

Diagnosis/Condition:	Generalized Anxiety Disorder (GAD)
Discipline:	ND, LAc
ICD-10 Codes:	F41.8, F41.9
Origination Date:	2014
Review/Revised Date:	10/2023
Next Review Date:	10/2025

Anxiety is a general term that encompasses several specific sub-conditions. The Diagnostic and Statistical Manual of Mental Disorders (5th Ed; DSM V) describes seven sub-categories of anxiety disorders, including the focus of this pathway, generalized anxiety disorder. In addition, the DSM V lists: 1) separation anxiety disorder; 2) selective mutism; 3) specific phobia; 4) social phobia; 5) panic disorder; 6) agoraphobia.¹ Generalized anxiety disorder (GAD) is a chronic mental health condition characterized by excessive and persistent worrying causing significant distress or impairment. It occurs more days than not for at least six months and may include other psychological symptoms, such as apprehensiveness, irritability, restlessness, difficult concentration, nervousness, and poor sleep. Physical (or somatic) symptoms may also occur, such as increased fatigue, headache, sweating, nausea, heart palpitations and muscular tension. It is one of the most common mental health conditions encountered in primary care and has a prevalence between 3.5-8% in the general population,^{2,3} although studies in 2020 indicate that this estimate has risen considerably to around 24% during the COVID-19 pandemic^{4,5,6} GAD is reported more commonly in women and in the elderly, but presents frequently in children, teenagers, and young adults.^{7,8,9,10}

GAD may exist with mental or physical comorbidities, including panic disorder, phobias, depression and PTSD. It may also be associated with substance abuse, and obsessive-compulsive disorder.¹¹ Patients with comorbid depression and anxiety tend to have a more severe and prolonged course of illness and greater social or occupational functional impairment. Patients may have co-existing chronic pain or other undiagnosed chronic physical illness, which must be ruled out.^{12,13,14}

There has been considerable research on the impact of the COVID-19 pandemic on the incidence of living with anxiety in many populations, including children, adolescents, adults, pregnancy, and health care professionals.^{15,16} International studies have indicated that on average, 1/3 adults experienced significant anxiety during and following the pandemic. The mental health consequences of COVID and other epidemics has been compared to that of armed conflicts and other major disasters worldwide.¹⁷ Studies also indicate that the incidence of anxiety is more prevalent in women.¹⁸

Predispositions to incident GAD include:¹⁹

- Female sex.
- Poverty.
- Recent adverse life events, personal trauma, and ongoing life stressors.
- Chronic physical illness (respiratory, cardiovascular, metabolic, chronic pain).
- Chronic mental disorder (depression, phobia, past GAD).
- Lack of emotional/physical support during childhood.
- History of family mental health problems.

There is a high prevalence of Complementary and Integrative Health (IH) use among those with GAD^{20,21,22,23,24,25} as well as depression and post-traumatic stress disorder.²⁶ Some patients with neuropsychiatric symptoms and chronic illness report improvement in quality of life (QoL) with use of IH.²⁷ The greater the number of symptoms, the more likely the use of IH.^{25,28}

In a large nationally representative survey, 56.7% of those with anxiety attacks and 53.6% of those with severe depression reported using IH in the past 12 months²⁹ Some populations of patients report using IH when they cannot afford counseling.^{30,31} Other reasons include: belief in its efficacy and ability to resolve symptoms more quickly than conventional care, dissatisfaction with conventional care, desire to work more cooperatively with their physician, decreased side effects from treatment, and a desire to improve overall health or because it offered a “different system of care aligned with their values”.^{32,33}

A 2017 multi-center study conducted in Seattle {The Natural Medicine Quality Improvement Project for the Treatment of Depression and Anxiety (NMQP-DA), assessed the quality of care received by patients with depression and anxiety who were seen by naturopathic physicians in a community health center. The study showed an overall improvement in symptoms of depression and anxiety that was highly significant ($p < 0.0001$) when comparing the group's average initial screening scores to their average final screening scores for both depression and anxiety.³⁴

Subjective Findings and History

- Genetic or familial predisposition.^{35,36,37}
- History of physical and/or psychogenic trauma.³⁸
- Poor sleep.
- Fatigue.
- Difficulty relaxing, irritability.
- Headaches.
- Pain in neck, shoulders, and back.
- Persistent worrying.
- Functional impairment.

Objective Findings

The following may or may not be present. Most patients present with normal affect and are oriented x 3 and cooperative, with normal cognition. There is generally no impairment in memory, language or speech. Positive findings below should be followed up with laboratory testing, and full PE to rule out physical disease.

- Hypertension, shortness of breath, tachycardia.
- Restless, anxious appearance.
- Dry mouth.
- Tense muscles.
- Patients with late-onset anxiety, weight loss, or cognitive impairment should be assessed for organic causes of anxiety.

