

Antidepressants Rarely Outperform Sugar Pills

STORY AT-A-GLANCE

- The serotonin hypothesis posits that low serotonin levels in your brain are responsible for symptoms of depression. However, there's little to no evidence for this. A number of studies have debunked the serotonin hypothesis, which is the basis upon which drug makers market SSRI antidepressants like Prozac, Lexapro and Zoloft
- According to recent research, "The main areas of serotonin research provide no consistent evidence of there being an association between serotonin and depression, and no support for the hypothesis that depression is caused by lowered serotonin activity or concentrations"
- The primary effect of SSRIs is to superimpose an abnormal drug state over your symptoms, much like recreational drugs and alcohol would. The small benefits seen in some drug trials are due to emotional numbing
- This numbing effect comes at a steep price, as it also prevents you from experiencing emotional highs and does little to counteract the loss of energy, interest and motivation that are so characteristic of depression
- Researchers at the U.S. Food and Drug Administration recently published the most comprehensive analysis of antidepressant clinical trial data submitted to the FDA, including unpublished trials. The evidence showed antidepressants outperformed placebo in only 15% of patients, and almost exclusively in those with the most severe depression

As of 2018, 13.2% — approximately 1 in 8 — of American adults over the age of 18 were on antidepressant medication, with more than twice as many women taking them (17.7%) than men (8.4%).¹ Curiously, though, only 7.2% had actually been diagnosed with a major depressive episode — a statistical discrepancy that hints at massive antidepressant overprescribing. As noted by Newsweek:²

"Although there is widespread agreement that SSRIs [selective serotonin reuptake inhibitors] help some people with severe depression, these patients are a small minority of people who take the drugs."

While those statistics are already staggering, depression rates have further risen since then, thanks to COVID lockdowns and the unprecedented fearmongering that has been a hallmark of this pandemic. As reported in "[What Does the Best Evidence Say About Antidepressants?](#)" 22.4% of American adults reported symptoms of depression in June 2022, compared to 7.1% in 2017.

No Evidence to Back Serotonin Hypothesis

The fact that antidepressants are still being used to this extent is a testament to how effectively the drug industry manipulates doctors and patients alike with less than truthful propaganda, as independent studies have repeatedly shown these drugs work no better than placebo.

As Irving Kirsch — associate director of the Program in Placebo Studies and the Therapeutic Encounter at Beth Israel Deaconess Medical Center and Harvard Medical School and a long-time critic of antidepressants — told Newsweek:³

"People do get better on the drug — but in the vast majority of cases it's not because of what's in the drug. There are other treatments that are at least equally effective, and that don't carry the risks."

Indeed, a number of studies have solidly debunked the serotonin hypothesis, which is the basis upon which drug makers market SSRI antidepressants like Prozac, Lexapro and Zoloft.

In short, the idea is that low serotonin levels in your brain is responsible for symptoms of depression. The problem is, there's little to no evidence for this. In fact, low serotonin is associated with long-term antidepressant use, which is basically the converse effect you'd expect if the serotonin theory was true. As reported in a systematic review published in Molecular Psychiatry July 20, 2022:⁴

"The serotonin hypothesis of depression is still influential. We aimed to synthesize and evaluate evidence on whether depression is associated with lowered serotonin concentration or activity in a systematic umbrella review of the principal relevant areas of research ...

17 studies were included: 12 systematic reviews and meta-analyses, 1 collaborative meta-analysis, 1 meta-analysis of large cohort studies, 1 systematic review and narrative synthesis, 1 genetic association study and 1 umbrella review ...

Two meta-analyses of overlapping studies examining the serotonin metabolite, 5-HIAA, showed no association with depression ... One meta-analysis of cohort studies of plasma serotonin showed no relationship with depression, and evidence that lowered serotonin concentration was associated with antidepressant use ...

One meta-analysis of tryptophan depletion studies found no effect in most healthy volunteers, but weak evidence of an effect in those with a family history of depression. Another systematic review and a sample of ten subsequent studies found no effect in volunteers.

No systematic review of tryptophan depletion studies has been performed since 2007. The two largest and highest quality studies of the SERT gene, one genetic association study and one collaborative meta-analysis, revealed no evidence of an association with depression, or of an interaction between genotype, stress and depression.

The main areas of serotonin research provide no consistent evidence of there being an association between serotonin and depression, and no support for the hypothesis that depression is caused by lowered serotonin activity or concentrations. Some evidence was consistent with the possibility that long-term antidepressant use reduces serotonin concentration."

