If patient is on 40 mg PO QAM of fluoxetine: (a) stop the fluoxetine and start paroxetine (or sertraline) the next day; or (b) decrease the fluoxetine to 20 mg per day and add in paroxetine 20 mg (or sertraline 50 mg) per day for 1–3 days and discontinue the fluoxetine.

2. SSRI to tricyclic antidepressant (TCA) or bupropion:

- Discontinue SSRI and then start tricyclic antidepressant (TCA) or bupropion
-or-
- Decrease SSRI to initiate TCA or bupropion at low dose to taper and discontinue SSRI, while gradually increasing TCA or bupropion as tolerated to therapeutic dose range.

Note: Both the TCAs and bupropion are associated with significant toxicity at elevated plasma concentrations. Since SSRIs increase the plasma concentrations of TCAs and bupropion (paroxetine > fluoxetine > sertraline > citalopram), caution is indicated when co-administering these agents or when therapy with bupropion or a TCA is undertaken in close proximity to cessation of an SSRI.

Case Example: If patient is on 40 mg PO QAM of fluoxetine: (a) stop the fluoxetine and start nortriptyline (or other TCA) or bupropion the next day; or (b) decrease the fluoxetine to 20 mg PO QAM and add in nortriptyline (25 mg PO QHS or another TCA) or bupropion (50–75 mg PO QD) for 1–3 days to discontinue fluoxetine, and increase nortriptyline or bupropion as tolerated to therapeutic dose range.

3. SSRI to nefazodone or venlafaxine:

- Discontinue SSRI and then start nefazodone or venlafaxine
-or-
- Decrease SSRI to initiate nefazodone (50–100 mg PO QHS) or venlafaxine (37.5–75 mg PO QD) to taper and discontinue SSRI, while gradually increasing nefazodone or venlafaxine as tolerated to therapeutic dose range.

Case Example: If patient is on 40 mg PO QAM of fluoxetine: (a) stop the fluoxetine and start nefazodone (50–100 mg PO QHS) or venlafaxine (37.5–75 mg PO QD) the next

day; or (b) decrease the fluoxetine to 20 mg PO QAM and add in nefazodone (50–100 mg PO QHS) or venlafaxine (37.5–75 mg PO QD) for 1–3 days to discontinue fluoxetine, and increase nefazodone and venlafaxine as tolerated to therapeutic dose range.

4. SSRI to monoamine oxidase inhibitor (MAOI):

- Discontinue SSRI and then after a 5-week washout period for fluoxetine or after a 2-week washout period (sertraline or paroxetine), MAOI therapy can be safely initiated.

SWITCHING FROM TCA, VENLAFAXINE, NEFAZODONE, OR BUPROPION

1. TCA/1 (or venlafaxine, nefazodone, or bupropion) to TCA/2:

- Discontinue TCA/1 (or venlafaxine, nefazodone, or bupropion) by taper and then start TCA/2
-or-
- Decrease TCA/1 (or venlafaxine, nefazodone, or bupropion) to initiate TCA/2 to taper and discontinue TCA/1 (or venlafaxine, nefazodone, or bupropion), while gradually increasing TCA/2 as tolerated.

Case Example: If patient is on 100 mg PO QHS of nortriptyline (or venlafaxine, nefazodone, or bupropion): (a) taper and then discontinue the nortriptyline (or venlafaxine, nefazodone, or bupropion) and start the other TCA the next day; or (b) decrease the nortriptyline (or venlafaxine, nefazodone, or bupropion) and add in doxepin (50–100 mg PO QHS or other TCA) for 1–3 days and then taper and discontinue the nortriptyline (or venlafaxine, nefazodone, or bupropion).

2. TCA (or venlafaxine, nefazodone, or bupropion) to SSRI:

- Taper and discontinue TCA (or venlafaxine, nefazodone, or bupropion) and then start SSRI
-or-
- Decrease TCA (or venlafaxine, nefazodone, or bupropion) to initiate SSRI at low dose to taper and discontinue TCA (or venlafaxine, nefazodone, or bupropion).

Case Example: If patient is on nortriptyline (or venlafaxine, nefazodone, or bupropion): (a) taper and discontinue the nortriptyline (or venlafaxine, nefazodone, or bupropion) and start fluoxetine (or other SSRI) the next day; or (b) decrease the nortriptyline (or venlafaxine, nefazodone, or bupropion) and add in fluoxetine (20 mg PO QAM or another SSRI) for 1–3 days to taper and discontinue nortriptyline (or venlafaxine, nefazodone, or bupropion).

3 TCA (or venlafaxine, nefazodone, or bupropion) to nefazodone, venlafaxine, or bupropion:

- Discontinue TCA (or venlafaxine, nefazodone, or bupropion) and then start nefazodone, venlafaxine, or bupropion
-or-

- Decrease TCA (venlafaxine, nefazodone, or bupropion) to initiate nefazodone (50–100 mg PO QHS), venlafaxine (37.5–75 mg PO QD), or bupropion (37.5–50 mg PO QD) to taper and discontinue TCA (venlafaxine, nefazodone, or bupropion), while gradually increasing nefazodone, venlafaxine, or bupropion as tolerated to therapeutic dose range.

Case Example: If patient is on nortriptyline (or venlafaxine, nefazodone, or bupropion): (a) stop the nortriptyline (or venlafaxine, nefazodone, or bupropion) and start nefazodone (50–100 mg PO QHS), venlafaxine (37.5–75 mg PO QD), or bupropion (37.5–50 mg PO QD) the next day; or (b) decrease the nortriptyline (or venlafaxine, nefazodone, or bupropion) and add in nefazodone (50–100 mg PO QHS), venlafaxine (37.5–75 mg PO QD), or bupropion (37.5–50 mg PO QD) for 1–3 days to discontinue nortriptyline (or venlafaxine, nefazodone, or bupropion) and increase nefazodone, venlafaxine, or bupropion as tolerated to therapeutic dose range.

TCA to MAOI:

- Discontinue TCA and then after a 2-week washout period, MAOI therapy can be safely initiated.

SWITCHING FROM AN MAOI

MAOI/1 to MAOI/2, SSRI, TCA, venlafaxine, bupropion, nefazodone:

- Discontinue MAOI/1 and then after a 2-week washout period, therapy with MAOI/2 (or SSRI, TCA, venlafaxine, or nefazodone) can be safely initiated.

Appendix G:

Process Measures

QUICK INVENTORY OF DEPRESSIVE SYMPTOMATOLOGY (SELF-REPORT) (QIDS-SR)

The QIDS-SR consists of 16 individual items that the patient is asked to read and rate based upon his/her individual perception of the presence and severity of common depression-related symptoms. If the patient has difficulty reading or interpreting an item, it is appropriate for a staff member to read the question to the patient, but staff should not lead or influence the patient's answer. Although some patients may have difficulty using the form for the first time, most individuals should be able to easily complete it after the second or third time. Most patients also appreciate the opportunity to be able to tell the physician and other staff about the symptoms that are bothering them. The QID-SR is constructed in order to capture a range of DSM-IV related depressive symptoms in an individual patient, while at the same time minimizing the tendency to overrate selected symptoms (e.g., sleep disturbance). For this reason, the patient does not answer all of the questions. For example, on questions 6 and 7, addressing appetite disturbance, the patient only answers one of the questions (addressing either decreased or increased appetite). If the patient has no appetite disturbance, they can answer either question. The same principles apply to questions 8 and 9. The QIDS-SR is also available in Spanish, and this version should be used for individuals who primarily read Spanish.

In scoring the QIDS-SR, the clinician does NOT sum all of the items to get the rating score. The scoring instructions are listed at the end of the form. If the form is scored correctly, only 12 of the questions will be summed to obtain the patient's depression rating score, with a maximum possible score of 27. The scoring criteria for the severity of depressive symptoms are listed below. Please note that these scoring criteria are a guideline, and they should never be used as a substitute for the clinician's judgment regarding the clinical status of the patient. Rather they are intended as a tool for the clinician to use in quantifying the severity of depressive symptoms and the response to treatment.

(QIDS-SR)

NAME: _____ TODAY'S DATE _____

Please circle the one response to each item that best describes you for the past seven days.

1. Falling Asleep:

- 0 I never take longer than 30 minutes to fall asleep.
- 1 I take at least 30 minutes to fall asleep, less than half the time.
- 2 I take at least 30 minutes to fall asleep, more than half the time.
- 3 I take more than 60 minutes to fall asleep, more than half the time.

2. Sleep During the Night:

- 0 I do not wake up at night.
- 1 I have a restless, light sleep with a few brief awakenings each night.
- 2 I wake up at least once a night, but I go back to sleep easily.
- 3 I awaken more than once a night and stay awake for 20 minutes or more, more than half the time.

3. Waking Up Too Early:

- 0 Most of the time, I awaken no more than 30 minutes before I need to get up.
- 1 More than half the time, I awaken more than 30 minutes before I need to get up.
- 2 I almost always awaken at least one hour or so before I need to, but I go back to sleep eventually.
- 3 I awaken at least one hour before I need to, and can't go back to sleep.

4. Sleeping Too Much:

- 0 I sleep no longer than 7-8 hours/night, without napping during the day.
- 1 I sleep no longer than 10 hours in a 24-hour period including naps.
- 2 I sleep no longer than 12 hours in a 24-hour period including naps.
- 3 I sleep longer than 12 hours in a 24-hour period including naps.

5. Feeling Sad:

- 0 I do not feel sad
- 1 I feel sad less than half the time.
- 2 I feel sad more than half the time.
- 3 I feel sad nearly all of the time.

Please complete either 6 or 7 (not both)

6. Decreased Appetite:

- 0 There is no change in my usual appetite.
- 1 I eat somewhat less often or lesser amounts of food than usual.
- 2 I eat much less than usual and only with personal effort.
- 3 I rarely eat within a 24-hour period, and only with extreme personal effort or when others persuade me to eat.

7. Increased Appetite:

- 0 There is no change from my usual appetite.
- 1 I feel a need to eat more frequently than usual.
- 2 I regularly eat more often and/or greater amounts of food than usual.
- 3 I feel driven to overeat both at mealtime and between meals.

Please complete either 8 or 9 (not both)

8. Decreased Weight (Within the Last Two Weeks):

- 0 I have not had a change in my weight.
- 1 I feel as if I've had a slight weight loss.
- 2 I have lost 2 pounds or more.
- 3 I have lost 5 pounds or more.

9. Increased Weight (Within the Last Two Weeks):

- 0 I have not had a change in my weight.
- 1 I feel as if I've had a slight weight gain.
- 2 I have gained 2 pounds or more.
- 3 I have gained 5 pounds or more.

10. Concentration/Decision Making:

- 0 There is no change in my usual capacity to concentrate or make decisions.
- 1 I occasionally feel indecisive or find that my attention wanders.
- 2 Most of the time, I struggle to focus my attention or to make decisions.
- 3 I cannot concentrate well enough to read or cannot make even minor decisions.

11. View of Myself:

- 0 I see myself as equally worthwhile and deserving as other people.
- 1 I am more self-blaming than usual.
- 2 I largely believe that I cause problems for others.
- 3 I think almost constantly about major and minor defects in myself.

12. Thoughts of Death or Suicide:

- 0 I do not think of suicide or death.
- 1 I feel that life is empty or wonder if it's worth living.
- 2 I think of suicide or death several times a week for several minutes.
- 3 I think of suicide or death several times a day in some detail, or I have made specific plans for suicide or have actually tried to take my life.

13. General Interest:

- 0 There is no change from usual in how interested I am in other people or activities.
- 1 I notice that I am less interested in people or activities.
- 2 I find I have interest in only one or two of my formerly pursued activities.
- 3 I have virtually no interest in formerly pursued activities.

14. Energy Level:

- 0 There is no change in my usual level of energy.
- 1 I get tired more easily than usual.
- 2 I have to make a big effort to start or finish my usual daily activities (for example, shopping, homework, cooking or going to work).
- 3 I really cannot carry out most of my usual daily activities because I just don't have the energy.

15. Feeling slowed down:

- 0 I think, speak, and move at my usual rate of speed.
- 1 I find that my thinking is slowed down or my voice sounds dull or flat.
- 2 It takes me several seconds to respond to most questions and I'm sure my thinking is slowed.
- 3 I am often unable to respond to questions without extreme effort.

16. Feeling restless:

- 0 I do not feel restless.
- 1 I'm often fidgety, wringing my hands, or need to shift how I am sitting.
- 2 I have impulses to move about and am quite restless.
- 3 At times, I am unable to stay seated and need to pace around.

To Score:

- 1. Enter the highest score on any 1 of the 4 sleep items (1-4) _____
- 2. Item 5 _____
- 3. Enter the highest score on any 1 appetite/ weight item (6-9) _____
- 4. Item 10 _____
- 5. Item 11 _____
- 6. Item 12 _____
- 7. Item 13 _____
- 8. Item 14 _____
- 9. Enter the highest score on either of the 2 psychomotor items (15 and 16) _____

Normal:	≤7
Mild:	8–12
Moderate:	13–16
Moderate to Severe:	17–20
Severe:	21+

Total Score (Range 0–27) _____

Appendix H:

Communications

IMPORTANT PHONE NUMBERS

TBA or delete

Appendix K:
Michigan Implementation of Medication Algorithms (MIMA)
Guidelines for Treating Bipolar Disorder
MIMA Physician Procedural Manual

Michigan Implementation of Medication Algorithms (MIMA)

Guidelines for Treating Bipolar Disorder

MIMA Physician Procedural Manual

2004

This manual is adapted from Trisha Suppes and Ellen B. Dennehy, *Texas Implementation of Medication Algorithms (TIMA) Procedural Manual, Bipolar Disorder Algorithms*, (Dallas, Texas: Bipolar Disorder Module Texas Medication Algorithm Project, August 27, 2002), available on the TIMA website: <http://www.mhmr.state.tx.us/centraloffice/medicaldirector/timasczman.pdf>.

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Notice

These guidelines reflect the state of knowledge, current at the time of publication, on effective and appropriate care, as well as clinical consensus judgments when knowledge is lacking. The inevitable changes in the state of scientific information and technology mandate that periodic review, updating, and revisions will be needed. These guidelines (algorithms) do not apply to all patients, and each must be adapted and tailored to each individual patient. Proper use, adaptation, modifications, or decisions to disregard these or other guidelines, in whole or in part, are entirely the responsibility of the clinician who uses the guidelines. The authors bear no responsibility for the use of these guidelines by third parties.

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Overview of MIMA

The Michigan Implementation of Medication Algorithms (MIMA) presented here are part of a broader action plan aimed at encouraging greater use of evidence-based practice (EBP) in mental health care in Michigan. As the name suggests, these medication algorithms for major depression, bipolar disorder, and schizophrenia were adapted from the Texas Implementation of Medication Algorithms (TIMA) project, implemented in that state over the past five years.

Funding for the Michigan EBP project was provided by the Ethel and James Flinn Foundation of Detroit, in partnership with Public Sector Consultants Inc. of Lansing. The project goal, simply stated, was to develop an action plan that would bridge the gap between what is known and what is done in psychiatry, between scientific evidence and actual practice.

Both the MIMA and the action plan of which the algorithms are a part were developed by the project Steering Committee, a diverse group of Michigan mental health experts with demonstrated expertise in EBP. Subcommittees of the Steering Committee reviewed various publicly available algorithms and guidelines and ultimately endorsed those used in Texas on the grounds that they were scientifically sound, had been field-tested and evaluated, were regularly updated, and were part of a broader disease management program.

The disease management component warrants special emphasis. The MIMA should not be viewed in isolation but as part of a program that includes clinical and technical support for physicians and patients, patient/family education, uniform documentation of patient outcomes, and a quality management program. The various components of this multifaceted program will be pilot-tested and evaluated in several Michigan locales over the next few years, with the results informing follow-up EBP programs in the future.

The Michigan EBP project, like other similar projects across the country, was devised in response to accumulating evidence that there is a significant gap between the state of knowledge and the treatment of patients in clinical practice. In many fields of medicine, psychiatry included, practice lags years behind research findings. Research also demonstrates that there are wide variations in practice even within a single state. It is therefore reasonable to conclude that the practices of at least some clinicians vary substantially from what is known to be effective.

Part of the problem is “information overload.” It is impossible for any psychiatrist to keep up with all the developments in his or her field. Another aspect of the problem is the uncritical acceptance of information from sources such as friends and colleagues, flawed studies, or pharmaceutical companies.

EBP has been criticized as a cost-cutting approach that undermines the “art” of medicine. The express intent of the MIMA, however, is actually the reverse. The MIMA in no way trivialize the clinician’s role, but rather formalize what has long been the ideal of practice: the use of science to inform the art of medicine. Clinical expertise continues to play an important role in the MIMA by allowing the clinician to rapidly integrate

research evidence and/or the practice judgments of the broader medical community in making decisions about patient care. Rather than being “cookbook medicine,” the MIMA empower clinicians to make their own decisions about patient care, guided by the best available evidence to support those decisions.

Introduction to Algorithm Implementation

Algorithms go beyond guidelines in providing an explicit framework for clinical decision making. Algorithms do not dictate decisions, but rather provide an approach to clinical decision making that should yield similar answers in similar situations. The MIMA are not just general recommendations for medication treatment, they are also a systematic guide to the treatment of individual patients, which includes a number of critical factors: initial medication and dosage, dosage changes, methods and frequency of assessment, and minimum and maximum treatment periods.

