Science to Services: Consumers Need "Real-World" Science

by Xavier F. Amador and Michael Fitzpatrick

Abstract

Over the past decade there has been a revolution in pharmacotherapy for schizophrenia and related disorders. The second generation, or atypical, antipsychotic medications have demonstrated efficacy and generally better side-effect profiles. However, from the perspective of policy makers the higher costs associated with these newer medications leads to tough decisions regarding their continued use in light of an escalating fiscal crisis. For consumers, both persons with the illness and their family caregivers, the budgetary cutbacks leave many scrambling for answers to questions that most treatment (efficacy) studies were never designed to answer. "Should we oppose formulary restrictions on principle alone, or is there scientific data that can be relied on to inform our position?" On a more personal note, many are asking whether or not to switch to one of the newer medications and which medication would be best for them.

Unlike CATIE, efficacy studies were never designed to answer such questions. In this article, we start by highlighting how CATIE will fill important gaps in translating the results of efficacy studies to effectiveness in the real world. Both the development of the CATIE methodology and the study design itself reflect what we will refer to as "real-world science": i.e., science that sheds light on effectiveness in vivo and can inform decisions consumers, clinicians, and policy makers are faced with day-to-day. We discuss CATIE in the context of the fiscal crisis hitting MEDICAID programs leading many policy makers to take the more expensive, atypical antipsychotics off the list of medications made available to patients. We argue that studies like CATIE will be highly informative and ultimately vital to policy makers wishing to create mental health policies that will succeed. Throughout, we highlight how CATIE, and real-world science more generally, are vital to consumers striving to find the medication(s) that works best for them. Given the organic research design process, which arguably relies on a fuller range of stakeholders than any study of its kind before, we remain hopeful that CATIE can succeed in generating an unprecedented amount of real-world science that consumers can use.

Keywords: Advocacy, MEDICAID, consumers, antipsychotic, atypicals, policy, schizophrenia and CATIE.

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Over the past decade there has been a revolution in pharmacotherapy for schizophrenia and related disorders. From the perspective of clinicians, researchers, and the pharmaceutical industry, the data are compelling: The second generation, or atypical, antipsychotics have demonstrated efficacy and generally better side-effect profiles. However, from the perspective of policy makers, the revolution is in the skyrocketing costs associated with these newer medications, leading to tough decisions regarding their continued use in light of an escalating fiscal crisis. The budgetary cutbacks leave many consumers, both people with the illness and their family caregivers, scrambling for answers to questions that most treatment (efficacy) studies were never designed to answer. Should we oppose formulary restrictions on principle alone, or are there data that can be relied on to support our concerns? On a more personal note, many are asking: Should I try one of these newer medications when I've been doing fairly well on one of the older ones? Which medication is best for me? Should I worry that my doctor has me on more than one antipsychotic drug?

Efficacy studies were never designed to answer such questions because they were primarily designed to obtain regulatory approval from the Food and Drug Administration, are short term in duration, and principally assess

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treatment effects on symptoms and not broader measures of treatment and cost-effectiveness. The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study grew out of a new National Institute of Mental Health (NIMH) initiative to establish a clinical research capability to address the pressing questions for mental health administrators and policy makers on one hand, and clinicians and consumers on the other. The data provided by these studies are more likely to answer many questions consumers have, with respect to both their advocacy agenda and personal treatment decisions.

In this article, we start by highlighting how CATIE will fill important gaps in translating the results of efficacy studies to effectiveness in the real world. Both the development of the CATIE methodology and the study design itself reflect what we will refer to as "real-world science"—that is, science that informs what will happen in actual practice. To illustrate the value of this approach from a consumer advocacy perspective, we discuss CATIE in the context of the fiscal crisis hitting Medicaid programs across the country. We start by describing how budget cutbacks are leading many policy makers to take the more expensive, second generation antipsychotics off the list of medications made available to patients. We argue that studies like CATIE will be highly informative and ultimately vital to policy makers wishing to create mental health policies that will succeed. Throughout, we highlight how CATIE, and real-world science more generally, are vital to consumers striving to find medication(s) that works for them and to their quest to recover. We end by noting that despite its numerous advantages over traditional treatment studies, CATIE has some limitations with respect to the real-world science that consumers need and want. Given CATIE's organic research design process, which arguably relies on a fuller range of stakeholders than any study of its kind before, we remain hopeful that CATIE can succeed in generating an unprecedented amount of real-world science that consumers can use and provide a model for the generation of real-world science for the future.

