

Mental Health Issues Today

Volume 6

Number 3

Polypharmacy of Psychotropic Drugs: A Critical Discussion

"He arose at the crack of dawn when he began to take his secret medicines, bromide to raise the spirits, salicylates for the aches in his bones when it rained, ergosterol drops for vertigo, belladonna for sound sleep. But in his pocket he always carried a little pad of camphor that he inhaled deeply when no one was watching, to calm his fear of so many medicines mixed together."

GABRIEL GARCIA MARQUEZ
Love in the Time of Cholera

In 21st Century American medicine, we are fortunate enough to have a large selection of prescription drugs available to treat disease. However, the advantage of multiple treatment options can be detrimental, especially when patients see multiple physicians and take numerous medications. Polypharmacy, the concurrent use of multiple medications, is a growing concern in all

areas of medicine, but it is an especially delicate matter in psychiatry where there are increased opportunities and risks when physicians use a combination of medications.

Lack of a standard definition notwithstanding, polypharmacy is often perceived, at worst, as dangerous, and at least, as potentially wasteful.

The latest resurgence in the long psychiatric polypharmacy debate was precipitated by the introduction of atypical antipsychotic medications and selective serotonin reuptake inhibitors (SSRI) for the treatment of depression. With the influx of new options for medical treatment, the issue of polypharmacy has become even more complex as prescribers try different combinations of the new agents, experimenting to pinpoint the formula that produces the most successful response with the fewest side effects.



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Supported by an educational grant from Janssen Pharmaceutica L.P., a member of the Johnson & Johnson family of companies.

Despite the clinical opportunity it represents, polypharmacy is often considered taboo in psychiatry, often implying inappropriate use of multiple medications to treat one condition. In fact, even the term is controversial; advocates will often refer to it as "combination therapy." Because "polypharmacy" can refer to a variety of therapeutic situations, it is difficult to capture the practice in one definition. According to a technical report by the National Association of State

Mental Health Program Directors (NASMHPD), the term polypharmacy can be divided into at least 5 categories:

Lack of a standard definition notwithstanding, polypharmacy is often perceived, at worst, as dangerous, and at least, as potentially wasteful. While the primary concern related to polypharmacy in any area of medicine is the increased potential for drug-drug interactions that may lead to morbidity

and iatrogenic complications, adherence and fiscal constraints are also important considerations in psychiatry.

Apart from issues of safety, combination therapies that are very complicated or produce intolerable side effects will often result in the patient disengaging from treatment, a possibility that must be considered by prescribers. In addition, both public and private payers are concerned about unnecessary expenses related to inappropriate polypharmacy and are taking steps to curb its use.

In this issue of *Mental Health Issues Today* we will examine whether polypharmacy is inherently a wasteful practice that implies a duplicative and even dangerous use of multiple psychotropic medications, or if it is an invaluable tool in the art of psychiatry. We will also describe ongoing state efforts to reduce polypharmacy and how programs such as the Texas Medication Algorithm Project (TMAP) can assist physicians in rational polypharmacy.

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Mental Health Issues Today is prepared for Janssen Pharmaceutica L.P. by PAREXEL, Centreville, Virginia, (703) 310-2041.

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Why is Polypharmacy Controversial?

The storm surrounding the practice of polypharmacy can be traced back to the mid-to-late 1970's, when new research that showed there was no advantage to same-class polypharmacy

TABLE 1.

CATEGORIES DESCRIBING THE USE OF POLYPHARMACY¹

Same-Class Polypharmacy: The use of more than one medication from the same medication class.

Example:

- Using two selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine plus paroxetine.

Multi-Class Polypharmacy: The use of full therapeutic doses of more than one medication from different medication classes for the same symptom cluster.

Example:

- Using lithium along with an atypical antipsychotic.

Adjunctive Polypharmacy: The use of one medication to treat the side effects or secondary symptoms of another medication from a different medication class.

Example:

- Using trazadone along with bupropion for insomnia.

Augmentation: The use of one medication at a lower than normal dose along with another medication from a different medication class at its full therapeutic dose, for the same symptom cluster.