Further, algorithms can be divided into *strategies* and *tactics*. Strategies are the various acceptable treatment regimen options for the care of an individual condition. Tactics address how optimally to implement a chosen regimen, and include such considerations as dose, monitoring, and how best to help an inadequately responding patient. Tactics also address the degree of symptom and functional improvement. As was the case with the TIMA, the MIMA presume that the aim of treatment is remission or the maximum possible improvement in cases where remission is not possible.

The MIMA approach is informed by the experience of Texas, which demonstrated that the successful implementation of algorithms is a human and social, as well as a technical, consideration. Assuring implementation of a treatment algorithm within a health care organization is a complex endeavor, requiring, in addition to research evidence, integrated changes in health care system design, patient and family education, and evaluation. Recommendations for just such a comprehensive, multifaceted approach are detailed in the Michigan EBP action plan.

Implementation of treatment algorithms is an evolutionary process, and change within systems does not occur without significant planning, goodwill, and effort. Yet the payoff in improved patient care is potentially enormous. Through an explicit process of algorithm implementation, evaluation, and revision, incremental improvements in many areas can result in major improvements in the overall quality of care.

At-a-Glance

Bipolar Disorder Medication Algorithms

Visit Frequency

While medications are being actively adjusted, patients should be seen every two weeks. As medications are stabilized and patients exhibit stable, positive response, visit intervals can be gradually lengthened to every four weeks. When patients enter continuation phase, visit frequency should be every 8–12 weeks, as individually determined. Support personnel may contact patients by phone if the physician is unable to see them.

Assessment Frequency

The Brief BD Symptom Scale (BDSS) may be completed at each visit.

Criteria for Medication Change

Medication changes are made after evaluation of tolerability, efficacy across multiple symptom domains, and safety. Clinicians consult Critical Decision Points (CDPs) and Tactics for the Treatment of Bipolar Disorder (see Exhibit 3, page 15) after review of symptom patterns and severity on the BDSS worksheet. The goals of treatment are full symptomatic remission, return of psychosocial functioning, and prevention of relapses and recurrences. Any symptoms, even those in the mild to moderate range, warrant consideration of tactics that may further optimize response.

Evaluations

At each visit, a physician will assess core symptom severity, overall functional impairment, and side effect severity. Physician can complete the BDSS and patient global self-rating of symptom severity and side effects.

Medication Doses

Recommended doses are provided in the Medications and Dosing section. **Doses outside of the ranges should have a chart note indicating “change from algorithm recommended” and documentation of rationale for change.**

Blood Levels

Serum levels should be obtained about five days (five half-lives) after reaching the minimum target dose (see Exhibit 5, page 19) for lithium (Li) or divalproex sodium (DVP). Levels should be ordered as necessary to ensure that dosing is within therapeutic window for individual patient. Intolerable side effects require immediate evaluation of serum levels.

Treatment of Depressive Symptoms

All patients will be maintained on the primary algorithm for treatment of hypomania/mania. If depressive symptoms warrant medication intervention, the clinician should utilize the strategies for treatment of bipolar depression in a similar, systematic, step-wise fashion as the primary algorithm, as an adjunct to the primary treatment stage (see Exhibits 1 and 2, pages 6–7).

EXHIBIT 1

Algorithm for the Treatment of Mania/Hypomania

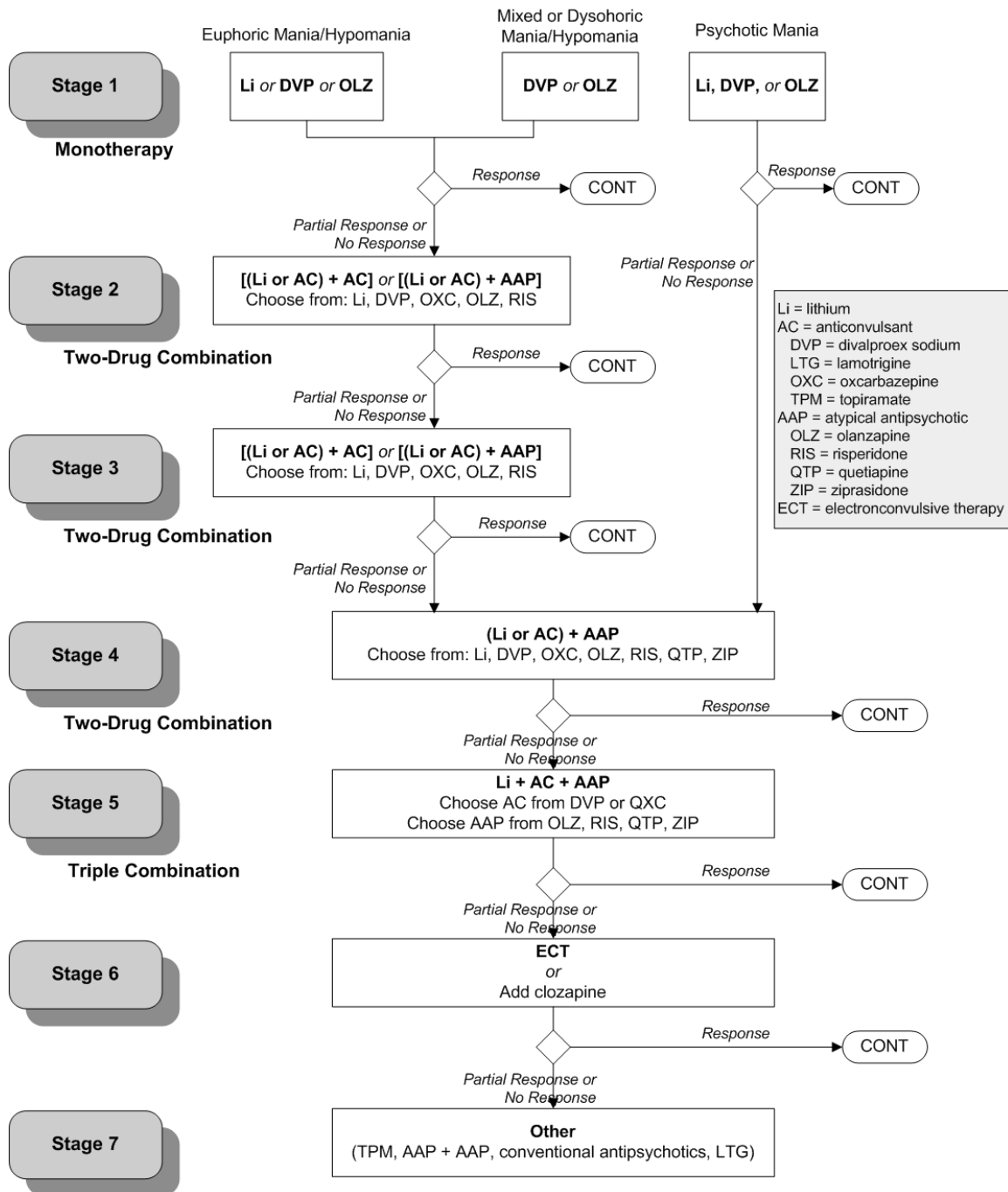
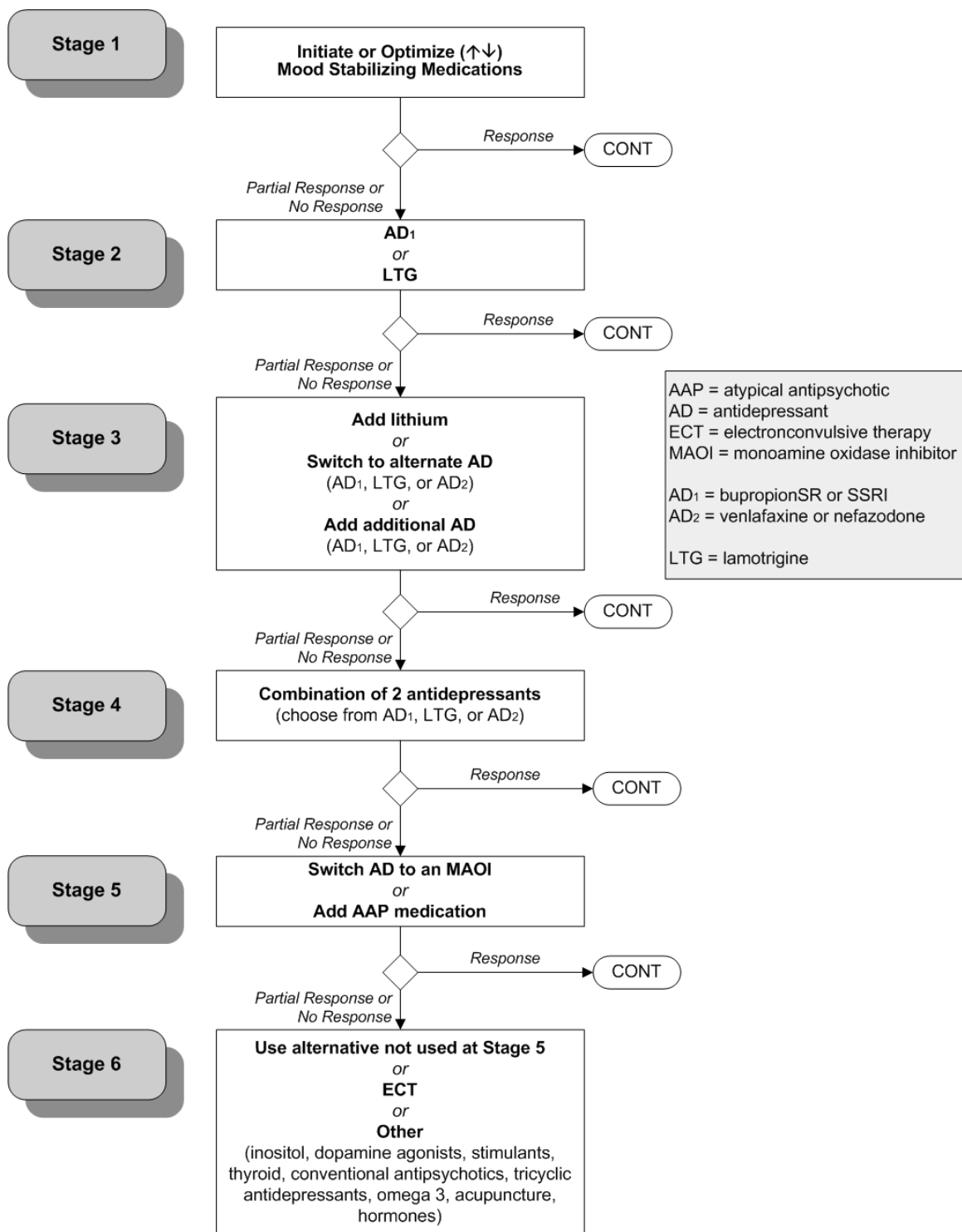


EXHIBIT 2

Algorithm for the Treatment of Depression in Bipolar Disorder*



*To be used in conjunction with primary treatment algorithm.

Description of Algorithm Stages¹

ALGORITHM FOR MANIA/HYPOMANIA

This is the primary treatment algorithm. All patients diagnosed with Bipolar I disorder should be treated with medication or medication combinations recommended within this guideline. Consistent with other published guidelines for treatment of bipolar disorder, the majority of treatment options consist of medication combinations. If possible, when adjusting medications, it is preferable to make adjustments to one agent at a time, to allow for evaluation of response.

When utilizing mood-stabilizing medications, it is recommended that the dose be pushed (either alone or in combination) as much as possible before moving to the second or third mood stabilizer. Switching to alternative mood stabilizers, versus adding, is recommended in cases of intolerance. If a patient has no or low-partial response to a medication, and **is tolerating** the medication, a new medication should be added using the overlap and taper tactics provided. It is recommended that the clinician try to taper the first medication at a later date if the patient's mood stabilizes.

When treating patients with hypomania or mania, a first consideration involves decreasing and/or discontinuing antidepressant medications. This taper should be done relatively quickly, except in cases where it is contraindicated. For those patients with rapid cycling, antidepressants should be tapered and discontinued. Some patients may still need an antidepressant plus mood stabilizers in order to minimize depressive symptoms and suicidality.

Serum Levels

If lithium (Li) or divalproex sodium (DVP) are utilized, serum levels are part of the consideration of response and tolerability. In practice, serum levels may not be available at each visit. It is recommended that by two weeks after initiating lithium or divalproex sodium the patient be receiving the minimum target dose. If possible, we recommend a serum level five days after reaching the target dose and before the first appointment to assess response (e.g., 2–3 weeks after starting the trial). While awaiting serum levels (e.g., four weeks), it is generally safe to gradually increase DVP and, more cautiously, Li if no side effects develop.

Target serum levels are provided in the Medications and Dosing section (see Exhibit 5, Summary of Recommended Doses of Medication Used for Acute Phase Treatment of Hypomania/Mania, page 19). For Li and DVP, evidence supports differences in clinical response for some patients between therapeutic and high therapeutic levels. Clinically, it is reasonably safe and well tolerated to exceed the recommended therapeutic range for DVP (>125 µg/ml), but few psychiatric patients appear to need these higher levels. The upper limits of Li (1.2 mEq/L) are usually associated with side effects, and levels over

¹T. Suppes, E. B. Dennehy, A. C. Swann, C. Bowden, J. Calabrese, R. Hirschfeld, P. E. Keck, G. Sachs, M. L. Crismon, M. Toprac, and S. P. Shon. "Report of the Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder 2000," *Journal of Clinical Psychiatry* (2002): 288–99.

these limits are potentially toxic, with the exception of patients in a full-blown manic episode who may tolerate and benefit from levels of Li between 1.0 and 1.2 mEq/L.

Similarly, it is necessary to obtain more frequent levels of DVP when used in combination with an auto-inducer such as carbamazepine. Once you have obtained a couple of levels for DVP or Li, it is generally possible to estimate the likely increase of serum levels with dose changes and collect serum levels somewhat less often. However, the development of side effects should always signal considering obtaining a serum level.

Stage 1

All the options for Stage 1 include monotherapy with lithium, divalproex, or olanzapine (see Exhibit 1, page 6). For patients presenting with euphoric mania/hypomania or psychotic mania, choice is from any of the three agents. For dysphoric or mixed mania, the recommendation is to choose between divalproex and olanzapine. Divalproex is recommended instead of valproic acid due to significantly better tolerability.

Generally, in the case of partial response with good tolerance, the recommendation will be to add a medication (move to combination therapy, i.e., Stage 2) versus switching. If the patient is intolerant in Stage 1, the recommendation will be to try an alternative mood stabilizer within Stage 1.

Stage 2

Stage 2 treatment includes combination treatment with two of the following: lithium, divalproex, oxcarbazepine, olanzapine, and risperidone. Oxcarbazepine and risperidone are added as options here. Oxcarbazepine is recommended over carbamazepine due to apparent similar efficacy with fewer drug interactions or adverse events, increased tolerability, and less physician supervision required. Therefore, the combination is lithium or anticonvulsant (Li or AC) + AC, or (Li or AC) + AAP (atypical antipsychotic medication).

Stage 3

In Stage 3, physicians are asked to attempt another combination of medications, drawing from the same group described in Stage 2. Preferably, they would keep one agent from the previous combination, and change to a different second agent. Again, the combination can be either lithium or anticonvulsant (Li or AC) + AC, or (Li or AC) + AAP.

Stage 4

This stage also includes combination therapy, but at this point, the physician is prompted directly to use an atypical antipsychotic agent in combination with lithium, divalproex, or oxcarbazepine. Therefore, it is a combination of Li or AC and an atypical antipsychotic medication [(Li or AC) + AAP]. For patients with psychotic mania, the recommendation is to progress immediately to this combination if Stage 1 monotherapy with lithium, divalproex, or olanzapine is ineffective or only partially effective. Quetiapine and ziprasidone are added as additional choices here.

Stage 5

Stage 5 includes “triple therapy,” with lithium, an anticonvulsant (choose from divalproex or oxcarbazepine), and an atypical antipsychotic medication (choose from olanzapine, risperidone, quetiapine, ziprasidone); therefore, Li + AC + AAP.

Stage 6

Electroconvulsive therapy (ECT) has demonstrated efficacy for treatment of acute mania. Safety, tolerability, and patient acceptance issues warrant its placement further down in the algorithm at Stage 6. Alternatively, clozapine could be added to other medications as a treatment option here. The placement of clozapine after other atypical antipsychotic medications is consistent with clinical recommendations to attempt treatment with other atypical antipsychotic medications before initiating clozapine treatment. If the patient is taking clozapine, weekly blood draws (WBCs) are necessary (for more information, see the medication descriptions in [Appendix A](#)).

Stage 7

This stage includes other options to be used as adjuncts to partially effective medication combinations. It includes topiramate, a combination of medications that includes two atypical antipsychotic medications, conventional antipsychotics, and lamotrigine.

ALGORITHM FOR THE TREATMENT OF DEPRESSION IN BIPOLAR DISORDER

This algorithm should be utilized in conjunction with the primary treatment algorithm for mania/hypomania. If a patient reports symptoms of depression significant enough to warrant intervention, the clinician is directed to utilize this algorithm as a concomitant treatment strategy, in addition to any stage of treatment within the Mania/Hypomania algorithm. As with any algorithm, if insufficient response in depressive symptoms is achieved, the clinician should continue through the algorithm until satisfactory symptom reduction is achieved.

It is important to carefully consider the addition of an antidepressant to a bipolar patient’s medication regimen. If the patient presents with a “pure” bipolar major depressive episode (BP-MDE), without mood lability or hypomania, the decision is relatively clear as the degree of suffering will justify initiating an antidepressant. However, many patients will have significant depressive symptoms, but also periods of dysphoric hypomania, mood lability, irritability, and other complicated states. Patients may need both a mood stabilizer and an antidepressant. The balancing of optimizing mood stabilizers, possibly adding Li, or adding an antidepressant must be done on a case-by-case basis.