Policy Relies on Science to Succeed

States have been hit hard by the weak economy since November 2001, with revenue losses not seen in decades and skyrocketing health care costs. A National Conference of State Legislatures April 2002 survey found that although the bulk of the budget problems were on the revenue side of the ledger, a growing number of States were facing cost overruns, even after adjusting their budgets. An increasingly popular response designed to reduce spending is to change policies to limit access to prescription medications used to treat mental illness. These changes in policy are clearly being made in response to the fiscal crisis, but *how* these decisions are being made and whether they are being made in a manner that is likely to optimize their success is unclear. Here, we describe the changing public services landscape and the different roles that research on drug efficacy versus real-world treatment studies should have in shaping the new landscape.

Today, more than 50 percent of all publicly funded State and local mental health services are funded by Medicaid. The costs associated with the program have skyrocketed in recent years, with a projected program growth of 9.5 percent between fiscal years 2002 and 2003. This growth in total spending follows on the heels of 11 percent growth between fiscal years 2001 and 2002. Without change at the Federal level, program growth is projected to be 8.5 percent annually over the next 10 years. This rate of spending growth is comparable to the growth that is occurring in the marketplace for health insurance.

Spending on prescription drugs is the fastest growing area of Medicaid spending. While spending on prescription drugs accounts for approximately 10 percent of total spending on health care in the United States, in recent years drug costs have contributed disproportionately to the sharp upturn in overall health costs. As a result, prescription drugs are consuming a growing share of Medicaid dollars. In 2000, the Medicaid program spent $16.6 billion on prescription drugs (Federal and State dollars combined). This acceleration of Medicaid spending growth has attracted the close attention of State and Federal policy makers.

As States seek to contain their spending on Medicaid, pharmaceuticals are the primary targets for cost savings. Every Medicaid cut affects local health care providers (and the local economy) and individuals who need health care services. States must cut total Medicaid spending $2 to $4 to save one State general fund dollar. States need Medicaid savings cuts now, but it takes time to achieve savings. Federal rules and political realities limit the choices that cost cutters have.

According to Congressional Budget Office projections, three-fourths of projected increases in Federal Medicaid spending will be due to care for the elderly and disabled. Cutting direct community and health services to elderly or disabled people places politicians squarely at odds with some well-organized communities. In short, the realistic choices for Medicaid budget cutters seeking immediate savings without a noisy battle are relatively few. States that continue to experience budget deficits will likely be forced to choose between raising new revenues and reducing the quality of and access to health care under their Medicaid program.

Why now?

Increased spending on prescription drugs for the Medicaid population, as with the privately insured population,

is being driven by four factors: (1) more drugs are being prescribed; (2) newer, more costly brand-name drugs are being substituted for older, lower cost drugs; (3) prices for prescription drugs are rising rapidly; and (4) newly approved medicines are being more heavily marketed to both doctors and consumers.

The Center for Medicaid and Medicare Services (CMS) projects that Medicaid's prescription drug expenditures will grow 70 percent faster than overall Medicaid growth between 2001 and 2006, especially for the elderly and disabled. Medicaid cost pressure is driven by enrollment growth and double-digit growth in the treatment marketplace where Medicaid operates. Even with a rebounding economy, increases in States' revenues will be dwarfed by Medicaid expenditure growth. Nationally, States spend 20 percent of their budgets on Medicaid, according to the National Conference of State Legislatures, and that is expected to rise to 25 percent in the next few years. Medicaid is the primary source of Federal grant support to States, representing almost 43 percent of all Federal grants to States. Given these pressures on State policy makers to contain costs, this is not a time to become old, sick, poor, or disabled.

The Policy Outlook for 2003

Prescription drugs are not a required benefit under Federal Medicaid rules. However, State Medicaid programs recognize the importance of this benefit. All States and the District of Columbia cover prescription drugs for at least some categories of Medicaid beneficiaries.