Assessment

- A medical history that focuses on possible contributory factors relating to current medical disorders or medication side effects.
- Assessment for self-harm ideation.
- Complete physical exam (PE), including heart, lungs, skin temperature especially in extremities, thyroid assessment, and muscle tension.
- Laboratory studies (CBC, thyroid panel, comprehensive metabolic panel, UA, EKG, urine, or serum toxicology).
- Substance abuse history (including alcohol, prescription drugs, caffeine, and nicotine use).
- Family psychiatric and medical history.
- Social history that screens for stressful life events and past sexual, physical and emotional abuse or neglect.
- There are several organizations that provide screening and assessment tools for the evaluation of GAD, listed at the end of this document. These include BAI, HADS, STAI, GAI, HADS-A, Dass, GADq-IV and others.^{39,40,41,42}

Differential Diagnoses:

- Depression, dysthymia.
- Social or other phobias.
- Hypochondriasis.
- Panic disorder.
- Adjustment disorder.
- Obsessive compulsive disorder (OCD).

Traditional Chinese Medicine Syndrome Differentiation:

- Spleen Qi Deficiency.
- Heart Yin/Blood Deficiency; Heart Fire.
- Liver Qi Stagnation, Liver Fire, LR Yin/Blood Deficiency, LR Yang rising (especially with associated migraine).

- Lung Qi Deficiency.
- Kidney Yin Deficiency, Kidney-Heart Disharmony (Kidney Yin failing to nourish Heart Yin, Heart Fire failing to nourish Kidney Yang).

Plan

Once a patient has been diagnosed with GAD, a clinical assessment of severity must be made to determine the extent of distress or impairment, and patient preference, whether treatment of the disorder is needed or wanted. Screening tools assist with establishment of severity (available below). Those patients whose symptoms do not limit functioning may decide to use mild or non-pharmacologic intervention. Patients should be assessed every 6 months to monitor the course of the disorder to alter or initiate therapies.

Naturopathic Treatment:

Botanical medicine:^{43,44,45,46,47} Kava-kava,^{48,49,50,51,52} valerian root, passion-flower,⁵³ chamomile,^{54,55} citrus aurantium blossom,⁵⁶ Eleutherococcus, St. John's Wort⁵⁷, black cohosh,⁵⁸ ashwagandha (Withania somnifera),^{59,60} Hypericum, Scutellaria, Magnolia, Rhodiola⁶¹, Lavendula, Valerian, Melissa, Humulus, Avena sativa, Ashwaganda,⁶²Lippia citriodora (lemon balm).⁶³

- Essential oils (aromatherapy).^{64,65,66,67}
- Bach flower remedies.
- Homeopathy as indicated by symptom picture.⁶⁸
- Nutraceuticals: vitamin B12, B complex, S-adenosylmethionine (SAM)⁶⁹ GABA.
- Whole systems naturopathic care.^{70,71}
- Nutraceutical for unipolar depression: omega-3 fatty acids, vitamin D, probiotics, zinc, methylfolate, S-adenosylmethionine (SAME).⁷²
- Phytoceuticals for unipolar depression: Lavender, St. John's wort, saffron, curcumin.
- Anxiety disorder: Ashwagandha, galphimia, lavender.

Traditional East Asian Medicine:

Acupuncture

More than 30 clinical trials have been published assessing the effects of acupuncture for the treatment of anxiety and most are summarized within recent systematic reviews.^{73,74,75,76,77,78,79} Based on the evidence the following conclusion can be drawn, The evidence is promising to suggest benefit from acupuncture for the treatment of Generalized Anxiety Disorders; more research is required to draw definitive conclusions.

- A recent systematic review (n=27; 1,782 participants) suggests promising effects, but calls for additional trials, "Acupuncture can effectively relieve the anxiety symptoms of generalized anxiety disorder patients with fewer side effects... high quality [RCTs] are also required to support the result."
 - Earlier systematic reviews drew similar conclusions.^{80,81,82}
- Two recent RCTs are not included in the most recent review.

- A 2021 trial (n=112) suggests that compared to SSRIs alone, "...acupuncture as an add-on therapy to SSRIs can significantly improve anxiety state... [at end of Tx, week 4]."⁸³
- An exploratory trial (n=56) suggests, "Acupuncture and electroacupuncture are effective in treating anxiety on their own or as adjuncts to pharmacological therapy."⁸⁴

Tai Chi

- A 2023 systematic review (n=23; 4,370 participants) suggests, "...Tai chi is more effective in reducing anxiety and depression and improving general mental health than non-mindful exercise [e.g. walking, stretching or aerobic exercise]."⁸⁵

Qi Gong

- A 2013 systematic review (n=12; 936 participants) suggests, "Qi gong may be potentially beneficial for management of depressive symptoms, but the results should be interpreted with caution due to the limited number of RCTs and associated methodological weaknesses."⁸⁶
 - This is supported by a 2023 RCT (n=200) that found the addition of QiGong (and music therapy) to usual care, was more effective than usual care alone to, "...relieve anxiety and depression, and improve the sleep quality in patients with COVID-19 infection."⁸⁷

Herbal Medicine (TEAM):

- Individualized herbal formulas are suggested as clinically effective adjunctive care (formulas recommendation based on syndrome differentiation).

Movement and Exercise Therapy:

- Yoga and breathing exercises (mixed reviews).^{88,89,90,91,92,93,94,95,96,97,98}
- Exercise.^{99,100,101}
- Massage and touch therapy (mixed reviews).¹⁰²
- Reiki¹⁰³, other whole person energy work.