The algorithm to treat bipolar depression ([see Exhibit 2, page 7](#)) assumes antidepressants will only be used in conjunction with a mood stabilizing medication, because of the risk of inducing manic symptoms. It may be necessary to adjust the mood stabilizer during treatment (i.e., increase dose with development of irritability or mood lability). In some cases, it may be clinically indicated to switch or combine mood stabilizers (i.e., an effective antidepressant is found and continued need for the medication is provided, but

the drug is associated with mild mood lability). It is expected that the physician will continue to utilize recommendations of the hypomania/mania algorithm even when prescribing antidepressant treatment.

Selection of a specific antidepressant medication should be made based on individual factors such as the expected side-effect profile, potential toxicity, concomitant medical problems, and medications. The initial algorithm stages focus on antidepressant monotherapy with medications associated with favorable risk-benefit ratios and for which there is evidence of efficacy in bipolar patients.

Stage 1

The first stage includes initiating and/or optimizing mood-stabilizing medications. The recommendation is that all patients diagnosed with Bipolar I disorder be prescribed antimanic medications, using the algorithm for treatment of mania/hypomania. Optimizing mood-stabilizing medications might mean either an increase or decrease in dosing, though no data is available to clearly direct tactics on this issue.

Stage 2

Patients entering Stage 2 of the algorithm should have a major depressive episode of sufficient severity to merit medication treatment. Stage 2 includes the addition of an SSRI, bupropion _{SR}, or lamotrigine to existing medications. The SSRI options are open, and include fluoxetine, paroxetine, sertraline, fluvoxamine, and citalopram. Bupropion _{SR} is an additional option; the sustained release version of bupropion is recommended, due to improved tolerability. While there is a risk of rash with lamotrigine, there is positive Level A data in support of its efficacy for treatment of bipolar depression.

Stage 3

At this point, the algorithm begins to rely more heavily on clinical consensus and expert opinion, as there is only limited data on treatment of bipolar depression following failure in Stage 2. The algorithm development philosophy was that when there are several options available, with little or no empirically derived reason to rank them, to offer the choices so that the clinician and patient can choose what is best for that individual. Therefore, Stage 3 offers the clinician and patient several options, including addition of lithium, switching to an alternative antidepressant medication (adding venlafaxine and nefazodone as options), or adding from Stage 2 options a second antidepressant or lamotrigine.

If Stage 2 treatment was unsuccessful primarily because of intolerable side effects, consider selecting an antidepressant from a different class with a contrasting side effect profile (e.g., if the patient experienced sexual dysfunction on an SSRI, consider bupropion _{SR} or nefazodone).

Stage 4

Stage 4 includes the combination of two antidepressant medications. This includes selection from the SSRI group, bupropion _{SR}, and lamotrigine. In choosing an antidepressant combination, it is recommended to use medications from different classes (i.e., not two SSRIs). The goal of combination antidepressant regimens is to combine

medications to enhance clinical response. In general, because of the potential for drug interactions, antidepressant combination treatment should be used carefully, and patients monitored closely.

Stage 5

Stage 5 includes changing the antidepressant medication to a monoamine oxidase inhibitor (MAOI), or adding an atypical antipsychotic medication. Because of potential health risks and the need to follow special dietary restrictions and avoid certain medications, MAOIs are located in Stage 5, after medications and medication combinations with less Level A and B data. Diet restriction guidelines should be provided to all patients receiving MAOI medications.

Stage 6

Recommendations at this stage include using the alternative not used in Stage 5, ECT, or Other. The “Other” category is exploratory, and includes a number of options to be considered in addition to partially effective medication combinations. It includes inositol, dopamine agonists, stimulant medications, thyroid, conventional antipsychotics, tricyclic antidepressants, omega 3, acupuncture, and hormones.

Critical Decision Points

Critical decision points (CDPs) are designed to prompt an assessment of symptoms and a determination of a need for a change in strategy or tactics. At each CDP, the physician should assess the patient for improvement and make a decision to either continue or change treatment based on improvement in symptoms or lack thereof. **Note:** Patients begin at CDP 1 at the beginning of each stage.

Exhibits 3 and 4 summarize the actions to be taken at each CDP.

EXHIBIT 3

Critical Decision Points (CDPs) and Tactics for the Treatment of Bipolar Disorder

CDP	Clinical status	Plan
Week 1 (CDP 1)	Symptomatic	Initiate medication; adjust dose to lower end of therapeutic dose range or serum level.
Week 2 (CDP 2)	Full response (No symptoms)	Continue current dose
	Mild to moderate symptoms	Continue current dose. Consider increasing dose.
	Severe symptoms	Increase dose.
Week 4 (CDP 3)	Full response (No symptoms)	Continue current dose.
	Mild to moderate symptoms	Increase dose. Consider the next stage.
	Severe symptoms	Increase dose. Consider the next stage.
Week 6 (CDP 4)	Full response (No symptoms)	Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Mild to moderate symptoms	Increase dose. Consider the next stage.
	Severe symptoms	Increase dose. Consider the next stage.
Week 8 (CDP 5)	Full response (No symptoms)	Go to continuation phase if full response is sustained for at least 4 weeks. Otherwise, continue current dose.
	Mild to moderate symptoms	Consider the next stage.
	Severe symptoms	Go to the next stage.

EXHIBIT 4

Critical Decision Points (CDPs) and Tactics for the Treatment of Bipolar Disorder*

Instructions: To identify the recommendations for the appropriate CDP, trace to the right to the degree of symptom severity indicated by the Bipolar Disorder Symptom Scale (BDSS).

		Symptoms							
CDP		NA	1	Mild to moderate			Severe		
				2	3	4	5	6	7
Week 1: CDP 1	Symptomatic.			Start medications.			Start medications.		
Week 2: CDP 2	Order serum levels (if applicable) to adjust dose.	Continue current dose.		Continue current dose. Consider increasing dose.			Increase dose.		
Week 4: CDP 3	Order serum levels (if applicable) to adjust dose.	Continue current dose.		Increase dose or consider next stage.			Increase dose or consider next stage.		
Week 6: CDP 4	All serum levels should be within therapeutic range.	Continue current dose.		Increase dose or consider next stage.			Increase dose or consider next stage.		
Week 8: CDP 5		Continue current dose.		Consider next stage.			Go to next stage.		

*Side Effects: Treatment recommendations assume that side effects are tolerable. Refer to the Medications, Dosage, and Side Effects Management section of this manual. Intolerable, unmanageable side effects may warrant changing to a different stage of treatment. Tolerability should be evaluated at all CDPs.

CDPs involve a consideration of efficacy among all symptom domains, tolerability, and safety. Clinicians must use their own judgment in evaluating the symptoms of the bipolar patient. Clinicians may evaluate the pattern and severity of symptoms by reviewing the BDSS worksheet (see page 56). For example, if most symptoms are contained within the light gray column, follow treatment recommendations within that column. Depending on the pattern and severity of symptom scores, the clinician may follow recommendations within the column that includes the most severe symptoms, or the column that contains the majority of clinical symptoms. The symptoms are loosely grouped by clinical presentation to allow for quicker assessment of potential treatment decisions. For example, if symptoms that are suggestive of hypomania/mania are elevated, the clinician would make adjustments to medications prescribed in the algorithm for hypomania/mania. If symptoms of psychosis are prominent, and an antipsychotic medication is included in the treatment regimen, the clinician may make the adjustment to that medication versus another antimanic agent. The Critical Decision Points and Tactics for treatment of the bipolar patient allow for physician judgment and choice in determining where to make adjustments to medications, responsive to the individual patient's presentation.

Patients should return to the physician's office or be contacted by office personnel every two weeks (office visit or by phone) until symptom patterns are primarily contained within the mild range on the BDSS. Patients will then be evaluated monthly, until the

clinician determines the patient may enter continuation phase treatment. It is recommended that clinicians see the patient every 8–12 weeks while they are in continuation phase. Support personnel may contact patients by phone if the physician is unable to see them.

All recommendations assume that side effects are tolerable. Please refer to the Side Effects Management section for suggestions on how to manage typical side effects. Intolerable, unmanageable side effects may warrant changing to a different stage of treatment. Tolerability should be evaluated at all CDPs.

The Critical Decision Points and Tactics for the Treatment of Bipolar Disorder assume that you are working on one clinical presentation at a time, i.e., hypomania/mania or depressive symptoms. If symptom patterns change, requiring a shift in algorithm focus, return to CDP 1 to evaluate and direct the change in treatment.

CDP 1, Week 1

All patients are treated with the algorithm for hypomania/mania. Treatment with this algorithm assumes that the clinician has made a thorough assessment of history and symptoms and determined that the patient has a diagnosis of Bipolar I disorder.

In addition, patients with depressive symptoms may require concomitant treatment with the algorithm for treatment of bipolar depression. The first stage of that algorithm recommends optimizing treatment with mood stabilizing medications. Therefore, the recommendation is to initiate treatment within the algorithm for hypomania/mania, stabilize those medications, and then assess symptoms of depression to determine if additional pharmacotherapy is needed.

At CDP 1, the clinician has determined that the patient requires medication treatment for symptoms associated with Bipolar I disorder. After review of patient symptoms, history, etc., a determination is made regarding where to initiate new treatment (in algorithm for mania/hypomania or depression, and at which stage). Each course through the CDP sequence is unique to one stage of treatment, in either algorithm. The recommendation is to minimize adjustments to multiple medications simultaneously as much as possible, to better allow for evaluation of the current stage of treatment.

CDP 2, Week 2

The next critical decision point occurs two weeks after the initiation of a new treatment stage. If medications that require serum levels have been prescribed, ideally the physician will have lab results to guide treatment decisions. Clinicians or support staff may administer the BDSS, and report scores on the BDSS worksheet. The rating of side effect severity may be entered on the worksheet as well.

At CDP 2, if the patient continues to experience symptoms within the mild to moderate range, the clinician may choose between continuing the current dosing or increasing the dose of medication(s). For symptoms within the severe range, the recommendation is to increase the dose of medication(s). If medications that require serum levels are adjusted (Li or DVP), order lab work so that dosage can be evaluated at CDP 3.

CDP 3, Week 4

If symptoms are not present, continue with current dosing. For symptoms within the mild to severe range, the clinician may choose between increasing the current dosing or moving to the next stage of treatment. If medications that require serum levels are adjusted (Li or DVP), order lab work so that dosage can be evaluated at CDP 4.

CDP 4, Week 6

Medications should be within the range of therapeutic dosing by this CDP. If symptoms are not present, continue with current dosing. The patient has been treated for six weeks with the current stage of treatment. Continued symptoms that are mild to severe warrant a further increase in dose, or consideration of the next stage of treatment.

CDP 5, Week 8

If symptoms are not present, continue with current dosing. If the patient is experiencing continued symptoms that are mild to moderate, the recommendation is to consider the next stage of treatment. However, it is possible that for some patients, this is a positive outcome, and continuing with the present treatment is a reasonable clinical decision. If severe symptoms are present, the clinician is directed to move to the next stage of treatment.

At any point within the CDPs, if medications are stabilized and patient outcomes remain positive and stable, visit intervals can be extended to every four weeks. All patients with Bipolar I disorder who achieve a satisfactory clinical response (preferably symptom remission) should receive continuation phase treatment. Please refer to the section on continuation and maintenance phase treatment for further recommendations.

Medications, Dosing, and Side Effects Management

EXHIBIT 5

Summary of Recommended Doses of Medications Used for Acute Phase Treatment of Mania/Hypomania*

Type/Class	Medication	Usual target dose	Usual maximum recommended dose (level)	Recommended administration schedule
	Lithium	(0.8–1.0 mEq/L)	(1.2 mEq/L)	BID or QHS
Anticonvulsants	Oxcarbazepine	600–2100 mg/day	2400 mg/day	BID or TID
	Divalproex Sodium	(80 ug/mL)	(125 mg/mL)	BID or QHS
Atypical Antipsychotics	Clozapine	100–300 mg/day	900 mg/day	QHS
	Olanzapine	10–15 mg/day	20 mg/day	BID or QHS
	Risperidone	2 mg/day	6 mg/day	BID or QHS
	Quetiapine	200–600 mg/day	800 mg/day	BID or QHS
	Ziprasidone	40–160 mg/day	160 mg/day	BID

*Doses used for maintenance treatment may be lower.

EXHIBIT 6

Doses of Medications Used for Acute Phase Treatment of Bipolar Depression*

Type/Class	Medication	Usual target dose	Usual maximum recommended dose (level)	Recommended administration schedule
SSRIs	Citalopram	20–40 mg/day	60 mg/day	QD
	Fluoxetine	20 mg/day	80 mg/day	QD
	Fluvoxamine	150–250 mg/day	250 mg/day	QD
	Paroxetine	20 mg/day	60 mg/day	QD
	Sertraline	50 mg/day	200 mg/day	QD
	Lamotrigine	200** mg/day	600 mg/day	QD
Others	Bupropion SR	300 mg/day	400 mg/day	BID (200 mg maximum in each dose)
	Nefazodone	300–600 mg/day	600 mg/day	QD
	Venlafaxine	150 mg/day	375 mg/day	BID or TID
	Venlafaxine XR	75 mg/day	225 mg/day	QD

*Doses used for maintenance treatment may be lower.

Please refer to Appendix A, Medications Descriptions, for instructions regarding initiation of this medication, due to risk of serious side effects associated **with rapid titration. For information on drug interactions, see Appendix C.

EXHIBIT 7

Side Effect Management and Recommendations*

Side effect	Recommendations*
GI Upset	<ul style="list-style-type: none"> —Administer medication with food and large quantities of liquid. —Consider lowering dose, if possible. —Use sustained release preparations of medications when available. —Some data suggest that this side effect can be successfully treated with H₂ blockers (e.g., cimetidine, ranitidine).
Tremor	<p>Enhanced physiologic tremor—A fine tremor of approximately 8–10 Hz; made worse with outstretched hands.</p> <ul style="list-style-type: none"> —Check blood levels of medication. —Decrease dose, divide dose, or change to slow release preparation of the medication. —Propranolol can be given at 20–30 mg TID. <p>Parkinsonian tremor – Coarse tremor at rest of approximately 4–6 Hz.</p> <ul style="list-style-type: none"> —Decrease dose, divide dosing, use QHS dosing, or switch to alternate medication. —Pharmacological treatments include benztropine 1–2 mg BID, amantadine 100 mg BID or TID, and diphenhydramine 25–50 mg BID or TID.
Sedation	<ul style="list-style-type: none"> —Change dosing to QHS. —Substitute a less sedating alternative medication.
Extrapyramidal Symptoms (EPS)	<ul style="list-style-type: none"> —Usually seen with typical antipsychotics. —Treat tremor as suggested above. —Reduce dose of antipsychotic medication. —Akathisia may respond to propranolol 20–30 mg TID, benztropine, amantadine, or diphenhydramine. If these are not effective, alternatives include clonidine 0.1 mg TID, and lorazepam 1 mg BID or TID. —Dystonic reactions can often be prevented by benztropine 1 mg BID or TID for the first few days of antipsychotic therapy. Acute dystonic reactions are generally managed with benztropine 1–2 mg IM or lorazepam 1 mg IM.
Tardive Dyskinesia	<ul style="list-style-type: none"> —Prescribe antipsychotics in the lowest dose necessary for the shortest time possible. —Consider alternatives for mood stabilization and control of agitation. —Use atypical antipsychotic medications. —Some evidence that vitamin E given in high doses (>1,000 units per day) may decrease some symptoms of tardive dyskinesia for some patients.
Insomnia	<ul style="list-style-type: none"> —Use QAM dosing, or divided dosing as early in the day as possible. —Use QHS dosing for any potentially sedating medications. —Use zolpidem at 5–10 mg QHS, zaleplon 5–20 mg (10 mg recommended dose) QHS, or benzodiazepine** such as temazepam 15–30 mg at night. Antipsychotics should always be considered second or third line agents for insomnia due to their risk of extrapyramidal side effects and tardive dyskinesia. Avoid use of trazodone for sleep as it is an antidepressant and thus has the potential for increasing symptoms of mania in bipolar patients.
Sexual Dysfunction	<ul style="list-style-type: none"> —Add yohimbine at 4–7.5 mg, TID, cyproheptadine at 4–8 mg given shortly before sexual intercourse, or bupropion given at dosages of 75–300 mg per day. Bupropion has the advantage of potentially also augmenting the antidepressant efficacy of the SSRI. However, a disadvantage of bupropion is possible induction or worsening of manic symptomatology with the use of two antidepressants.

*In general, treatment-emergent side effects should be addressed first by dose reduction or medication switching.

**Benzodiazepines are best avoided in patients with prior history of substance abuse/dependence or who are at risk for substance abuse. Nonaddicting agents are preferred.

EXHIBIT 8

Common Side Effects for Medications in the Algorithm for Hypomania/Mania

Medication	Common side effects*
Lithium	Tremor, drowsiness, nausea/vomiting, polyuria, muscle weakness, thirst, dry mouth, cognitive impairment
Anticonvulsants	
Oxcarbazepine	Dizziness, somnolence, diplopia, fatigue, nausea, vomiting, ataxia, abnormal vision, abdominal pain, tremor, dyspepsia, abnormal gait
Divalproex sodium	Nausea/vomiting, increased appetite with weight gain, sedation
Atypical Antipsychotics	
Clozapine	Sedation, anticholinergic effects, hypotension, weight gain, hypersalivation, constipation, nausea, vomiting
Olanzapine	Weight gain, sedation, anticholinergic effects, mild EPS, hypotension, potential TD
Risperidone	EPS, weight gain, mild sedation, anticholinergic effects, changes in blood pressure, sexual dysfunction, potential TD
Quetiapine	Sedation, blood pressure, weight gain
Ziprasidone	Rash, nausea and vomiting, constipation, somnolence, EPS, dizziness

* For more information about potential side effects, please consult the *Physician's Desk Reference* (PDR) or package inserts.

