One in six people who stop antidepressants will experience discontinuation symptoms as a direct result, says study

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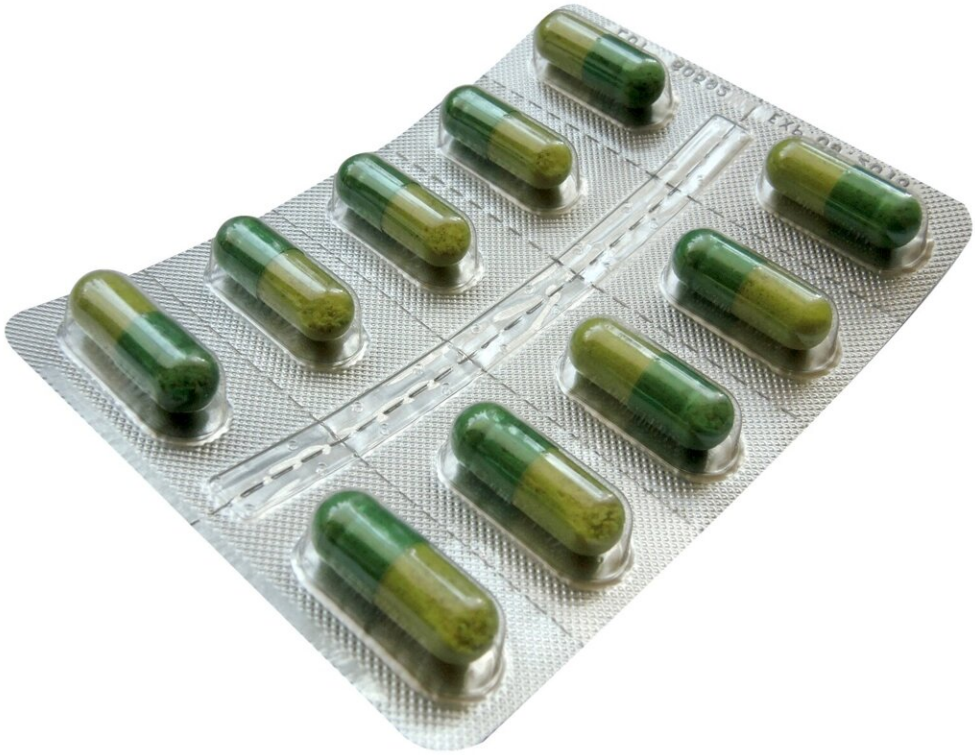

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For someone stopping taking antidepressants, the risk of experiencing one or more discontinuation symptoms (also called withdrawal symptoms), such as dizziness, headache, nausea, insomnia and irritability due directly to stopping the medication is 15% (equivalent to one in six to seven people), according to a systematic review and meta-analysis published in *The Lancet Psychiatry.*

The analysis also found discontinuation symptoms that patients describe as severe, and which may have led to patients dropping out of a study or restarting on antidepressants, occurred in about 3% (one in 35) of patients stopping antidepressants.

"There's strong evidence that antidepressants can be effective for many people who are experiencing a depressive disorder, either alone or alongside other treatments such as psychotherapy. However, they do not work for everyone, and some patients may experience unpleasant side-effects. In patients who have recovered with the help of antidepressants, the decision from doctors and patients may be to stop taking them in time. Therefore, it's important both doctors and patients have an accurate, evidence-based picture of what might happen when patients stop taking antidepressants," says Dr. Jonathan Henssler from Charité-Universitätsmedizin Berlin.

He continues, "Our study confirms that a number of patients coming off antidepressants will experience discontinuation symptoms, and for a few, these will be of a more severe extent. It's important to note that antidepression discontinuation symptoms are not due to antidepressants being addictive. There is a crucial need for all patients stopping antidepressants to be counseled, monitored and supported by heath care professionals. However, our findings, which consolidate data from a large number of studies, should also provide reassurance that rates of

discontinuation symptoms are not as high as some previous single studies and reviews have suggested."

Previous studies have estimated that over half of patients experience discontinuation symptoms when stopping antidepressants, and that half of the symptoms are severe. However, many of these estimates are based on observational studies which cannot reliably determine cause and effect.