Pharmacology:

A stepped pharmacotherapy approach with combination therapy should be used for initial treatment, based on availability, side effects experienced, and patient preference. A referral can be made to a mental health care provider and prescriber as needed. Serotonergic antidepressants and CBT are the most often studied treatments found to be efficacious for GAD.^{104,105,106}

- Selective-serotonin reuptake inhibitors (SSRIs) (e.g., paroxetine, sertraline, citalopram, escitalopram, fluoxetine, and fluvoxamine).
- Serotonin-norepinephrine reuptake inhibitors (SNRIs) (e.g., venlafaxine, duloxetine).
- Tricyclic antidepressants (e.g., Imipramine).
- Benzodiazepines (e.g., clonazepam, diazepam, lorazepam).
- Buspirone.
- Pregabalin.
- other antidepressants (e.g., mirtazapine).

- antipsychotic medications.
- Hydroxyzine.

Mind-body Therapies:

- Cognitive Behavioral therapy.^{107,108,109,110}
- Psychotherapy.
- Group therapy.
- Emotional Freedom Technique.¹¹¹
- Biofeedback.^{112,113}
- Music therapy.¹¹⁴
- Relaxation Interventions (including hypnosis).^{115,116,117}
- Multi-modal therapy based on self-care behavior.¹¹⁸
- A 2023 systematic review (n=10; 1311 participants) assessed the effects of a web-based mindfulness meditation program for front-line healthcare workers during COVID. The authors state that more research needs to be performed, but concluded, “Web-based mindfulness-based interventions may be effective in reducing the symptoms of anxiety, depression, and stress.”¹¹⁹
- A 2023 scoping review (n=8; 626 participants) assessed the effects of mindfulness interventions and concluded, “...highlighted the significance of mindfulness intervention to reduce anxiety, distress, and depression among patients with chronic diseases.”¹²⁰

Referrals

A referral should be made to professionals specializing in treating behavioral/mental health/substance abuse conditions, especially in recalcitrant or severe cases, acute states, in cases where there is currently or a past history of suicidal or homicidal ideation, or if the patient presents with a complicating dual diagnosis. This might include a psychologist, behavioral health consultants, psychiatrist, case manager, licensed social worker (LSW), or other counselor who may have experience in treating or finding appropriate resources for the patient. The National Alliance for Mental Illness (NAMI) provides extensive resources and has local emergency and suicide helplines listed for all areas of the United States (U.S.) at <http://www.NAMI.org>. In addition, all states have differing laws in regards to reporting suicidal or homicidal ideation to local authorities.

Resources for Clinicians

The primary care or IH provider is often a gateway to specialist care and can provide patients with the resources they need to access a specialist. Recognizing and referring patients with serious health conditions is also sometimes necessary when patients have a complex condition underlying their symptoms. The recommended treatment of mental and behavioral health conditions is a team-based therapeutic model, with team consultation, assessment, and management of these patients. Many patients do not reveal their IH use to their various medical providers, or these providers may not be educated on or open to the efficacy of IH. These are

just some of the factors that may complicate the integration of IH with conventional medical care.^{121,122}

Mental illness is treatable. Most people diagnosed with a serious mental illness can experience relief from their symptoms by actively participating in an ongoing individual treatment plan. Patients who are currently under the medical supervision of other licensed providers and are taking medications for behavioral health conditions should be encouraged to remain on these, unless constructive contact can be made between the patient's different providers.

The Integrative Behavioral Health Project provides a virtual toolkit for primary care providers to "to provide hotlinks to screening tools and resources recommended for use in primary care". Their complete electronic resource guide, "Integrated Behavioral Health Screening Tools for Primary Care" is available at: <http://www.ibhp.org/>

National Association for Mental Illness (NAMI) – resources for primary care providers
http://www.nami.org/Template.cfm?Section=child_and_teen_support&Template=/ContentManagement/ContentDisplay.cfm&ContentID=120673

SAMHSA-HRSA Center for Integrated Health Solutions. Integrating Behavioral Health into Primary Care:
<http://www.integration.samhsa.gov/integrated-care-models/behavioral-health-in-primary-care>

Bazzan AJ, Zabrecky G, Monti DA, Newberg AB. Current evidence regarding the management of mood and anxiety disorders using complementary and alternative medicine. *Expert Rev Neurother*. 2014;14 (4):411-23.

Society for Acupuncture Research. Acupuncture for the Treatment of Anxiety: An Overview of Research. October 2021. www.AcupunctureResearch.org.

Resources for Patients

National Association for Mental Illness (NAMI).
http://www.nami.org/Template.cfm?Section=By_Illness

Crisistextline.org: Text the word HOME to 741741

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¹ American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.

² Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. *Ann Intern Med*. 2007 Mar 6;146(5):317-25. doi: 10.7326/0003-4819-146-5-200703060-00004.PMID: 17339617

³ Refractory generalized anxiety disorder. Pollack MH. *J Clin Psychiatry*. 2009;70 Suppl 2:32-8. doi: 10.4088/jcp.s.7002.06.PMID: 19371505 Review.