Researcher's Personal Experience With Antidepressants

An interesting backstory to this serotonin paper is that one of its coauthors, Mark Horowitz, Ph.D., a research scientist at the University College London, was on the antidepressant Lexapro for 15 years. His incentive to dive deeper into the truth behind antidepressants emerged when he tried to wean off the drug and found he couldn't.

Panic attacks, insomnia and debilitating depression actually forced him to move back with his parents. All of these symptoms were far worse than what he suffered before taking the drug, and many others find themselves in the same situation — they can't quit the drug because of the side effects. In essence, the addictive nature of these drugs ensures you'll be a lifelong cash cow for the drug maker.

"Ever since beginning his calamitous effort to get off SSRIs, Horowitz has devoted himself to disproving the claims used to justify their widespread use, and lobbying lawmakers to take a second look," Newsweek writes.⁵ "He now describes himself as no more neurotic than anyone in a Woody Allen movie and believes he should never have been prescribed SSRIs in the first place."

We've Been Lied to About Antidepressants

But if the serotonin hypothesis is false, what is it that makes antidepressants appear to be working? In short, it's the [placebo effect](#). As reported by Newsweek:⁶

"The pharmaceutical industry used [the serotonin hypothesis] ... to market the drugs to consumers for many years ... As a result, according to the study's authors,

between 85 and 90% of the public believe that low serotonin levels cause depression.

After reviewing data from previous studies involving hundreds of thousands of individuals, Horowitz and his colleagues concluded that there is little to no evidence that this is true. 'The drug companies convinced us that if you're sad, you should go to your doctor and seek treatment,' Horowitz told Newsweek.

'They've made us all believe that normal aspects of the human condition are a medical illness called major depressive disorder – that normal reactions to difficult situations are a chemical brain problem that needs a medical solution. They convinced people these are very 'mild' drugs that are very easy to stop. None of this is true' ...

Horowitz and the paper's other co-authors ... call for a fundamental reassessment of how mental illness is treated. 'We have a mistaken view of what psychiatric drugs are doing,' says Dr. Joanna Moncrieff, professor of Critical and Social Psychiatry at University College London.

She is also Horowitz's boss and the lead author of the serotonin paper. 'This idea that they work by targeting the underlying biological mechanisms that produce the symptoms of mental disorders is actually not supported by evidence for any type of mental disorder, whether that's depression or schizophrenia or whatever,' she told Newsweek.

Instead, she argues, the drugs change 'normal brain states' and 'normal mental states and processes' in ways not that much different than recreational drugs like alcohol."

Negative Emotions Are Part of the Human Condition

As explained by Moncrieff, the primary effect of SSRI's is to "superimpose an abnormal drug state" over your symptoms, much like recreational drugs and alcohol would. She also stresses that the small benefits seen in some drug trials are due to emotional numbing.

This numbing effect comes at a steep price, however, as it also prevents you from experiencing emotional highs, and does little to counteract the loss of energy, interest and motivation that are so characteristic of depression. Moncrieff continues:⁷

"It's not helpful to think of depression as a brain disease. I think that we should be thinking of it as an emotional reaction to life circumstances and life events. And

indeed, there is very strong evidence that people who suffer from adverse life events are much more likely to get depressed."

Adverse life events tend to be stressful, and stress is strongly linked to depression. People with depression typically report experiencing a stressful episode, such as the death of a loved one, a job loss or onset of a chronic disease, shortly before the onset of their depression.

The question is how to treat it. While many psychiatrists believe stress can cause changes in the brain that can be reversed by antidepressants, others, like Moncrieff, Horowitz and Kirsch, believe psychotherapy that centers on strengthening coping skills and emotional resiliency is a far better — and safer — option.

Most Comprehensive Analysis to Date

In 2022, another team, which included researchers at the U.S. Food and Drug Administration, also came out with the most comprehensive analysis of antidepressant clinical trial data ever published.

This paper,⁸ published in The BMJ, included all antidepressant clinical trial data submitted to the FDA between 1979 and 2016, including unpublished trials. In all, 232 randomized, double-blind, placebo-controlled trials involving 73,388 patients diagnosed with depression were analyzed.

Here, the evidence showed antidepressants outperformed placebo in only 15% of patients, and almost exclusively in those with the most severe depression. In short, the reason many believe they're getting a benefit from these drugs is because of the placebo effect and nothing else.

