

OPTIONS MD

*Groundbreaking* + experimental therapies  
for treatment-resistant depression

Explore innovative treatments that might be right for you.

# You've got Options MD.

Options MD uses medical research–built technology to connect you with proven treatments and expert clinicians who understand severe, treatment-resistant depression—so you can find the relief you deserve.

## Options tailored to your *unique* experience.

Our groundbreaking software offers:

- Comprehensive assessment that captures your complete mental health history
- Over 200 treatment options—from FDA-approved pharmaceuticals to next-level clinical trials
- Access to clinicians specialized in treatment-resistant depression who are confident prescribing a wide range of treatment options and up to date on the newest innovations
- Robust community of people who have experienced and witnessed treatment-resistant depression—so you're never alone on your path to relief

While this guide is not meant to provide medical advice, it may spark your interest in novel treatment approaches that you might not have considered.

You can also get to know the Options MD Fundamentals plan, which utilizes Options MD's proprietary software to give you personalized education on your treatment options.



# Switching + Augmenting Antidepressants

Like everything in life, depression is not a universal experience, and clinicians must adapt their strategies for truly effective treatment.

Of people experiencing major depression, only 30% will have symptoms that subside after their first antidepressant trial. For those who continue to have depression despite trying an antidepressant—especially those who have at least some improvement in their symptoms—adding another antidepressant can lead to a greater response and even remission of depression entirely.<sup>1</sup>

## What is augmentation treatment?

Broadly, augmentation—or combination—therapy is when a new medication is added with the goal of boosting the effects of a medication you are already on. Many combinations of medications exist to boost your current medication's effects.<sup>1</sup>

Common classes of medications used for augmentation include: atypical antipsychotics, lithium, some stimulants, and psychiatric treatments.

## How Options MD can help:

It's always worth asking your clinician about treatments beyond typical first-line approaches. Options MD makes that process easier with our comprehensive assessment. It delves into your lifestyle, medical and mental health history, side effect sensitivity, demographic factors, and more to provide a range of options that you can discuss with a clinician.

With a deeper understanding of your depression, conversations about more innovative treatments will be more productive, informed, and—hopefully—lead to more relief.

## To switch or not to switch?

Switching antidepressants is a tactic used when little to no symptom relief is experienced or the side effect profile is too intolerable and impactful on daily life. This may be a clinician's first approach when an initial treatment option has not been helpful.

## More meds = more side effects?

Inherent with any pharmaceutical approach is the potential for adverse effects; however, it's important to speak with your clinician about what side effects you want to avoid and what cannot be taken with your current antidepressant.

## The Fundamentals:

The Options MD Fundamentals plan will analyze your mental health and medical history to give you personalized recommendations for new treatments you may want to consider. Plus you can join our community of users (for free!) who know exactly what it's like to live with treatment-resistant depression. Because we've been there.



# Ketamine

First in our list of groundbreaking treatments is ketamine. When administered by a professional, ketamine can produce a rapid and powerful antidepressant response. Numerous studies from leaders in the field have shown that ketamine can play an impactful role in reducing life-threatening thoughts that could lead to suicide.<sup>2,3</sup>



## How it works:

Used for fast results, ketamine blocks a special receptor in the brain and is believed to help restore balance to parts of the brain affected by stress. It may also promote the growth or strengthening of neural pathways that affect mood, cognition, and thought patterns. Available in IV infusions or a nasal spray, you should consider factors like symptom severity, health insurance coverage, and your clinician's recommendation before choosing a ketamine treatment route.

Ketamine treatments are often administered 2–3 times per week for the first 4–6 weeks. When ketamine produces a positive response, maintenance treatments are typically required to sustain the antidepressant effect and occur once or twice a month.

## What it costs:

An increasing number of insurance companies are seeing the benefit of this groundbreaking treatment. Most commercial insurance and even some Medicare plans now cover treatment with ketamine, typically the nasal spray esketamine. However, both commercial insurance and Medicare have specific requirements that must first be met, such as how many other medications must have been tried first. IV treatments are also available with out-of-pocket costs typically ranging from \$350 to \$650 per session. Consult your provider for specific coverage information.