⁴ Impact of COVID-19 pandemic on mental health in the general population: A systematic review. Xiong J, Lipsitz O, Nasri F, Lui LMW, Gill H, Phan L, Chen-Li D, Iacobucci M, Ho R, Majeed A, McIntyre RS. *J Affect Disord*. 2020 Dec 1;277:55-64. doi: 10.1016/j.jad.2020.08.001. Epub 2020 Aug 8.PMID: 32799105

⁵ Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: a systematic review and meta-analysis. Salari N, Hosseini-Far A, Jalali R, Vaisi-Raygani A, Rasoulpoor S, Mohammadi M, Rasoulpoor S, Khaledi-Paveh B. *Global Health*. 2020 Jul 6;16(1):57. doi: 10.1186/s12992-020-00589-w.PMID: 32631403

⁶ Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. Cénat JM, Blais-Rochette C, Kokou-Kpolou CK, Noorishad PG, Mukunzi JN, McIntee SE, Dalexis RD, Goulet MA, Labelle PR. *Psychiatry Res*. 2021 Jan;295:113599. doi: 10.1016/j.psychres.2020.113599. Epub 2020 Nov 26.PMID: 33285346

Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: A systematic review and meta-analysis. Cénat JM, Blais-Rochette C, Kokou-Kpolou CK, Noorishad PG, Mukunzi JN, McIntee SE, Dalexis RD, Goulet MA, Labelle PR. *Psychiatry Res*. 2021 Jan;295:113599. doi: 10.1016/j.psychres.2020.113599. Epub 2020 Nov 26.PMID: 33285346

⁷ Wittchen HU, Jacobi F, Rehm J, et al. The size and burden of mental disorders and other disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol*. 2011;21(9):655-79.

⁸ Wittchen HU, Kessler RC, Beesdo K, Krause P, Höfler M, Hoyer J. Generalized anxiety and depression in primary care: prevalence, recognition, and management. *J Clin Psychiatry*. 2002;63 Suppl 8:24-34.

⁹ Wittchen HU, Zhao S, Kessler RC, Eaton WW. DSM-III-R generalized anxiety disorder in the National Comorbidity Survey. *Arch Gen Psychiatry*. 1994;51(5):355-64.

⁴ Refractory generalized anxiety disorder. Pollack MH. *J Clin Psychiatry*. 2009;70 Suppl 2:32-8. doi: 10.4088/jcp.s.7002.06.PMID: 19371505 Review.

⁵ Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. Kroenke K, Spitzer RL,

Williams JB, Monahan PO, Löwe B. *Ann Intern Med*. 2007 Mar 6;146(5):317-25. doi: 10.7326/0003-4819-146-5-200703060-00004. PMID: 17339617

¹⁰ Generalized Anxiety Disorder Health Guide; Harvard Health Topics; Updated Dec. 29, 2020. *J Altern Complement Med*. 2021 May;27(5):416-422. doi: 10.1089/acm.2020.0305. Epub 2021 Apr 27.

¹¹ Tyrer P, Seivewright H, Johnson T. The Nottingham Study of Neurotic Disorder: predictors of 12-year outcome of dysthymic, panic and generalized anxiety disorder. *Psychol Med*. 2004;34(8):1385-94.

¹² Beesdo K, Hoyer J, Jacobi F, Low NC, Höfler M, Wittchen HU. Association between generalized anxiety levels and pain in a community sample: evidence for diagnostic specificity. *J Anxiety Disord*. 2009; 23(5): 684-93.

¹³ Allgulander C. Morbid anxiety as a risk factor in patients with somatic diseases: A review of recent findings. *Mind Brain*, 2010.

¹⁴ Allgulander C. Generalized Anxiety Disorder: A Review of Recent Findings. *Journal of Experimental and Clinical Medicine. J Exp Clin Med* 2012; 4(2): 88e91.

¹⁵ A systematic review of the prevalence of anxiety among the general population during the COVID-19 pandemic. Pashazadeh Kan F, Raoofi S, Rafiei S, Khani S, Hosseini-fard H, Tajik F, Raoofi N, Ahmadi S, Aghalou S, Torabi F, Dehnad A, Rezaei S, Hosseini-palangi Z, Ghashghaee A *J Affect Disord*. 2021 Oct 1;293:391-398. doi: 10.1016/j.jad.2021.06.073. Epub 2021 Jul 2. Erratum in: *J Affect Disord*. 2022 Sep 1;312:337. PMID: 34246947; PMCID: PMC8712560.

¹⁷ Mental disorders following COVID-19 and other epidemics: a systematic review and meta-analysis. Leung CMC, Ho MK, Bharwani AA, Cogo-Moreira H, Wang Y, Chow MSC, Fan X, Galea S, Leung GM, Ni MY *Transl Psychiatry*. 2022 May 17;12(1):205. doi: 10.1038/s41398-022-01946-6. PMID: 35581186; PMCID: PMC9110635.

¹⁸ Gender and COVID-19 related fear and anxiety: A meta-analysis. *J Affect Disord*. 2022 Aug 1;310:384-395. Metin A, Erbiçer ES, Şen S, Çetinkaya A. doi: 10.1016/j.jad.2022.05.036. Epub 2022 May 11. PMID: 35561885; PMCID: PMC9090872

¹⁹ Zhang X, Norton J, Carrière I, Ritchie K, Chaudieu I, Ancelin ML. Risk factors for late-onset generalized anxiety disorder: results from a 12-year prospective cohort (the ESPRIT study). *Transl Psychiatry*. 2015;5:e536.

²⁰ Kessler RC, Soukup J, Davis RB, et al. The use of complementary and alternative therapies to treat anxiety and depression in the United States. *Am J Psychiatry*. 2001;158(2): 289-94.