This supports previous research, which found the placebo effect accounts for anywhere between 30%⁹ and 67%¹⁰ of the antidepressant treatment effect, and that placebo is just as effective as antidepressants in those with mild to moderate depression.¹¹

Drug Makers Use Placebo Effect to Their Advantage

As you might expect, such a strong placebo effect is a problem for drug makers who need to prove their drug works better than a sugar pill. To get around this problem, they devise studies that capitalize on the placebo effect while hiding that fact. As reported by Newsweek:¹²

“The FDA study provides a glimpse of the true power of the SSRI placebo effect and the efforts of the pharmaceutical industry to use these effects to bolster the data on their own drugs. To win approval for a new drug, FDA requires drug makers to submit the results from ‘two well-designed clinical trials’ that demonstrate the drug itself is more potent than the placebo effect ...

But the rules place no limit on how many clinical trials a drug company can conduct to get those two positive results. And though negative trial results must be registered with the FDA, there is no requirement that drug companies publish them.

As a result, the failure rate of trials of antidepressants is far higher than most people understand, says Dr. Erick Turner, a former FDA clinical reviewer, who is now a professor of psychiatry and pharmacology at Oregon Health and Science University ...

By 2015, Dr. Turner had left the agency for academia. He conducted a review of the publication status of 74 studies involving 12 antidepressant agents with 12,564 patients and found that the drugs beat the placebo in only 51% of the studies in the FDA files – an outcome that was not reflected in the published medical literature at the time.

Of 33 studies that had negative or questionable results, 22 were never published and 11 were published in a way that falsely conveyed a positive outcome ... Even though half of the trial had failed, 94% of the published trials reported positive trial results.”

Antidepressants Are Not for Long-Term Use

Importantly, SSRIs, even when they do work for someone, should not be used for years on end. As noted in a recent PLOS ONE paper:¹³

“The real-world effect of using antidepressant medications does not continue to improve patients’ HRQoL [health-related quality of life] over time. Future studies should not only focus on the short-term effect of pharmacotherapy, it should rather investigate the long-term impact of pharmacological and non-pharmacological interventions on these patients’ HRQoL.”

Dr. Michael Thase, professor of psychiatry at UPenn's Perelman School of Medicine, agrees. While he believes antidepressants can be helpful by interrupting the damaging release of glutamate in the brain, he also believes the drugs should not be used for more than six to nine months. Beyond that, you need to have another treatment plan in place.¹⁴

This could go a long way toward avoiding the withdrawal symptoms that afflict 56% of those trying to wean off SSRIs.¹⁵ Since 2004, the average duration patients stay on SSRIs has doubled,¹⁶ and avoiding withdrawal symptoms appears to be a huge part of this trend. Doctors and patients also often misconstrue withdrawal symptoms for a relapse of depression.

Limiting their duration of use will also minimize other risks to your health, as antidepressants come with a long list of potential side effects, including:^{17,18}

- Self-harm, suicide and violence against others. Many [mass shooters have been on antidepressants](#)
- Increased risk of developing Type 2 diabetes,¹⁹ even after adjusting for risk factors such as body mass index²⁰
- Thickening of the greater carotid intima-media (the lining of the main arteries in your neck that feed blood to your brain),²¹ which could contribute to the risk of heart disease and stroke. This is true both for SSRIs and antidepressants that affect other brain chemicals. Users of tricyclic antidepressants have a 36% increased risk of heart attack²²
- An increased risk of dementia; as the dose increases, so does the risk for dementia²³
- Depletion of various nutrients. In the case of tricyclic antidepressants this includes coenzyme Q10 and vitamin B12, which are needed for proper mitochondrial function. SSRIs have been linked to iodine and folate depletion²⁴

Depression Treatments That Actually Work

If you're at all interested in following science-based recommendations, you'd place antidepressants at the very bottom of your list of treatment candidates. Far more effective treatments for depression include:

Exercise — A number of studies have shown exercise outperforms drug treatment. Exercise helps create new GABA-producing neurons that help induce a natural state of calm, and boosts serotonin, dopamine and norepinephrine, which helps buffer the effects of stress.

Studies have shown there is a strong correlation between improved mood and aerobic capacity, but even gentle forms of exercise can be effective. Yoga, for example, has received particular attention in a number of studies. One study found 90-minute yoga sessions three times a week reduced symptoms of major depression by at least 50%.²⁵

Nutritional intervention — Keeping inflammation in check is an important part of any effective treatment plan. If you're gluten sensitive, you will need to remove all gluten from your diet. A food sensitivity test can help ascertain this. Reducing lectins may also be a good idea.

As a general guideline, eating a whole food diet as described in my [optimal nutrition plan](#) can go a long way toward lowering your inflammation level. A cornerstone of a healthy diet is limiting sugar of all kinds, ideally to no more than 25 grams a day.