## Side effects:

When treating severe depression and suicidal ideations, the benefits may outweigh the side effects. Possible temporary side effects include: drowsiness or a dream-like state, double or blurred vision, dizziness, vomiting or nausea, a loss of appetite, sleep disturbances, jerky muscle movements, and high blood pressure.

Ketamine may be more harmful than helpful for some people seeking relief. Patients with a history of uncontrolled hypertension or other cardiac disease should talk to their doctor before starting a ketamine treatment. Patients with a history of psychosis or negative experiences with psychedelic substances should not use ketamine or esketamine.

## Treatment outcome:

Cost aside, ketamine offers hope to those suffering treatment-resistant depression. Here to help in a crisis, Ketamine delivers rapid results as research and clinical trials continue to demonstrate its positive effect on severe depression symptoms.

Options MD's Fundamentals plan can help you understand if ketamine is a good treatment option for you. Because it is an intensive treatment, we can also help you find a clinician specialized in ketamine and other innovative therapies to double verify ketamine's appropriateness for your unique experience.



## rTMS

A model for the new era of treatment, repetitive transcranial magnetic stimulation (rTMS) is a non-invasive approach that may improve symptoms of depression when other options have failed. Over the course of a few weeks, depressive episodes decrease, and treatment-resistant patients report feeling significant relief of their symptoms.<sup>4,5,6</sup>

### How it works:

Harnessing the power of electromagnetism, rTMS delivers short magnetic pulses to active nerve cells involved in mood control and depression. Administered by a clinician, electromagnetic coils are strategically placed on the head and then switched on and off to provide increased amounts of magnetic energy stimulation.

rTMS is typically administered in daily sessions that last about 20–40 min and occur 5 days per week for up to 4–6 weeks.

### What it costs:

While many health insurance plans cover rTMS for treatment-resistant depression, it's important to find a physician who advocates for coverage and maintains a proven record of medication resistance for major depression.

### Side effects:

Though relatively well tolerated, some side effects may arise. Those include headaches, lightheadedness, tingling, twitching face muscles, and scalp irritation where stimulation occurred. Rare cases of seizures and hearing loss (due to improper ear protection) have occurred. Patients with non-removable metal in their heads (with the exception of braces or dental fillings) should not use rTMS.

### Treatment outcome:

rTMS has shown to be effective at reducing symptoms of depression and anxiety in patients who have not responded to traditional antidepressant medications.<sup>7</sup> In patients who respond to rTMS, the positive effects typically last between 6 months to 1 year. Repeat rounds of rTMS are sometimes helpful for those whose response has faded.





# EMDR



Originally developed for post-traumatic stress disorder, eye movement desensitization and reprocessing (EMDR) is a psychotherapy that facilitates the accessing and processing of traumatic memories and life experiences to alleviate their associated stress and symptoms. By mimicking the body’s healing processes, psychologists create a sequence for the mind to heal.<sup>8</sup>

## How it works:

Depression’s association with negative life events makes its symptoms an apt target for EMDR. By identifying adverse events from childhood to present—not limited to life-threatening trauma—therapists help transform the meaning of painful events. Working with a therapist to target specific memories, clinicians use stimulating eye movements related to REM sleep cycles, so patients’ intellectual and emotional processes accelerate and negative associations become empowering ones.

## What it costs:

EMDR sessions typically cost between \$100 to \$250 a session, with each session lasting between one to two hours. Fortunately, EMDR is covered under most insurance plans with therapy coverage.

## Side effects:

While there is little potential for physical harm with EMDR, psychotherapy intentionally delves into sensitive and traumatic subject matter that could cause short-term distress or increase depressive symptoms. It is important for patients to establish a strong relationship with their therapists for full transparency throughout treatment.

## Treatment outcome:

People with trauma-related treatment-resistant depression have seen clinically significant improvement in symptoms after EMDR therapy. Though no therapy will have universal effects, EMDR’s direct intervention in negative belief processing makes it a hopeful approach when other treatments have failed.

Options MD’s Fundamentals plan can help you understand if EMDR is a good fit for you. We can also help you find an EMDR-certified therapist before fully committing to this therapy.