To balance budgets for fiscal year 2003, States employed a variety of cost containment schemes to control pharmaceutical expenditures. States have focused their efforts on changing Medicaid recipient behavior through copayments and limits on how much and how often recipients can fill prescriptions. They have also focused on changing physician prescribing behavior. In their 2002 legislative sessions, 16 States approved measures to implement one or a combination of the following cost control measures:

- preferred drug lists
- prior authorization for prescriptions
- supplemental drug rebates
- Fail First procedures
- generic substitutions
- prescribing and dispensing limitations
- increased copayments
- reduced dispensing fees to pharmacists

In June 2002, the Pharmaceutical Research and Manufacturers of America filed a lawsuit in Federal district court against the U.S. Department of Health and Human Services and the CMS. The lawsuit asks that the prior authorization and supplemental rebate aspects of Michigan's Medicaid pharmacy cost containment plan be invalidated.

In recent months, pharmacy chains in Washington, Massachusetts, and Maine have threatened to stop serving Medicaid recipients if States follow through with planned cuts in payments.

State legislatures in 2003 will again be the legislative and regulatory battleground for cost containment in Medicaid. Growth in health care costs is unlikely to abate, and States face spending pressures in other areas, such as education and homeland security. Policy makers are faced with the complex challenge of managing this change wisely. Medicaid is the only health care option for many children and adults. Yet Medicaid costs are now threatening the stability of other legal and programmatic aspects of State budgets. Tough decisions lie ahead.

Consumer advocates must provide impact information and alternatives to policy makers. For this reason, the National Alliance for the Mentally Ill (NAMI) has organized a medication access task force within its Policy Research Institute to study the problem. The task force is considering several points:

- Prescription drugs are essential to the recovery of many people with mental illness. Ensuring access to prescription drugs is essential. Pharmaceutical spending has skyrocketed in recent years; however, it is not clear that this is undesirable. Rapid growth in one category of spending is not necessarily bad because increasing the use of some services may decrease the use of more expensive services and lower costs over time.
- For mental illness, pharmaceuticals enhance recovery and serve as an alternative to more expensive care or procedures. Cutting reimbursement rates often hurts access. If policy makers choose to do less for people, someone else will pay. The task force will review the impact of prior authorization and other cost containment policies and the resulting tradeoffs regarding quality of life and cost shifts to other parts of State government and society.
- Policy makers should weigh the costs of any strategy being considered against the anticipated benefits. How does the State propose to measure costs and health consequences? What are the risks inherent in a strategy, and who will bear them? Improving clinical quality by using evidence-based prescribing practices may require short-term investments and garner long-term savings.
- Many of the cost containment methods being experimented with in State Medicaid programs

have been tested in the private health insurance marketplace. The private insurance industry is now moving away from using prior authorization routinely as a means of cost control. Using prior authorization programs along with other cost controls may discourage people with mental illness from obtaining their prescription medication. Experience with the "Michigan initiative" and a study by the Center for Studying Health System Change (2002) seem to indicate this trend. Does the implementation of multiple cost containment schemes lead to a significant number of people with mental illness not receiving their medications? Programs to review may include

- Indiana's limit of four brand-name drugs per month (mental health drugs are exempt),
- Massachusetts's, Idaho's, and Maine's requirement that Medicaid enrollees use generic drugs unless brand-name drugs are medically necessary,
- Florida's negotiations with drug companies that provide the State with disease management programs in exchange for inclusion of their drugs on the State's Medicaid preferred drug list,
- Maryland's limit of 10 prescriptions a month and voluntary preferred drug list, and
- Michigan's removal of drugs from its formulary if the drug companies do not agree to a certain price.

