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Risks Found for Youths in New Antipsychotics

By [BENEDICT CAREY](#)

A new government study published Monday has found that the medicines most often prescribed for [schizophrenia](#) in children and adolescents are no more effective than older, less expensive drugs and are more likely to cause some harmful side effects. The standards for treating the disorder should be changed to include some older medications that have fallen out of use, the study's authors said.

The results, being published online by The American Journal of Psychiatry, are likely to alter treatment for an estimated one million children and teenagers with schizophrenia and to intensify a broader controversy in child [psychiatry](#) over the newer medications, experts said.

Prescription rates for the newer drugs, called atypical antipsychotics, have increased more than fivefold for children over the past decades and a half, and doctors now use them to settle outbursts and aggression in children with a wide variety of diagnoses, despite serious side effects.

A consortium of state [Medicaid](#) directors is currently evaluating the use of these drugs in children on state Medicaid rolls, to ensure they are being prescribed properly.

The study compared two of the newer antipsychotics, Zyprexa from Eli Lilly and Risperdal from Janssen, with an older medication and found that all three relieved symptoms of schizophrenia, like auditory [hallucinations](#), in many young patients. Yet half of the children in the study stopped taking their drug within two months, either because it had no effect or was causing serious side effects, like rapid weight gain. The children receiving Zyprexa gained so much weight that a government oversight panel monitoring safety ordered that they be taken off the drug.

The long-anticipated study, financed by the National Institute of Mental Health, is the most rigorous, head-to-head trial of the drugs in children and adolescents with this disorder. About three million Americans suffer from schizophrenia, and perhaps 40 percent first show symptoms in their teens or earlier.

"This is really a landmark study, because these newer drugs have been around for 12 years or so now, and there were fundamental questions for which we really didn't have answers," said Dr. Sanjiv Kumra, director of the division of child and adolescent psychiatry at the [University of](#)

[Minnesota](#), who was not involved in the study.

Dr. Kumra said the results revealed significant differences in the drugs' side effects that should help doctors and patients choose among them.

"What this is saying is that all treatments work, at least for some people, and have serious risks for others," he said. "It's a trial-and-error process" to match people with the right medication.

Dr. Jon McClellan of the [University of Washington](#), a co-author of the new study and of the current guidelines for treating childhood schizophrenia, said in a telephone interview that older schizophrenia drugs should now be considered as an alternative in some cases.

"Some of the children in this study gained 15 pounds or more in eight weeks," Dr. McClellan said. "That's as much as adults gain in a year on these medications. Children are especially susceptible to these side effects, and this has broad implications across the board, for the use of these agents to treat any disorder."

Studies have found that more than 80 percent of [prescriptions](#) for atypical antipsychotics for children are to treat something other than schizophrenia, like [autism](#)-related aggression, [bipolar disorder](#) or attention-deficit problems. Some of these are approved uses; others are not.

The researchers, led by Dr. Linmarie Sikich of the [University of North Carolina](#), recruited 119 young people, ages 8 to 19, who suffer from [psychotic](#) symptoms. The children received either Zyprexa, Risperdal or molindone, an older drug used to blunt psychosis. Neither the young patients nor the doctors treating them knew which drug was being taken, but the researchers told the youngsters and their parents that, if the medication was not working out, the family could switch to another one.

After eight weeks, 34 percent of the children taking Zyprexa, 46 percent of those on Risperdal, and 50 percent of those receiving molindone showed significant improvement.

But by that time so many of the patients had stopped taking the drug they were on that it was not clear that those differences were significant. Many had gained a lot of weight: an average of about nine pounds for those in the Risperdal group, and 13 pounds in the Zyprexa group.

Both groups also showed changes in [cholesterol](#) and insulin levels that are [risk factors for diabetes](#). Those taking molindone gained less than a pound, on average, and had little metabolic changes.

"I thought the extra weight was putting a lot of pressure on me," said Brandon Constantineau, 18,

a study participant in Wilmington, N.C., who gained 35 pounds while taking Risperdal for several months. “Kids at school were making fun of me, all that. I knew I had to get rid of it. I exercised a lot, but it didn’t happen until I changed drugs.”

Mr. Constantineau said he was now doing well on a medication not offered in the study.

Dr. Sikich, the study’s lead researcher, said, “One implication of this study is that the guidelines for treating schizophrenia need to be revised, so that some of the milder, traditional or older medications are considered first-line treatments in some cases.” She added: “The other significant thing is that none of these medications were as well tolerated as we had hoped. We really need to find better alternatives.”

Spokesmen for Eli Lilly and Janssen said that their drugs were not approved to treat schizophrenia in children and that, given the limited number of options for such patients, there was a need for new therapies.

Jamaison Schuler, a spokesman for Eli Lilly, pointed out that the new study, at eight weeks in length, had not lasted long enough to pick up the most worrisome side effect associated with the older drugs: [Parkinson’s](#)-like movement problems, which are often irreversible. Patients in the study taking molindone also took another drug to reduce this risk.

Beginning in the early 1990s, [psychiatrists](#) turned to the newer drugs in large part to spare their patients those problems. Several large studies since then have shown that that shift — while perhaps sparing some patients movement problems — has had a cost.

A landmark comparison of older and newer drug in adults with schizophrenia, published in 2005, had findings similar to the new report. Most patients in the earlier study stopped taking the drug they were put on, and some of the medications were associated with rapid weight gain and other problems.

“I think the reason the use of these newer drugs has gone up so fast is that there was this widespread assumption that they were safer and more effective than what we had before,” Dr. McClellan said. “Well, we’re seeing now that that’s not the whole story.”

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