# Lithium

The gold standard of bipolar disorder treatment, lithium has shown to be a rapidly effective augmentation for treatment-resistant depression—especially in the prevention of early relapses and reducing suicidality.<sup>9,10</sup>



## How it works:

While lithium has been used for over 70 years to treat mood disorders, scientists remain unsure as to how it produces its antidepressant effect. This is because lithium is a salt and interacts with cells in a variety of ways. Lithium affects different neurotransmitters including dopamine, norepinephrine, serotonin, GABA, and glutamate. It also affects different types of internal cellular machinery.<sup>11</sup>

Depending on a patient's weight, lithium doses range from 600 mg/day to up to 1500 mg/day through tablets and capsules. Solutions range from 10 mL two or three times a day up to 25 mL two or three times a day.

## What it costs:

Generic lithium is covered by Medicare Part D prescription drug plans. Eskalith, the extended-release version of lithium, is also covered by Medicare. Consult your provider for specific pricing and coverage information.

## Side effects:

As with any medication, some side effects may occur, including: confusion, poor memory, lack of awareness, fainting, irregular heartbeat, frequent urination, increased thirst, muscle stiffness, trouble breathing during strenuous activity, unusual tiredness, and weight gain. More rare side effects include headache, noise in ears, vision problems, and dizziness.

## Treatment outcome:

Lithium augmentation's rapid onset and demonstrated efficacy in reducing suicidality make it an appealing therapy for severe, treatment-resistant depression. Clinical studies show people who use it in addition to TCAs, SSRIs, or other antidepressants are 2–3 times more likely to experience relief from depression.<sup>12</sup>

Options MD's Fundamentals plan can help you understand if lithium is a good fit for you.



# Intermittent Fasting

A novel approach still in the experimental phase, intermittent fasting has demonstrated antidepressant efficacy. Simply defined as short-term, regular periods of calorie restriction, intermittent fasting as an antidepressant may stem from multiple physiological processes, including evident effects on the neuroendocrine system and mood condition.<sup>13</sup>

Despite its antidepressant appeal, calorie restriction is not without controversy, and has the potential to cause long-term detrimental effects via inhibiting the function of 5-HT system and decreasing leptin levels.<sup>13</sup> Plus its association with disordered eating must be taken into account prior to beginning an intermittent-fasting regimen.

## How it works:

Scientists are just beginning to understand how intermittent fasting affects the brain. So far fasting has been shown to have many benefits for brain function, health, and mood and is associated with a reduction in inflammation, an increase in neuroprotective factors, improved insulin sensitivity, and changes in neurotransmitter systems.<sup>14</sup>

The most common intermittent-fasting methods include daily time-restricted feeding, alternate-day fasting, and the 5:2 schedule. Daily time-restricted feeding involves scheduling a daily time window for eating (typically a 6–8-hour period) and fasting for the rest of the time. In alternate-day fasting, a person will eat on one day then fast the next day, while the 5:2 schedule refers to fasting two days a week.

## What it costs:

Intermittent fasting is free beyond food expenses—all you need is the motivation to start it and guidance to do it right. With an abundance of online resources, you can discover an approach, diet, and fasting balance that works well for your unique depression symptoms.

## Side effects:

Intermittent fasting is relatively safe and has a number of health benefits, including improving outcomes for those with diabetes, high-blood pressure, and high cholesterol.<sup>15</sup> Those new to fasting may notice headache, dizziness, lightheadedness, and fatigue. It is important to listen to your body when fasting and to slowly work up to longer fasts. When fasting, always remember to stay hydrated. For those with diabetes or other health conditions, talk to your doctor before starting a fasting regimen.

## Treatment outcome:

While clinical studies reviewing intermittent fasting's impact on treatment-resistant depression have yet to be conducted, numerous studies have shown that intermittent fasting is associated with reductions in symptoms of anxiety and depression in general<sup>16</sup> and may improve cognitive function.<sup>17</sup>



## Studies have shown...

As researchers learn more about depression and why some people experience such chronic, untreatable symptoms, more treatments emerge that show promise as adjunctive—or standalone—therapies. Options MD's Fundamentals plan can match you with ongoing clinical trials to see if you qualify and if the tested therapy aligns with your background and symptom profile.

