Impact of the CATIE Findings on State Mental Health Policy

Joseph J. Parks, M.D.
Alan Q. Radke, M.D.
Rajiv Tandon, M.D.

The authors, who are medical directors of three state mental health agencies and members of the Medical Directors' Council of the National Association of State Mental Health Program Directors (NASMHPD), describe the impact on public mental health policy of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). Before publication of the CATIE results, the preponderance of information indicated substantial and broad-ranging advantages of second-generation antipsychotics over first-generation agents. State mental health authorities focused on improving access to and increasing utilization of the newer agents. In many states, expenditures for these agents accounted for 10% of the total pharmacy budget of the Medicaid program. After CATIE, state policy makers have had to take a more critical look at the data and formulate more nuanced approaches. The authors summarize policy recommendations of the NASMHPD Medical Directors' Council, which reviewed efficacy studies of antipsychotics and formulated a position statement. The recommendations cover three broad areas of policy. First, neither complete open access for all patients at all times nor a uniform fail-first trial of a first-generation antipsychotic is an optimal approach. A more nuanced middle ground is necessary. Second, excessive emphasis on the cost of second-generation antipsychotics has led to a lack of focus on optimizing use of all antipsychotic medication in usual practice. More research and management attention must be focused on improving how these medications are prescribed for individual patients. Third, more resources should be invested in clinical trials that more clearly and accurately reflect current practice. (*Psychiatric Services* 59:534–536, 2008)

The views presented in this article arise from our years of experience as the medical directors of state agencies responsible for mental health in Missouri, Florida, and Minnesota. Those years have included substantial amounts of time assisting the state's Medicaid agency on mental health policy issues. In addition, the views arise from our experience with the Medical Directors Council of the National Association of State Mental Health Program Directors (NASMHPD). Over the past two years the council, which is made up of the medical directors of all state departments of mental health, has engaged in ongoing review of new research findings and has discussed policy implications (1). Although the views presented here are informed by these experiences, they our personal views and do not represent the policy of the mental health or Medicaid agencies in the three states or of NASMHPD.

The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) (2) in schizophrenia was a landmark study. In terms of duration (18 months) and number of patients (1,460), CATIE is the most comprehensive randomized clinical trial of chronic schizophrenia ever conducted. Because of increasing skepticism about discrepancies and biases in industry-sponsored clinical trials that provide much of the data guiding current antipsychotic practice (3), the field keenly awaited the results of this government-funded study, which addressed several key questions about the comparative effectiveness of antipsychotics. The results of the study have been impressive—surprising, revealing, and very significant (2,4–8).

Webster's *Third New International Dictionary* defines "policy" as "Prudence or wisdom in the management of public affairs; a definite course or method of action and selected from among alternatives and in the light of given conditions to guide and determine present and future decisions." The policy questions raised by CATIE are an excellent example of how difficult it is to be prudent, wise, and certain at the same time.

The mission of a state mental health system is to minimize the adverse impact of mental illness on the lives of citizens in the state and facilitate their ability to lead productive and meaningful lives. The state is mandated to focus on serving those with severe mental illness. Toward this end, public mental health policy attempts to provide maximally effective services in the context of limited resources, promul-

Dr. Parks is chief clinical officer, Missouri Department of Mental Health, 1706 East Elm St., P.O. Box 687, Jefferson City, MO 65102 (e-mail: joe.parks@dmh.mo.gov). Dr. Radke is medical director of the Minnesota Department of Human Services, St. Paul. Dr. Tandon is chief of psychiatry, Florida Department of Children and Families, Tallahassee. *This article is part of a special section on the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) and its implications. Marvin S. Swartz, M.D., served as guest editor of the special section.*

gate clear service standards in the context of scientific uncertainty, and work to harmonize frequently conflicting needs and objectives of multiple stakeholders (patients, families, providers, other payers, general citizenry, and so forth). The CATIE findings have shifted our understanding of how to best achieve the first two goals and have complicated the third. Choosing which services to provide in a public mental health system is always a matter of balancing clinical effectiveness, cost, and political will. Political will has never been sufficient to support the full cost of all that we believe to be clinically effective, and therefore difficult choices are always necessary.

Before CATIE

Before publication of the CATIE results, the preponderance of information in the past decade indicated substantial and broad-ranging advantages of second-generation antipsychotics over first-generation agents (9,10). Given the consensus that second-generation antipsychotics were superior, state mental health authorities focused on improving access to and increasing utilization of these agents. The years preceding CATIE saw a steady increase in the portion of our budgets allocated to procuring second-generation antipsychotics. In many state Medicaid programs, expenditures for these agents became one of the top three medication costs, typically representing over 10% of the total pharmacy expenditures (11). Even though the incremental cost of second-generation agents was formidable, there seemed sufficient assurance of greater clinical effectiveness and sufficient political will to make availability of second-generation antipsychotics a winning priority in the competition over which treatment resources merited increased and continued funding.

