

# Ketamine effective for treatment-resistant depression: Clinical trial

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One 10 ml vial of 1000 mg ketamine. Credit: Psychonaught/Wikipedia

A low-cost version of ketamine to treat severe depression has performed

strongly in a double-blind trial that compared it with placebo.

In research published today in the *British Journal of Psychiatry*, researchers led by UNSW Sydney and the affiliated Black Dog Institute found that more than one in five participants achieved total remission from their symptoms after a month of bi-weekly injections, while a third had their symptoms improve by at least 50 percent. The study was a collaboration between six academic clinical mood disorder units in Australia and one in New Zealand and was funded by the Australian National Health and Medical Research Council (NHMRC).

"For people with treatment-resistant [depression](#)—so those who have not benefitted from different modes of talk-therapy, commonly prescribed antidepressants, or electroconvulsive therapy—20 percent remission is actually quite good," lead researcher Professor Colleen Loo says.

"We found that in this trial, ketamine was clearly better than the placebo—with 20 percent reporting they no longer had [clinical depression](#) compared with only 2 percent in the placebo group. This is a huge and very obvious difference and brings definitive evidence to the field which only had past smaller trials that compared ketamine with placebo."

## How the trial worked

The researchers recruited 179 people with treatment-resistant depression. All were given an injection of either a generic form of ketamine that is already widely available in Australia as a drug for anesthesia and sedation—or placebo. Participants received two injections a week in a clinic where they were monitored for around two hours while acute dissociative and sedative effects wore off—usually within the first hour. The treatment ran for a month and participants were asked to assess their mood at the end of the trial and one month

later.

As a [double-blind trial](#), neither participants nor researchers administering the drug were aware which patients received generic ketamine or placebo, to ensure psychological biases were minimized. Importantly, a placebo was chosen that also causes sedation, to improve treatment masking. Midazolam is a sedative normally administered before a general anesthetic, while in many previous studies the placebo was saline.

"Because there are no subjective effects from the saline, in previous studies it became obvious which people were receiving the ketamine and which people received placebo," Prof. Loo says.

"In using midazolam—which is not a treatment for depression, but does make you feel a bit woozy and out of it—you have much less chance of knowing whether you have received ketamine, which has similar acute effects."

Other features of the recent trial that set it apart from past studies included accepting people into the trial who had previously received [electroconvulsive therapy](#) (ECT).

"People are recommended ECT treatment for their depression when all other treatments have been ineffective," Prof. Loo says.

"Most studies exclude people who have had ECT because it is very hard for a new treatment to work where ECT has not."

Another difference about this trial was that the drug was delivered subcutaneously (injected into the skin) rather than by drip, thus greatly reducing time and medical complexity. The study is also the largest in the world to date that compares generic ketamine with [placebo](#) in

treating [severe depression](#).

## **Much more affordable**

Apart from the positive results, one of the standout benefits of using generic ketamine for [treatment-resistant depression](#) is that it is much cheaper than the patented S-ketamine [nasal spray](#) currently in use in Australia. Where S-ketamine costs about \$800 per dose, the generic ketamine is a mere fraction of that, costing as little as \$5, depending on the supplier and whether the hospital buys it wholesale.

On top of the cost for the drug, patients need to pay for the medical care they receive to ensure their experience is safe—which at Black Dog Institute clinics, comes to \$350 per session.

"With the S-ketamine nasal spray, you are out of pocket by about \$1200 for every treatment by the time you pay for the drug and the procedure, whereas for generic ketamine, you're paying around \$300-350 for the treatment including the drug cost," Prof. Loo says.

She adds that for both S-ketamine and generic ketamine treatments, the positive effects often wear off after a few days to weeks, so ongoing treatment may be required, depending on someone's clinical situation. But the prohibitive costs of the drug and procedure make this an unsustainable proposition for most Australians.

"This is why we're applying for a Medicare item number to fund this treatment now, because it's such a powerful treatment."

"And if you consider that many of these people might spend many months in hospital, or be unable to work and are often quite suicidal, it's quite cost effective when you see how incredibly quickly and powerfully it works. We've seen people go back to work, or study, or leave hospital

because of this treatment in a matter of weeks."

The researchers will next be looking at larger trials of generic [ketamine](#) over longer periods, and refining the safety monitoring of [treatment](#).

**More information:** Colleen Loo et al, Efficacy and safety of a 4-week course of repeated subcutaneous ketamine injections for treatment-resistant depression (KADS study): randomised double-blind active-controlled trial, *The British Journal of Psychiatry* (2023). [DOI: 10.1192/bjp.2023.79](#)

Provided by University of New South Wales

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