EXHIBIT 9

Common Side Effects for Medications in the Algorithm for Treatment of Depression in Bipolar Disorder

Medication	Common side effects*
SSRIs	Dizziness, dry mouth, insomnia, agitation, nausea, sexual dysfunction, headache
Citalopram	
Fluoxetine	
Paroxetine	
Sertraline	
Fluvoxamine	
Bupropion SR	Headache, agitation, weight loss, insomnia, nausea
Lamotrigine	Headache, nausea, dizziness, ataxia, somnolence, rhinitis, rash
Nefazodone	Dizziness, headache, nausea, somnolence, insomnia
Venlafaxine XR	Dizziness, somnolence, insomnia, decreased appetite, anxiety, headache, nausea, sexual dysfunction
MAOIs	Restlessness, dizziness, blurred vision, diarrhea, insomnia, weakness, arrhythmias, headache, sexual dysfunction
Phenelzine	
Tranylcypromine	

*For more information about potential side effects, please consult the *Physician's Desk Reference* (PDR) or package inserts.

Overlap and Taper Guidelines

Considerable evidence in patients with bipolar disorder suggests that a sudden discontinuation of lithium maintenance treatment is associated with a greater relapse of affective illness than a gradual taper (Suppes et al. 1996). Some evidence in patients with schizophrenia suggests that the abrupt discontinuation of maintenance antipsychotic treatment is also associated with a greater risk of relapse than is a gradual taper (Viguera et al. 1997). Thus, a gradual tapering of psychotropic medications in persons with bipolar disorder is strongly recommended when possible to minimize exacerbation or relapse of mood symptoms. Exceptions to this rule would be when severe or potentially life-threatening side effects occur or if manic symptoms should develop during antidepressant therapy.

In general, if a medication is to be discontinued, the new medication should be started and brought to a therapeutic level. Then the medication to be discontinued is gradually tapered over a period of at least one month. For example, if a patient was nonresponsive and had side effects during an adequate trial of lithium monotherapy at 1200 mg per day and the decision was made to discontinue lithium and begin therapy with divalproex sodium, the guidelines would recommend beginning divalproex sodium at 500–750 mg per day, checking blood levels and bringing the patient to a therapeutic level of divalproex sodium (≥ 50 $\mu\text{g/mL}$). At this point, the lithium could then be tapered at 300 mg per one to two weeks monitoring for evidence of increased symptoms of mania during this time.

If during the increasing dose period of the second medication, presumptive side effects from the first medication increase, it would be reasonable to begin tapering the first med prior to reaching full therapeutic dose of the second, new medication. On the other hand, if, during the taper of a medication, the patient shows a good response to a particular combination, it would be reasonable to continue with both medications. At a later time, the taper could be resumed to further evaluate the need for both medications.

Continuation and Maintenance Guidelines

ALGORITHM FOR TREATMENT OF HYPOMANIA/MANIA

Continuation Guidelines

If patient received pharmacotherapy during acute phase:

At baseline and throughout treatment, other psychosocial or nonmedication treatment modalities such as concomitant psychotherapy should be considered. After full response, the medication(s) should be continued for three months at the dose effective during the acute phase. Patients should be evaluated at least every three months during continuation treatment (if possible, every 1–2 months).

Importantly, once the patient is stabilized during the latter portion of continuation phase, it is recommended that efforts be made to simplify the medication regimen. When discontinuing one of the ongoing medications, the dosage should be tapered no more rapidly than 25 percent per week and not before three months of full remission have occurred. Tapering and discontinuation usually can be completed over a 1–2 month period. Patients should be educated concerning the signs and symptoms of recurrence of depressive symptoms.

At this time, little is scientifically known about the relative need for combined mood stabilizers long term. Thus, treatment decisions should be empiric. Once the patient is stabilized, consideration of tapering a medication either associated with side effects or limited partial response, while continuing other medications, is reasonable.

If mood instability recurs, prompt treatment with the medication previously effective should be initiated (i.e., initiate algorithm stage and tactic that previously resulted in remission of symptoms).

If patient received ECT during acute phase:

Continuation phase treatment with mood stabilizers is recommended after the initial treatment phase of ECT is completed. Selecting a mood stabilizer(s) that the patient has not previously received or one that the patient has responded to during a previous episode is generally recommended. However, if necessary, a previously partially effective mood stabilizer may be used alone or in combination with other mood stabilizers. Dosing, duration of treatment, monitoring, and medication tapering are as above.

If a patient relapses during continuation phase treatment, continuation ECT should be considered.

Maintenance Guidelines

Guidelines are limited due to relatively few scientific studies on the long-term management of bipolar patients. Treatment should be empirically based. In practice, usually all patients will need mood stabilizers to prevent return of symptoms. The lowest possible dose is recommended, while maintaining the mood stabilizing treatment at therapeutic levels. General practice at this time is lifetime mood stabilizers following two

manic episodes, or one episode if there is a severe episode and/or significant family history of bipolar or major depressive disorder. For a first episode of bipolar mania with no family history of bipolar or major depression, medication tapering and discontinuation may be considered after the continuation period is completed (usually six months in remission), depending on the severity of the first episode, surrounding factors, and prodromal history.

Active discussions regarding the initiation and duration of maintenance treatment are an important element in the clinician-patient collaboration for this as well as other phases of pharmacological management of bipolar disorder. The patient's personal preference as well as the risk factors for recurrence should be considered in the decision process.

ALGORITHM FOR THE TREATMENT OF DEPRESSION IN BIPOLAR DISORDER

Continuation Guidelines

If patient received pharmacotherapy during acute phase:

At baseline and throughout treatment, other psychosocial or nonmedication treatment modalities such as concomitant psychotherapy should be considered. After full response, the antidepressant medication(s) should be continued for 1–3 months at the dose effective during the acute phase. Patients should be evaluated at least every three months during continuation treatment (if possible, every 1–2 months).

For initial episodes of bipolar major depression and in all bipolars without a proven continued need for antidepressants, medication tapering and discontinuation should be considered after the continuation period is completed. If previous depressive episodes occurred with antidepressant discontinuation, maintenance treatment should be considered.

When discontinuing the antidepressant, the dosage should be tapered no more rapidly than 25 percent per week and not before 1–3 months of full remission have occurred. Tapering and discontinuation usually can be completed over a 1–2 month period. In major depressive disorder (unipolar), a new depressive episode is most likely to occur within the first eight months of medication discontinuation; therefore, patients should be evaluated every two to four months during that period. Patients should be educated concerning the signs and symptoms of recurrence of depressive symptoms.

If depression recurs, prompt treatment with the medication previously effective should be initiated (i.e., initiate algorithm stage and tactic that previously resulted in remission of depressive symptoms). At this time, little is scientifically known about the relative need for combined antidepressants long term. Thus, treatment decisions should be empiric, and once the patient is stabilized, consideration of tapering one of the antidepressants is reasonable.

If patient received ECT during acute phase:

Continuation phase treatment with mood stabilizers is recommended after the initial treatment phase of ECT is completed. Selecting a mood stabilizer(s) that the patient has

not previously received or one that the patient has responded to during a previous episode is generally recommended. However, if necessary, a previously partially effective mood stabilizer may be used alone or in combination with other mood stabilizers. Generally, mood stabilizers would be used prior to initiating an antidepressant. Dosing, duration of treatment, monitoring, and medication tapering are as above.

If a patient relapses during continuation phase treatment with an antidepressant, continuation ECT should be considered.

MAINTENANCE GUIDELINES

Guidelines are limited due to few scientific studies on the long-term management of antidepressants in bipolar patients. Treatment should be empirically based. In practice, some patients will need antidepressants to prevent return of symptoms. The lowest possible dose is recommended, while maintaining the mood-stabilizing treatment at therapeutic levels.

Active discussions regarding the initiation and duration of maintenance treatment are an important element in the clinician-patient collaboration for this as well as other phases of pharmacological management of bipolar disorder. The patient's personal preference, as well as the risk factors for recurrence, should be considered in the decision process.

MODIFICATIONS FOR INPATIENT USE

Patients who have been hospitalized for symptoms of bipolar disorder require fast-acting interventions to achieve stabilization and discharge. It is likely that a clinician may make the following modifications to these algorithms to achieve these goals.

Adjustment to Critical Decision Points

The CDPs are set at two-week intervals, assuming outpatient treatment. Of course, opportunities to evaluate the patient and make clinical decisions and medication adjustments will happen on an expedited schedule for inpatients. The recommendation is to observe the patient at least every 48 hours to evaluate symptoms, assess side effects to medications, and judge response.

Accelerated movement to advanced treatment stage

The clinician may use an advanced stage of treatment to achieve quick symptom relief and stabilization. If this is indicated as the best course of treatment, it is recommended to document the rationale for this decision. The clinician might suggest medications to taper and discontinue at a later point in discharge documentation, once the patient is stable, in order to minimize medication combinations and simplify medication regimens.

Use of alternate medications

If clinicians prescribe lithium and/or divalproex, it is unlikely that they will have the opportunity to monitor effects through blood levels over the course of a brief hospitalization. In this case, again, documentation of the prescribing intent would be helpful to ensure consistency when the patient continues in outpatient care. For example,

at the time of discharge, please include instructions for follow-up procedures, including target dose, expected blood levels, and intended taper of short-term medications.

In addition, clinicians may utilize faster acting forms of medications contained in these algorithms. Oral loading of divalproex sodium can be utilized for quick stabilization of manic patients (20 mg/kg is the standard formula). Additionally injectable and deconate forms of atypical antipsychotic medications may be available before the next substantial revision of this algorithm and manual.

INPATIENT TO OUTPATIENT TRANSITION

The transition between inpatient and outpatient care is often unsuccessful. Most inpatient clinicians have dealt with the frustration of discharging a patient only to see him or her return to the hospital within a few weeks as a result of not receiving outpatient follow-up and/or not filling prescriptions. Managed care's insistence on brief stays further aggravates the problem by forcing clinicians to discharge patients before they are truly stabilized. By the same token, outpatient clinicians must constantly revise their treatment plans when their long-term treatment intentions are not followed by the inpatient physician. The following three strategies may improve transitions between the two treatment settings:

1. **Document the treatment plan.** It is imperative that all clinicians document the rationale behind treatment decisions and outline the expected treatment plan. This would include detailing expected changes in medications, such as "I expect Mr. Doe will discontinue use of Ambien for sleep once manic symptoms are controlled by increased dosing of olanzapine and divalproex into recommended therapeutic ranges." Inpatient clinicians may want to start notes to their outpatient colleagues with "transfer" rather than "discharge" (I am *transferring* the acute care of this patient...) because the former term implies a continuation of care while the latter suggests a termination.
2. **Ensure that patients leave the hospital with enough medication to see them through to the first follow-up appointment.** If administrative policies prevent adequate supplies of medication from being dispensed, these policies need to be challenged. The future availability of long-acting second generation antipsychotics may help resolve this problem.
3. **Establish communication between the inpatient and outpatient treatment teams.** Physicians working in both arenas should get to know each other and brainstorm about ways to improve coordination between the two settings. Two possible strategies for improving communication are (1) having a team member (on each side) whose job it is to coordinate and follow up on transfers and (2) organizing quarterly meetings with key inpatient and outpatient staff members.

Appendix A:

Medication Descriptions

MEDICATIONS INCLUDED IN ALGORITHM FOR MANIA/HYPOMANIA

(Please refer to the PDR, package inserts, or other sources for more complete information.)

Lithium

Startup and Dosing

The initial dosing strategy for acute phase treatment of mania is 900 mg/day and obtaining a lithium level after 5–7 days. The approximate target dose range and schedule is 900–2400 mg/day given BID or, if appropriate, given QD (up to 1200 mg in a single bedtime dose as tolerated). If available, the slow release formulations are often better tolerated and provide a more even serum level once daily dosing is stabilized.

Side Effects

Patients should be monitored closely for emergence of side effects during initiation of treatment. Common side effects include: thirst, polyuria, cognitive changes, tremor, weight gain, sedation, weakness, diarrhea, nausea (watch for dehydration leading to toxicity), abdominal pain, ECG changes, acne, psoriasis, hypothyroidism, and acute renal dysfunction. Lithium use during pregnancy has been associated with birth defects including Epstein's anomaly. A recent analysis of these data suggested that the risk of this malformation may be less than previously thought, but nonetheless the use of lithium in pregnant women should be avoided.

Baseline Labs

A general health screen should be completed prior to initiation of lithium therapy. This should include a chemistry panel, creatinine and creatinine clearance, complete blood count, thyroid function tests, a human chorionic gonadotropin urine test (HCG) if appropriate, and an electrocardiogram (ECG) if the patient is more than 50 years of age and/or has a history of cardiac disease. After initiation of lithium therapy, patients should have a follow-up serum creatinine drawn, then another after reaching a therapeutic blood level. Follow-up ECGs should be performed as clinically indicated.

Monitoring and Blood Levels

During long-term lithium use, serum levels can be obtained every three months. Serum creatinine, BUN, and TSH should be drawn every six months or if signs of renal or thyroid toxicity appear. Serum lithium levels of 0.8–1.2 mEq/L generally provide a therapeutic response to episodes of acute mania. For maintenance phase, treatment levels above 0.6 mEq/L are recommended.

Drug Interactions

Central nervous system depressants, including alcohol, antidepressants, antipsychotics, and antihypertensive agents, may interact with lithium to produce sedation or confusional states. The following drug interactions may raise lithium levels: thiazide diuretics, nonsteroidal anti-inflammatory agents, and angiotensin-converting enzyme inhibitors. In addition, the following drug interactions may lower lithium levels: acetazolamide, theophylline, aminophylline, caffeine, and osmotic diuretics.

Divalproex Sodium (enteric-coated valproic acid)

Startup and Dosing

This medication is generally started at 250 mg/day x 2 days; 500 mg/day x 2 days; 750 mg/day until the next visit, at which time a serum blood level should be drawn. The approximate target dose range is 750–2000 mg/day. For the treatment of acute mania, one can also load 20 mg/kg over 1–1½ days. However, this loading technique is generally reserved for hospitalized patients. In many cases, it is possible to give the entire dose in the evening—especially when the enteric-coated form is used. This will help minimize daytime sedation.

Side Effects

Common side effects associated with divalproex include tremor, vomiting, heartburn, ataxia, sedation, diarrhea, nausea, weight gain, hair loss, and mild elevation of liver function tests. The sedation and tremor generally subside with chronic use and/or decreased dosage. Administration with food and the use of enteric-coated preparations or H₂ antagonists, such as ranitidine, may help diminish gastrointestinal effects. Divalproex may also cause mild impairment of cognitive function. The most severe side effects include hepatitis, hepatic failure, pancreatitis, and drug rashes including erythema multiform. Should significant liver function abnormalities or symptoms of hepatitis occur, the drug should be discontinued and the patient carefully monitored.

Baseline Labs

A general health screen should be completed prior to initiation of divalproex including a chemistry panel, liver function tests, a complete blood count (CBC) with platelets, and a HCG test if appropriate. Divalproex should not be given to patients with known liver disease.

Monitoring and Blood Levels

Optimal blood levels appear to be in the range of 50–125 µg/mL, and blood levels may be obtained weekly until the patient is stable. Since blood levels are trough measurements, levels should be drawn 12 hours post-dose or immediately prior to taking the next dose. Many clinicians also obtain LFTs and a CBC at the same time blood levels are assessed, and these should be repeated after beginning divalproex therapy. In asymptomatic patients receiving stable dosages, blood levels, LFTs, and a CBC may be obtained every six months.

Drug Interactions

Divalproex may have pharmacodynamic interactions with other psychotropic drugs, including carbamazepine, lithium, and antipsychotic drugs. In addition, divalproex produces pharmacokinetic interactions with many drugs. It will increase the levels of lamotrigine and may increase levels of tricyclic antidepressants and possibly selective serotonin reuptake inhibitors (SSRIs), phenytoin, phenobarbital, and other drugs. Divalproex may also change the effective levels of other protein-bound drugs by competing for protein binding sites. Furthermore, divalproex combinations may be decreased by drugs, such as carbamazepine, that induce hepatic microsomal enzymes. Its concentrations can be increased by drugs, such as SSRIs, that inhibit hepatic microsomal enzymes. Thus blood levels of divalproex should be carefully monitored when used in combination with other medications.

Carbamazepine

Startup and Dosing

For acute mania, dosages of 400–1200 mg/day are frequently used. Patients must be carefully observed after a therapeutic dose is established, because after several weeks carbamazepine may induce its own metabolism, requiring a dosage increase. The initial dosing strategy for acute phase treatment of mania is 200–400 mg/day, increasing by 200 mg/day every 2–4 days. Due to decreased toxic metabolite and drug interactions, oxcarbazepine is recommended if available.

Side Effects

Common side effects include dizziness, ataxia, rash, nystagmus, headache, sedation, dysarthria, diplopia, nausea and gastrointestinal upset, reversible mild leukopenia, and reversible mild increases in liver function tests. Less common dosage-related side effects include tremor, memory disturbance, confusional states, cardiac conduction delay, and syndrome of inappropriate antidiuretic hormone (SIADH) secretion. Some idiosyncratic toxicities include lenticular opacities, hepatitis, and blood dyscrasias.