In one study,²⁶ men consuming more than 67 grams of sugar per day were 23% more likely to develop anxiety or depression over the course of five years than those whose sugar consumption was less than 40 grams per day. Certain nutritional deficiencies are also notorious contributors to depression, especially:

- **Marine-based omega-3 fats** — Omega-3 fats have been shown to improve major depressive disorder,²⁷ so make sure you're getting enough omega-3s in your diet, either from wild Alaskan salmon, sardines, herring, mackerel and anchovies, or a high-quality supplement. I recommend getting an omega-3 index test to make sure you're getting enough. Ideally, you want your omega-3 index to be 8% or higher.
- **B vitamins (including B1, B2, B3, B6, B9 and B12)** — Low dietary folate can raise your risk by as much as 300%.^{28,29} One of the most recent studies^{30,31} showing the importance of vitamin deficiencies in depression involved suicidal teens. Most turned out to be deficient in cerebral folate and all of them showed improvement after treatment with folic acid.
- **Magnesium** — Magnesium supplements led to improvements in mild-to-moderate depression in adults, with beneficial effects occurring within two weeks of treatment.³²
- **Vitamin D** — Studies have shown vitamin D deficiency can predispose you to depression and that depression can respond favorably to optimizing your vitamin D stores, ideally by getting sensible sun exposure.^{33,34} In one study,³⁵ people with a vitamin D level below 20 nanograms per milliliter (ng/mL) had an 85% increased risk of depression compared to those with a level greater than 30 ng/mL.
- A double-blind randomized trial³⁶ published in 2008 concluded that supplementing with high doses of vitamin D “seems to ameliorate [depression] symptoms indicating a possible causal relationship.” Other research³⁷ also claims that low vitamin D levels appear to be associated with suicide attempts. For optimal health, make sure your vitamin D level

is between 60 and 80 ng/mL year-round. Ideally, get a vitamin D test at least twice a year to monitor your level.

Light therapy — Light therapy alone and placebo were both more effective than Prozac for the treatment of moderate to severe depression in an eight-week study.³⁸ Spending time outdoors in broad daylight is the least expensive and likely most effective option.

Probiotics — Keeping your gut microbiome healthy also has a significant effect on your moods, emotions and brain.

Emotional Freedom Techniques (EFT) — EFT is a form of psychological acupressure that has been shown to be quite effective for depression and anxiety.^{39,40,41,42} For serious or complex issues, seek out a qualified health care professional who is trained in EFT to guide you through the process. That said, for most of you with depression symptoms, this is a technique you can learn to do effectively on your own.

Other Helpful Treatment Strategies

Additional strategies that can help improve your mental health include the following:⁴³

Minimize electromagnetic field (EMF) exposure — In 2016, Martin Pall, Ph.D., published a review⁴⁴ in the Journal of Neuroanatomy showing how microwave radiation from cellphones, Wi-Fi routers and computers and tablets not in airplane mode is clearly associated with many neuropsychiatric disorders.

These electromagnetic fields (EMFs) increase intracellular calcium and trigger the production of extremely damaging free radicals by acting on your voltage gated calcium channels (VGCCs), and the tissue with the highest density of VGCCs is your brain. Once these VGCCs are stimulated they also cause the release of neurotransmitters and neuroendocrine hormones, which contribute to anxiety and depression.

So, be sure to limit your exposure to wireless technology. Simple measures include turning your Wi-Fi off at night, not carrying your cellphone on your body unless it's in airplane mode, and not keeping portable phones, cellphones and other electric devices in your bedroom.

Clean up your sleep hygiene — Make sure you're getting enough high quality sleep, as sleep is essential for optimal mood and mental health. The inability to fall asleep and stay asleep can be due to elevated cortisol levels, so if you have

trouble sleeping, you may want to get your saliva cortisol level tested with an Adrenal Stress Index test.

Adaptogens, herbal products that help lower cortisol and adjust your body to stress, can be helpful if your cortisol is running high. There are also other excellent herbs and amino acids that help you to fall asleep and stay asleep.

Optimize your gut health — A number of studies have confirmed gastrointestinal inflammation can play a critical role in the development of depression.⁴⁵ Optimizing your gut microbiome will also help regulate a number of neurotransmitters and mood-related hormones, including GABA and corticosterone, resulting in reduced anxiety and depression-related behavior.⁴⁶

To nourish your gut microbiome, be sure to eat plenty of fresh vegetables and traditionally fermented foods such as fermented vegetables, lassi, kefir and natto. If you do not eat fermented foods on a regular basis, taking a high-quality probiotic supplement is recommended. Also remember to severely limit sugars and grains, to rebalance your gut flora.