Or, the addition of a medication that would not be used alone for the same symptom cluster.

Example:

- The addition of lithium in a person with major depression who is currently taking an antidepressant.

Total Polypharmacy: The total count of medication used in patient, or total drug load. Consideration of total pharmacy should include prescription medications, over-the-counter medications, alternative medical therapies, and illicit pharmacological agents.

Source: NASMHPD Medical Directors' Technical Report on Psychiatric Polypharmacy, September 2001.

with typical antipsychotics, and that it could cause additional problems.² As a result, physician education and drug utilization review (DUR) procedures began to focus on discouraging this practice.

In the 1990s, further developments in the practice of clinical psychopharmacology, coupled with the introduction of new atypical antipsychotic medications, changed circumstances once again. Once more, polypharmacy

became a concern as prescribers experimented with combining the new agents, albeit without the support of hard clinical evidence.

Joseph Parks, M.D., Director of the **Missouri** Department of Mental Health explained, "Older therapies had so many more side effects that it usually was not possible to give a patient more than two or three medications simultaneously without them being too sedated or falling down. The new therapies have such lower rates of side effects that patients can tolerate taking seven or eight at once. Since psychiatrists want to help their patients and believe that medications will be effective in combination even though there is not yet research on combinations of more than two medications, we tend to keep adding more until the patient says 'enough.'"

Thomas A.M. Kramer, M.D., Director of the Student Counseling and Resource Service at the University of Chicago agreed. "The good news is that the number of therapeutic agents that are available to us has increased exponentially, so we have a lot more to offer our patients. It was not that long ago that there were only two kinds of antidepress-

¹ NASMHPD Medical Directors' Technical Report on Psychiatric Polypharmacy, September 2001.

² NASMHPD, "Medical Directors' Technical Report on Psychiatric Polypharmacy." (September 2001).

sants and there was not a whole lot of evidence that if you failed to improve on one, you would get better on another one within the same class."

"Now, we have all kinds of different medications and polypharmacy has become a bigger deal in psychiatry because of the increased number of possibilities we have to make a cocktail that may actually make somebody better," Dr. Kramer continued.

However, polypharmacy is still somewhat of a "fighting word" in psychiatry because it implies an "inappropriate or irrational use of multiple medications."³ "Polypharmacy literally means multiple drugs. It does not have anything more to it than that," Sheldon H. Preskorn, M.D., Professor and Chair for the Department of Psychiatry and Behavioral Sciences at the University of Kansas School of Medicine said, adding,

"Unfortunately, polypharmacy in the literature has frequently been used as a synonym for 'bad' polypharmacy. Rarely do people talk about 'good' polypharmacy. It has a negative connotation to it. Physicians often become defensive when they hear the word."

Current Prevalence of Polypharmacy

According to the National Association of State Mental Health Program Directors (NASMHPD), polypharmacy is common practice and has been increasing steadily over the last decade. For example, in **Missouri**, 25 percent of acute care patients and 33 percent of hospitalized patients are using more than one antipsychotic agent.⁴ A study by the DUR Committee of California Medi-Cal found that polypharmacy of any two antipsychotics (either atypicals or conventionals) was 11 percent. In **Massachusetts**, Medicaid officials were recently surprised to find that nearly 5,000 patients were on two or more antidepressants and more than 1,100 patients were on five, six or seven different psychiatric medications.

Other reasons for the increasing prevalence of polypharmacy that are often cited in discussions is adding a second drug too quickly and the complexity of switching a patient from one drug to another. The time constraints associated with treating acutely ill

³ NASMHPD, "Medical Directors' Technical Report on Psychiatric Polypharmacy." (September 2001).

⁴ NASMHPD, "Medical Directors' Technical Report on Psychiatric Polypharmacy." (September 2001).

⁵ Stephen Stahl et al. "Frequency of High Cost Utilization of Atypical Antipsychotics within Medi-Cal, the California Medicaid Program: Polypharmacy, High Dosing and Augmentation." (July 2002).

patients are often to blame. Dr. Parks explains, "Not adding drugs slowly enough and failed cross-tapers are major reasons for escalating polypharmacy."