Currently under investigation and showing great promise for individuals living with treatment-resistant depression is the compound psilocybin.

### Psilocybin

A compound found in mushrooms with hallucinogenic properties, psilocybin has been explored as a depression treatment for some time. Recently gaining traction and clinical legitimacy, Columbia University, New York Psychiatric Institute, and London-based Compass Pathways released a phase 2 clinical trial using COMP360 (a compound of psilocybin) for treatment-resistant depression.<sup>18</sup>

Phase 2 trials aim to provide preliminary evidence of a specific compound's actions by testing it on a small group of patients. In this case, the trial aimed to answer the question: Is psilocybin an effective therapy for treatment-resistant depression?

#### The future of psilocybin:

After phase 2 trials come phase 3 trials. Phase 3 trials aim to show a compound is effective on a large number of patients and are crucial for FDA approval.

With a phase 3 trial planned for mid-2022, the COMP360 research has further refined the ideal dosage of psilocybin for depression treatment and the adverse effects associated with that amount of treatment. By understanding the adverse effects associated with a given dosage, clinicians can better develop risk-management strategies and optimize treatment outcomes.<sup>18</sup>

#### Exploring safe, effective doses:

Doses ranging from 1 mg to 25 mg were given to individuals under the watchful eye of clinicians trained in psychedelic-assisted therapy, and participants taking 25 mg reported a steep decline in depressive symptoms when taking the highest dose. They also reported rapid remission around the three-week mark, and sustained remission after three months. More common side effects included headache, nausea, fatigue, and insomnia, while 12 of the 233 participants reported severe adverse events, including suicidal ideation.

#### Disclaimer:

Options MD NEVER recommends trying psilocybin in recreational settings. Any recreational use risks serious side effects such as suicidal thoughts, paranoia, distorted reality, convulsions, triggering of substance use disorders, and more.

That said, some patients have asked us how they may be able to safely undergo psilocybin treatment in clinical settings. We recommend going to [clinicaltrials.gov](https://clinicaltrials.gov) and searching for psilocybin related clinical trials in your state. If you have any history of substance use disorder, we highly recommend avoiding psilocybin and/or psychedelic-related trials.

# *Final Thoughts*

While we hope these leading-edge treatments piqued your interest, they represent only a small portion of groundbreaking therapies for severe, treatment-resistant depression.

At Options MD, we've compiled a database of over 200 treatments for depression, including tried-and-tested antidepressants, behavioral and natural treatments, intensive therapies, and innovative treatments like some of the ones explored in this article.

For a small, one-time fee, you can access our Fundamentals Plan to receive personalized education around the treatment options that fit your unique experience with treatment-resistant depression. And for free, you can [join the Options MD private community](#) and ask for insights from fellow patients with their own journeys in treatment-resistant depression.

As people who have suffered from mental illness ourselves, we always want to help. Do you have questions, concerns, or just want to share your story? Contact us any time by emailing [founders@optionsmd.com](mailto:founders@optionsmd.com)