However, at the same time the overall budget available to public mental health systems remained stagnant, which forced difficult choices in resource allocation. In Missouri, for example, second-generation antipsychotics remained on completely open access in the formulary, even as Medicaid eligibility criteria were made more stringent so that our state Medicaid program could stay within budget. Thus our understanding of the evidence and the politics was such that we placed a higher value on maintaining unlimited access to second-generation antipsychotics for a smaller number of Medicaid beneficiaries than we did on maintaining a larger number of Medicaid beneficiaries on a more limited formulary. Similarly, to meet the increasing demands for funding the formulary, funds for state-operated psychiatric hospitals in Missouri have been reallocated from mental health interventions, such as occupational therapy, recreational therapy, and psychology.

CATIE and beyond

The initial CATIE report in September 2005 indicated that the first-generation antipsychotic perphenazine is as effective as various second-generation antipsychotics in the treatment of schizophrenia (2). When differences in switching rates were controlled for, olanzapine was also found to be no more effective than perphenazine. CATIE results published over the past two years (6–8) have provided additional strong support for the initial findings.

Our first response to the CATIE results was disbelief, and we scrutinized the reports for reasons to question the validity of the findings. We had repeatedly spoken publicly about the "clear clinical superiority" and "proven cost-neutrality" of second-generation antipsychotics. The CATIE findings explicitly contradicted those assertions. The policy options considered in this early stage were simple and straightforward. If CATIE is deeply flawed and the findings are incorrect and the previous research is valid, then all second-generation antipsychotics should remain on open access and the service system must continue to bear the escalating costs. If CATIE is valid and the previous research is misleading, then we should require a patient to undergo a trial of a first-generation antipsychotic before coverage for a second-generation antipsychotic is authorized, and we must bear the political consequences of this abrupt policy change.

However, an abrupt 180-degree policy shift can be disastrous and harmful unless it is truly warranted by the science. What is CATIE really telling us? After the initial findings were published, we became more critical in our review of the methodologies used in the pre-CATIE studies and in CATIE itself. CATIE, after all, reminded us of the value of careful critical analysis of data and of the importance of always remaining skeptical of that which we think we know or appear to see.

Our thinking has been substantially influenced by the deliberations of the NASMHPD Medical Directors' Council, which rigorously reviewed studies of antipsychotic efficacy over the past two years. The council recently formulated its position statement (1). During our deliberations, it became clear that much of the pre-CATIE data suggesting the substantial superiority of second-generation over first-generation agents was "biased" in favor of second-generation antipsychotics by the use of high-dose haloperidol as the first-generation comparator (12) and other study design elements (3). What CATIE, in turn, was telling us is that when first-generation antipsychotics are used at low to moderate dosages and perhaps in a certain population—one at relatively low risk for extrapyramidal symptoms, which was the CATIE population—they can be as effective as second-generation antipsychotics.

Thus the CATIE findings of clinical equivalence of first- and second-generation agents are applicable to persons with schizophrenia who are at relatively low risk for extrapyramidal symptoms (13–15). Neither CATIE nor the many pre-CATIE studies by themselves told the full story. Differences in the results of CATIE and the pre-CATIE studies do not invalidate one another but instead provide important information about efficacy and cost-effectiveness when second- and first-generation antipsychotics are used in different ways and in different populations. The differences in outcomes are the result of how the drugs were used in these studies, in addition to any intrinsic differences.

The analogy of constructing a house is useful: good tools make a difference, but how they are used might make a much bigger difference. We need to use all the available information, conduct needed studies to better characterize and discriminate between tools, disseminate current and accurate information about these tools to all who

use them, and articulate practice standards that promote appropriate use of these tools. We need to do this continually and repeatedly, collectively and with mutual respect, and inclusively—that is, both in terms of participants and information. We also need to do it transparently, objectively, and independently. We believe the NASMHPD Medical Directors' Council recommendations (1) meet these standards.

NASMHPD recommendations

Three broad areas of policy conclusions from CATIE are covered in detail in the NASMHPD recommendations.

First, neither complete open access for all patients at all times nor a uniform fail-first trial of a first-generation drug are optimal approaches. A more nuanced middle ground will be necessary for optimal balance of competing needs. Several, but not all, second-generation drugs should be available for first use. These should include a choice for each generally predictable difference in side effect profiles or route of administration. All second-generation antipsychotics should be in the formulary, even if not all are in the open-access category. A completely open formulary impedes price negotiations with pharmaceutical companies. However, a fail-first policy will harm many individuals, particularly those at higher risk for extrapyramidal symptoms and tardive dyskinesia.

Second, excessive emphasis on the cost of second-generation antipsychotics has led to a lack of focus on optimizing use of all antipsychotics in usual clinical practice. We must focus more research and management attention on improving how these drugs are prescribed for individuals (16,17).