Psychiatry may be even more vulnerable to a high prevalence of polypharmacy than other areas of medicine. For one, patients often take the medications for a long time. In addition, patients frequently have multiple symptoms, and some individuals may require more than one medication to achieve the desired therapeutic effect.

"There are many patients who only will get better with multiple medications. The newer therapies are very good, but often patients require more than one of them to get the complete effect," Dr. Kramer observed, also noting that, "Sometimes, polypharmacy can ease side effects instead of cause them. For example, if you give somebody an activating drug and a sedating drug, they may cancel each other out."

Another problematic situation is that while a psychiatrist may be mindful of the interactions between the medications he or she is prescribing, things can get complicated or dangerous when there are multiple practitioners prescribing for one patient.⁶ These factors, combined with the reality that

⁶ Thomas AM Kramer, "Polypharmacy," *Medscape Psychiatry & Mental Health eJournal*, 5(3) (March 2000).

outpatient medication management is usually far less expensive than other forms of psychiatric treatment, such as in-patient or partial hospitalization, add up to the increasing prevalence of polypharmacy.

When is Polypharmacy "Bad?"

The concern related to inappropriate polypharmacy is the increased potential for unintended results including drug-drug interactions and side effects. According to Dr. Kramer, the most frightening examples of "bad" polypharmacy are combinations of medications that have drug interactions that might have catastrophic consequences. "There are combinations of medications that can cause cardiac toxicity, arrhythmia, and death," Kramer explained.

Another example would be prescribing combinations of medications that produce intolerable side effects, are too complicated, or that lead to a worsening of symptoms "If the medicine makes you feel so awful you don't take it, or if the regime is so complicated that you cannot keep track of it, there is little hope of it working. In addition, a particular combination of medications might also exacerbate the very problems that you are trying to treat. All of those things are possibilities," Kramer said.

Fortunately, most examples of inappropriate polypharmacy do not lead to catastrophic outcomes; they just have little or no benefit. Dr. Kramer observed that most cases are just "stupid" polypharmacology. "For example, if a patient has severe depression, you do not want to concurrently prescribe two SSRIs."

Apart from issues of safety, combination therapies that are complicated or produce intolerable side effects will often result in the patient not complying with treatment. Moreover, both public and private payers are concerned about the potential to ramp up costs unnecessarily due to inappropriate polypharmacy.

Rational Polypharmacy

The debate over polypharmacy inevitably leads one to question whether it ever makes sense to consider using more than one medication to treat a single condition. Many psychiatrists see polypharmacy as part of the art of treating patients with serious and complicated mental illnesses. In addition, it is difficult to predict which drugs, or which combination of drugs, will help which patients.

Because there is little research on polypharmacy, there are often conflicting opinions. Many experts say that there is no indication that using two drugs

within the same class increases effectiveness. However, others assert that even similar drugs in the same class work on different neurotransmitters in the brain, and a combination therapy may be most effective.

Annette Hanson, M.D., Medical Director for **Massachusetts** Medicaid provided an example of some of the mixed information providers and policymakers have to confront.

"Our research indicates that there is absolutely no indication for using more than one SSRI. However, there may be some rationale for using more than one antipsychotic.

In particular, if you pushed one drug as far as the patient can tolerate the side effects, but the patient still seems to be having difficulties, a physician may want to add another drug that has a different side effect profile. The problem with polypharmacy is that prescribers switch to or add another antipsychotic before an adequate trial of the initial drug is completed."

Dr. Parks agreed, adding that, "Polypharmacy within a drug class with the same mechanisms -- using one or more of fluoxetine, paroxetine,

or sertraline -- or using more than one benzodiazepine is not rational. However, using more than one drug within a class, if each has a difference mechanism of action, may be rational: for example, a tricyclic and a SSRI."