Sincerely,

Morgan and Kyle,  
the founders of Options MD

# References

1. Thase ME. Using adjunctive treatments when first-line antidepressants fail. *J Clin Psychiatry*. 2012 Jan;73(1):e01. doi: 10.4088/JCP.10126tx4c. PMID: 22316580.
2. Fu DJ, Ionescu DF, Li X, et al. Esketamine Nasal Spray for Rapid Reduction of Major Depressive Disorder Symptoms in Patients Who Have Active Suicidal Ideation With Intent: Double-Blind, Randomized Study (ASPIRE I). *J Clin Psychiatry*. 2020;81(3). doi:10.4088/jcp.19m13191
3. Ionescu DF, Fu DJ, Qiu X, et al. Esketamine Nasal Spray for Rapid Reduction of Depressive Symptoms in Patients With Major Depressive Disorder Who Have Active Suicide Ideation With Intent: Results of a Phase 3, Double-Blind, Randomized Study (ASPIRE II). *Int J Neuropsychoph*. 2020;24(1):22-31. doi:10.1093/ijnp/pyaa068
4. Dunner DL, Aaronson ST, Sackeim HA, et al. A Multisite, Naturalistic, Observational Study of Transcranial Magnetic Stimulation for Patients With Pharmacoresistant Major Depressive Disorder: Durability of Benefit Over a 1-Year Follow-Up Period. *J Clin Psychiatry*. 2014;75(12):1394-1401. doi:10.4088/jcp.13m08977
5. Levkovitz Y, Isserles M, Padberg F, et al. Efficacy and safety of deep transcranial magnetic stimulation for major depression: a prospective multicenter randomized controlled trial. *World Psychiatry*. 2015;14(1):64-73. doi:10.1002/wps.20199
6. Hung YY, Yang LH, Stubbs B, et al. Efficacy and tolerability of deep transcranial magnetic stimulation for treatment-resistant depression: A systematic review and meta-analysis. *Prog Neuro-psychopharmacology Biological Psychiatry*. 2019;99:109850. doi:10.1016/j.pnpbp.2019.109850
7. Leggett LE, Soril LJ, Coward S, Lorenzetti DL, MacKean G, Clement FM. Repetitive Transcranial Magnetic Stimulation for Treatment-Resistant Depression in Adult and Youth Populations: A Systematic Literature Review and Meta-Analysis. *Prim Care Companion CNS Disord*. 2015;17(6):10.4088/PCC.15r01807. Published 2015 Nov 5. doi:10.4088/PCC.15r01807
8. Wood E, Ricketts T, Parry G. EMDR as a treatment for long-term depression: A feasibility study. *Psychol Psychother*. 2018;91(1):63-78. doi:10.1111/papt.12145
9. Berghöfer A. Lithium in the prevention of suicide in mood disorders: Updated systematic review and meta-analysis. *BMJ*. 2013. doi:10.1136/sbmj.f5578
10. Bschor T. Lithium in the Treatment of Major Depressive Disorder. *Drugs* 74, 855–862 (2014). <https://doi.org/10.1007/s40265-014-0220-x>
11. CG; LRHH. Overview of the mechanism of action of lithium in the brain: Fifty-year update. *The Journal of clinical psychiatry*. <https://pubmed.ncbi.nlm.nih.gov/10826655/>. Published 2000. Accessed February 13, 2022.
12. Nelson JC, Baumann P, Delucchi K, Joffe R, Katona C. A systematic review and meta-analysis of lithium augmentation of tricyclic and second generation antidepressants in major depression. *J Affect Disorders*. 2014;168:269-275. doi:10.1016/j.jad.2014.05.053
13. Zhang Y, Liu C, Zhao Y, Zhang X, Li B, Cui R. The Effects of Calorie Restriction in Depression and Potential Mechanisms. *Curr Neuropharmacol*. 2015;13(4):536-542. doi:10.2174/1570159x13666150326003852
14. Igwe O, Sone M, Matveychuk D, Baker GB, Dursun SM. A review of effects of calorie restriction and fasting with potential relevance to depression. *Prog Neuro-psychopharmacology Biological Psychiatry*. 2020;111:110206. doi:10.1016/j.pnpbp.2020.110206
15. Cabo R de, Mattson MP. Effects of Intermittent Fasting on Health, Aging, and Disease. *New Engl J Med*. 2019;381(26):2541-2551. doi:10.1056/nejmra1905136
16. Berthelot E, Etchecopar-Etchart D, Thellier D, Lancon C, Boyer L, Fond G. Fasting Interventions for Stress, Anxiety and Depressive Symptoms: A Systematic Review and Meta-Analysis. *Nutrients*. 2021;13(11):3947. doi:10.3390/nu13113947
17. Leclerc E, Trevizol AP, Grigolon RB, et al. The effect of caloric restriction on working memory in healthy non-obese adults. *Cns Spectrums*. 2020;25(1):2-8. doi:10.1017/s1092852918001566
18. Cantor C. Psilocybin found to rapidly improve depressive symptoms in clinical trial. Columbia University Department of Psychiatry. <https://www.columbiapsychiatry.org/news/psilocybin-found-rapidly-improve-depressive-symptoms-clinical-trial>. Published November 18, 2021. Accessed February 10, 2022.