Third, we need to invest more resources in clinical trials that more clearly and accurately reflect current practice and on research into mental health services utilization and the outcomes that these services produce (15). We have far too little information given the scale of resources that are being expended. CATIE has been an excellent move in this direction. However the current business model for procuring antipsychotic medication will never be able to support the type of research needed to determine the optimal use of antipsychotic medication. One option for improved financing of clinical and outcomes research is to include it in our purchasing model. If we wish to obtain good clinical outcomes for patients, then at least in part that is what we should contract to purchase. Instead of buying individual pills at a particular price regardless of how they are used or the outcomes they produce, we should be paying for patient-days on a medication treatment, with bonus payments if a patient meets or exceeds certain defined clinical or functional outcomes. This would force all parties concerned to develop more extensive and accurate service utilization and outcome data and to focus their efforts on actual patient outcomes. It would result in resources currently expended on sales and marketing being redirected to improving and optimizing the practices through which these medications are utilized. In addition, such resources could be redirected toward fuller and more clinically relevant characterization of these medications and timely support for trials such as CATIE.

Paying for clearly defined patient outcomes that are associated with use of particular medications would require both purchasers and the manufacturers of the medication to focus much more on their optimal use, which would greatly benefit our patients.

Acknowledgments and disclosures

CATIE was supported by grant N01-MH-90001 from the National Institute of Mental Health. A list of study locations and principal investigators can be found at www.catie.unc.edu/schizophrenia/locations.html.

The authors report no competing interests.

References

1. Radke A, Parks J, Parker G, et al: Principles of antipsychotic prescribing for policy makers: the comparative effectiveness of available antipsychotic medications. Schizophrenia Bulletin, in press
2. Lieberman JA, Stroup ST, McEvoy JP, et al: Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. New England Journal of Medicine 353:1209–1223, 2005
3. Heres S, Davis J, Maino K, et al: Why olanzapine beats risperidone, risperidone beats quetiapine, and quetiapine beats olanzapine: an exploratory analysis of head-to-head comparison studies of second-generation antipsychotics. American Journal of Psychiatry 163: 185–194, 2006
4. McEvoy JP, Lieberman JA, Stroup TS, et al: Effectiveness of clozapine versus olanzapine, quetiapine, and risperidone in patients with chronic schizophrenia who did not respond to prior antipsychotic treatment. American Journal of Psychiatry 163:600–610, 2006
5. Stroup TS, Lieberman JA, McEvoy JP, et al: Effectiveness of olanzapine, quetiapine, risperidone, and ziprasidone in patients with chronic schizophrenia following discontinuation of a previous atypical antipsychotic. American Journal of Psychiatry 163:611–622, 2006
6. Rosenheck RA, Leslie DL, Sindelar J, et al: Cost-effectiveness of second-generation antipsychotics and perphenazine in a randomized trial of treatment for chronic schizophrenia. American Journal of Psychiatry 163: 2080–2089, 2006
7. Keefe RSE, Bilder RM, Davis SM, et al: Neurocognitive effects of antipsychotic medications in patients with chronic schizophrenia in the CATIE trial. Archives of General Psychiatry 64:633–647, 2007
8. Swartz MS, Perkins DO, Stroup ST, et al: Effects of antipsychotic medications on psychosocial functioning in patients with chronic schizophrenia: findings from the NIMH CATIE study. American Journal of Psychiatry 164:428–436, 2007
9. Kane JM, Leucht S, Carpenter D, et al: Expert Consensus Guideline Series: optimizing pharmacologic treatment of psychotic disorders. Journal of Clinical Psychiatry 64(suppl 12):1–100, 2003
10. Falkai P, Wobrock T, Lieberman J, et al: World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for biological treatment of schizophrenia: part 1. acute treatment of schizophrenia. World Journal of Biological Psychiatry 6:132–191, 2005
11. Polinski JM, Wang Ps, Fischer MA: Medicaid's prior authorization program and access to atypical antipsychotic medications. Health Affairs 26:750–760, 2007
12. Hugenholtz GW, Heerdink ER, Stolker JJ, et al: Haloperidol dose when used as active comparator in randomized controlled trials with atypical antipsychotics in schizophrenia: comparison with officially recommended doses. Journal of Clinical Psychiatry 67:897–903, 2006
13. Tandon R, Carpenter WT, Davis JM: First- and second-generation antipsychotics: learning from CUtLASS and CATIE (reply to letter). Archives of General Psychiatry 64:977–980, 2007
14. Rosenheck R, Stroup ST, Keefe RSE, et al: Study samples key to assessing risk (reply to letter). Current Psychiatry 6:3–19, 2007
15. Tandon R, Moller H-J, Belmaker R, et al: World Psychiatry Association Pharmacopsychiatry Section statement on comparative effectiveness of antipsychotics in schizophrenia. Schizophrenia Research, in press
16. Constantine RJ, Richard SM, Surles RC, et al: Optimizing pharmacotherapy of schizophrenia: tools for the psychiatrist. Current Psychosis and Therapeutics Reports 4:5–11, 2006
17. Parks J, Surles R: Using best practices to manage psychiatric medications under Medicaid. Psychiatric Services 55:1227–1229, 2004