This latter point is espoused by Dr. Alen J. Salerian, the medical director of the Psychiatric Institute of Washington's outpatient facility, the Washington Psychiatric Center. Salerian refers to the three key mood-regulating neurotransmitters in the brain (serotonin, dopamine and norepinephrine) as "the three tenors" -- when they "sing" in harmony and balance, depressed patients feel best. Thus, it sometimes makes sense to provide different drugs that target each of these "three tenors" for optimal treatment effect of depression -- particularly if a string of single-medication therapies has already failed. For example, this approach might prescribe Wellbutrin (for dopamine levels), Paxil (for serotonin levels) and Effexor (for norepinephrine and serotonin levels). Alternately, augmentation therapy might entail the use of Wellbutrin and Paxil, with Adderall (a stimulant often used for attention deficit hyperactivity disorder) added to further boost dopamine levels. In an article published in the Washington Post, Dr. Salerian notes that he has "treated hundreds of patients who have responded well to combination strate-

gies," adding that, "Just as the three tenors sing best when they work together, the three neurotransmitters make the best mood music for the brain when they're balanced harmoniously."⁷ Salerian also points out that often, experimentation with different drugs or dosages of the medications is needed before finding a perfect harmony.

Dr. Kramer agreed that changes in course are part of the territory, underscoring that it is the nature of mental illness to change over time. "Patients experience symptoms that wax and wane," Dr. Kramer said. "As symptoms change, medication needs to change. Monotherapy is sometimes not adequate and the use of polypharmacy may be better for a given patient because it is more easily adapted to subtle but important changes in effectiveness and side effects that the patient may experience over time."

"We have to be careful not to throw the baby out with the bath water here. I understand that people have to cut costs and that everyone is in a budget crisis. But that fact of the matter is, you want to get rid of 'bad' polypharmacy and encourage rational polypharmacy. On the whole, newer generation medications and rational polypharmacy saves the system huge amounts of money because it keeps folks out of the hospital," Dr. Kramer continued.

State Efforts to Reduce Inappropriate Polypharmacy

With budgets stretched thin due to the staggering economy, States are looking at ways to reduce spending. In the last few years, pharmaceuticals have been a major cost driver for states and State Medicaid and mental health officials have focused their attention on controlling spending in this area of the budget. To control pharmaceutical spending, a number of states have adopted or are considering restrictions on access to certain types of more expensive medications, including psychotropic medications, in their Medicaid programs. One way that states are accomplishing this goal is to monitor and manage inappropriate polypharmacy.

For example, **Illinois** established a DUR system to minimize polypharmacy of antipsychotics. Under the program, prescribers must receive approval for greater than ten days of concurrent antipsychotic use. After the program was implemented, long-term use of concurrent, multiple antipsychotics seemed to be lower in Illinois than observed in other states.⁸

⁷ Salerian, Alen J. "Making the Three Tenors Sing." The Washington Post, June 20, 2000, Health Section.

⁸ NASMHPD, "Medical Directors' Technical Report on Psychiatric Polypharmacy." (September 2001).

According to Dr. Parks, polypharmacy is very prevalent, but the profession has not yet thought it through rationally. "The first question a provider needs to ask is: does it make sense clinically, and second: does it make sense fiscally? Therapy for a patient on new antipsychotic costs \$3,000 to \$6,000 a year. If a patient is on two of the new antipsychotics, that increases to \$10,000 to \$12,000 per annually," Dr. Parks observed.

Allison Jorgenson, Pharm.D., R.Ph., a former Medicaid DUR Director in Nebraska, recognized that currently, there is heightened interest in polypharmacy on the public payer side because states are under enormous budget pressure. "It isn't that we want to cut mental health prescription spending, but that we want to save money rationally. State Medicaid programs are focusing on polypharmacy because they want to ensure that if they reduce instances where patients are receiving multiple medications, that everyone will still be okay," Jorgenson explains.

"In mental health care, this is critical. If a 21-year-old man with schizophrenia or a new mother with postpartum depression is suddenly not allowed to have the combination therapy that was keeping him or her stable, the consequences could be devastating," Jorgenson continued.