On the other hand, well-conducted randomized controlled trials (where half of the trial population is offered a placebo, or dummy pill, and the other half is offered the medication) can more reliably distinguish between symptoms directly caused by the medication and non-specific symptoms that might be driven by patients' or practitioners' expectations.

The aim of this study was to review all available evidence to establish the probable incidence of discontinuation symptoms caused directly by stopping antidepressant use, the probable incidence of severe symptoms and the differences between different types of antidepressant. The researchers conducted a review and meta-analysis of 79 trials (44 RCTs and 35 observational studies) which included data from 21,002 patients, 16,532 discontinuing from antidepressants and 4,470 from placebo, with an average age of 45 years, and with 72% women.

Overall, the analysis found that a third (31%) of people who stopped taking an antidepressant experienced at least one symptom, such as dizziness, headache, nausea, insomnia or irritability. Severe symptoms occurred in about 3% (one in 35). Stopping imipramine (Tofranil), paroxetine (Seroxat) and (des-)venlafaxine (Pristiq) was associated with a higher risk of severe symptoms compared with other antidepressants.

When looking specifically at the results from randomized controlled trials, one in six patients (17%) experienced discontinuation-like

symptoms when stopping a placebo drug. This suggests approximately half of all symptoms experienced in those stopping antidepressants might be due to negative expectations (the "nocebo effect") or non-specific symptoms which could occur at any time in the general population. In conclusion, the authors estimate that one in six to seven (15%) of patients will experience one or more discontinuation symptoms that are directly caused by stopping antidepressants.

The analysis did not find a difference between studies that applied tapering of the antidepressant and studies with a sudden stopping of the medication. However, the authors caution that substantial variation in study designs--such as the duration of taper and type of antidepressant used--mean that these are not firm conclusions, and further research is needed. They also highlight how previous single study results indicate that tapering may be helpful in decreasing severity and incidence of discontinuation symptoms.

"We hope the findings from this study will inform health-care professionals and patients about the risk of experiencing discontinuation symptoms when stopping antidepressants without causing unnecessary alarm. Like all medications, antidepressants present important benefits, but also carry risks—including discontinuation symptoms which are also common among a variety of general medications, like drugs for high blood pressure or mild painkillers, and it is important that patients are able to access accurate, evidence-based information under the care of a clinician to discuss the balance of benefits vs. risks for them personally.

"Our findings do not imply that some symptoms experienced by people during antidepressant discontinuation are not 'real' or that all discontinuation symptoms are due to expectations on the part of patients. Any symptoms that cause patients discomfort or distress should be taken seriously, and the patient should be supported. The patient and clinician should discuss which of the symptoms might be directly caused by

stopping antidepressants and how best to manage all symptoms," says Christopher Baethge, University of Cologne.

The researchers note some limitations of their study, cautioning that the studies included in the systematic review and meta-analysis used a variety of methodologies. Additionally, a challenge in all studies on antidepressant discontinuation symptoms is the possibility of symptoms of re-occurring depression after stopping antidepressants, which may be interpreted as discontinuation symptoms. Although the main analysis included 62 studies, only seven antidepressants were investigated in three or more studies, and there were no studies found on several widely used antidepressants, for example, mirtazapine, bupropion, or amitriptyline.

Writing in a linked Comment, Glyn Lewis and Gemma Lewis from University College London, who were not involved in the study, say, "…the difference between the active and placebo groups is the important one from a scientific point of view. A rough estimate of the true prevalence of discontinuation symptoms is about 8–14% and of severe withdrawal syndromes about 2%. Reports of withdrawal symptoms that are not compared with a placebo will give a large overestimate of the frequency of such symptoms. Future study of withdrawal symptoms should ensure that comparisons are made with a placebo when possible."

More information: Incidence of antidepressant discontinuation symptoms: a systematic review and meta-analysis, *The Lancet Psychiatry* (2024). DOI: 10.1016/S2215-0366(24)00133-0 , www.thelancet.com/journals/lan … (24)00133-0/fulltext

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