²¹ Moss AS, Monti DA, Amsterdam JD, Newberg AB. Complementary and alternative medicine therapies in mood disorders. *Expert Rev Neurother*. 2011; 11(7): 1049-56.

²² Mcpherson F, McGraw L. Treating generalized anxiety disorder using complementary and alternative medicine. *Altern Ther Health Med*. 2013; 19(5): 45-50.

²³ Bystritsky A, Hovav S, Sherbourne C, et al. Use of complementary and alternative medicine in a large sample of anxiety patients. *Psychosomatics*. 2012; 53(3): 266-72.

²⁴ Qureshi NA, Al-bedah AM. Mood disorders and complementary and alternative medicine: a literature review. *Neuropsychiatr Dis Treat*. 2013; 9:639-58.

²⁵ Purohit MP, Zafonte RD, Sherman LM, et al. Neuropsychiatric symptoms and expenditure on complementary and alternative medicine. *J Clin Psychiatry*. 2015;76(7):e870-6.

²⁶ Asher GN, Gerkin J, Gaynes BN. Complementary Therapies for Mental Health Disorders. *The Medical clinics of North America*. 2017;101(5):847-64.

²⁷ Bar-sela G, Danos S, Visel B, Mashiach T, Mitnik I. The effect of complementary and alternative medicine on quality of life, depression, anxiety, and fatigue levels among cancer patients during active oncology treatment: phase II study. *Support Care Cancer*. 2015;23(7):1979-85.

²⁸ Purohit MP, Zafonte RD, Sherman LM, et al. Neuropsychiatric symptoms and expenditure on complementary and alternative medicine. *J Clin Psychiatry*. 2015;76(7):e870-6.

²⁹ Kessler RC, Soukup J, Davis RB, et al. The use of complementary and alternative therapies to treat anxiety and depression in the United States. *Am J Psychiatry* 2001;158:289–294.

³⁰ Kemper KJ, Gardiner P, Birdee GS. Use of complementary and alternative medical therapies among youth with mental health concerns. *Acad Pediatr*. 2013;13(6):540-5.

-
- ³¹ Burnett-zeigler I, Schuette S, Victorson D, Wisner KL. Mind-Body Approaches to Treating Mental Health Symptoms Among Disadvantaged Populations: A Comprehensive Review. *J Altern Complement Med.* 2016;22(2):115-24.
- ³² Oberg EB, Thomas M-S, McCarty M, et al. Older adults' perspectives on naturopathic medicine's impact on healthy aging. *Explore (NY)* 2014;10:34-43.
- ³³ Knaudt PR, Connor KM, Weisler RH, et al. Alternative therapy use by psychiatric outpatients. *J Nerv Ment Dis* 1999;187:692-695.
- ³⁴ Breed C, Berezney C. Treatment of Depression and Anxiety by Naturopathic Physicians: An Observational Study of Naturopathic Medicine Within an Integrated Multidisciplinary Community Health Center. *J Altern Complement Med.* 2017;23(5):348-354.
- ³⁵ Kendler KS. Major depression and generalised anxiety disorder. Same genes,(partly) different environments--revisited. *Br J Psychiatry Suppl.* 1996;(30): 68-75.
- ³⁶ Hetttema JM, Prescott CA, Kendler KS. Genetic and environmental sources of covariation between generalized anxiety disorder and neuroticism. *Am J Psychiatry.* 2004;161(9):1581-7.
- ³⁷ Mackintosh MA, Gatz M, Wetherell JL, Pedersen NL. A twin study of lifetime Generalized Anxiety Disorder (GAD) in older adults: genetic and environmental influences shared by neuroticism and GAD. *Twin Res Hum Genet.* 2006; 9(1):30-7.
- ³⁸ Safren SA, Gershuny BS, Marzol P, Otto MW, Pollack MH. History of childhood abuse in panic disorder, social phobia, and generalized anxiety disorder. *J Nerv Ment Dis.* 2002; 190(7):453-6.
- ³⁹ GENERALIZED ANXIETY DISORDER 7 – GAD-7 ADULTS
Spitzer, R. L., Kroenke, K., Williams, J. B., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine*, 166(10), 1092.
- ⁴⁰ HOSPITAL ANXIETY AND DEPRESSION SCALE – HADS Adults
Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta psychiatrica scandinavica*, 67(6), 361-370.
- ⁴¹ GENERALIZED ANXIETY DISORDER QUESTIONNAIRE-IV – GADQ-IV ([LINK](#)). Adults
Newman, M. G., Zuellig, A. R., Kachin, K. E., Constantino, M. J., & Cashman, L. (2002). The reliability and validity of the GAD-Q-IV: a revised self-report diagnostic measure of generalized anxiety disorder. *Behavior Therapy*, 33, 215-233.
- ⁴² Accuracy of the Hospital Anxiety and Depression Scale Depression subscale (HADS-D) to screen for major depression: systematic review and individual participant data meta-analysis. Wu Y, Levis B, Sun Y, He C, Krishnan A, Neupane D, Bhandari PM, Negeri Z, Benedetti A, Thombs BD; DEPRESSION Screening Data (DEPRESSD) HADS Group.BMJ. 2021 May 10;373:n972. doi: 10.1136/bmj.n972.PMID: 33972268
- ⁴³ Liu L, Liu C, Wang Y, Wang P, Li Y, Li B. Herbal Medicine for Anxiety, Depression and Insomnia. *Curr Neuropsychopharmacol.* 2015;13(4):481-93.
- ⁴⁴ Sarris J, McIntyre E, Camfield DA. Plant-based medicines for anxiety disorders, part 2: a review of clinical studies with supporting preclinical evidence. *CNS Drugs.* 2013;27(4):301-19.
- ⁴⁵ SaeedSA, BlochRM, AntonacciDJ. Herbal and dietary supplements for treatment of anxiety disorders. *Am Fam Physician* 2007;76:549-556.
- ⁴⁶ Sarris J. Herbal medicines in the treatment of psychiatric disorders: 10-year updated review. *Phytother Res.* 2018;32(7):1147-1162.
- ⁴⁷ Yeung KS, Hernandez M, Mao JJ, Haviland I, Gubili J. Herbal medicine for depression and anxiety: A systematic review with assessment of potential psycho-oncologic relevance. *Phytother Res.* 2018;32(5):865-891.
- ⁴⁸ Pittler MH, Ernst E. Kava extract for treating anxiety. *Cochrane Database Syst Rev.* 2003;(1):CD003383.
- ⁴⁹ Smith K, Leiras C. The effectiveness and safety of Kava Kava for treating anxiety symptoms: A systematic review and analysis of randomized clinical trials. *Complement Ther Clin Pract.* 2018;33:107-117.
- ⁵⁰ Pittler MH, Ernst E. Kava extract versus placebo for treating anxiety. *Cochrane Database of Systematic Reviews.* 2003;(1):CD003383 [edited 2010]. Accessed at www.thecochranelibrary.com on March 6, 2020.
- ⁵¹ Sarris J, Stough C, Bousman CA, et al. Kava in the treatment of generalized anxiety disorder. A double-blind, randomized, placebo-controlled study. *Journal of Clinical Psychopharmacology.* 2013;33(5):643-648 Sarris J, Stough C,
-