States Explore Ways to Optimize Utilization of Antipsychotics

Faced with budget pressures and accelerating spending on mental health drugs, states are under increasing pressure to develop formulary restrictions to cut costs. However, much of the increased use in this area is due to the therapeutic advantages of the newer atypical antipsychotics and a restrictive formulary would limit this clinical opportunity.

While restricting access to newer, expensive medications may seem to be the logical choice at first glance, strict controls could harm patients by creating time consuming and onerous processes for prescribers.

In addition, psychiatric drugs keep people who suffer from mental illness stable and, hopefully, out of hospitals and jails, in turn, saving state dollars.

In order to avoid this action, some states are first studying how these medications are currently being used, and then developing educational programs to reduce inappropriate and costly uses. Through voluntary awareness and education programs, these states are attempting to encourage

prescribers to optimize the use of certain mental health drugs to assure unrestricted access to these resources. **California** and **Massachusetts** provide examples of educational initiatives.

California: "Fiscal Pharmacology of Atypical Antipsychotic Drugs"

In California, the DUR Board has been studying the use and costs of atypical antipsychotics in Medi-Cal, its Medicaid program. Led by Stephen M. Stahl, M.D., Ph.D., and supported by unrestricted educational grants from four manufacturers of atypical antipsychotics, the Medi-Cal DUR Educational Committee on atypical antipsychotics developed evidence-based continuing medical education (CME) programs throughout the state to inform prescribers, providers and mental health professionals about how these drugs are utilized in the fee-for-service Medicaid program. The program's goal was to create a therapeutic resource that would enhance best practices with these agents and be more effective than formulary restrictions in changing clinical practices.⁹

Before the educational programs were developed, a baseline analysis of the Medi-Cal database was con-

⁹ Glen L. Stimmel, "Fiscal Pharmacology of Atypical Antipsychotics: Strategies to Limit Costs Yet Maintain Full Formulary Options." *Psychiatric Times* (June 2002).

ducted to identify possible high-cost, low evidence-based uses of atypical antipsychotics drugs that would become the focus of the educational effort. From the analysis, the state found that polypharmacy and high dosing were frequent practices within the Medi-Cal program and that these practices have "well documented costs and poorly documented benefits."

In developing the CME program content, the California Medi-Cal DUR Review Committee chose to target three issues: high dose use, polypharmacy of multiple antipsychotic drugs and augmentation of an antipsychotic with other psychotropic drugs. Both evidence-based and cost efficient uses were highlighted and contrasted from unproven and cost inefficient uses. Educational objectives included:

- To review the current uses of atypical antipsychotics within the fee-for-service Medi-Cal sector, including cost trends, dosing, polypharmacy and concomitant therapies.
- To compare these uses with national patterns and with various treatment algorithms including best practices.
- To highlight three areas of high-cost use for atypical antipsychotics, including polypharmacy, high doses, and concomitant administration of augmenting agents.
- To review the evidence for the utility of these high dose uses and how to optimize clinical and economic out-

comes by recognizing the uniqueness of the atypical medications and individualizing patient therapy in a cost-effective, evidence-based best practices algorithm.¹⁰

The Medi-Cal educational program focuses on optimizing monotherapy with one atypical antipsychotic drug.

According to the program, monotherapy has the best literature support for efficacy and is also the least costly treatment.

Additionally, a key message of the Medi-Cal educational program is that monotherapy is optimized when enough time is allowed for clinical response before moving on to other treatment strategies such as high doses, polypharmacy, or augmentation.

