

Generalized Anxiety Disorder (GAD)



What is GAD?

Generalized anxiety disorder, or GAD, is one of the most common psychiatric disorders, affecting approximately 26 million U.S. adults.¹ People with GAD experience constant, overwhelming worry that's hard to control and lasts for six or more months. Common symptoms include fatigue, muscle tension, trouble concentrating, and difficulty sleeping.² GAD is vastly undertreated and often occurs alongside other health problems like chronic physical symptoms, depression, other anxiety disorders, and trauma-related conditions. Together, these issues can seriously impact a person's daily life, including substantial functional, economic, and quality-of-life burdens, and are associated with increased healthcare utilization and costs.³⁻⁶

What causes GAD?

GAD involves disrupted activity, connectivity, or neuroplasticity in key regions of the brain such as the prefrontal cortex, amygdala, and thalamus, leading to impaired emotional regulation and clinical symptoms.^{7,8} GAD may run in families, but the exact cause of the disorder is unknown. Research suggests that GAD results from a mix of genetics, brain chemistry, biology, and environment. Researchers have found that external causes, such as experiencing a traumatic event or being in a stressful environment, may put a person at higher risk for developing GAD.⁹

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Definium is developing a new generation of therapeutics intended to address the underlying causes of psychiatric and neurological disorders. The mission of Definium Therapeutics is to forge a new era of psychiatry by applying scientific rigor to psychedelics, with the goal of developing accessible treatments that unlock healing at scale.

Definium is currently advancing its controlled clinical trials of DT120 Orally Disintegrating Tablet (ODT) – its proprietary, pharmaceutically optimized form of LSD. Currently, four Phase 3 clinical trials are underway to explore the potential of DT120 ODT for the treatment of GAD and MDD, with a fifth trial in PTSD planned, all without adjunctive psychotherapeutic interventions.

How is GAD diagnosed?

The U.S. Preventive Services Task Force (USPSTF) currently recommends screening for GAD in adults aged 64 and younger.

In 2006, researchers developed the Generalized Anxiety Disorder-7 (GAD-7) as a diagnostic criterion for GAD in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). The GAD-7 is a self-reported questionnaire with a brief format, primarily used to identify probable cases of GAD and assess the severity of anxiety symptoms in primary care settings.

How is GAD treated?

While several GAD pharmacotherapies are approved, many patients do not experience sustained relief, and approximately 50% inadequately respond to first-line treatments.¹⁰ Serotonin reuptake inhibitors (SRIs) are commonly used first-line, but a lack of efficacy and side effects can contribute to disease burden, treatment nonadherence, and discontinuation.¹¹ Benzodiazepines have shown acute efficacy in GAD, but their use is limited by side effects and risks of misuse and dependence.^{13,14}

Despite the significant personal and societal burden of GAD, there has been little innovation in the treatment of GAD in the past several decades, with the last new drug approval occurring in 2007, leaving patients and providers with few effective options.¹⁴

What is the relationship between GAD, Major Depressive Disorder (MDD) and Posttraumatic Stress Disorder (PTSD)?

Mental health conditions like GAD, major depressive disorder (MDD) and post-traumatic stress disorder (PTSD) often overlap. More than 50% of patients with GAD also have MDD. Co-occurring MDD and GAD is associated with increases in mean annual per-patient inpatient visits, office visits, emergency department visits, annual drug costs, and total medical costs.^{15,16} Approximately 80% of individuals with PTSD meet the criteria for another psychiatric diagnosis, underscoring the interconnection across these disorders and the urgent need for more effective treatment options.²