Cognitive behavioral therapy (CBT) — CBT has been used successfully to treat depression.^{47,48} This therapy assumes mood is related to the pattern of thought. CBT attempts to change mood and reverse depression by directing your thought patterns.

Make sure your cholesterol levels aren't too low for optimal mental health — You may also want to check your cholesterol to make sure it's not too low. Low cholesterol is linked to dramatically increased rates of suicide, as well as aggression toward others.⁴⁹

This increased expression of violence toward self and others may be due to the fact that low membrane cholesterol decreases the number of serotonin receptors in the brain, which are approximately 30% cholesterol by weight.

Lower serum cholesterol concentrations therefore may contribute to decreasing brain serotonin, which not only contributes to suicidal-associated depression, but prevents the suppression of aggressive behavior and violence toward self and others.

Ecotherapy — Studies have confirmed the therapeutic effects of spending time in nature. Ecotherapy has been shown to lower stress, improve mood and significantly reduce symptoms of depression.⁵⁰ Outdoor activities could be just about anything, from walking a nature trail to gardening, or simply taking your exercise outdoors.

Breathing exercises — Breath work also has enormous psychological benefits and can quickly reduce anxiety by increasing the partial pressure of carbon dioxide in your body.

Helpful supplements — A number of herbs and supplements can also be used in lieu of drugs to reduce symptoms of anxiety and depression, such as:

- **St. John's Wort (*Hypericum perforatum*)** — This medicinal plant has a long historical use for depression, and is thought to work similarly to antidepressants, raising brain chemicals associated with mood such as serotonin, dopamine and noradrenaline.⁵¹
- **S-Adenosyl methionine (SAME)** — SAME is an amino acid derivative that occurs naturally in all cells. It plays a role in many biological reactions by transferring its methyl group to DNA, proteins, phospholipids and biogenic amines. Several scientific studies indicate that SAME may be useful in the treatment of depression.
- **5-Hydroxytryptophan (5-HTP)** — 5-HTP is another natural alternative to traditional antidepressants. When your body sets about manufacturing serotonin, it first makes 5-HTP. Taking 5-HTP as a supplement may raise serotonin levels. Evidence suggests 5-HTP outperforms a placebo when it comes to alleviating depression,⁵² which is more than can be said about antidepressants.
- **XingPiJieYu** — This Chinese herb, available from doctors of traditional Chinese medicine, has been found to reduce the effects of “chronic and unpredictable stress,” thereby lowering your risk of depression.⁵³

Guidelines for Safe Drug Withdrawal

If you're currently on an antidepressant and want to get off it, ideally, you'll want to have the cooperation of your prescribing physician. It would also be wise to do some homework on how to best proceed.

Dr. Peter Breggin's book, “Psychiatric Drug Withdrawal: A Guide for Prescribers, Therapists, Patients and Their Families,”⁵⁴ and/or “The Antidepressant Solution: A Step-by-Step Guide to Overcoming Antidepressant Withdrawal, Dependence, and Addiction”⁵⁵ by Dr. Joseph Glenmullen can be helpful.

You can also turn to an organization with a referral list of doctors who practice more biologically or naturally, such as the American College for Advancement in Medicine at www.ACAM.org. A holistic psychiatrist will have a number of

treatment options in their tool box that conventional doctors do not, and will typically be familiar with nutritional supplementation.

Once you have the cooperation of your prescribing physician, start lowering the dosage of the medication you're taking. There are protocols for gradually reducing the dose that your doctor should be well aware of. At the same time, it may be wise to add in a multivitamin and/or other nutritional supplements or herbs. Again, your best bet would be to work with a holistic psychiatrist who is well-versed in the use of nutritional support.

If you have a friend or family member who struggles with depression, perhaps one of the most helpful things you can do is to help guide them toward healthier eating and lifestyle habits, as making changes can be particularly difficult when you're feeling blue — or worse, suicidal.

Encourage them to unplug and meet you outside for walks. We should not underestimate the power of human connection, and the power of connection with nature. Both, I believe, are essential for mental health and emotional stability.

If you are feeling desperate or have any thoughts of suicide and reside in the U.S., please call the National Suicide Prevention Lifeline by dialing 988, or call 911, or simply go to your nearest hospital emergency department.

You cannot make long-term plans for lifestyle changes when you are in the middle of a crisis. U.K. and Irish helpline numbers can be found on [TherapyRoute.com](https://www.therapyroute.com). For other countries, do an online search for “suicide hotline” and the name of your country.

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