- Escalating costs raise many issues. The most important from a mental health care financing perspective is whether the growing uses of prescription drugs will, over time, add to overall health care costs or yield savings as they supplant and reduce the need for other, more costly treatments. Patients should receive care based on the best available scientific knowledge. Although most payment methods have an objective of cost containment or reflect consideration of issues of access, they do not have the explicit goal of ensuring quality care. Care should not vary illogically from State to State or from clinician to clinician based on cost containment decisions made by policy makers. The NAMI task force (see below) should review the best available scientific knowledge regarding the costs and benefits of the new medications to treat mental illness.
- States have taken other actions to manage their Medicaid pharmacy budgets:
  - The Texas Medication Algorithm Project (TMAP) has produced treatment algorithms (including prescription drug therapy) for three serious mental illnesses: schizophrenia, major depressive disorder, and bipolar disorder. This project, which began in Texas, is being piloted in 10 States. The task force should review the effectiveness of the TMAP approach and whether it provides an alternative in the cost containment debate surrounding Medicaid.
  - Massachusetts's Medicaid and Mental Health Departments have introduced a voluntary polypharmacy approach with doctor education and compliance tracking as an alternative to a preferred drug list. Do the data support this approach as a method of managing Medicaid pharmacy costs and changing doctors' prescribing patterns?
  - Political and economic environments vary from State to State. What is feasible politically in one State may not be feasible in another. Kentucky, Maine, Minnesota, Mississippi, New Mexico, Vermont, and West Virginia have implemented or are in the process of implementing prior authorization programs passed by their legislatures. What are fallback approaches to protect Medicaid recipients, if prior authorizations and preferred drug lists become State Medicaid policy?

The NAMI task force is exploring legal, regulatory, and political options. To assist this task force, one of us (X.F.A.) convened a workgroup of leading researchers to provide a peer-reviewed analysis of existing data to assist in making recommendations. This report will be published in early 2003. However, despite comprehensive data on the efficacy and safety of atypical antipsychotics, many questions may be difficult, if not impossible, to answer based on evidence from traditional treatment studies.

There is limited evidence to support the superior effectiveness of atypical antipsychotics over conventional antipsychotics, and the data that do exist are based almost exclusively on short-term efficacy studies. Although demonstrating efficacy, these studies do not address effectiveness in the real world. Also, the evidence does not adequately address long-term effectiveness and cost issues. The studies to date, which were for the most part sponsored by pharmaceutical companies and designed to achieve regulatory approval, are mostly short term, involve initially hospitalized patients, and focus mainly on the diagnostically relevant symptoms of schizophrenia (e.g., positive and negative symptoms) and on the more notorious side effects (e.g., extrapyramidal symptoms). These studies do not readily address the relevant questions policy

makers and consumers have, nor were they designed to do so. Consequently, although we are hopeful that NAMI's Scientific Council can produce an authoritative summary of the extant data and its value in shaping policy, more definitive recommendations regarding the real-world effectiveness of the less expensive antipsychotics compared to the more expensive atypical antipsychotics may have to wait until new studies are completed.

Existing evidence suggests some, albeit inconsistent, advantages in efficacy and tolerability for the newer atypical antipsychotics over the conventional antipsychotics for patients with schizophrenia. However, the limited types of assessment measures used and short study durations do not provide adequate information about treatment for this heterogeneous condition. Inclusion and exclusion criteria needed to complete these studies necessarily limit generalizability. We need new data from studies not sponsored by pharmaceutical companies and focused solely on efficacy and safety, to inform clinicians and policy makers about the appropriate role of atypicals. Several studies are currently ongoing or in preparation that examine the comparative effectiveness of atypical drugs. In this issue of the *Bulletin*, a description of the CATIE project is given in articles by Keefe et al., Rosenheck et al., Schneider et al., Stroup et al., and Swartz et al. CATIE represents a major NIMH research initiative that will assess the effectiveness of the second generation antipsychotics in a broad range of patients with schizophrenia and in patients with Alzheimer's disease. Importantly, the CATIE schizophrenia trial combines elements of efficacy and effectiveness trials. Medications are randomly assigned and double blinded, but long-term followup is planned, and the study will even examine what to do when a patient fails an initial trial of an atypical antipsychotic drug (e.g., should a second newer atypical drug be prescribed, or is clozapine the best choice?). And perhaps most important from the perspective of Medicaid directors, cost-effectiveness and cost-benefit analyses will be conducted to help identify the value of any advantages that atypicals may have over the conventional drug or over each other. Another study that promises to provide real-world effectiveness data related to this issue is the Medical Networks in Medicine (MEDNET) study being conducted in Germany. Studies like this will contribute to the body of evidence that is needed to definitively evaluate the effectiveness of the atypical antipsychotic drugs and determine their proper use in the present fiscal crisis. It is imperative that we have the results of these studies for the future. In particular, if all aspects of the CATIE study are indeed completed, it will yield invaluable data that will be vital to not only policy makers but also providers and consumers.

Reference

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