-
- Bousman CA, et al. Kava in the treatment of generalized anxiety disorder. A double-blind, randomized, placebo-controlled study. *Journal of Clinical Psychopharmacology*. 2013;33(5):643-648
- ⁵² Smith K, Leiras C. The effectiveness and safety of kava kava for treating anxiety symptoms: a systematic review and analysis of randomized clinical trials. *Complementary Therapies in Clinical Practice*. 2018;33:107-117
- Smith K, Leiras C. The effectiveness and safety of kava kava for treating anxiety symptoms: a systematic review and analysis of randomized clinical trials. *Complementary Therapies in Clinical Practice*. 2018;33:107-117
- ⁵³ Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166 (10):1092-7.
- ⁵⁴ Amsterdam JD, Li Y, Soeller I, Rockwell K, Mao JJ, Shults J. A randomized, double-blind, placebo-controlled trial of oral *Matricaria recutita* (chamomile) extract therapy for generalized anxiety disorder. *J Clin Psychopharmacol*. 2009; 29(4):378-82.
- ⁵⁵ Putative Antidepressant Effect of Chamomile (*Matricaria chamomilla* L.) Oral Extract in Subjects with Comorbid Generalized Anxiety Disorder and Depression.
Amsterdam JD, Li QS, Xie SX, Mao JJ. *J Altern Complement Med*. 2020 Sep;26(9):813-819. doi: 10.1089/acm.2019.0252. Epub 2019 Dec 5. PMID: 31808709 Clinical Trial.
Objectives: This exploratory analysis examined the putative antidepressant effect of *Matricaria chamomilla* L. (chamomile) extract in subjects
- ⁵⁶ Akhlaghi M, Shabani G, Rafieian-kopaei M, Parvin N, Saadat M, Akhlaghi M. *Citrus aurantium* blossom and preoperative anxiety. *Rev Bras Anesthesiol*. 2011; 61(6): 702-12.
- ⁵⁷ Pirotta M, Willis K, Carter M, Forsdike K, Newton D, Gunn J. 'Less like a drug than a drug': the use of St John's wort among people who self-identify as having depression and/or anxiety symptoms. *Complement Ther Med*. 2014 Oct;22(5):870-6.
- ⁵⁸ Geller SE, Studee L. Botanical and dietary supplements for mood and anxiety in menopausal women. *Menopause*. 2007;14(3 Pt 1):541-9.
- ⁵⁹ Pratte MA, Nanavati KB, Young V, Morley CP. An alternative treatment for anxiety: a systematic review of human trial results reported for the Ayurvedic herb ashwagandha (*Withania somnifera*). *J Altern Complement Med*. 2014;20(12):901-8.
- ⁶⁰ Lopresti AL, Smith SJ, Malvi H, Kodgule R. An investigation into the stress-relieving and pharmacological actions of an ashwagandha (*Withania somnifera*) extract: A randomized, double-blind, placebo-controlled study. *Medicine (Baltimore)*. 2019;98(37):e17186.
- ⁶¹ Angheliescu I-G, Edwards D, Seifritz E, et al. Stress management and the role of *Rhodiola rosea*: a review. *International Journal of Psychiatry in Clinical Practice*. 2018;22(4):242-252
- ⁶² Clinical evaluation of the pharmacological impact of ashwagandha root extract on sleep in healthy volunteers and insomnia patients: A double-blind, randomized, parallel-group, placebo-controlled study *J Ehnopharmacol* 2021 Jan 10;264:113276.doi: 10.1016/j.jep.2020.113276. Epub 2020 Aug 17.
- ⁶³ Anxiolytic Effect and Improved Sleep Quality in Individuals Taking *Lippia citriodora* Extract. *Nutrients*. Martínez-Rodríguez A, Martínez-Olcina M, Mora J, Navarro P, Caturla N, Jones J. 2022 Jan 4;14(1):218. doi: 10.3390/nu14010218. PMID: 35011093; PMCID: PMC8747367.
- ⁶⁴ National Cancer Institute: PDQ® Aromatherapy and Essential Oils. Bethesda, MD: National Cancer Institute. Available at: <https://www.cancer.gov/about-cancer/treatment/cam/patient/aromatherapy-pdq> (Accessed 10/2021)
- ⁶⁵ Meghani N, Tracy MF, Hadidi NN, Lindquist R. Part II: The Effects of Aromatherapy and Guided Imagery for the Symptom Management of Anxiety, Pain, and Insomnia in Critically Ill Patients: An Integrative Review of Current Literature. *Dimens Crit Care Nurs*. 2017;36(6):334-348.
- ⁶⁶ Moslemi F, Alijaniha F, Naseri M, Kazemnejad A, Charkhkar M, Heidari MR. Aroma for Anxiety in Patients with Acute Coronary Syndrome: A Double-Blind Placebo-Controlled Trial. *J Altern Complement Med*. 2019;25(8):833-839.
- ⁶⁷ Generoso MB, Soares A, Taiar IT, et al. Lavender oil preparation (Silexan) for treating anxiety: an updated meta-analysis. *Journal of Clinical Psychopharmacology*. 2017;37(1):115-117.
- ⁶⁸ Mathie RT, Robinson TW. Outcomes from homeopathic prescribing in medical practice: a prospective, research-targeted, pilot study. *Homeopathy*. 2006; 95:199-205.
-