Baseline Labs

Prior to initiation of carbamazepine, the physician should order and evaluate the results of a general health screen including a chemistry panel, CBC, liver function tests, and human chorionic gonadotropin (HCG) test, if appropriate.

Monitoring and Blood Levels

Blood levels may be obtained weekly until the patient is stable. Collection of electrolytes, CBC, and platelets is recommended weekly or biweekly during initial titration. The therapeutic blood levels of carbamazepine in the treatment of mania is not known; however, blood levels of about 4–12 µg/mL appear to be effective in epilepsy. This has been debated, however, resulting in many clinicians refraining from using blood levels to titrate efficacy in bipolar disorder. During maintenance therapy serum level should be obtained every 3–6 months, and a CBC and LFTs every six months.

Drug Interactions

Carbamazepine can induce the metabolism of many psychotropics including lamotrigine, divalproex, benzodiazepines, antipsychotics, and tricyclic antidepressants, and frequently prescribed nonpsychotropics including doxycycline, phenytoin, corticosteroids, theophylline, and coumadin. Carbamazepine can decrease the efficacy of oral contraceptives. Erythromycin, diltiazem, verapamil, cimetidine, and divalproex and other medications have been reported to increase levels of carbamazepine or its epoxide metabolite, potentially resulting in increased side effects. Phenobarbital, phenytoin, theophylline, and tricyclic antidepressants are among the medications reported to potentially decrease carbamazepine levels. Because of concern about agranulocytosis the FDA currently does not recommend the concurrent use of clozapine and carbamazepine. The use of carbamazepine with monoamine oxidase inhibitors may increase risk of hypertensive crises and should be used with great caution.

Oxcarbazepine

Startup and Dosing

Recommended daily dose is between 600–2100 mg/day, to a maximum 2400 mg/day, in a BID or TID dosing schedule. No autoinduction has been observed with oxcarbazepine. For patients with renal impairment, initial dosing should begin at one-half the usual starting dose, increased, if necessary, at a slow rate.

Side Effects

Clinically significant hyponatremia (sodium <125 mmol/L) can develop during oxcarbazepine use. Patients who have had hypersensitivity reactions to carbamazepine may have a similar reaction to oxcarbazepine. Common side effects include dizziness, somnolence, diplopia, fatigue, nausea, vomiting, ataxia, abnormal vision, abdominal pain, tremor, dyspepsia, and abnormal gait.

Baseline Labs

Prior to initiation of oxcarbazepine, the physician should order and evaluate the results of a general health screen including a chemistry panel, CBC, liver function tests, and human chorionic gonadotropin (HCG) test, if appropriate.

Monitoring and Blood Levels

Measurement of serum sodium levels should be considered for patients on oxcarbazepine. Routine blood serum levels are not necessary.

Drug Interactions

Oxcarbazepine may reduce the efficacy of hormonal contraceptives. Oxcarbazepine may lower the plasma concentrations of dihydropyridine calcium antagonists (e.g., felodipine and verapamil). It can inhibit CYP2C19 and induce CYP3A4/5. Protein binding is low (40 percent).

Risperidone

Start-up and Dosing

The effective dosage in bipolar disorder is not known. In patients with schizophrenia, BID dosing beginning with 1 mg BID and increasing to a target dose of 2–4 mg BID over a period of several weeks is often used. However, clinical experience would suggest beginning at a low dose, 1–2 mg per day or less, and increasing as needed to control target symptoms including psychosis. The maximum recommended dose is 16 mg daily. Half the usual dose should be used in persons with renal impairment.

Side Effects

Side effects include orthostatic hypotension, and extrapyramidal side effects at higher doses, including possible tardive dyskinesia and somnolence.

Baseline Labs

Baseline liver function tests and renal function should be assessed, since risperidone is hepatically metabolized and has active metabolites that are renally eliminated.

Monitoring and Blood Levels

None.

Drug Interactions

This medication is metabolized by the P4502D6 system. Therefore, concurrent use of medication that inhibits this system, which includes selective serotonin reuptake inhibitors, may increase plasma levels of risperidone and thus, increase side effects.

Olanzapine

Start-up and Dosing

The effective dose of this medication in bipolar disorder is 5–20 mg per day. A commonly prescribed dose for schizophrenia is 5–15 mg per day. The patient should generally be started at 2.5–5 mg daily and increased to control target symptoms including psychosis to a maximum dose of 20 mg daily.

Side Effects

The side effects of this medication include somnolence, weight gain, elevations in triglycerides and serum glucose, and extrapyramidal side effects including a possible risk of tardive dyskinesia.

Baseline Labs

Weight, blood glucose, and lipid panel.

Monitoring and Blood Levels

Weight, blood glucose, and lipid panel.

Drug Interactions

Elevated levels of olanzapine can result when the medication is used in conjunction with fluvoxamine. In addition, olanzapine interacts with carbamazepine, which can cause up to a 50 percent increase in the clearance of olanzapine from the system.

Clozapine

Start-up and Dosing

The effective dose of this medication in bipolar disorder is not known. A commonly prescribed starting dose is 25–50 mg per day. This is then increased in 25 mg increments no more frequently than every 2–3 days to control target symptoms including psychosis. Daily dosages of 100–400 mg per day are typical.

Side Effects

The most common side effects include somnolence, sedation, weight gain, hypersalivation, tachycardia, dizziness, constipation, weight gain, and nausea and vomiting. A less common but potential life-threatening side effect is agranulocytosis, which has been reported in about 1–2 percent of patients receiving clozapine. An additional side effect is seizures, which is a dose-dependent side effect reported in about 3–4 percent of patients receiving clozapine at daily dosages greater than 600 mg.

Baseline Labs

A general health screen that includes a complete blood count, LFTs, and an EKG is recommended.

Monitoring and Blood Levels

White blood count is to be obtained weekly during the first six months of clozapine therapy. If no change in white blood count is measured over the first six months, then white blood count monitoring can be reduced to every two weeks. The current guidelines recommend discontinuing the medication if the white blood count drops to less than 2000 mm³ or if the granulocyte count drops to less than 1000 mm³.³ The monitoring of blood levels is not currently a standard of practice with clozapine; however, some data suggest a trough level of at least 350 µg/mL may be effective.

Drug Interactions and Laboratory Interferences

Clozapine should not be given with other drugs that are associated with the risk of agranulocytosis. This includes carbamazepine, propylthiouracil, sulfonamides, and captopril. No laboratory interferences are known with clozapine. Since a large percentage of clozapine is metabolized via Cyt P450 1A2 and 3A3/3A4, fluvoxamine and nefazodone may inhibit its metabolism, raising the levels of clozapine.

Quetiapine

Start-up and Dosing

The effective dose of this medication in bipolar disorder is not known. Commonly prescribed dosages for schizophrenia begin at 25 mg BID and increase by 25–50 mg per

day to a target dose of 300 mg. In general, dosages of 300–700 mg appear to be effective in schizophrenia. Bipolar patients may respond to lower dosing.

Side Effects

Side effects include orthostatic hypotension, sedation, and limited weight gain. In some animal studies, this medication has been demonstrated to increase the risk of cataracts. Currently, the manufacturer recommends a baseline and follow-up eye exams.

Baseline Labs

None.

Monitoring and Blood Levels

None.

Drug Interactions

This medication is metabolized by the P4503A4 system; therefore, medications that inhibit this enzyme system, including fluvoxamine and nefazodone, may increase blood levels of quetiapine. Medications that enhance this metabolic system, such as carbamazepine and phenytoin, may decrease blood levels of this medication.

Ziprasidone

Start-up and Dosing

The effective dose of this medication in bipolar disorder is not known. A commonly prescribed dose for schizophrenia begins at 20 mg BID taken with food and increasing to a target dose of 20–80 mg BID per day with a total maximum dose of 160 mg per day.

Side Effects

The side effects of this medication include somnolence, extrapyramidal effects, nausea, insomnia, akathisia, dyspepsia, dizziness, and constipation.

Baseline Labs

None needed unless a patient is at risk for significant electrolyte disturbances, hypokalemia in particular. Such patients should have baseline serum potassium and magnesium measurements. An ECG is also recommended.

Monitoring and Blood Levels

None.

Drug Interactions

This medication should not be used with drugs that prolong the QT interval, including quinidine, dofetilidone, sotalol, thioridazine, moxifloxacin, and sparfloxacin. In addition, this drug has the potential to antagonize levo-dopa and other dopamine agonists and can enhance the effects of serotonin agonists. Carbamazepine has also been shown to decrease levels of ziprasidone.

Topiramate

Start-up and Dosing

The effective dose of this medication in bipolar disorder is not known. Commonly prescribed dosages for epilepsy are 200–400 mg daily, with a maximum recommended dose of 1600 mg per day.

Side Effects

Side effects include somnolence, dizziness, ataxia, nistagmus, parasthesias, fatigue, anxiety, decreased appetite, weight loss, and tremor. An additional risk is kidney stones, which were reported in 1.5 percent of patients receiving this medication. The concurrent use of carbonic anhydrase inhibitors such as acetazolamide or zonisamide appear to increase the risk of kidney stones. Patients are advised to drink adequate amounts of fluid to possibly decrease the risk of kidney stones.

Baseline Labs

None.

Monitoring and Blood Levels

None.

Drug Interactions

This medication can potentially decrease divalproex levels. Also, divalproex and carbamazepine appear to decrease topiramate levels; therefore, careful monitoring of divalproex and carbamazepine levels are useful when topiramate is prescribed.

MEDICATIONS INCLUDED IN ALGORITHM FOR DEPRESSION IN BIPOLAR DISORDER

(Please refer to the PDR, package inserts, or other sources for more complete information.)

Lamotrigine

Start-up and Dosing

The effective dose of this medication in bipolar depression is targeted at 200 mg. However, doses of 200–500 mg daily may be effective in the control of seizures. In general, this medication is started at 25 mg daily for the first two weeks and increased in 25 mg increments every two weeks thereafter. *If the bipolar patient is concurrently taking divalproex*, the medication should be started at 25 mg every other day and increased by 25 mg every two weeks. *If the bipolar patient is concurrently taking carbamazepine*, the dosage should be 50 mg per day for the first two weeks and then increased in 25–50 mg increments every two weeks thereafter. If divalproex is also being used, the dose should be 12.5 mg per day for two weeks, then increased to 25 mg for two weeks.

Side Effects

Common side effects include headache, nausea, dizziness, ataxia, somnolence, and rhinitis. These side effects can often be treated by slowing the rate of upper titration or decreasing the dose. An additional side effect is a rash that has been reported to occur in 3–4 percent of patients receiving lamotrigine and which in some cases can become severe and life threatening (<1 percent). If a drug rash develops, the current guidelines recommend immediately discontinuing the medication and having the rash evaluated by a dermatologist or internist. Rapid titration and the current use of divalproex appear to be risk factors for rash.

Baseline Labs

None.

Monitoring and Blood Levels

Blood levels are not currently recommended and no routine labs are currently recommended.

Drug Interactions

Divalproex inhibits the metabolism of lamotrigine; therefore, care should be used when these medications are combined and lamotrigine should be increased slowly. Carbamazepine induces the metabolism of lamotrigine; therefore, higher dosages of lamotrigine are required when used concurrently with carbamazepine.

Fluoxetine

Start-up and Dosing

This medication is generally started at 20 mg in the morning and this is often the target dose. If dose increases are needed, they should not be done for at least four weeks, then the dose can be increased by 10–20 mg to a maximum dose of 80 mg per day.

Common Side Effects

Common side effects include headache, nervousness, insomnia, somnolence, nausea, diarrhea, dry mouth, and weight loss.

Baseline Labs

None.

Monitoring and Blood Levels

Blood levels are not currently obtained on a regular basis with this medication.

Drug Interactions

This medication inhibits the P450 enzyme system and will result in increased concentrations of medications metabolized by this system, such as tricyclic antidepressants, antipsychotics, and carbamazepine. In addition, this medication should not be taken in combination with MAOIs or in a patient who has recently discontinued taking an MAOI.

Paroxetine

Start-up and Dosing

This medication is generally started at 20 mg usually taken in the morning. The target dose is often 20 mg per day; however, the dose can be increased up to 50 mg per day.

Side Effects

The side effects of this medication include nausea and vomiting, headaches, dry mouth, and sedation.

Baseline Labs

None.

Monitoring and Blood Levels

None.

Drug Interactions

This medication has a number of drug interactions with medications inhibited by the P450 enzyme system, including tricyclic antidepressants, propranolol, and coumadin, causing increased plasma levels of these medications. Careful monitoring for side effects is advised when these medications are given together.

Sertraline

Start-up and Dosing

This medication is generally started at 50 mg in the morning and this is often the target dose. The medication can be increased in 50 mg increments to a maximum dose of 200 mg per day.

Side Effects

The side effects of this medication include nausea, vomiting, dry mouth, diarrhea, insomnia, and somnolence.

Baseline Labs

None.

Monitoring and Blood Levels

None

Drug Interactions

This medication inhibits the P450 enzyme system resulting in elevated plasma levels of drugs metabolized by that system such as the TCAs.

Bupropion SR

Start-up and Dosing

This medication is generally started at 150 mg in the morning. The target dose is generally 150 mg BID. The medication can be increased up to 200 mg BID.

Side Effects

Common side effects include constipation, headache, dizziness, and insomnia. Another potential side effect of this medication is seizures. This appears to be a dose-dependent side effect increasing to about 5 percent at dosages greater than 450 mg per. The use of bupropion in persons with seizure disorders or eating disorders is not advised.

Baseline Labs

None

Monitoring and Blood Levels

None.

Drug Interactions

Bupropion should not be given along with monoamine oxidase inhibitors because of the possible increased risk of hypertensive crisis.

Nefazodone

Start-up and Dosing

This medication is generally started at 50 mg BID with the target dose of 300–600 mg per day. The maximum dose of this medication is 600 mg per day.

Side Effects

Common side effects with this medication include headache, dry mouth, nausea, constipation, and somnolence.

Baseline Labs

None.

Monitoring and Blood Levels

None.

Drug Interactions

Nefazodone inhibits the cytochrome P450 3A4 system and therefore can decrease the metabolism of other medications metabolized through this system including terfenadine, astemizole, or cisapride. These medications should not be given along with nefazodone. Nefazodone can increase plasma concentrations of drugs that are highly protein bound, including monoamine oxidase inhibitors, haloperidol, lorazepam, triazolam, alprazolam, digoxin, and propranolol.

Venlafaxine

Start-up and Dosing

This medication is generally started at 37.5 mg bid. The target dose is generally 150–225 mg given daily in divided doses. The maximum daily dose for this medication is 375 mg per day.

Side Effects

Common side effects include decreased appetite, nausea, vomiting, anxiety, dizziness, insomnia, somnolence, sweating, and abnormalities of visual accommodation.

Baseline Labs

None.

Monitoring and Blood Levels

None.

Drug Interactions

Venlafaxine is contraindicated with the MAOIs. Do not begin treatment with venlafaxine until at least two weeks after discontinuation of an MAOI. MAOI treatment should not begin until at least seven days after discontinuation of venlafaxine.

Fluvoxamine

Start-up and Dosing:

This medication is generally started at 50 mg per day. The target dose is 100–200 mg per day. The maximum daily dose is 300 mg per day.

Side Effects:

Side effects include nausea, somnolence, insomnia, nervousness, and dizziness.

Baseline Labs:

None.

Monitoring and Blood Levels:

None.

Drug Interactions

Fluvoxamine inhibits certain P450 enzymes 1A2 and therefore increases the plasma levels of medications metabolized through these enzymes. These include terfenadine, astemizole, and cisapride. In addition, alprazolam and diazepam may also have their plasma levels increased with fluvoxamine. It is not recommended that fluvoxamine be used in combination with these medications.

Citalopram

Start-up and Dosing

This medication is generally started at 20 mg, usually taken in the morning. It can be increased in 10 mg increments to a target dose of 20–40 mg. Maximum daily dose is 60 mg; for adults older than 65, maximum daily dose is 40 mg.

Side Effects

Side effects include dizziness, headache, sleep disturbance, dry mouth, and/or nausea.

Baseline Labs

None.

Monitoring and Blood Levels

None.

Drug Interactions

This medication should not be used in combination with an MAOI. Citalopram is 80% protein-bound, and has a low potential for interactions with drugs metabolized by the CYP2D6 system or other CYP isoenzymes. It is less cardiotoxic than tricyclic and tetracyclic antidepressants.

Monoamine Oxidase Inhibitors

Phenelzine

Tranylcypromine

Start-up and Dosing

Two monoamine oxidase inhibitors are currently available in the United States, phenelzine and tranylcypromine. Phenelzine is generally started at 15 mg TID with a target dose of 60–90 mg per day. Tranylcypromine is generally started at 30 mg per day in divided doses with a target dose of 30–40 mg per day in divided doses.

Side Effects

Common side effects include orthostatic hypotension, weight gain, edema, sexual dysfunction and insomnia. A potentially life-threatening side effect is hypertensive crisis. This can be brought on by combining monoamine oxidase inhibitors with certain medications including meperidine; over-the-counter cold, hay fever, and sinus medications; and stimulants including amphetamines, cocaine, methylphenidate, dopamine, epinephrine, norepinephrine, and isoproterenol. Hypertensive crisis can also be brought on by ingesting foods with a high tyramine content, including certain alcohol beverages (e.g., Chianti wine), fava beans, aged cheeses, and beef or chicken liver. All patients should be given information about tyramine-rich foods and medications to be avoided before beginning monoamine oxidase inhibitors.

