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Reviewed by Virginia Lindahl, Ph.D.

When Susan Gayhart heard about ketamine as a depression treatment, she wasn't optimistic. "I'd been hopeful in the past, trying [different medications](#), waiting for weeks to see any kind of improvement," said Gayhart, a writer and photographer. "And I just never did. I didn't have any hope that ketamine would be better."

Despite her reservations, Gayhart — who struggled with severe depression for decades — decided to give it a try. Within a week, she

noticed changes. “At the time, even taking a shower seemed overwhelming,” she said. “After my first week of treatment, I was thinking, ‘Hmm, taking a shower might be a good idea.’ The shifts were small, but significant.” Continued treatment was so successful that Gayhart eventually started [a blog called My Ketamine Story](#) to advocate for ketamine treatment and share her experience with others.

How does depression affect you?

Clinical depression, or major depressive disorder, is a serious illness that's steadily become **more prevalent**, especially **during the pandemic**. While **situational depression** (technically called adjustment disorder with depressed mood) is triggered by specific circumstances and tends to get better in a shorter time, clinical depression can last for longer and have devastating consequences. It robs you of your ability to enjoy life and experience pleasure, consumes your energy, and makes you feel both helpless and hopeless. Over time, depression can also harm your physical health and increase your risk of **suicide**.

How common is depression?

The National Institute of Mental Health estimates that **21 million adults had at least one major depressive episode** in 2020. And depression is almost **twice as common** among women, particularly during reproductive ages — 21% will experience a major depressive episode (versus 13% of men) in their lifetimes, and the rates are **even higher** for **women of color**. Socioeconomic factors play a role, as well: **The rate of depression** decreases as family income increases.

While depression is a highly treatable disease, traditional antidepressants have **side effects** ranging from anxiety to weight gain, and, for about **30% of** people treated with medication, they offer no relief. “Antidepressants are widely used and often effective, but they have their limitations,” said **David Spiegel, M.D.**, the Willson Professor and associate chair of psychiatry at Stanford University School of

Medicine. “There are some people who don’t respond to them.” Fortunately, research is uncovering new ways to target depression.

The science behind new treatments for depression

“For the last 70 years in the United States, depression has typically been treated with two forms of antidepressants, which are very similar in the way they modulate serotonin, norepinephrine and dopamine in the brain,” explained [Emil Tsai, M.D., Ph.D., M.A.S.](#), professor at the Department of Psychiatry and Behavioral Sciences at UCLA. Tsai explained that new treatments like ketamine affect a different [part of the brain](#) than other antidepressants, so they may help patients who don’t respond to those.

“These new treatments are interesting because they seem to work in different ways,” said Spiegel. For example, [Transcranial Magnetic Stimulation \(TMS\)](#) stimulates [an area of the brain](#) that helps control mood. With TMS, Spiegel said, there are two benefits: patients can get rapid relief from depression symptoms, and over time, they also get a “tune-up” on the parts of the brain that don’t work correctly when they’re depressed.

Overall, the newer treatments for clinical depression show great promise: They work quickly and have few—if any—side effects. Availability is still limited in some areas, however, and not all treatments are covered by insurance — but that’s changing. “We’re beginning to redefine the range of treatments for depression,” said Spiegel. “For example, TMS is spreading rapidly and is now used in some emergency rooms.”

The latest treatments for clinical depression

Dextromethorphan/bupropion

Dextromethorphan/bupropion is the first new type of oral treatment for depression to be FDA-approved in 60 years. An NMDA receptor antagonist, it is generally [well-tolerated](#) by patients and shows [significant improvements](#) of depressive symptoms, even within a week of starting treatment. According to the manufacturer, it should be [commercially available](#) by late 2022.

Ketamine and other psychedelics

Ketamine is one of the most promising new treatments for depression, with years of research behind it. It's been shown to be [safe and effective](#) as a treatment for moderate to severe depression. And, with the [FDA's 2019 approval](#) of a nasal spray, it's easy to deliver.

Other ketamine delivery methods include [intravenous](#) and [intramuscular](#). In both instances, one would typically go to an outpatient clinic for a 45-60-minute session. Patients might start with an intense dosing period, and then ease into a more sustainable schedule. "Ketamine cuts the NMDA receptor off altogether," Tsai said. "This is why employing this therapy treatment requires such a deft hand. The goal is to work within the delicacy of the NMDA receptor, and employ a gentle touch." Ketamine not only [treats symptoms quickly](#), but may also stimulate [long-term brain change](#) over time.

Other psychedelics, such as [psilocybin](#) (the active ingredient in "magic mushrooms") and [dimethyltryptamine](#) (found in the Amazonian plant ayahuasca), show promise as well, but are in earlier stages of research and trial.

Transcranial magnetic stimulation (TMS)

Depression treatment with a giant magnet may seem like a sci-fi invention, but it's very real and very effective. In fact, studies at Stanford show [nearly 80% efficacy](#) for TMS, often [within days](#).

In a TMS session, a large piece of equipment is angled carefully over your head, sending electric currents from a magnetic coil to work on a specific region of the brain. "TMS can rapidly reverse depression and suicidal ideation in people who are very sick," Spiegel said. And with new protocols such as [high-dose spaced theta burst](#), he explained, it's possible to deliver the treatments in one week, with effects lasting six months to a year.

Digital therapy options

[The pandemic](#) forced many to rely on digital for therapy and help, and new tools and research have grown from that shift. For example, some studies have shown that computer-assisted cognitive behavior therapy (CCBT) had [significantly better effects](#) than standard treatment, particularly in treating [marginalized adults](#). Digital mental health apps are accessible in a way that other treatments are not. "We're learning to use digital approaches for some of the best aspects of psychological treatments," Spiegel said. "Even [dealing with insomnia](#) can be a huge help. They're particularly helpful for people at the moderate end of the depression spectrum."

Perhaps the most exciting possibility is what can happen with the right combination of tools and treatment. For Gayhart, ketamine provided her with enough relief from the severe symptoms of depression that she could start using the tools she'd learned in therapy over the years. There's now huge hope as treatments like TMS and ketamine push back the darkness of depression, and [digital apps](#) make therapy and tools more accessible for more people.

“I had almost succeeded in a suicide attempt,” Gayhart said. “That’s why I really advocate for this medication. It saved my life.”

If you or someone you know is having a mental health crisis, please call or text the Suicide and Crisis Lifeline at 988.

Resources

[American Foundation for Suicide Prevention](#)

[988 Suicide and Crisis Lifeline](#)

[National Institute for Mental Health Depression Overview Page](#)