

Study Shows Possible Link Between Deaths and ADHD Drugs

By [Shankar Vedantam](#)

Washington Post Staff Writer

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Children taking stimulant drugs such as Ritalin to treat attention-deficit hyperactivity disorder are several times as likely to suffer sudden, unexplained death as children who are not taking such drugs, according to a study published yesterday that was funded by the Food and Drug Administration and the National Institute of Mental Health.

While the numbers involved in the study were very small and researchers stopped short of suggesting a cause and effect, the study is the first to rigorously demonstrate a rare but worrisome connection between ADHD drugs and sudden death among children. In doing so, the research adds to the evolving puzzle parents and doctors face in deciding whether to treat children with medication.

Doctors have speculated about such a connection in the past because stimulants increase heart rate and have other cardiovascular effects. Physicians are currently advised to evaluate patients for cardiac risks before prescribing the drugs, and FDA officials said yesterday that those guidelines do not need strengthening in light of the new study. About 2.5 million children in the United States take ADHD medications such as Ritalin and Adderall.

In a press briefing called on short notice yesterday, FDA officials said that given the seriousness of ADHD and the rarity of sudden death -- which strikes fewer than 1 in 10,000 children -- the benefits of the drugs outweigh their risks. Agency officials urged parents to discuss concerns with doctors rather than deciding on their own to discontinue a child's medication. The study's lead author, Madelyn Gould, a professor in child psychiatry and epidemiology at Columbia University, said she agreed with the FDA's advice.

"This study reports a significant association or 'signal' between sudden unexplained death and the use of stimulant medication, specifically methylphenidate," the study researchers concluded, referring to the chemical name of Ritalin. "While the data have limitations that preclude a definitive conclusion, our findings draw attention to the potential risks of stimulant medications for children and adolescents."

Since an experimental study comparing the risk of sudden death among children taking medications with those not taking medications would have had to include millions of children to generate a useful scientific result, Gould and a number of colleagues conducted what is known as a matched case-control study: They obtained information about 564 children in the United States who died suddenly and inexplicably between 1985 and 1996. The researchers evaluated how many of the children who died had been taking stimulant drugs by asking their parents and caregivers and by reviewing medical documents.

For every child who died suddenly and inexplicably, the researchers then found another child closely matched in terms of age, sex and other variables who died in a traffic accident. Taking a stimulant drug is unlikely to have played any role in a child getting killed in an accident. If stimulant drugs had nothing to do with sudden, unexplained death, then the number of victims on stimulant drugs who suffered such deaths and the number of victims on stimulant drugs who died in traffic accidents ought to have been about the same.

But Gould found that 10 children in the group that suffered sudden, unexplained death had been taking stimulant drugs, whereas only two children in the group killed in traffic accidents were taking such medications.

Robert Temple, director of the Office of Drug Evaluation at the Center for Drug Evaluation and Research at the FDA, said that the study had been well conducted, but that he was concerned that not all parents may accurately recall whether children who died were taking stimulant drugs. When a child dies suddenly, he said, it is natural for a parent to pay close attention to all the medications the child was taking at the time and to report that to researchers. By contrast, he said, parents whose children die in traffic accidents may be less likely to note whether their children are taking medications -- and less able to report it years later.

In an editorial accompanying the study, Benedetto Vitiello of the National Institute of Mental Health said that ADHD itself might have increased the risk for sudden, unexplained death. If that were the case, he said, it would explain why more children taking stimulant drugs were found in the group that suddenly died than among the children who died in traffic accidents.

The researchers who conducted the peer-reviewed study acknowledged that its design precluded definitive answers, but they said that they had taken care to eliminate each of these potential confounders. They did not consider cases of sudden death in which children had asthma or cardiac abnormalities -- conditions known to be associated with ADHD -- because those factors might have independently raised the risk of sudden death. They also included one child who died in a traffic accident who seemed to have been abusing amphetamines, rather than taking an ADHD medication.

Gould said she had her colleagues had compensated for biases not only on the part of parents, but in medical records -- medical examiners are more likely to conduct toxicology tests among children who die suddenly than among children who die in traffic accidents. The researchers first eliminated all records that relied on parental memories and looked only at medical records. They then eliminated all cases that had medical records and looked only at what parents reported. No matter how the data were sliced, Gould said, there were significantly more children taking stimulant drugs who suffered sudden, unexplained death than those who were killed in traffic accidents.

Vitiello said Gould's study underscores that ADHD drugs are not innocuous. Indiscriminate prescription of the drugs for general behavioral problems and the growing number of healthy teenagers and adults using the drugs to boost mental performance could have deadly consequences, he added.