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Psychiatrists, Children and Drug Industry's Role

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When Anya Bailey developed an eating disorder after her 12th birthday, her mother took her to a psychiatrist at the University of Minnesota who prescribed a powerful antipsychotic drug called Risperdal.

Created for schizophrenia, Risperdal is not approved to treat eating disorders, but increased appetite is a common side effect and doctors may prescribe drugs as they see fit. Anya gained weight but within two years developed a crippling knot in her back. She now receives regular injections of Botox to unclench her back muscles. She often awakens crying in pain.

Isabella Bailey, Anya's mother, said she had no idea that children might be especially susceptible to Risperdal's side effects. Nor did she know that Risperdal and similar medicines were not approved at the time to treat children, or that medical trials often cited to justify the use of such drugs had as few as eight children taking the drug by the end.

Just as surprising, Ms. Bailey said, was learning that the university psychiatrist who supervised Anya's care received more than $7,000 from 2003 to 2004 from Johnson & Johnson, Risperdal's maker, in return for lectures about one of the company's drugs.

Doctors, including Anya Bailey's, maintain that payments from drug companies do not influence what they prescribe for patients.

But the intersection of money and medicine, and its effect on the well-being of patients, has become one of the most contentious issues in health care. Nowhere is that more true than in psychiatry, where increasing payments to doctors have coincided with the growing use in children of a relatively new class of drugs known as atypical antipsychotics.

These best-selling drugs, including Risperdal, Seroquel, Zyprexa, Abilify and Geodon, are now being prescribed to more than half a million children in the United States to help parents deal with behavior problems despite profound risks and almost no approved uses for minors.

A New York Times analysis of records in Minnesota, the only state that requires public reports

of all drug company marketing payments to doctors, provides rare documentation of how financial relationships between doctors and drug makers correspond to the growing use of atypicals in children.

From 2000 to 2005, drug maker payments to Minnesota psychiatrists rose more than sixfold, to $1.6 million. During those same years, prescriptions of antipsychotics for children in Minnesota's Medicaid program rose more than ninefold.

Those who took the most money from makers of atypicals tended to prescribe the drugs to children the most often, the data suggest. On average, Minnesota psychiatrists who received at least $5,000 from atypical makers from 2000 to 2005 appear to have written three times as many atypical prescriptions for children as psychiatrists who received less or no money.

The Times analysis focused on prescriptions written for about one-third of Minnesota's Medicaid population, almost all of whom are disabled. Some doctors were misidentified by pharmacists, but the information provides a rough guide to prescribing patterns in the state.

Drug makers underwrite decision makers at every level of care. They pay doctors who prescribe and recommend drugs, teach about the underlying diseases, perform studies and write guidelines that other doctors often feel bound to follow.

But studies present strong evidence that financial interests can affect decisions, often without people knowing it.

In Minnesota, psychiatrists collected more money from drug makers from 2000 to 2005 than doctors in any other specialty. Total payments to individual psychiatrists ranged from $51 to more than $689,000, with a median of $1,750. Since the records are incomplete, these figures probably underestimate doctors' actual incomes.

Such payments could encourage psychiatrists to use drugs in ways that endanger patients' physical health, said Dr. Steven E. Hyman, the provost of Harvard University and former director of the National Institute of Mental Health. The growing use of atypicals in children is the most troubling example of this, Dr. Hyman said.

"There's an irony that psychiatrists ask patients to have insights into themselves, but we don't connect the wires in our own lives about how money is affecting our profession and putting our patients at risk," he said.

The Prescription

Anya Bailey is a 15-year-old high school freshman from East Grand Forks, Minn., with pictures of the actor Chad Michael Murray on her bedroom wall. She has constant discomfort in her neck that leads her to twist it in a birdlike fashion. Last year, a boy mimicked her in the lunch room.

"The first time, I laughed it off," Anya said. "I said: 'That's so funny. I think I'll laugh with you.' Then it got annoying, and I decided to hide it. I don't want to be made fun of."

Now she slumps when seated at school to pressure her clenched muscles, she said.

It all began in 2003 when Anya became dangerously thin. "Nothing tasted good to her," Ms. Bailey said.

Psychiatrists at the University of Minnesota, overseen by Dr. George M. Realmuto, settled on Risperdal, not for its calming effects but for its normally unwelcome side effect of increasing appetite and weight gain, Ms. Bailey said. Anya had other issues that may have recommended Risperdal to doctors, including occasional angry outbursts and having twice heard voices over the previous five years, Ms. Bailey said.

Dr. Realmuto said he did not remember Anya's case, but speaking generally he defended his unapproved use of Risperdal to counter an eating disorder despite the drug's risks. "When things are dangerous, you use extraordinary measures," he said.

Ten years ago, Dr. Realmuto helped conduct a study of Concerta, an attention deficit hyperactivity disorder drug marketed by Johnson & Johnson, which also makes Risperdal. When Concerta was approved, the company hired him to lecture about it.

