

New study supports psilocybin's potential as an antidepressant

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Credit: Marek Piwnicki from Pexels

Psilocybin—the active ingredient in "magic" mushrooms—is a more effective treatment for symptoms of depression than controls, providing further support for its potential as an antidepressant, suggests a study published by *The BMJ* today.

The researchers say the findings are encouraging but "further research is

needed to clarify the factors that maximize psilocybin's treatment potential for symptoms of [depression](#)."

Depression affects an estimated 300 million people worldwide and is a leading cause of disability.

Psilocybin has shown promise in reducing symptoms of depression after one or two doses with few [side effects](#) and no current evidence of causing addiction. However, studies published to date have not investigated factors that may moderate psilocybin's effects, including type of depression, past use of psychedelics, dosage, and publication biases.

To address this, a team of UK researchers examined databases looking for randomized controlled trials that compared psilocybin as a treatment for symptoms of depression with controls, such as placebo, niacin (vitamin B), or micro doses of psychedelics.

They included studies where psychotherapy was present in both the experimental and the control conditions, so that the effects of psilocybin could be distinguished from those of psychotherapy.

They found seven relevant trials for analysis involving 436 participants with depression (52% female; 90% white). Changes in depression scores were measured using a statistical method called Hedges' *g*. A Hedges' *g* of 0.2 indicates a small effect, 0.5 a moderate effect, and 0.8 or more a large effect.

The change in depression scores was significantly greater after treatment with psilocybin than with a comparator treatment, with an overall Hedge's *g* of 1.64 indicating a large effect size favoring psilocybin.

Further analyses to account for trial differences indicated that having

secondary depression (related to an underlying disease) rather than primary depression, being assessed with a self-reported scale rather than a clinician assessed scale, older age, and previous use of psychedelics, were correlated with greater improvements.

The study authors acknowledge that high levels of variation (heterogeneity) between trials resulted in a low certainty of evidence to support a strong antidepressant effect of psilocybin, and generalizability of findings were limited by the lack of participant diversity.

Pre-treatment expectations and the extent to which participants knew they were being treated with psilocybin or placebo, were also not measured.

Furthermore, in [clinical trials](#), patients receive psilocybin in a calm living room with soothing music, supervised by a psychotherapist, which is unlikely to be achievable in a health care system.

As such, the authors conclude that, although this review's findings are encouraging for psilocybin's potential as an effective antidepressant, issues such as cost, lack of regulatory guidelines and legal safeguards associated with psilocybin treatment need to be dealt with before it can be established in clinical practice.

This study is an important contribution to the evidence base for the use of psilocybin in depression, but it cannot answer several questions, say researchers unconnected to the study in a linked editorial.

For instance, they argue that it cannot provide evidence for psilocybin's effectiveness (performance under 'real-world' conditions) in depression until more information about potential effect modifiers is gathered, and that pragmatic clinical trials and real-world data could help to deliver that.

Furthermore, there is still ongoing debate on whether psychedelics can express antidepressant activity on their own rather than by assisting specific forms of psychotherapy.

Finally, and perhaps most importantly, the editorial authors say that, as per all analyses using aggregate data, we cannot differentiate between those individuals most likely to benefit from psilocybin and those who might instead experience adverse events.

As such, they conclude that these promising findings "support a prudent approach in both scholarly and public settings, because more and better evidence is needed before any clinical recommendation can be made about therapeutic use of [psilocybin](#)."

More information: Efficacy of psilocybin for treating symptoms of depression: systematic review and meta-analysis, *The BMJ* (2024). [DOI: 10.1136/bmj-2023-078084](#)

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