In the Medi-Cal educational program, many reasons are given for using polypharmacy on a short-term basis. For example, cross-titration between two antipsychotic drugs results in temporary polypharmacy and short-term conventional-atypical polypharmacy may often occur in emergency department settings or when patients are being switched from one drug to another. This type of short-term use is unlikely to interfere

with the long-term benefits of atypicals. However, patients may become caught in cross-titration, resulting in continuation of atypical-atypical polypharmacy for extended periods of time. In the Medi-Cal analysis, 4.4 percent of patients had received long-term atypical-atypical polypharmacy. This practice is not supported by evidence in the literature and the cost of such therapy is excessively high.¹¹

In addition, the education program discusses that the addition of a conventional antipsychotic to an atypical may be useful for the purpose of increasing positive symptom efficacy. However, this type of polypharmacy may eliminate the positive side-effect profile of the atypical and there is no evidence that it increases effectiveness.¹²

The Medi-Cal educational program also targets the practices of high-dose use and augmentation of an antipsychotic with other psychotropic drugs. The Medi-Cal data analysis suggested that treating patients with high doses costs an estimated \$64 million per year and that \$8 to \$15 million could be saved if half of those patients were

¹⁰ Medi-Cal DUR Educational Program on Atypical Antipsychotics.

¹¹ Glen L. Stimmel, "Fiscal Pharmacology of Atypical Antipsychotics: Strategies to Limit Costs Yet Maintain Full Formulary Options." *Psychiatric Times* (June 2002).

¹² Glen L. Stimmel, "Fiscal Pharmacology of Atypical Antipsychotics: Strategies to Limit Costs Yet Maintain Full Formulary Options." *Psychiatric Times* (June 2002).

switched to alternative treatments. In addition, according to the educational program, augmentation is described as more expensive than atypical monotherapy. However, augmentation is less expensive than high doses or atypical-atypical polypharmacy and has more evidence to support its use.

Massachusetts Polypharmacy Program: Focusing on Awareness

Like most other states, **Massachusetts** is facing a major budget crisis and budget-makers have focused on one of the fastest-growing line items in the budget, Medicaid. In particular, state budget officers have zeroed in on psychiatric drugs, which consume 47 cents of every dollar spent on the prescriptions Massachusetts Medicaid fills each month.

To reduce spending on psychiatric medicines, the Massachusetts Division of Medical Assistance (DMA), which administers Medicaid, has asked providers to reconsider using the common practice of polypharmacy. While state officials recognize that the treatment of some psychiatric patients requires a sort of "drug cocktail," for various reasons, they contend that polypharmacy has gotten out of hand.

According to Annette Hanson, M.D., Massachusetts' Medicaid

Medical Director, a review of Medicaid claims data for psychiatric drugs revealed that about 1,000 Massachusetts physicians had at least one patient on six or more medications. Of those 1,000 physicians, about fifty percent of those had just one such patient.

Dr. Hanson, herself a psychiatrist, explained that a multidisciplinary task force was assembled to determine how best to reduce the level of inappropriate polypharmacy.

"First, we put together a work group of psychopharmacologists, internists, pediatricians, practicing psychiatrists, child psychiatrists and pharmacists. Next, we started thinking about how we could make changes as evidence-based as possible. Right away, we knew we would have to begin by educating the "docs."

The voluntary program, which started in August 2002, advised physicians of potential adverse drug interactions (ADIs) and provided evidence that multiple medications in the same class does not increase successful outcomes. The DMA sent out a letter asking the 500 to 600 physicians with

two or more patients on multiple psychiatric medications to review and possibly change patterns of prescribing multiple and duplicative drugs within the same class. The Agency will then track the prescribing habit of these providers to see if improvements are made.

"What we did was send a series of letters telling providers how much the pharmacy budget was, how much was devoted to psychiatric drugs, what were some of the problems that we found (using the criteria of the concomitant treatment with two SSRIs or two atypicals), and then how much the drugs cost. We also sent them a list of their patients that fit this category and asked them to respond or think about the care they were giving these patients," Dr. Hanson explained.

If the most frequent "polypharmacy offenders" do not voluntarily cut back on unnecessary prescribing within three months, they will receive a visit from state-employed pharmacists to discuss their prescribing habits. This type of effort is generally referred to as "counter-detailing."

Dr. Hanson has been pleased with the responses she has gotten from physicians thus far and she feels most have embraced the effort. "You know, I never heard from the physician with 41 patients on seven or more psychiatric drugs. But, some of the physicians with

patients on five or more drugs responded and were upset because they thought they had been labeled as a 'bad doc.' I explained that we just wanted to make them aware of the polypharmacy issue, and encourage them to examine whether their patients needed to be on so many medications."