Baseline Labs

None.

Monitoring and Blood Levels

Blood levels are not routinely obtained for these medications.

Drug Interactions

See Medications, Dosage, and Side Effects Management section. These medications should not be administered along with serotonin selective reuptake inhibitors or stimulants.

Appendix B:

Process Measures

Brief Bipolar Disorder Symptom Scale

Critical Decision Points and Tactics for the Treatment of Bipolar Disorder

BDSS/CDP Worksheet

Scoring Criteria for Overall Symptom and Side Effect Ratings

Patients with a diagnosis of Bipolar I disorder may be evaluated using the Brief Bipolar Disorder Symptoms Scale, or BDSS. This scale is derived from items included on the 24-item Brief Psychiatric Rating Scale.² The 10-item version assesses hostility, elevated mood, grandiosity, excitement, motor hyperactivity, depressed mood, anxiety, emotional withdrawal, blunted affect, and unusual thought content.

Physicians can use the worksheet (see page 60) to graph patient scores on each of these 10 symptom domains. While the presence of one or more of these symptoms might be suggestive of different things, they are loosely grouped within the categories of mania/hypomanic symptoms, depressive symptoms, and psychotic symptoms. Of course, physician judgment will be necessary to evaluate the source of particular symptoms. For example, blunted affect may be a result of increased depression, increased psychosis, or other sources. Elevated mood may be related to increased hypomania/mania or a manifestation of increased delusional/psychotic symptoms. The grouping is intended to help facilitate decision making within the algorithms, but is not exclusive.

²J. E. Overall and D. R. Gorham. "Introduction - the Brief Psychiatric Rating Scale (BPRS): Recent developments in ascertainment and scaling." *Psychopharmacol Bulletin* 24 (1988): 97–99.

BRIEF BIPOLAR DISORDER SYMPTOM SCALE

1. **HOSTILITY:** Animosity, contempt, belligerence, threats, arguments, tantrums, property destruction, fights, and any other expression of hostile attitudes or actions. Do not infer hostility from neurotic defenses, anxiety, or somatic complaints. Do not include incidents of appropriate anger or obvious self-defense.

How have you been getting along with people (family, co-workers, etc.)?

Have you been irritable or grumpy lately? (How do you show it? Do you keep it to yourself?)

Were you ever so irritable that you would shout at people or start fights or arguments? (Have you found yourself yelling at people you didn't know?)

Have you hit anyone recently?

NA—Not Assessed

1—Not Present

2—Very Mild

Irritable or grumpy, but not overtly expressed.

3—Mild

Argumentative or sarcastic.

4—Moderate

Overtly angry on several occasions OR yelled at others excessively.

5—Moderately Severe

Has threatened, slammed about, or thrown things.

6—Severe

Has assaulted others but with no harm likely, e.g., slapped or pushed, OR destroyed property, e.g., knocked over furniture, broken windows.

7—Extremely Severe

Has attacked others with definite possibility of harming them or with actual harm, e.g., assault with a household object or weapon.

2. **ELEVATED MOOD:** A pervasive, sustained and exaggerated feeling of well-being, cheerfulness, euphoria (implying a pathological mood), optimism that is out of proportion to the circumstances. Do not infer elation from increased activity or from grandiose statements alone.

Have you felt so good or high that other people thought that you were not your normal self?

Have you been feeling cheerful and “on top of the world” without any reason?

If patient reports elevated mood/euphoria, ask the following:

Did it seem like more than just feeling good? How long did that last?

NA—Not Assessed

1—Not Present

2—Very Mild

Seems to be very happy, cheerful without much reason.

3—Mild

Some unaccountable feelings of well-being that persist.

4—Moderate

Reports excessive or unrealistic feelings of well-being, cheerfulness, confidence or optimism inappropriate to circumstances, some of the time. May frequently joke, smile, be giddy or overly enthusiastic OR few instances of marked elevated mood with euphoria.

5—Moderately Severe

Reports excessive or unrealistic feelings of well-being, confidence or optimism inappropriate to circumstances much of the time. May describe feeling “on top of the world,” “like everything is falling into place,” or “better than ever before,” OR several instances of marked elevated mood with euphoria.

6—Severe

Reports many instances of marked elevated mood with euphoria OR mood definitely elevated almost constantly throughout interview and inappropriate to content.

7—Extremely Severe

Patient reports being elated or appears almost intoxicated, laughing, joking, giggling, constantly euphoric, feeling invulnerable, all inappropriate to immediate circumstances.

3. **GRANDIOSITY:** Exaggerated self-opinion, self-enhancing conviction of special abilities or powers, or identity as someone rich or famous. Rate only patients' statements about themselves, not their demeanor. **Note:** If the subject rates a "6" or "7" due to grandiose delusions, you must rate unusual thought content at least a "4" or above.

Is there anything special about you? Do you have any special abilities or powers? Have you thought that you might be somebody rich or famous?

If the patient reports any grandiose ideas/delusions, ask the following:

How often have you been thinking about [use patient's description]? Have you told anyone about what you have been thinking? Have you acted on any of these ideas?

NA—Not Assessed

1—Not Present

2—Very Mild

Feels great and denies obvious problems, but not unrealistic.

3—Mild

Exaggerated self-opinion beyond abilities and training.

4—Moderate

Inappropriate boastfulness, claims to be brilliant, insightful, or gifted beyond realistic proportions, but rarely self-discloses or acts on these inflated self-concepts. Does not claim that grandiose accomplishments have actually occurred.

5—Moderately Severe

Same as 4 but often self-discloses and acts on these grandiose ideas. May have doubts about the reality of the grandiose ideas. Not delusional.

6—Severe

Delusional—claims to have special powers like ESP, to have millions of dollars, invented new machines, worked at jobs when it is known that he was never employed in these capacities, be Jesus Christ, or the president. Patient may not be very preoccupied.

7—Extremely Severe

Delusional—Same as 6 but subject seems very preoccupied and tends to disclose or act on grandiose delusions.

4. **DEPRESSION:** Sadness, unhappiness, anhedonia, preoccupation with depressing topics (can't attend to TV, conversations due to depression), hopelessness, and loss of self-esteem (dissatisfied or disgusted with self or feelings of worthlessness). Do not include vegetative symptoms, e.g., motor retardation, early waking, or the amotivation that accompanies the deficit syndrome.

How has your mood been recently? Have you felt depressed (sad, down, unhappy, as if you didn't care)?

Are you able to switch your attention to more pleasant topics when you want to?

Do you find that you have lost interest in or get less pleasure from things you used to enjoy, like family, friends, hobbies, watching TV, eating?

If subject reports feelings of depression, ask the following:

How long do these feelings last? Have they interfered with your ability to perform your usual activities/work?

NA—Not Assessed

1—Not Present

2—Very Mild

Occasionally feels sad, unhappy, or depressed.

3—Mild

Frequently feels sad or unhappy but can readily turn attention to other things.

4—Moderate

Frequent periods of feeling very sad, unhappy, moderately depressed, but able to function with extra effort.

5—Moderately Severe

Frequent, but not daily, periods of deep depression OR some areas of functioning are disrupted by depression.

6—Severe

Deeply depressed daily but not persisting throughout the day OR many areas of functioning are disrupted by depression.

7—Extremely Severe

Deeply depressed daily OR most areas of functioning are disrupted by depression.

5. **ANXIETY:** Reported apprehension, tension, fear, panic, or worry. Rate only the patient's statements, not observed anxiety that is rated under TENSION.

Have you been worried a lot during [mention time frame]? Have you been nervous or apprehensive? (What do you worry about?)

Are you concerned about anything? How about finances or the future?

When you are feeling nervous, do your palms sweat or does your heart beat fast (or do you experience shortness of breath, trembling, choking)?

If patient reports anxiety or autonomic accompaniment, ask the following:

How much of the time have you been [use patient's description]?

Has it interfered with your ability to perform your usual activities/work?

NA—Not Assessed

1—Not Present

2—Very Mild

Reports some discomfort due to worry OR infrequent worries that occur more than usual for most normal individuals.

3—Mild

Worried frequently but can readily turn attention to other things.

4—Moderate

Worried most of the time and cannot turn attention to other things easily but no impairment in functioning OR occasional anxiety with autonomic accompaniment but no impairment in functioning.

5—Moderately Severe

Frequent, but not daily, periods of anxiety with autonomic accompaniment, OR some areas of functioning are disrupted by anxiety or worry.

6—Severe

Anxiety with autonomic accompaniment daily but not persisting throughout the day OR many areas of functioning are disrupted by anxiety or constant worry.

7—Extremely Severe

Anxiety with autonomic accompaniment persisting throughout the day OR most areas of functioning are disrupted by anxiety or constant worry.

6. **UNUSUAL THOUGHT CONTENT:** Unusual, odd, strange, or bizarre thought content. Rate the degree of unusualness, not the degree of disorganization of speech. Delusions are patently absurd, clearly false, or bizarre ideas that are expressed with full conviction. Consider the patient to have full conviction if he/she has acted as though the delusional belief were true. Ideas of reference/persecution can be differentiated from delusions in that ideas are expressed with much doubt and contain more elements of reality. Include thought insertion, withdrawal, and broadcast. Include grandiose, somatic and persecutory delusions even if rated elsewhere. **Note:** If somatic concern, guilt, suspiciousness, or grandiosity are rated “6” or “7” due to delusions, then unusual thought content must be rated a “4” or above.

Have you been receiving any special messages from people or from the way things are arranged around you? Have you seen any references to yourself on TV or in the newspapers?

Can anyone read your mind?

Do you have a unique relationship with God?

Is anything like electricity, X-rays, or radio waves affecting you?

Are thoughts put into your head that are not your own?

Have you felt that you were under the control of another person or force?

If patient reports any odd ideas/delusions, ask the following:

How often do you think about [use patient’s description]?

Have you told anyone about these experiences? How do you explain the things that have been happening [specify]?

NA—Not Assessed

1—Not Present

2—Very Mild

Ideas of reference (people may stare or may laugh at him/her), ideas of persecution (people may mistreat him/her). Unusual beliefs in psychic powers, spirits, UFOs, or unrealistic beliefs in his/her or patient’s own abilities. Not strongly held, some doubt.

3—Mild

Same as 2, but degree of reality distortion is more severe as indicated by highly unusual ideas or greater conviction. Content may be typical of delusions (even bizarre), but without full conviction. The delusion does not seem to have fully formed, but is considered as one possible explanation for an unusual experience.

4—Moderate

Delusion present but no preoccupation or functional impairment. May be an encapsulated delusion or a firmly endorsed absurd belief about past delusional circumstances.

5—Moderately Severe

Full delusion(s) present with some preoccupation OR some areas of functioning disrupted by delusional thinking.

6—Severe

Full delusion(s) present with much preoccupation OR many areas of functioning are disrupted by delusional thinking.

7—Extremely Severe

Full delusions present with almost total preoccupation OR most areas of functioning are disrupted by delusional thinking.

Rate the following items on the basis of observed behavior and speech.

7. **EXCITEMENT:** Heightened emotional tone, or increased emotional reactivity to interviewer or topics being discussed, as evidenced by increased intensity of facial expressions, voice tone, expressive gestures or increase in speech quantity and speed.

NA—Not Assessed

1—Not Present

2—Very Mild

Subtle and fleeting or questionable increase in emotional intensity. For example, at times, seems keyed-up or overly alert.

3—Mild

Subtle but persistent increase in emotional intensity. For example, lively use of gestures and variation in voice tone.

4—Moderate

Definite but occasional increase in emotional intensity. For example, reacts to interviewer or topics that are discussed with noticeable emotional intensity. Some pressured speech.

5—Moderately Severe

Definite and persistent increase in emotional intensity. For example, reacts to many stimuli, whether relevant or not, with considerable emotional intensity. Frequent pressured speech.

6—Severe

Marked increase in emotional intensity. For example reacts to most stimuli with inappropriate emotional intensity. Has difficulty settling down or staying on task. Often restless, impulsive, or speech is often pressured.

7—Extremely Severe

Marked and persistent increase in emotional intensity. Reacts to all stimuli with inappropriate intensity, impulsiveness. Cannot settle down or stay on task. Very restless and impulsive most of the time. Constant pressured speech.

8. **MOTOR HYPERACTIVITY:** Increase in energy level evidenced in more frequent movement and/or rapid speech. Do not rate if restlessness is due to akathisia.

NA—Not Assessed

1—Not Present

2—Very Mild

Some restlessness, difficulty sitting still, lively facial expressions, or somewhat talkative.

3—Mild

Occasionally very restless, definite increase in motor activity, lively gestures, 1–3 brief instances of pressured speech.

4—Moderate

Very restless, fidgety, excessive facial expressions or nonproductive and repetitious motor movements. Much pressured speech, up to one-third of the interview.

5—Moderately Severe

Frequently restless, fidgety. Many instances of excessive nonproductive and repetitious motor movements. On the move most of the time. Frequent pressured speech, difficult to interrupt. Rises on 1–2 occasions to pace.

6—Severe

Excessive motor activity, restlessness, fidgety, loud tapping, noisy, etc., throughout most of the interview. Speech can only be interrupted with much effort. Rises on 3–4 occasions to pace.

7—Extremely Severe

Constant excessive motor activity throughout entire interview, e.g., constant pacing, constant pressured speech with no pauses, interviewee can only be interrupted briefly and only small amounts of relevant information can be obtained.

9. **EMOTIONAL WITHDRAWAL:** Deficiency in patient's ability to relate emotionally during interview situation. Use your own feeling as to the presence of an "invisible barrier" between patient and interviewer. Include withdrawal apparently due to psychotic processes.

NA—Not Assessed

1—Not Present

2—Very Mild

Lack of emotional involvement shown by occasional failure to make reciprocal comments; occasionally appears preoccupied or smiles in a stilted manner, but spontaneously engages the interviewer most of the time.

3—Mild

Lack of emotional involvement shown by noticeable failure to make reciprocal comments; appears preoccupied or lacking in warmth, but responds to interviewer when approached.

4—Moderate

Emotional contact not present much of the interview because subject does not elaborate responses, fails to make eye contact, doesn't seem to care if interviewer is listening, or may be preoccupied with psychotic material.

5—Moderately Severe

Same as "4" but emotional contact not present during most of the interview.

6—Severe

Actively avoids emotional participation. Frequently unresponsive or responds with yes/no answers (not solely due to persecutory delusions). Responds with only minimal affect.

7—Extremely Severe

Consistently avoids emotional participation. Unresponsive or responds with yes/no answers (not solely due to persecutory delusions). May leave during interview or just not respond at all.

10. **BLUNTED AFFECT:** Restricted range in emotional expressiveness of face, voice, and gestures. Marked indifference or flatness even when discussing distressing topics. In the case of euphoric or dysphoric patients, rate Blunted Affect if a flat quality is also clearly present. Use the following probes at end of interview to assess emotional responsivity:

Have you heard any good jokes lately? Would you like to hear a joke?

NA—Not assessed

1—Not Present

2—Very Mild

Emotional range is slightly subdued or reserved; but patient displays appropriate facial expressions and tone of voice that are within normal limits.

3—Mild

Emotional range overall is diminished; patient is subdued or reserved, without many spontaneous and appropriate emotional responses. Voice tone is slightly monotonous.

4—Moderate

Emotional range is noticeably diminished; patient doesn't show emotion, smile, or react to distressing topics except infrequently. Voice tone is monotonous or there is noticeable decrease in spontaneous movements. Displays of emotion or gestures are usually followed by a return to flattened affect.

5—Moderately Severe

Emotional range very diminished; patient doesn't show emotion, smile or react to distressing topics except minimally; few gestures; facial expression does not change very often. Voice tone is monotonous much of the time.

6—Severe

Very little emotional range or expression. Mechanical in speech and gestures most of the time. Unchanging facial expression. Voice tone is monotonous most of the time.

7—Extremely Severe

Virtually no emotional range or expressiveness; stiff movements. Voice tone is monotonous all of the time.

Sources of information (check all applicable):		Explain here if validity of assessment is questionable:	
<input type="checkbox"/> Patient	<input type="checkbox"/> Parents/Relatives	<input type="checkbox"/> Symptoms possibly drug-induced	<input type="checkbox"/> Underreported due to lack of rapport
<input type="checkbox"/> Mental Health Professionals	<input type="checkbox"/> Chart	<input type="checkbox"/> Underreported due to negative symptoms	<input type="checkbox"/> Patient uncooperative
<input type="checkbox"/> Difficult to assess due to formal thought disorder			
Confidence in assessment:		Other: _____	
<input type="checkbox"/> (Rate on a scale of 1–5, where 1=Not confident at all, and 5=Very confident.)			

CRITICAL DECISION POINTS AND TACTICS FOR THE TREATMENT OF BIPOLAR DISORDER*

Instructions: To identify the recommendations for the appropriate CDP, trace to the right to the degree of symptom severity indicated by the BDSS Chart.

Critical decision point		SYMPTOMS							
		Mild		Mild to moderate				Severe	
		NA	1	2	3	4	5	6	7
Clinical status									
Week 1: CDP 1	Symptomatic.			Start medications.			Start medications.		
Week 2: CDP 2	Order serum levels (if applicable) to adjust dose.	Continue current dose.		Continue current dose. Consider increasing dose.			Increase dose.		
Week 4: CDP 3	Order serum levels (if applicable) to adjust dose.	Continue current dose.		Increase dose or consider next stage.			Increase dose or consider next stage.		
Week 6: CDP 4	All serum levels should be within therapeutic range.	Continue current dose.		Increase dose or consider next stage.			Increase dose or consider next stage.		
Week 8: CDP 5		Continue current dose.		Consider next stage.			Go to next stage.		

