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## **APA Says New CATIE Results Don't Support Change in Reimbursement Policies – Changes that Could Risk Patients' Wellbeing**

**Arlington, Va.** - Three articles published in today's *American Journal of Psychiatry (AJP)* “underscore the complexities of designing and conducting research to assess the comparative clinical- and cost-effectiveness of alternate medications for treating psychotic disorders,” according to the American Psychiatric Association (APA). Taken together, the articles and accompanying editorials suggest that preliminary data from clinical trials do not yield information needed to ascertain cost effectiveness. Moreover, basing reimbursement policies on such research poses potential risks to the wellbeing of patients with schizophrenia.

The articles include:

- an in-depth critique prepared by Daniel Polsky, Ph.D., of University of Pennsylvania, and colleagues, of research methodologies used to evaluate costs associated with different antipsychotic medications;
- an assessment by Susan Essock, Ph.D., of New York's Mt. Sinai School of Medicine, and colleagues, of the clinical implications of switching a patient's medication during a course of treatment; and
- a cost-effectiveness study, by Robert Rosenheck, M.D., of Yale University, and colleagues, that introduces a pilot measure – a rating of Quality Adjusted Life Years (QALYs) – for ascertaining changes in the overall clinical status of patients who are administered different medications for chronic psychotic disorders.

The new reports were developed in the wake of the federally funded Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study – a large-scale, multi-year project that examined the clinical outcomes of patients with psychotic disorders who were treated either with an early, “first generation” antipsychotic (FGA) medication or any of four more recently introduced atypical or “second generation” antipsychotic (SGA) medications.

Darrel A. Regier, M.D., M.P.H., director of the APA's Division of Research, provides this analysis of the studies and their implications for mental health treatment policy and patient care:

The CATIE studies are best understood in the context of Dr. Polsky's methodologic analysis, in which the authors define appropriate scientific criteria for assessing the policy relevance and utility of various types of treatment effectiveness research.

The Polsky article discusses sources of “threats to validity” of policy-oriented, cost-effectiveness studies that utilize data drawn from clinical trials. The investigators reviewed eight studies that examined the cost of first- and second-generation antipsychotic medications in treating schizophrenia. In these studies, they identified the weakness of existing QALY outcome measures, high drop-out rates, and a primary focus, typical of clinical trials, on the “internal validity” of findings, which are drawn from small numbers of highly similar patients.

In contrast to clinical trials, cost-effectiveness research is intended to inform allocation of societal resources and thus must emphasize the “external validity” of findings to the larger and more heterogeneous population who receive such treatments for acute or chronic care. In addition, the time-frame of cost-effectiveness research typically is longer than short-term clinical efficacy or effectiveness trials in order to fully evaluate the effectiveness and side-effects of the intervention under study. Cost-effectiveness studies also must take into account social costs associated with a given illness as well as direct treatment costs.

Essock’s study re-examined strategies employed in the CATIE study to randomly assign patients to one of the five medications investigated. These were the first-generation antipsychotic, perphenazine, and four second-generation antipsychotics: olanzapine, quetiapine, risperidone, and ziprasidone. In the new analysis, the investigators identified patients who, in phase one of CATIE, were randomly assigned to receive the same drug they had been taking before the study. Their outcomes, measured as the time until the patient discontinued treatment with the assigned medication, were compared with those of patients who were randomly assigned to begin a new medication.

Essock found that patients who had been taking olanzapine or risperidone before entering the CATIE trial and were randomly assigned to receive the same medication in the study had longer times to discontinuation than those who were newly switched to one of these medications at the beginning of the study. Of those who stayed with olanzapine or risperidone, only about half discontinued it during the trial, compared to more than 70 percent of patients who were switched to olanzapine or risperidone from their previous antipsychotic medication or from no medication.

An editorial by Carol Tamminga, M.D., of the University of Texas Southwestern Medical Center, and colleagues on the Essock group’s findings observes that “the CATIE patients had been treated with antipsychotics for an average of more than 14 years.” Over the course of their illness patients had opportunity to identify which medication was most effective for them with fewest adverse effects and those patients did well if the study maintained them on the same drug. She noted that “those who switched, no matter from what drug or to what medication, always fared worse. Switching is not a risk-free decision for the patient.”

With regard to the policy implications of these findings for public payers such as Medicare or Medicaid, this study has good internal validity, as described by Polsky, for assessing clinical outcomes for this chronically ill population. It demonstrates that requiring patients stabilized on one antipsychotic to switch to a “preferred” or cheaper formulary medication may come at a cost of decreasing effectiveness and increased risk of adverse side effects.

The economic analysis of the CATIE study led by Rosenheck examined direct treatment costs of care – i.e., the prices of medications and health care services – and assessed the effectiveness of treatment in terms of symptoms and side effects, measures that lead to changes in QALYs.

Although the total cost of health care was \$300 to \$500 per month lower for perphenazine than for the SGAs, this difference was accounted for during the average time of approximately five months that patients received the less-expensive perphenazine before discontinuing or switching to another medication.

Since there was no significant difference in outcomes between this relatively brief exposure to perphenazine and the second-generation antipsychotics as measured by quality-adjusted life years, the authors concluded that it was more cost-effective for these chronically ill patients. However, the study was limited by a high dropout rate (only 25.9 percent of all patients completed 18 months with their original assigned treatment) and potential longer-term side effects that require further study.

The short period that patients were followed and the high drop-out rates did not permit the investigators to assess the risk and cost implications of metabolic syndromes or tardive dyskinesia – an irreversible side effect associated with long-term use of first generation antipsychotics that has carried substantial liability issues for treating physicians.

As interesting as the study is from a methodology development perspective, failures to assess social costs, to demonstrate the prior validity of the QALY outcome measure, or to meet the “external validity” criteria outlined by Polsky, make this study an insufficient base for broad policy decisions that would restrict access to any particular medication.

The *American Journal of Psychiatry* is the official journal of the American Psychiatric Association (APA).

**Note to Editors:** Contact APA’s Office of Communications and Public Affairs at 703-907-8640 or [press@psych.org](mailto:press@psych.org) for an embargoed copy of the article and editorial.

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