He said he gives marketing lectures for several reasons.

"To the extent that a drug is useful, I want to be seen as a leader in my specialty and that I was involved in a scientific study," he said.

The money is nice, too, he said. Dr. Realmuto's university salary is $196,310.

"Academics don't get paid very much," he said. "If I was an entertainer, I think I would certainly do a lot better."

In 2003, the year Anya came to his clinic, Dr. Realmuto earned $5,000 from Johnson & Johnson for giving three talks about Concerta. Dr. Realmuto said he could understand someone's worrying that his Concerta lecture fees would influence him to prescribe Concerta

but not a different drug from the same company, like Risperdal.

In general, he conceded, his relationship with a drug company might prompt him to try a drug. Whether he continued to use it, though, would depend entirely on the results.

As the interview continued, Dr. Realmuto said that upon reflection his payments from drug companies had probably opened his door to useless visits from a drug salesman, and he said he would stop giving sponsored lectures in the future.

Kara Russell, a Johnson & Johnson spokeswoman, said that the company selects speakers who have used the drug in patients and have either undertaken research or are aware of the studies. "Dr. Realmuto met these criteria," Ms. Russell said.

When asked whether these payments may influence doctors' prescribing habits, Ms. Russell said that the talks "provide an educational opportunity for physicians."

No one has proved that psychiatrists prescribe atypicals to children because of drug company payments. Indeed, some who frequently prescribe the drugs to children earn no drug industry money. And nearly all psychiatrists who accept payments say they remain independent. Some say they prescribed and extolled the benefits of such drugs before ever receiving payments to speak to other doctors about them.

"If someone takes the point of view that your doctor can be bought, why would you go to an E. R. with your injured child and say, 'Can you help me?' " said Dr. Suzanne A. Albrecht, a psychiatrist from Edina, Minn., who earned more than $188,000 from 2002 to 2005 giving drug marketing talks.

The Industry Campaign

It is illegal for drug makers to pay doctors directly to prescribe specific products. Federal rules also bar manufacturers from promoting unapproved, or off-label, uses for drugs.

But doctors are free to prescribe as they see fit, and drug companies can sidestep marketing prohibitions by paying doctors to give lectures in which, if asked, they may discuss unapproved uses.

The drug industry and many doctors say that these promotional lectures provide the field with invaluable education. Critics say the payments and lectures, often at expensive restaurants, are disguised kickbacks that encourage potentially dangerous drug uses. The issue is particularly important in psychiatry, because mental problems are not well understood, treatment often

involves trial and error, and off-label prescribing is common.

The analysis of Minnesota records shows that from 1997 through 2005, more than a third of Minnesota's licensed psychiatrists took money from drug makers, including the last eight presidents of the Minnesota Psychiatric Society.

The psychiatrist receiving the most from drug companies was Dr. Annette M. Smick, who lives outside Rochester, Minn., and was paid more than $689,000 by drug makers from 1998 to 2004. At one point Dr. Smick was doing so many sponsored talks that "it was hard for me to find time to see patients in my clinical practice," she said.

"I was providing an educational benefit, and I like teaching," Dr. Smick said.

Dr. Steven S. Sharfstein, immediate past president of the American Psychiatric Association, said psychiatrists have become too cozy with drug makers. One example of this, he said, involves Lexapro, made by Forest Laboratories, which is now the most widely used antidepressant in the country even though there are cheaper alternatives, including generic versions of Prozac.

"Prozac is just as good if not better, and yet we are migrating to the expensive drug instead of the generics," Dr. Sharfstein said. "I think it's the marketing."

Atypicals have become popular because they can settle almost any extreme behavior, often in minutes, and doctors have few other answers for desperate families.

Their growing use in children is closely tied to the increasingly common and controversial diagnosis of pediatric bipolar disorder, a mood problem marked by aggravation, euphoria, depression and, in some cases, violent outbursts. The drugs, sometimes called major tranquilizers, act by numbing brain cells to surges of dopamine, a chemical that has been linked to euphoria and psychotic delusions.

Suzette Scheele of Burnsville, Minn., said her 17-year-old son, Matt, was given a diagnosis of bipolar disorder four years ago because of intense mood swings, and now takes Seroquel and Abilify, which have caused substantial weight gain.

"But I don't have to worry about his rages; he's appropriate; he's pleasant to be around," Ms. Scheele said.

The sudden popularity of pediatric bipolar diagnosis has coincided with a shift from antidepressants like Prozac to far more expensive atypicals. In 2000, Minnesota spent more

than $521,000 buying antipsychotic drugs, most of it on atypicals, for children on Medicaid. In 2005, the cost was more than $7.1 million, a 14-fold increase.

The drugs, which can cost $1,000 to $8,000 for a year's supply, are huge sellers worldwide. In 2006, Zyprexa, made by Eli Lilly, had $4.36 billion in sales, Risperdal $4.18 billion and Seroquel, made by AstraZeneca, $3.42 billion.