*Side Effects: Treatment recommendations assume that side effects are tolerable. Refer to the Side Effects Management section of the physician manual. Intolerable, unmanageable side effects may warrant changing to a different stage of treatment. Tolerability should be evaluated at all critical decision points.

BDSS/CDP WORKSHEET

Visit date: _____

Instructions: Indicate the score for each item in the appropriate cell to the right of the item. Evaluate the pattern and severity of symptom(s) to guide clinical decision making.

Overall side effect severity (from 1–7): _____

Presence of **mild to moderate symptoms** may indicate need for medication adjustment.

Any score > 4 is within the range of **severe symptoms**, and indicates a need to make treatment changes.

NA = Not assessed, 1 = Not present, 2 = Very mild, 3 = Mild, 4 = Moderate, 5 = Moderately severe, 6 = Severe, 7 = Extremely severe

Symptom group	Symptoms	NA	1	2	3	4	5	6	7
Manic/Hypomanic	Hostility								
	Elevated mood								
	Grandiosity								
	Excitement								
	Motor hyperactivity								
Major Depressive	Depressed mood								
	Anxiety								
	Emotional withdrawal								
	Blunted affect								
Psychotic	Unusual thought content								
		SYMPTOMS							
		Mild		Mild to moderate			Severe		
Critical decision points and tactics*		NA	1	2	3	4	5	6	7
Week 1: CDP 1	Symptomatic.			Start medications.			Start medications.		
Week 2: CDP 2	Order serum levels (if applicable) to adjust dose.	Continue current dose.		Continue current dose. Consider increasing dose.			Increase dose.		
Week 4: CDP 3	Order serum levels (if applicable) to adjust dose.	Continue current dose.		Increase dose or consider next stage.			Increase dose or consider next stage.		
Week 6: CDP 4	All serum levels should be within therapeutic range.	Continue current dose.		Increase dose or consider next stage.			Increase dose or consider next stage.		
Week 8: CDP 5		Continue current dose.		Consider next stage.			Go to next stage.		

*Side Effects: Treatment recommendations assume that side effects are tolerable. Refer to the Medications, Dosing, and Side Effects Management section of this manual. Intolerable, unmanageable side effects may warrant changing to a different stage of treatment. Tolerability should be evaluated at all CDPs.

Appendix C:

*Drug Interactions**

Medication	Interacting medication	Effect
Lithium	Benzodiazepines	Increased risk for CNS depressant effects (mild)
	Carbamazepine	Increased neurotoxicity of lithium
	Clozapine	Few cases of seizure and diabetic ketoacidosis
	Divalproex sodium	Slightly increased concentrations of divalproex sodium
	Haloperidol	Altered mental status, extrapyramidal symptoms (rare)
	MAOIs	Few reports of myoclonic jerks in patients
Anticonvulsants		
Carbamazepine	Antiepileptics	Increased toxicity of carbamazepine
	Benzodiazepines	Decreased levels of benzodiazepines
	Clozapine	Increased risk for agranulocytosis
	Divalproex Sodium	Toxic levels of carbamazepine; decreased levels of valproate
	Fluoxetine	Increased levels of carbamazepine
	Haloperidol & other antipsychotics	Decreased levels of haloperidol and other antipsychotics
	Lamotrigine	Decreased levels of lamotrigine and possible increase in carbamazepine
	Lithium	Increased neurotoxicity of lithium
	Olanzapine	May get a 50% increase in the clearance of olanzapine
	Quetiapine	Decreased levels of quetiapine
	TCAs	Decreased levels of TCAs
	Ziprasidone	Decreased levels of ziprasidone
Divalproex sodium	Carbamazepine	Decreased levels of divalproex sodium
	Fluoxetine	Increased levels of divalproex sodium
	Lamotrigine	Increased levels of lamotrigine
	Lithium	Slightly increased levels of divalproex sodium
	Phenobarbital	Increased levels of phenobarbital
	Phenytoin	Increased levels of phenytoin
	Topiramate	Decreased levels of divalproex sodium and topiramate
	TCAs	Increased levels of TCAs
Atypical Antipsychotics		
Clozapine	Carbamazepine	Potential increased risk for agranulocytosis
	Fluvoxamine	Increased levels of clozapine

Medication	Interacting medication	Effect
	Nefazodone	Increased levels of clozapine
Olanzapine	Carbamazepine	May get a 50% increase in the clearance of olanzapine
	Fluvoxamine	Increased levels of olanzapine and quetiapine
Quetiapine	Carbamazepine	Decreased levels of quetiapine
	Nefazodone	Increased levels of quetiapine
	Phenytoin	Decreased levels of quetiapine
Risperidone	SSRIs	Enhanced side effects of risperidone
Ziprasidone	Carbamazepine	Decreased levels of ziprasidone
SSRIs		
Citalopram	MAOIs	Risk of serotonin syndrome – possibly death
Fluoxetine	Benzodiazepines	Increased levels of benzodiazepines
	Carbamazepine	Increased levels of carbamazepine
	Clozapine	Increased levels of clozapine
	Divalproex Sodium	Increased levels of divalproex sodium
	Haloperidol	Increased levels of haloperidol
	TCAs	Increased levels of TCAs
Fluvoxamine	Carbamazepine	Increased levels of carbamazepine
	Clozapine	Increased levels of clozapine
	Imipramine	Increased levels of imipramine
	Olanzapine	Increased levels of olanzapine
	Quetiapine	Increased levels of quetiapine
	TCAs	Increased levels of TCAs
Paroxetine	TCAs	Increased levels of TCAs
Sertraline	TCAs	Increased levels of TCAs
Bupropion_{SR}	MAOIs	Increased risk of hypertensive crisis
Lamotrigine	Carbamazepine	Decreased levels of lamotrigine
	Divalproex Sodium	Increased levels of lamotrigine
Nefazodone	Alprazolam, Triazolam, Lorazepam	Highly increased levels of these benzodiazepines
	Clozapine	Increased levels of clozapine
	Haloperidol	Increased levels of haloperidol
	MAOIs	Increased levels of MAOIs
	Quetiapine	Increased levels of quetiapine
Venlafaxine XR	MAOIs	Increased risk for neuroleptic malignant-like syndrome, hypertensive crisis, or a serotonin-like syndrome
Topiramate	Carbamazepine	Decreased levels of topiramate
	Divalproex Sodium	Decreased levels of divalproex sodium and topiramate
Ziprasidone	Carbamazepine	Decreased levels of ziprasidone

* More detailed information about drug interactions can be obtained from the PDR or individual package inserts.

Appendix L:
Survey Instrument, Protocols, and Frequencies

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You may either complete this survey and return it in the postage-paid envelope provided or take the survey on the Internet by going to **www.pscinc.com** and clicking on the ***Psychotropic Medication Prescribing Survey*** link located on the left side of the Web page. On the Web-based survey, you will be asked to type the code that appears below on the bottom right corner of the paper survey.

Thank you!

- Use a No. 2 pencil or a blue or black ink pen only.
- Do not use pens with ink that soaks through the paper.
- Make solid marks that fill the response completely.
- Make no stray marks on this form.

INCORRECT:

1. Type of health care professional (*select one*):

2. Type of medical/clinical setting in which you treat the majority of your patients (*check all that apply*):

- [illegible]



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[SERIAL]

Continued page 2

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3. Do you have the ability to transmit/receive patient information electronically, via the Internet or electronic data interchange (EDI)? YES (Y) NO (N)

4. Do you have access to the Internet from your place of work? (Y) (N)

4a. If yes, do you use the Internet from your place of work? (Y) (N)

5. What is the estimated percentage of the total number of patients that you treat whose diagnosis includes one of the following?

a) Major depression %

b) Bipolar disorder %

c) Schizophrenia %

6. In the past year, have you prescribed medication for any of the following? YES NO

a) Major depression (Y) (N)

b) Bipolar disorder (Y) (N)

c) Schizophrenia (Y) (N)

7. How easy is it for you to access the following sources of information to stay abreast of the latest developments in the treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 is "not at all easy" and 5 is "very easy."

	NOT AT ALL EASY 1	2	3	4	VERY EASY 5
a) Professional peer-reviewed journals	(A)	(A)	(A)	(A)	(A)
b) Non-peer-reviewed journals/newsletters	(B)	(B)	(B)	(B)	(B)
c) Professional organizations	(C)	(C)	(C)	(C)	(C)
d) Workshops/conferences	(D)	(D)	(D)	(D)	(D)
e) Online sources	(E)	(E)	(E)	(E)	(E)
f) Pharmaceutical company representatives and materials	(F)	(F)	(F)	(F)	(F)
g) Patients	(G)	(G)	(G)	(G)	(G)
h) Colleagues	(H)	(H)	(H)	(H)	(H)

i) Other

8. How **useful** do you find these sources of information for staying abreast of the latest developments in the treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 is "not at all useful" and 5 is "very useful."

	NOT AT ALL USEFUL 1	2	3	4	VERY USEFUL 5
a) Professional peer-reviewed journals	A	A	A	A	A
b) Non-peer-reviewed journals/newsletters	B	B	B	B	B
c) Professional organizations	C	C	C	C	C
d) Workshops/conferences	D	D	D	D	D
e) Online sources	E	E	E	E	E
f) Pharmaceutical company representatives	F	F	F	F	F
g) Patients	G	G	G	G	G
h) Colleagues	H	H	H	H	H
i) Other					

9. To what extent is your ability to prescribe psychotropic medications limited or restricted by the following?

	NEVER	RARELY	SOMETIMES	OFTEN	ALWAYS
a) Private health plan formularies	A	A	A	A	A
b) The state's Medicaid preferred drug list	B	B	B	B	B
c) A patient's lack of insurance coverage	C	C	C	C	C

FAMILIARITY WITH CURRENT ALGORITHMS AND GUIDELINES

10. How familiar are you with any of the following pharmaceutical treatment algorithms or published guidelines? Please select a value from 1 to 5, where 1 is "not at all familiar" and 5 is "very familiar."

	NOT AT ALL FAMILIAR 1	2	3	4	VERY FAMILIAR 5
a) Texas Medication Algorithm Project	A	A	A	A	A
b) Michigan Quality Improvement Consortium (MQIC) Guidelines	B	B	B	B	B
c) Harvard Algorithms Project	C	C	C	C	C
d) American Psychiatric Association Guidelines	D	D	D	D	D
e) Private health plan or insurance company guidelines	E	E	E	E	E
f) Expert Consensus Guidelines (e.g., Allen Francis, et al.)	F	F	F	F	F
g) Other					

USE OF ALGORITHMS AND GUIDELINES

11. Do you refer to or rely upon **any** algorithms or published guidelines when treating patients? YES NO
 (Y) (N)

12. How **often** do you refer to or rely upon the following pharmaceutical treatment algorithms or published guidelines when developing a treatment plan for patients with major depression, bipolar disorder, or schizophrenia?

	NEVER	RARELY	SOMETIMES	OFTEN	ALWAYS
a) Texas Medication Algorithm Project	(A)	(A)	(A)	(A)	(A)
b) Michigan Quality Improvement Consortium (MQIC) Guidelines	(B)	(B)	(B)	(B)	(B)
c) Harvard Algorithms Project	(C)	(C)	(C)	(C)	(C)
d) American Psychiatric Association Guidelines	(D)	(D)	(D)	(D)	(D)
e) Private health plan or insurance company guidelines	(E)	(E)	(E)	(E)	(E)
f) Expert Consensus Guidelines (e.g., Allen Francis, et al.)	(F)	(F)	(F)	(F)	(F)
g) Other					

13. When you use algorithms and/or published guidelines, to what extent is your decision to use them influenced by the following factors? Please select a value from 1 to 5, where 1 is “not at all an influence” and 5 is “a major influence.”

	1 NOT AT ALL AN INFLUENCE	2	3	4	5 MAJOR INFLUENCE
a) Recommended by experts in the field	(A)	(A)	(A)	(A)	(A)
b) Recommended for use in my practice by health plans or payers	(B)	(B)	(B)	(B)	(B)
c) Easy to understand and use	(C)	(C)	(C)	(C)	(C)
d) Influence from colleagues	(D)	(D)	(D)	(D)	(D)
e) Significant evidence that they improve patient outcomes	(E)	(E)	(E)	(E)	(E)
f) Financial incentives	(F)	(F)	(F)	(F)	(F)
g) Allows for prescriber autonomy	(G)	(G)	(G)	(G)	(G)
h) Saves time without jeopardizing patient outcomes	(H)	(H)	(H)	(H)	(H)
i) Patient request or preference	(I)	(I)	(I)	(I)	(I)
j) Recommendation by a professional group	(J)	(J)	(J)	(J)	(J)
k) Recommendation by a pharmaceutical manufacturer	(K)	(K)	(K)	(K)	(K)
l) Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	(L)	(L)	(L)	(L)	(L)
m) Training in the use of algorithm	(M)	(M)	(M)	(M)	(M)
n) Other					

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a) Don't need to; I already do what the guidelines and algorithms recommend	A	A	A	A	A
b) Not easy for me to use when I'm seeing patients	B	B	B	B	B
c) Patients need individualized treatment	C	C	C	C	C
d) Formulary restrictions	D	D	D	D	D
e) Patient preferences	E	E	E	E	E
f) Lack of evidence that they improve patient outcomes	F	F	F	F	F
g) Lack of financial incentives	G	G	G	G	G
h) Adds paperwork	H	H	H	H	H
i) Adds too much time	I	I	I	I	I
j) Infrastructure requirements (e.g., new technology needed)	J	J	J	J	J
k) Compromises prescriber autonomy	K	K	K	K	K
l) Recommendation by a pharmaceutical manufacturer	L	L	L	L	L
m) Lack of decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	M	M	M	M	M
n) Lack of endorsement from professional groups	N	N	N	N	N
o) Lack of training in the use of algorithm/guideline	O	O	O	O	O
p) Other					

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	NOT INCREASE LIKELIHOOD OF USE 1	2	3	4	DEFINITELY INCREASE LIKELIHOOD OF USE 5
a) Increased reimbursement from payers	(A)	(A)	(A)	(A)	(A)
b) CE/CME credit	(B)	(B)	(B)	(B)	(B)
c) Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	(C)	(C)	(C)	(C)	(C)
d) Ongoing training in the use of the algorithm	(D)	(D)	(D)	(D)	(D)

16. Are there any other strategies that would affect your decision to adopt consensus guidelines or algorithms for the pharmaceutical treatment of major depression, bipolar disorder and schizophrenia?

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18. Please give us any additional comments on this topic or project.

Thank you very much for your time and insights!

PLEASE DO NOT WRITE IN THIS AREA



[SERIAL]



Practitioner Survey

The survey to 6,208 practitioners was fielded in November; 531 practitioners completed the survey, for a response rate of 8.6 percent. Complete survey results are presented in Appendix A.

Profile of Respondents (Q1–6)

- 40% psychiatrists/60% PCPs
 - Psychiatrists (214): 84% treat adults, 16% treat children
 - PCPs (277): 51% general or family practice practitioners
- Half of respondents can transmit and receive patient information electronically
- Most have access to the Internet and use it from their place of work
- Psychiatrists more often than PCPs have patients with major depression, bipolar disorder, or schizophrenia
- Major depression is the most prevalent diagnosis and is more prescribed

Information Sources (Q7 and Q8)

- Peers and interactions with peers are most important sources of information
- Peer reviewed journals are easiest source to access, followed by non-peer-reviewed journals and pharmaceutical representatives
- Peer-reviewed journals also top pick for usefulness
- Workshops, colleagues, and professional organizations are most useful ways of keeping abreast but not easy to access
- No great difference in responses of psychiatrists and PCPs

Limitations on Prescribing (Q9)

- More PCPs perceive/experience restrictions or limitations in their ability to prescribe
- This is especially true for private health plans and Medicaid

Algorithm/Guideline Familiarity (Q10)

- Psychiatrists
 - 59% “somewhat/very familiar” with APA guidelines
 - 38% “somewhat/very familiar” with TMAP
- PCPs
 - 8% “somewhat/very familiar” with APA guidelines
 - Practically no one is familiar with TMAP (<2%)
 - Most familiar with private health plan guidelines (11%)

Use and Barriers (Q11–14)

- Little difference in the use of *any* guideline
 - 48% of psychiatrists report using or relying on *any* guideline and algorithm

- 42% of PCPs report using any guideline or algorithm
- Drop-off in use among psychiatrists
 - 59% familiar with APA guidelines; only 24% “often or always” use them in treatment
 - 38% familiar with TMAP; 10% “often or always” use it
- Nearly all PCPs who are familiar with guidelines also use them
 - 8% are familiar with APA guidelines and report often or always using the those guidelines

Facilitating Factors (Q13)

Both groups use algorithms and guidelines for the same reasons:

- Significant evidence that they improve patient outcomes
- Easy to understand and use
- Influence of colleagues
- Recommendations by professional group
- Recommendations from experts in the field

Barriers (Q14): Psychiatrists

Top five reasons for not using algorithms/guidelines

- Patients need individualized treatment
- Already do what guidelines recommend
- Lack of training in how to use them
- Patient preferences
- Lack of evidence that they improve patient outcomes

Barriers (Q14): PCPs

Top five reasons for not using algorithms/guidelines

- Patients need individualized treatment
- Lack of training in how to use them
- Formulary restrictions
- Not easy to use when they are seeing patients
- Adds too much time

Bottom Line: What Will it Take? (Q15)

Top factor for both groups: more evidence that guidelines make a difference in patient outcomes

Preliminary Analysis: Big Picture

- “Messengers”

- All respondents are similar in the information sources they have access to and find useful
 - They value expert opinion, evidence, and the ability to interact in various ways with colleagues
 - Peer reviewed journals cited as accessible and useful to all. Other venues, such as workshops and professional organizations are rated as useful, but are not as accessible as other sources, e.g., pharmaceutical representatives
- Systemic barriers encountered by the two groups of practitioners may be different
- Any plan that tackles systemic barriers needs to address how and why these groups differ and how they may experience the system of mental health care differently
 - While the venues for education, training, and dissemination can be similar for both groups, the plan may need to diverge when it comes to tackling barriers to implementation
- Facilitating use
- Evidence
 - Make it easy to use

Practitioner Survey Results

SURVEY FREQUENCIES

Practitioner Profile

1. Type of health care professional (*select one*):

a) Psychiatrist—Adult	34%
b) Psychiatrist—Child	06
c) Primary care physician—General/family practice	26
d) Primary care physician—Internist	11
e) Primary care physician—Pediatrician	07
f) Primary care physician—Ob/Gyn	07
g) Psychiatric nurse	<1
h) Other	<1
Missing	06
Multiple entries	01

2. Type of medical/clinical setting in which you treat the majority of your patients (*check all that apply*):

	Entire Sample	Psychiatrists
a) Private medical office—Solo practice	33%	41%
b) Private medical office—Group practice	37	19
c) Community Mental Health	12	27
d) Hospital/medical center	27	40
e) Federally Qualified Health Center (FQHC)/public health clinic	03	<1
f) Other (e.g., homeless shelters, mobile health vans, etc.)	03	01

3. Do you have the ability to transmit/receive patient information electronically?

	Entire Sample	Psychiatrists
Yes	51%	49
No	45	48
Missing	04	03

4. Do you have access to the Internet from your place of work?

	Entire Sample	Psychiatrists
Yes	77%	69%
No	19	28
Missing	03	03

4a. If yes, do you use the Internet from your place of work?