The state hopes to save \$10 million a year from this effort, approximately two percent of current spending on psychiatric drugs. However, this effort is not likely to stop the growth of pharmacy spending. Rather, Massachusetts hopes that it will help to contain the rate of growth in costs of providing drugs to MassHealth members. When asked if there is a next step planned after the education campaign, Dr. Hanson commented: "The next step depends on the results of this effort and the seriousness of our budget problems. We may decide to look at an evidence-based algorithm or take a more aggressive approach with some of these drugs."

The Texas Medication Algorithm Project (TMAP)

Several states have implemented, or are considering using, evidence-based algorithms to assist providers in prescribing medications for individuals with certain mental illness diagnoses. While these algorithms were con-

ceived as a way to provide a very detailed protocol that physicians could use in prescribing medications to patients with certain disorders, they may also reduce polypharmacy.

Beginning in 1995, the Texas Medication Algorithm Project (TMAP) was developed by the Texas Department of Mental Health and Mental Retardation (TDMHMR) in collaboration with academic pharmacists and physicians to assess the value of algorithms in the pharmacological management of mentally ill patients with diagnoses of schizophrenia, major depression, and bipolar disorder.

The mandatory algorithms are evidence-based, relying on thorough literature studies and input from stakeholders such as practitioners, patients, families, and administrators to ensure both efficacy and practicality.

TMAP's specific treatment sequences, tactical recommendations and patient education materials are designed to facilitate clinical decision-making and meet the objectives of long-term safety, tolerability, and full symptom remission – not just

response.¹³ The state hopes to see a decrease in the use of crisis/hospital services and an increase in the efficiency of patient care.

A by-product of the TMAP project may be a reduction in polypharmacy. According to Steven Shon, M.D., Medical Director of TDMHR, the algorithms give a step-by-step approach to using medication starting with monotherapy. "Only after one has had a long enough trial on a particular medication will you move to another medication. What the algorithm process recommends is going through at least two monotherapies before one considers using a combination like polypharmacy," Dr. Shon said.

Another key feature of the algorithm process is that physicians should only move on to another medication if there is a clear-cut failure after appropriate dosing duration. "What I mean by dosing duration is that if a medication takes ten to fourteen days to see full effect, then you keep the person on it ten to fourteen days at that initial dose and then you raise the dose after that. Sometimes, what you'll find is people will start switching medications way too early, after four days, and the medication really has not had time to achieve full effect. So the issue with going with an initial trial of monotherapy on a single

¹³Texas Implementation of Medication Algorithms (January 2000).

medication is that you have appropriate dose and appropriate duration, Dr. Shon explained.

This protocol is expected to lead to a natural reduction in polypharmacy. "A physician must go through three, or even four trials of monotherapy before he or she considers going to a combination of medications. This tends to reduce polypharmacy because the physician is sure the patient failed on medication A, medication B, and medication C. In this structured mechanism, combination therapy or polypharmacy is not considered until later in the treatment cycle versus jumping to it very quickly, which is a tendency that many psychiatrists have," Dr. Shon said.

According to Pablo Hernandez, M.D., Administrator at the **Wyoming State Hospital**, the Texas Medication Algorithm project is a best practice guideline that other states are watching carefully. "As more and more issues about cost containment arise in all of the states, developing a scientific-based response from the clinical perspective, as well as the cost containment perspective, will be of great interest to clinicians and administrators," Dr. Hernandez said. Several states have implemented one or more of the Texas algorithms including: **Pennsylvania, Illinois, Ohio, Georgia, New Mexico, Nevada, and South Carolina.**

In **South Carolina**, state officials are trying to initiate a Medication Algorithm Project for individuals with severe mental illness that is based on the Texas model. According to Stephen McLeod-Bryant, M.D., Medical Director for the South Carolina Department of Mental Health, one of the program's potential benefits will be a reduction in the use of unnecessary polypharmacy.