→ References

1. Ringeisen, H., et al. (2023). Mental and Substance Use Disorders Prevalence Study (MDPS): Findings report. RTI International and current U.S. Census data and internal company estimates.
2. American Psychiatric Association. (2022). Diagnostic and statistical manual of mental disorders (5th ed., text rev.). American Psychiatric Association Publishing.
3. DeMartini, J., Patel, G., & Fancher, T. L. (2019). Generalized anxiety disorder. *Annals of Internal Medicine*, 170(4), ITC49–ITC64. <https://doi.org/10.7326/AITC201904020>
4. Barrera, T. L., & Norton, P. J. (2009). Quality of life impairment in generalized anxiety disorder, social phobia, and panic disorder. *Journal of Anxiety Disorders*, 23, 1086–1090. <https://doi.org/10.1016/j.janxdis.2009.07.011>
5. Armbrecht, E., Shah, R., Poorman, G. W., et al. (2021). Economic and humanistic burden associated with depression and anxiety among adults with non-communicable chronic diseases (NCCDs) in the United States. *Journal of Multidisciplinary Healthcare*, 14, 887–896. <https://doi.org/10.2147/jmdh.s280200>
6. Newman, M. G., Llera, S. J., Erickson, T. M., Przeworski, A., & Castonguay, L. G. (2013). Worry and generalized anxiety disorder: A review and theoretical synthesis of evidence on nature, etiology, mechanisms, and treatment. *Annual Review of Clinical Psychology*, 9, 275–297. <https://doi.org/10.1146/annurev-clinpsy-050212-185544>
7. Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry*, 164(10), 1476–1488. <https://doi.org/10.1176/appi.ajp.2007.07030504>
8. Hilbert, K., Lueken, U., & Beesdo-Baum, K. (2014). Neural structures, functioning, and connectivity in generalized anxiety disorder: A systematic review. *Journal of Affective Disorders*, 169, 117–126. <https://doi.org/10.1016/j.jad.2014.01.022>
9. National Institute of Mental Health. (2025, August). Generalized anxiety disorder: What you need to know. U.S. Department of Health and Human Services, National Institutes of Health. <https://www.nimh.nih.gov/health/publications/generalized-anxiety-disorder-gad>
10. Ansara, E. D. (2020). Management of treatment-resistant generalized anxiety disorder. *Mental Health Clinician*, 10(4), 326–334. <https://doi.org/10.9740/mhc.2020.11.326>
11. Gartlehner, G., Hansen, R. A., Morgan, L. C., Thaler, K., Lux, L., Van Noord, M., & Lohr, K. N. (2011). Comparative benefits and harms of second-generation antidepressants for treating major depressive disorder: An updated meta-analysis. *Annals of Internal Medicine*, 155, 772–785. <https://doi.org/10.7326/0003-4819-155-11-201112060-00009>
12. Garakani, A., Murrough, J. W., Freire, R. C., Thomé, J. P., Larkin, K., & Mathew, S. J. (2021). Pharmacotherapy of anxiety disorders: Current and emerging treatment options. *Focus*, 19, 222–242. <https://doi.org/10.3389/fpsyg.2020.595584>
13. Strawn, J. R., Geraciotti, L., Rajdev, N., Clemenza, K., & Levine, A. (2018). Pharmacotherapy for generalized anxiety disorder in adult and pediatric patients: An evidence-based treatment review. *Expert Opinion on Pharmacotherapy*, 19, 1057–1070. <https://doi.org/10.1080/14656566.2018.1491966>
14. Kessler, R. C., & collaborators. (2015). Anxious and non-anxious major depressive disorder in the World Health Organization World Mental Health Surveys. *Epidemiology and Psychiatric Sciences*, 24(4), 210–226. <https://doi.org/10.1017/S2045796015000189>
15. U.S. Food and Drug Administration. (2007, August 9). FDA approves Cymbalta for treatment of generalized anxiety disorder [Press release]. <https://www.fda.gov/oc/2007/08/09/fda-approves-cymbalta-for-treatment-of-generalized-anxiety-disorder>
16. Armbrecht, E., Shah, R., Poorman, G. W., Luo, L., Stephens, J. M., Li, B., Pappadopulos, E., Haider, S., & McIntyre, R. S. (2021). Economic and humanistic burden associated with depression and anxiety among adults with non-communicable chronic diseases (NCCDs) in the United States. *Journal of Multidisciplinary Healthcare*, 14, 887–896. <https://doi.org/10.2147/JMDH.S280200>