-
- ⁶⁹ Cerutti R, Sichel MP, Perin M, et al. Psychological distress during puerperium: a novel therapeutic approach using S-adenosylmethionine. *Curr Ther Res.* 1993; 53:707–716.
- ⁷⁰ Cooley K, Szczurko O, Perri D, et al. Naturopathic care for anxiety: A randomized controlled trial ISRCTN78958974. *PLoS One* 2009;4:e6628.
- ⁷¹ Breed C, Berezney C. Treatment of Depression and Anxiety by Naturopathic Physicians: An Observational Study of Naturopathic Medicine Within an Integrated Multidisciplinary Community Health Center. *J Altern Complement Med.* 2017;23(5):348-354.
- ⁷² Sarris J, et al. Clinician guidelines for the treatment of psychiatric disorders with nutraceuticals and phytoceuticals: The World Federation of Societies of Biological Psychiatry (WFSBP) and Canadian Network for Mood and Anxiety Treatments (CANMAT) Taskforce, *World J Biol Psychiatry.* 2022 Jul;23(6):424-455. doi: 10.1080/15622975.2021.2013041. Epub 2022 Mar 21.
- ⁷³ Errington-Evans, N., Acupuncture for anxiety. *CNS Neurosci Ther,* 2012. 18(4): p. 277-84.
- ⁷⁴ Pilkington, K., et al., Acupuncture for anxiety and anxiety disorders--a systematic literature review. *Acupunct Med,* 2007. 25(1-2): p. 1-10.
- ⁷⁵ Allan, F., et al., Acupuncture for anxiety in dental patients: Systematic review and meta-analysis. *Eur J Integrat Med,* 2018. 20: p. 22-35.
- ⁷⁶ Amorim, D., et al., Acupuncture and electroacupuncture for anxiety disorders: A systematic review of the clinical research. *Complement Ther Clin Pract,* 2018. 31: p. 31-37.
- ⁷⁷ Li, M., et al., Acupuncture for treatment of anxiety, an overview of systematic reviews. *Complement Ther Med,* 2019. 43: p. 247-252.
- ⁷⁸ Tong, Q.Y., et al., Can acupuncture therapy reduce preoperative anxiety? A systematic review and meta-analysis. *J Integr Med,* 2021. 19(1): p. 20-28.
- ⁷⁹ Li, M., et al., Efficacy of acupuncture for generalized anxiety disorder: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore),* 2022. 101(49): p. e30076.
- ⁸⁰ Errington-Evans, N., Acupuncture for anxiety. *CNS Neurosci Ther,* 2012. 18(4): p. 277-84.
- ⁸¹ Pilkington, K., et al., Acupuncture for anxiety and anxiety disorders--a systematic literature review. *Acupunct Med,* 2007. 25(1-2): p. 1-10.
- ⁸² Amorim, D., et al., Acupuncture and electroacupuncture for anxiety disorders: A systematic review of the clinical research. *Complement Ther Clin Pract,* 2018. 31: p. 31-37.
- ⁸³ Sabbagh Gol, A., et al., Additive effects of acupuncture in alleviating anxiety: A double-blind, three-arm, randomized clinical trial. *Complement Ther Clin Pract,* 2021. 45: p. 101466.
- ⁸⁴ Amorim, D., et al., Electroacupuncture and acupuncture in the treatment of anxiety - A double blinded randomized parallel clinical trial. *Complement Ther Clin Pract,* 2022. 46: p. 101541.
- ⁸⁵ Yin, J., et al., The comparative effects of Tai chi versus non-mindful exercise on measures of anxiety, depression and general mental health: A systematic review and meta-analysis. *J Affect Disord,* 2023. 337: p. 202-214.
- ⁸⁶ Wang, C.W., et al., The effect of qigong on depressive and anxiety symptoms: a systematic review and meta-analysis of randomized controlled trials. *Evid Based Complement Alternat Med,* 2013. 2013: p. 716094.
- ⁸⁷ Wang, X., et al., The effect of Baduanjin Qigong combined with five-elements music on anxiety and quality of sleep in asymptomatic patients with COVID-19 infection: A randomised controlled trial. *Heliyon,* 2023. 9(8): p. e18962.
- ⁸⁸ Ndetan H, Evans MW, Williams RD, Woolsey C, Swartz JH. Use of movement therapies and relaxation techniques and management of health conditions among children. *Altern Ther Health Med.* 2014; 20(4): 44-50.
- ⁸⁹ Michalsen A, Grossman P, Acil A, et al. Rapid stress reduction and anxiolysis among distressed women as a consequence of a three-month intensive yoga program. *Med Sci Monit.* 2005;11(12):CR555-561.
- ⁹⁰ Rao MR, Raghuram N, Nagendra HR, et al. Anxiolytic effects of a yoga program in early breast cancer patients undergoing conventional treatment: a randomized controlled trial. *Complement Ther Med.* 2009;17(1):1-8.
- ⁹¹ Kirkwood G, Rampes H, Tuffrey V, Richardson J, Pilkington K. Yoga for anxiety: a systematic review of the research evidence. *Br J Sports Med.* 2005;39 (12):884-91.
-

