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Psychiatric Drugs' Use Drops for Children

Suicide Warnings Raise Bigger Fears On Testing Process

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Warnings that drugs such as Prozac, Paxil and Effexor can increase suicidal behavior in some children have resulted in a nearly 20 percent drop in U.S. pediatric prescriptions of the widely used antidepressants and have triggered deep concerns about the quality of current data on psychiatric drugs, doctors and regulators said.

The unprecedented fall of what were once considered wonder drugs comes as a series of taxpayer-funded analyses have systematically undermined the claims of industry-funded drug trials, raising thorny questions about the ways in which psychiatric drugs are being tested, marketed and used.

No one knows the consequences of such a steep decline in children's drug prescriptions: Critics of the drugs say regulators ought to crack down further, as British health authorities did last month, but many American psychiatrists are worried that reduced access to medications could cause an increase in suicide as a result of untreated depression.

As with many disputes over these and other psychiatric drugs, opinions are more readily available than definitive data. The fundamental problem, many experts said, is that there are not enough systematic long-term studies about psychiatric drugs.

"The problem is we don't have enough good data," said Thomas Laughren, director of the division of psychiatry products at the Food and Drug Administration. "All of our data are focused on the short term."

As a result, he and others said, a consensus is growing that the system of approving psychiatric drugs based on industry-run trials that sometimes last just 12 weeks is not providing doctors with the information they need -- many physicians place patients on the drugs for years. Senior FDA officials say they are weighing whether companies should be required to conduct longer trials to reveal the true risks and benefits of the drugs.

Pharmaceutical makers say that profound change would increase the time and expense of bringing new medications to market.

Although the agency does ask that companies pursue long-term trials after drugs are approved, few do. At a meeting this month, Laughren said, regulators will debate whether long-term trials "should be asked for at initial approval."

Alan Goldhammer, associate vice president for regulatory affairs at the Pharmaceutical Research and Manufacturers of America, said long-term studies should be conducted by public health agencies at taxpayer expense.

"I don't think they fall within the province of the pharmaceutical industry because they are so costly and time-consuming that it would probably bring drug development to a halt," he said. "There would not be the funds to develop new drugs if one focused on one drug and tried to know everything about it."

In the absence of long-term data, however, doctors, parents and patients have been confused by a steady stream of concerns that have recently emerged:

- An FDA review last year found that newer antidepressants increase suicidal behavior among some children, and the agency ordered that a "black box" warning be placed on them.
- British authorities last month went even further, telling doctors there never to prescribe medications to depressed children without first trying multiple alternatives, and never to prescribe drugs without also providing psychotherapy. Doctors were also warned not to prescribe the antidepressants Paxil and Effexor to depressed children under any circumstances.
- On Sept. 28, the FDA announced that the drug Strattera, prescribed widely to children with attention deficit disorder, had also been found to increase the risk of suicidal behavior in some, and told manufacturer Eli Lilly and Co. to add a black-box warning.
- Also last month, a major government analysis of antipsychotic medications found newer, expensive drugs were neither safer nor more effective than an older generic medication that doctors rarely use. The drugs had never been systematically compared in a long-term trial. Another study in older patients, paid for by Canadian health authorities, found the newer drugs "are not necessarily safer" when it came to causing uncontrolled movements; for years, doctors have believed the newer drugs were significantly less likely to cause that side effect.

Reflecting the confusion caused by the lack of good data, FDA regulators have drawn the ire both of critics who say the agency has not gone far enough to protect patients who take the drugs and of many psychiatrists who say the agency is going too far.

Antidepressant prescriptions for children fell nearly 20 percent in the last year, according to a recent report by the American Psychiatric Association and data from NDCHealth, a health care information company. Experts at the association worry that patients have been scared into thinking the drugs are dangerous, when the bigger danger of suicide lies in untreated depression.

Again, the FDA's Laughren said there is little data on whether the drop in prescriptions is a good thing or a bad thing.

"It could mean that physicians are prescribing more rationally and that explains the drop, or it could mean there is a decreased access of medications," he said. "Ultimately, systematic controlled trials are the best way to figure out the risks and benefits."

Many experts said without long-term studies, doctors are left to rely on trial and error -- and drug company marketing. Millions of dollars have been spent to boost the profile of newer antipsychotic drugs, for example. Although some patients clearly benefit, the study paid for by the federal government suggests doctors have embraced the new products without clear evidence that they are superior.

Many psychiatrists, in fact, were so certain the new drugs were better that they questioned the need to pit the new medications against an older drug, said Yale psychiatrist Robert Rosenheck, who helped conduct the study that found all of them did about as well.

Such misjudgments cannot be corrected when doctors are so dependent on short industry-sponsored trials, said Columbia University psychiatrist Jeffrey Lieberman, who led the antipsychotics study. Short-term studies do not tell clinicians which drug to try first or which is more cost-effective.

Many industry trials also carefully select the patients being studied in order not to muddy the results, whereas doctors routinely deal with patients with multiple conditions and complex problems. And companies have been legally allowed to keep short-term trials with inconvenient results out of public view. Studies that showed antidepressants were ineffective in children, for example, were systematically excluded from the medical literature. The result was that the data available to doctors painted a rosy picture of the drugs.

"If we only had the public evidence, we would have recommended the use of all the [drugs]," said Tim Kendall, a British psychiatrist who led a two-year analysis of both the public and secret data.

When the unpublished trials were taken into account, the evidence, he said, led them to rule out the use of Paxil and Effexor for children and to severely curtail the use of the other antidepressants.

Children with milder forms of major depression -- who are persistently teary, emotionally flat, or uninterested in activities for several weeks -- ought not to be candidates for the drugs at all, he said. Instead, the new British guidelines call for watchful waiting.

Children with severe forms of major depression -- losing weight, not sleeping, and showing suicidal behavior -- should get talk therapy for at least three months, Kendall said, before doctors consider adding a medication.

But Thomas Insel, director of the National Institute of Mental Health in Bethesda, said requiring three months of talk therapy before giving medication is unrealistic, because talk therapy is not widely available.

"It is not clear to me that most 16-year-olds would get any treatments at all," he said. "It is hard to imagine that is an improvement."

Depriving doctors of antidepressants could also prompt clinicians to venture into uncharted territory with even less data, Insel said. He is concerned that physicians are already switching children from antidepressants to antipsychotic drugs, none of which have been approved for children. The federal government's top mental health researcher said it "was amazing" that nearly a quarter of all antipsychotic prescriptions for children are going to those younger than 9, the vast majority of them boys.

"I am concerned we are going to see an increase in . . . antipsychotics in this population," said Insel. "Have we gone from one set of medications of known benefit and of questionable risks to a group of medications with unknown benefits and well-known risks?"