Many Minnesota doctors, including the president of the Minnesota Psychiatric Society, said drug makers and their intermediaries are now paying them almost exclusively to talk about bipolar disorder.

The Diagnoses

Yet childhood bipolar disorder is an increasingly controversial diagnosis. Even doctors who believe it is common disagree about its telltale symptoms. Others suspect it is a fad. And the scientific evidence that atypicals improve these children's lives is scarce.

One of the first and perhaps most influential studies was financed by AstraZeneca and performed by Dr. Melissa DelBello, a child and adult psychiatrist at the University of Cincinnati.

Dr. DelBello led a research team that tracked for six weeks the moods of 30 adolescents who had received diagnoses of bipolar disorder. Half of the teenagers took Depakote, an antiseizure drug used to treat epilepsy and bipolar disorder in adults. The other half took Seroquel and Depakote.

The two groups did about equally well until the last few days of the study, when those in the Seroquel group scored lower on a standard measure of mania. By then, almost half of the teenagers getting Seroquel had dropped out because they missed appointments or the drugs did not work. Just eight of them completed the trial.

In an interview, Dr. DelBello acknowledged that the study was not conclusive. In the 2002 published paper, however, she and her co-authors reported that Seroquel in combination with Depakote "is more effective for the treatment of adolescent bipolar mania" than Depakote alone.

In 2005, a committee of prominent experts from across the country examined all of the studies of treatment for pediatric bipolar disorder and decided that Dr. DelBello's was the only study involving atypicals in bipolar children that deserved its highest rating for scientific rigor. The

panel concluded that doctors should consider atypicals as a first-line treatment for some children. The guidelines were published in The Journal of the American Academy of Child and Adolescent Psychiatry.

Three of the four doctors on the panel served as speakers or consultants to makers of atypicals, according to disclosures in the guidelines. In an interview, Dr. Robert A. Kowatch, a psychiatrist at Cincinnati Children's Hospital and the lead author of the guidelines, said the drug makers' support had no influence on the conclusions.

AstraZeneca hired Dr. DelBello and Dr. Kowatch to give sponsored talks. They later undertook another study comparing Seroquel and Depakote in bipolar children and found no difference. Dr. DelBello, who earns $183,500 annually from the University of Cincinnati, would not discuss how much she is paid by AstraZeneca.

"Trust me, I don't make much," she said. Drug company payments did not affect her study or her talks, she said. In a recent disclosure, Dr. DelBello said that she received marketing or consulting income from eight drug companies, including all five makers of atypicals.

Dr. Realmuto has heard Dr. DelBello speak several times, and her talks persuaded him to use combinations of Depakote and atypicals in bipolar children, he said. "She's the leader in terms of doing studies on bipolar," Dr. Realmuto said.

Some psychiatrists who advocate use of atypicals in children acknowledge that the evidence supporting this use is thin. But they say children should not go untreated simply because scientists have failed to confirm what clinicians already know.

"We don't have time to wait for them to prove us right," said Dr. Kent G. Brockmann, a psychiatrist from the Twin Cities who made more than $16,000 from 2003 to 2005 doing drug talks and one-on-one sales meetings, and last year was a leading prescriber of atypicals to Medicaid children.

The Reaction

For Anya Bailey, treatment with an atypical helped her regain her appetite and put on weight, but also heavily sedated her, her mother said. She developed the disabling knot in her back, the result of a nerve condition called dystonia, in 2005.

The reaction was rare but not unknown. Atypicals have side effects that are not easy to predict in any one patient. These include rapid weight gain and blood sugar problems, both risk factors

for diabetes; disfiguring tics, dystonia and in rare cases heart attacks and sudden death in the elderly.

In 2006, the Food and Drug Administration received reports of at least 29 children dying and at least 165 more suffering serious side effects in which an antipsychotic was listed as the "primary suspect." That was a substantial jump from 2000, when there were at least 10 deaths and 85 serious side effects among children linked to the drugs. Since reporting of bad drug effects is mostly voluntary, these numbers likely represent a fraction of the toll.

Jim Minnick, a spokesman for AstraZeneca, said that the company carefully monitors reported problems with Seroquel. "AstraZeneca believes that Seroquel is safe," Mr. Minnick said.

Other psychiatrists renewed Anya's prescriptions for Risperdal until Ms. Bailey took Anya last year to the Mayo Clinic, where a doctor insisted that Ms. Bailey stop the drug. Unlike most universities and hospitals, the Mayo Clinic restricts doctors from giving drug marketing lectures.

Ms. Bailey said she wished she had waited to see whether counseling would help Anya before trying drugs. Anya's weight is now normal without the help of drugs, and her counseling ended in March. An experimental drug, her mother said, has recently helped the pain in her back.

This article is by Gardiner Harris, Benedict Carey and Janet Roberts.