

HEALTH NEWS

High Doses of ADHD Drugs Linked to Higher Risks of Psychosis and Mania: Harvard Study

Researchers call for dose considerations in ADHD treatment as study shows 81 percent of high-dose psychosis cases might be preventable.

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People taking high doses of amphetamines, often prescribed for treating attention-deficit/hyperactivity disorder (ADHD), may have higher risks of developing psychosis and mania, a new study has found.

Researchers at McLean Hospital, the largest psychiatric affiliate of Harvard Medical School, found that people taking high doses of the stimulant amphetamine, the active ingredient in ADHD drugs such as Adderall, face a 5.3-fold higher chance of experiencing a psychotic or manic episode.

"Stimulant medications don't have an upper dose limit on their labels," Dr. Lauren Moran, a pharmacoepidemiology researcher at McLean Hospital and lead author of the study, said in a [press release](#). "Our results show that it is clear that dose is a factor in psychosis risk and should be a chief consideration when prescribing stimulants."

For this study, a high dose was defined as 30 milligrams (mg) of dextroamphetamine, equivalent to 40 mg of Adderall. The generally recommended dose for adults is 20 mg of Adderall.

People taking doses above 30 mg of dextroamphetamine equivalents face a much higher risk of mental health issues. Older adults are even more susceptible to these risks.

Dr. Alex Dimitriu, founder of Menlo Park Psychiatry and Sleep Medicine, who was not involved in the study, told The Epoch Times that in his practice, most patients only require up to 40 mg of Adderall. "As would be expected, some with more severe ADHD or other comorbid conditions such as OCD or depression may benefit from higher doses," he said. "However, the number of patients in ranges above 40 mg is not many."

First-Onset Psychosis and Mania in Stimulant Takers

The team analyzed electronic health records from the Mass General Brigham health care system, covering patient encounters between 2005 and 2019. Published in The American Journal of Psychiatry, the study compared patients aged 16 to 35 who were hospitalized for their first episode of psychosis or mania with those hospitalized for depression or anxiety.

Psychosis affects how the brain processes information, leading to a loss of touch with reality through hallucinations and delusions. Mania, on the other

hand, is characterized by elevated mood, high energy, and euphoria.

The research found a 63 percent attributable risk for any amphetamine use. This means that if people hadn't taken amphetamines, 63 percent of those cases might have been avoided. Additionally, 81 percent of cases involving high doses could have been avoided by not using such high amounts.

The researchers found that individuals who took high-dose amphetamines in the past month had a 5.3-fold increased risk of being hospitalized for their first psychotic or manic episode compared to those hospitalized for other psychiatric conditions. When compared to outpatient controls, high-dose amphetamine users showed a 13.4-fold higher risk of developing psychosis or mania.

There's limited evidence for prescription amphetamines being more effective in high doses, Moran said. A [clinical study](#) by the U.S. Food and Drug Administration (FDA) found that doses exceeding 20 mg per day didn't provide additional benefits.

The FDA doesn't specify a maximum recommended dose on approved labels.

Additionally, only amphetamines prescribed for children state on their labels that it is rarely necessary to exceed a total of 40 mg per day, Moran said. There is no such upper limit label for adults that doctors can adhere to, she added.

Psychosis Linked to Only 1 Drug

Recent studies show a difference in the risk profiles of two commonly prescribed ADHD medications. Amphetamines, such as Adderall, have been linked to an increased risk of psychosis and mania, while methylphenidates, like Ritalin, do not appear to carry this risk.

According to the study, both types of stimulants work by increasing dopamine levels in the brain, but amphetamines cause four times more dopamine release than methylphenidates, while methylphenidates are more effective at preventing dopamine reabsorption.

The current study, consistent with previous research, found that the risk of psychosis and mania was present only in patients taking amphetamines, not in those using methylphenidates.

"Adderall is more potent but also has more side effects and a greater risk of triggering mania and psychosis," Dimitriu said. "Ritalin generally is more gentle and easier to tolerate with fewer risks of adverse reactions."

While the study does not establish causality, researchers hypothesize that the higher levels of dopamine released by amphetamines may be a key factor. This higher dopamine release mimics the increased dopamine levels seen in people with psychotic disorders, potentially explaining the stronger association between amphetamines and these mental health conditions.

"It does not surprise me that amphetamine presents with a higher risk of psychosis given its binding affinity and effects on serotonin and dopamine concentrations," Oliver Grundmann, a clinical professor in pharmaceutical chemistry and clinical toxicology at the University of Florida College of Pharmacy, told The Epoch Times via email. "The mechanism of action for amphetamine is also different from Ritalin, so it does make sense to see a difference."

What to Look Out For

The researchers advised close monitoring and screening for symptoms of psychosis and mania in ADHD patients taking more than 30 mg of dextroamphetamine, as patients often overlook these symptoms themselves.

"Individuals with a predisposition to mood disorders or a family history of psychiatric conditions are particularly at risk," Dr. Dara Abraham, founder and psychiatrist at Dr. Dara Psychiatry, told The Epoch Times.

Moran, who has extensive experience working with ADHD patients, suggests that people seek help when they notice early warning signs such as insomnia, agitation, and difficulty maintaining thoughts, especially if others comment that they're not acting like themselves.

Family members should seek help immediately, she added, if they observe changes in behavior along with self-reporting by the patient that he or she is hearing voices, having beliefs that don't make sense, speaking rapidly, and jumping between topics without making sense.

"If someone develops psychosis ... the stimulant should be stopped immediately, and a doctor should be consulted," Dimitriu said. He also emphasized the importance of quality sleep for optimal effects from prescription stimulants and warned that extensive use of substances, such as alcohol and cannabis, can diminish the drug's effectiveness.

Risk of Schizophrenia and Bipolar Disorder?

ADHD is linked to both schizophrenia and bipolar disorder, conditions where psychosis and mania can occur.

A 2021 [study](#) found that childhood ADHD is associated with an increased risk of developing psychotic disorders in adulthood. Another [study](#), from 2014, found that children and adolescents with ADHD are 4.3 times more likely to develop schizophrenia.

ADHD is also highly likely to co-occur with bipolar disorder. The [age of onset](#) of bipolar disorder is earlier in those with ADHD.

Moran said she believes that ADHD itself is a risk factor for both conditions independent of stimulant use. "Cognitive symptoms precede the onset of psychosis and are common in bipolar disorder," she said.

While the study shows that prescription amphetamines are associated with a greater risk of new-onset psychosis and mania, this doesn't mean that all cases of schizophrenia/bipolar disorder with ADHD diagnoses are due to stimulants, she noted.

ADHD, schizophrenia, and bipolar disorder share neurobiological features, particularly concerning dopamine dysregulation, Abraham said. "For individuals predisposed to bipolar disorder or schizophrenia, stimulants might trigger or worsen symptoms," she noted.

"ADHD may be seen in higher frequency in schizophrenia and bipolar, but medication and stimulant use alone is not the most likely explanation," Dimitriu said. Children with ADHD who are properly treated with stimulants are less likely to abuse drugs—showing that stimulant use could protect against both schizophrenia and bipolar disorder, he added.



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Rachel Melegrito worked as an occupational therapist, specializing in neurological cases. Melegrito also taught university courses in basic sciences and professional occupational therapy. She earned a master's degree in childhood development and education in 2019. Since 2020, Melegrito has written extensively on health topics for various publications and brands.

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