Dr. McLeod-Bryant explained some of the details of the upcoming clinician training for the initial pilot of the program. "We will discuss some of the components of the algorithm and the fact that it is more than just guiding physicians as to what the most appropriate choice of medication should be. We want clinicians to know that it also involves a change in the way the system works and how it involves consumer and family education."

The pilot will start off with the algorithm for schizophrenia and consider others gradually. "We plan to establish proficiency in that algorithm, then, in six months or so, we can add one of the other algorithms," Dr. McLeod-Bryant said.

The new program stems from collaboration between the Medical University of South Carolina's Department of Psychiatry and community mental health center sites. "We will be focused on the

Department of Mental Health consumers who are being treated in those mental health centers, but the medical university will use the algorithms with all patients with schizophrenia who are admitted to the hospital," Dr. McLeod-Bryant explained.

Conclusions

In the last few years, much attention has been focused on the unproven but well-established practice of polypharmacy in psychiatry. The influx of new medications over the last decade has refueled the fires of this old debate and the recent state budget crises have kept it going.

Although it is common practice, the word "polypharmacy" has a negative connotation in psychiatry because it often implies wasteful and potentially dangerous over-prescribing. However, many psychiatrists increasingly believe that combinations of drugs, even drugs in the same class, may be more effective when combined. Others disagree, asserting that polypharmacy is not clinically beneficial and inflates health care costs.

Public payers in particular have been focusing on how they can reduce inappropriate polypharmacy. State Medicaid agencies and Mental

Health Departments are intervening with education campaigns and evidence-based best practice guidelines like TMAP to improve patients' health by avoiding unnecessary medications, as well as reduce costs associated with polypharmacy. These initiatives have avoided the fierce criticism from advocates that has befallen states like Michigan that have adopted restrictive prior authorization policies. In fact, the National Alliance for the Mentally Ill (NAMI) lists development of explicit protocols such as TMAP as one of the strategies states should include.

However, experts like Dr. Preskorn caution that the downside of algorithms is that they are based on responses for the "usual" person. "You want a roadmap, but on the other hand, if the roadmap doesn't show you that a road up ahead is barricaded, you'll just keep mindlessly trying to go down that one road and getting nowhere. You have to be able to back up and allow for individual differences."

Dr. Kramer brings up another interesting argument. "The fact of the matter is that there are not enough psychiatrists out there to treat everybody in need. As the result, a lot of primary care doctors are treating the simplest of mental disorders. Whether we meant to or not, we have essentially abdicated the role of uncomplicated

treatment of depression to the primary care doctor. As a result, patients that are visiting psychiatric practices tend to be relatively complicated. What we have to offer as psychopharmacologists is the ability to say that 'I know how to put together a rational, effective combination of medications for you,'" Dr. Kramer observed.

Currently, data on the safety and efficacy of using psychotropic drugs in combination is very limited. While there is anecdotal evidence that polypharmacy can result in successful treatment for patients who were previously unresponsive to monotherapy, there is no hard research available and there are risks and concerns related to cost. Leaders in the field of psychiatry agree that rigorous scientific evidence is necessary to further explore the use of multiple psychiatric medications and that practitioners would benefit from guidelines that clarify when it is appropriate to use multiple psychiatric medications concurrently.

Ultimately, more definitive clinical trials should be conducted to substantiate the clinical benefits of polypharmacy and build best practices for its use using a rational application of our understanding of psychopharmacology.

Resources:

To view the National Association of State Mental Health Program Directors Technical Report on Psychiatric Polypharmacy, please visit: <http://www.nasmhpd.org/Polypharmacy.pdf>.

For more information on the TMAP research project, please visit: <http://www.mhmr.state.tx.us/centraloffice/medicaldirector/TMAPtoc.html>. For updated algorithms and other materials to be implemented in daily practice, go to the TIMA website: <http://www.mhmr.state.tx.us/centraloffice/medicaldirector/TIMA.html>.

If you would like to learn about the potential complexity of polypharmacy, please visit Dr. Sheldon Preskorn's applied clinical psychopharmacology web-site: <http://www.preskorn.com/column1.html>.