	Entire Sample	Psychiatrists
Yes	80%	79%
No	20	20
Missing	00	00

5. What is the estimated percentage of the total number of patients that you treat whose primary diagnosis includes one of the following?

	Entire Sample (median)	Psychiatrists (median)
a) Major depression	20%	40%
b) Bipolar disorder	05	20
c) Schizophrenia	02	10

6. In the past year, have you prescribed medication for any of the following?

	Yes	No	Missing
Entire Sample			
a) Major depression	88%	09%	03%
b) Bipolar disorder	71	25	04
c) Schizophrenia	56	39	05
Psychiatrists			
a) Major depression	94	03	02
b) Bipolar disorder	94	05	01
c) Schizophrenia	89	09	01

7. How easy is it for you to access the following sources of information to stay abreast of the latest developments in the treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 is "not at all easy" and 5 is "very easy."

	Not at all easy 1	2	3	4	Very easy 5	Missing
Entire Sample						
a) Professional peer-reviewed journals	03%	07%	21%	28%	37%	03%
b) Non-peer-reviewed journals/newsletters	07	11	25	24	29	06
c) Professional organizations	06	18	30	24	17	05
d) Workshops/conferences	06	16	31	28	15	04
e) Online sources	11	12	21	26	25	06
f) Pharmaceutical company representatives and materials	08	09	23	29	27	04
g) Patients	12	14	29	20	17	07
h) Colleagues	06	12	31	27	19	05
i) Other = 01						

8. How **useful** do you find these sources of information for staying abreast of the latest developments in the treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 is “not at all useful” and 5 is “very useful.”

	Not at all useful 1	2	3	4	Very useful 5	Missing
Entire Sample						
a) Professional peer-reviewed journals	03%	07%	14%	34%	37%	04%
b) Non-peer-reviewed journals/newsletters	07	20	32	24	11	05
c) Professional organizations	06	15	34	28	12	06
d) Workshops/conferences	02	08	22	35	28	05
e) Online sources	12	17	25	25	14	07
f) Pharmaceutical company representatives	15	24	29	20	08	05
g) Patients	17	33	28	09	05	07
h) Colleagues	04	10	24	36	18	08
i) Other = <1						

9. To what extent is your ability to prescribe psychotropic medications limited or restricted by the following?

	Never	Rarely	Sometimes	Often	Always	Missing
Entire Sample						
a) Private health plan formularies	07%	14%	39%	30%	05%	04%
b) The state's Medicaid formulary	09	10	26	38	13	06
c) A patient's lack of insurance coverage	06	08	33	38	10	05
Psychiatrists						
a) Private health plan formularies	09	19	42	24	03	02
b) The state's Medicaid formulary	12	15	29	32	10	01
c) A patient's lack of insurance coverage	08	08	37	36	10	01

Familiarity with Current Algorithms and Guidelines

10. How familiar are you with any of the following pharmaceutical treatment algorithms or published guidelines? Please select a value from 1 to 5, where 1 is “not at all familiar” and 5 is “very familiar.”

	Not at all familiar 1	2	3	4	Very familiar 5	Missing
Entire Sample						
a) Texas Medication Algorithm Project	63%	09%	08%	11%	06%	03%
b) Michigan Quality Improvement Consortium (MQIC) Guidelines	58	17	14	05	03	03
c) Harvard Algorithms Project	72	12	08	02	<1	05
d) American Psychiatric Association	31	17	19	20	09	04

		Not at all familiar 1	2	3	4	Very familiar 5	Missing
	Guidelines						
e)	Private health plan or insurance company guidelines	41	26	19	08	02	04
f)	Expert Consensus Guidelines (i.e., Allen Francis, et al.)	56	17	14	07	02	04
g)	Other = 02						
	Psychiatrists						
a)	Texas Medication Algorithm Project	31	14	16	23	15	01
b)	Michigan Quality Improvement Consortium (MQIC) Guidelines	58	20	13	05	03	01
c)	Harvard Algorithms Project	59	18	14	05	01	03
d)	American Psychiatric Association Guidelines	08	10	22	40	19	01
e)	Private health plan or insurance company guidelines	42	28	22	04	03	02
f)	Expert Consensus Guidelines (i.e., Allen Francis, et al.)	36	20	24	14	03	03
g)	Other = 02						

Use of Algorithms and Guidelines

11. Do you refer to or rely upon any algorithms or published guidelines when treating patients?

	Entire Sample	Psychiatrists
Yes	45%	48%
No	47	45
Missing	8	7

12. How **often** do you refer to or rely upon the following pharmaceutical treatment algorithms or published guidelines when developing a treatment plan for patients with major depression, bipolar disorder, or schizophrenia?

		Never	Rarely	Sometimes	Often	Always	Missing
	Entire Sample						
a)	Texas Medication Algorithm Project	66%	10%	10%	05%	00%	09%
b)	Michigan Quality Improvement Consortium (MQIC) Guidelines	66	10	10	03	<1	10
c)	Harvard Algorithms Project	75	10	03	01	<1	11
d)	American Psychiatric Association Guidelines	39	13	20	12	04	11
e)	Private health plan or insurance company guidelines	53	16	15	06	01	10
f)	Expert Consensus Guidelines (e.g., Allen Francis, et al.)	59	12	11	05	01	11
g)	Other = 04						
	Psychiatrists						

		Never	Rarely	Sometimes	Often	Always	Missing
a)	Texas Medication Algorithm Project	48	19	19	10	00	04
b)	Michigan Quality Improvement Consortium (MQIC) Guidelines	73	14	07	01	<1	05
c)	Harvard Algorithms Project	76	17	03	<1	00	06
d)	American Psychiatric Association Guidelines	23	15	31	19	06	04
e)	Private health plan or insurance company guidelines	56	21	14	04	<1	04
f)	Expert Consensus Guidelines (e.g., Allen Francis, et al.)	52	16	16	07	02	06
g)	Other = 04						

13. When you **use** algorithms and/or published guidelines, to what extent is your decision to use them influenced by the following factors? Please select a value from 1 to 5, where 1 is “not at all an influence” and 5 is “a major influence.”

		Not at all an influence 1	2	3	4	Major influence 5	Missing
Entire Sample							
a)	Recommended by experts in the field	07%	03%	18%	28%	26%	18%
b)	Recommended for use in my practice by health plans or payers	22	19	26	11	04	18
c)	Easy to understand and use	09	06	20	31	17	18
d)	Influence from colleagues	08	12	23	30	08	18
e)	Significant evidence that they improve patient outcomes	06	03	11	28	35	17
f)	Financial incentives	47	19	08	06	02	18
g)	Allows for prescriber autonomy	15	12	28	18	08	19
h)	Saves time without jeopardizing patient outcomes	15	14	21	23	10	18
i)	Patient request or preference	15	14	28	21	04	18
j)	Recommendation by a professional group	11	08	26	29	08	18
k)	Recommendation by a pharmaceutical manufacturer	28	29	18	06	01	18
l)	Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	25	16	20	17	04	18
m)	Training in the use of algorithm	23	13	20	16	07	19
n)	Other = 05						
Psychiatrists							
a)	Recommended by experts in the field	10	04	18	28	30	10
b)	Recommended for use in my practice by health plans or payers	35	25	19	06	02	12
c)	Easy to understand and use	14	09	24	26	14	13
d)	Influence from colleagues	13	17	27	27	07	10
e)	Significant evidence that they improve patient outcomes	08	05	12	27	39	09
f)	Financial incentives	55	20	08	05	01	11
g)	Allows for prescriber autonomy	17	12	25	22	11	14

		Not at all an influence 1	2	3	4	Major influence 5	Missing
h)	Saves time without jeopardizing patient outcomes	21	18	19	21	10	12
i)	Patient request or preference	21	14	24	24	05	11
j)	Recommendation by a professional group	17	11	28	28	06	10
k)	Recommendation by a pharmaceutical manufacturer	39	31	15	03	<1	11
l)	Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	38	14	19	15	02	12
m)	Training in the use of algorithm	31	15	19	14	08	13
n)	Other = 03						

14. When you **do not use** algorithms and/or published guidelines, how significant are the following reasons? Please select a value from 1 to 5, where 1 is “not a reason” and 5 is a “significant reason.”

		Not a reason 1	2	3	4	Significant reason 5	Missing
Entire Sample							
a)	Don't need to; I already do what the guidelines and algorithms recommend	23%	08%	21%	21%	14%	12%
b)	Not easy for me to use when I'm seeing patients	20	13	19	22	14	12
c)	Patients need individualized treatment	07	07	21	21	32	11
d)	Formulary restrictions	14	17	26	22	10	11
e)	Patient preferences	13	17	35	19	04	12
f)	Lack of evidence that they improve patient outcomes	23	14	21	16	13	12
g)	Lack of financial incentives	59	13	10	04	01	12
h)	Adds paperwork	31	18	16	15	09	12
i)	Adds too much time	24	15	20	20	10	11
j)	Infrastructure requirements (e.g., new tech. needed)	30	17	20	12	08	13
k)	Compromises prescriber autonomy	29	18	23	11	06	13
l)	Recommendation by a pharmaceutical manufacturer	41	22	18	04	02	13
m)	Lack of decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	28	21	22	14	03	13
n)	Lack of endorsement from professional groups	24	17	24	16	07	12
o)	Lack of training in the use of algorithm/guideline	16	13	19	23	17	12
p)	Other = 04						
Psychiatrists							
a)	Don't need to; I already do what the guidelines and algorithms recommend	18%	06%	16%	29%	24%	05%
b)	Not easy for me to use when I'm seeing patients	28	15	21	21	09	06
c)	Patients need individualized treatment	07	04	20	30	34	05

	Not a reason 1	2	3	4	Significant reason 5	Missing
d) Formulary restrictions	21	24	27	16	06	06
e) Patient preferences	13	19	34	21	05	08
f) Lack of evidence that they improve patient outcomes	24	15	21	17	15	06
g) Lack of financial incentives	69	11	10	04	<1	06
h) Adds paperwork	44	20	14	11	06	06
i) Adds too much time	35	15	21	18	07	05
j) Infrastructure requirements (e.g., new tech. needed)	39	15	20	12	07	07
k) Compromises prescriber autonomy	28	14	30	12	09	06
l) Recommendation by a pharmaceutical manufacturer	49	23	16	03	02	06
m) Lack of decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	37	20	20	14	03	06
n) Lack of endorsement from professional groups	28	21	22	15	06	06
o) Lack of training in the use of algorithm/guideline	23	17	19	20	13	07
p) Other = 03						

15. Which of the following would *increase the likelihood that you would use* consensus guidelines or algorithms for the pharmaceutical treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 means the item would “not increase the likelihood of use” and 5 means the item would “most definitely increase the likelihood of use.”

	Not an increase likelihood of use 1	2	3	4	Most Definitely an increase likelihood of use 5	Missing
Entire Sample						
a) Increased reimbursement from payers	31%	12%	17%	18%	15%	08%
b) CE/CME credit	18	13	23	23	15	08
c) Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	13	11	25	17	<1	09
d) Ongoing training in the use of the algorithm	10	11	24	29	19	08
e) More evidence that they made a difference in patient outcome	05	05	12	29	42	07
Psychiatrists						
a) Increased reimbursement from payers	43	14	14	16	10	03
b) CE/CME credit	25	14	18	22	16	04
c) Includes decision support (e.g., laminated cards, computer/Web-based support,	20	14	25	20	16	05

		Not an increase likelihood of use 1	2	3	4	Most Definitely an increase likelihood of use 5	Missing
	one-page summaries)						
d)	Ongoing training in the use of the algorithm	15	14	25	22	20	05
e)	More evidence that they made a difference in patient outcome	05	07	11	22	53	03

16. Are there any other factors that would affect your decision to adopt consensus guidelines or algorithms for the pharmaceutical treatment of major depression, bipolar disorder and schizophrenia? [*Open-ended*]

17. Please give us any additional comments on this topic or project. [*Open-ended*]

AVERAGE RATINGS FOR SELECT QUESTIONS

The following is a presentation of average ratings for questions 7,8, 13,14 and 15—all questions where respondents were asked to use a scale from 1 to 5 to rate the items under consideration. They have been arranged in descending order so they are in a different order than they appear on the survey.

Access to Information Sources

7. How easy is it for you to access the following sources of information to stay abreast of the latest developments in the treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 is "not at all easy" and 5 is "very easy."

	Average
a) Professional peer-reviewed journals	3.92
b) Non-peer-reviewed journals/newsletters	3.60
f) Pharmaceutical company representatives and materials	3.60
e) Online sources	3.43
h) Colleagues	3.42
d) Workshops/conferences	3.31
c) Professional organizations	3.29
g) Patients	3.18

Usefulness of Information Sources

8. How **useful** do you find these sources of information for staying abreast of the latest developments in the treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 is “not at all useful” and 5 is “very useful.”

	Average
a) Professional peer-reviewed journals	4.01
d) Workshops/conferences	3.81
h) Colleagues	3.59
c) Professional organizations	3.26
e) Online sources	3.13
b) Non-peer-reviewed journals/newsletters	3.12
f) Pharmaceutical company representatives	2.82
g) Patients	2.52

Influencing Factors

13. When you **use** algorithms and/or published guidelines, to what extent is your decision to use them influenced by the following factors? Please select a value from 1 to 5, where 1 is “not at all an influence” and 5 is “a major influence.”

	Average
e) Significant evidence that they improve patient outcomes	3.99
a) Recommended by experts in the field	3.76
c) Easy to understand and use	3.48
d) Influence from colleagues	3.23
j) Recommendation by a professional group	3.18
h) Saves time without jeopardizing patient outcomes	3.00
g) Allows for prescriber autonomy	2.91
i) Patient request or preference	2.80
m) Training in the use of algorithm	2.64
l) Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	2.50
b) Recommended for use in my practice by health plans or payers	2.46
k) Recommendation by a pharmaceutical manufacturer	2.04
f) Financial incentives	1.74

Barriers to Implementation

14. When you **do not use** algorithms and/or published guidelines, how significant are the following reasons? Please select a value from 1 to 5, where 1 is “not a reason” and 5 is a “significant reason.”

		Average
c)	Patients need individualized treatment	3.60
o)	Lack of training in the use of algorithm/guideline	3.14
a)	Don't need to; I already do what the guidelines and algorithms recommend	2.97
b)	Not easy for me to use when I'm seeing patients	2.97
d)	Formulary restrictions	2.96
e)	Patient preferences	2.83
f)	Lack of evidence that they improve patient outcomes	2.78
i)	Adds too much time	2.75
n)	Lack of endorsement from professional groups	2.62
h)	Adds paperwork	2.45
j)	Infrastructure requirements (e.g., new technology needed)	2.43
k)	Compromises prescriber autonomy	2.40
m)	Lack of decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	2.36
l)	Recommendation by a pharmaceutical manufacturer	1.91
g)	Lack of financial incentives	1.56

Increasing the Likelihood of Use

15. Which of the following would *increase the likelihood that you would use* consensus guidelines or algorithms for the pharmaceutical treatment of major depression, bipolar disorder, and/or schizophrenia? Please select a value from 1 to 5, where 1 means the item would “not increase the likelihood of use” and 5 means the item would “most definitely increase the likelihood of use.”

		Average
e)	More evidence that they made a difference in patient outcome	4.07
d)	Ongoing training in the use of the algorithm	3.38
c)	Includes decision support (e.g., laminated cards, computer/Web-based support, one-page summaries)	3.23
b)	CE/CME credit	3.04
a)	Increased reimbursement from payers	2.72