- ⁹² Gupta N, Khera S, Vempati RP, Sharma R, Bijlani RL. Effect of yoga based lifestyle intervention on state and trait anxiety. *Indian J Physiol Pharmacol*. 2006;50(1):41-7.
- ⁹³ Lavey R, Sherman T, Mueser KT, Osborne DD, Currier M, Wolfe R. The effects of yoga on mood in psychiatric inpatients. *Psychiatr Rehabil J*. 2005; 28:399–402.
- ⁹⁴ Mullur LM, Khodnapur JP, Bagali S, Aithala M, Dhanakshirur GB. Role of yoga in modifying anxiety level in women. *Indian J Physiol Pharmacol*. 2014;58(1):92-5.
- ⁹⁵ Weaver LL, Darragh AR. Systematic Review of Yoga Interventions for Anxiety Reduction Among Children and Adolescents. *Am J Occup Ther*. 2015;69(6):6906180070p1-9.
- ⁹⁶ Cramer H, Lauche R, Anheyer D, et al. Yoga for anxiety: A systematic review and meta-analysis of randomized controlled trials. *Depress Anxiety*. 2018;35(9):830-843.
- ⁹⁷ Mccall M. Yoga intervention may improve health-related quality of life (HRQL), fatigue, depression, anxiety and sleep in patients with breast cancer. *Evid Based Nurs*. 2018;21(1):9.
- ⁹⁸ Albracht-schulte K, Robert-mccomb J. The effects of yoga and quiet rest on subjective levels of anxiety and physiological correlates: a 2-way crossover randomized trial. *BMC Complement Altern Med*. 2018;18(1):280.
- ⁹⁹ Ravindran AV, Da silva TL. Complementary and alternative therapies as add-on to pharmacotherapy for mood and anxiety disorders: a systematic review. *J Affect Disord*. 2013; 150(3): 707-19.
- ¹⁰⁰ Otto MW, Church TS, Craft LL, Greer TL, Smits JA, Trivedi MH. Exercise for mood and anxiety disorders. *J Clin Psychiatry*. 2007; 68: 669–676.
- ¹⁰¹ Oeland AM, Laessoe U, Olesen AV, Munk-Jørgensen P. Impact of exercise on patients with depression and anxiety. *Nord J Psychiatry*. 2010 May 4;64(3):210-7.
- ¹⁰² Kukimoto Y, Ooe N, Ideguchi N. The Effects of Massage Therapy on Pain and Anxiety after Surgery: A Systematic Review and Meta-Analysis. *Pain Manag Nurs*. 2017;18(6):378-390.
- ¹⁰³ Bowden D, Goddard L, Gruzelier J. A randomised controlled single-blind trial of the efficacy of Reiki at benefiting mood and well-being. *Evid Based Complement Alternat Med*. 2011; 2011:381862.
- ¹⁰⁴ Hunot V, Churchill R, Silva de lima M, Teixeira V. Psychological therapies for generalised anxiety disorder. *Cochrane Database Syst Rev*. 2007;(1):CD001848.
- ¹⁰⁵ Hendriks GJ, Oude voshaar RC, Keijsers GP, Hoogduin CA, Van balkom AJ. Cognitive-behavioural therapy for late-life anxiety disorders: a systematic review and meta-analysis. *Acta Psychiatr Scand*. 2008;117(6):403-11.
- ¹⁰⁶ Wetherell JL, Petkus AJ, White KS, et al. Antidepressant medication augmented with cognitive-behavioral therapy for generalized anxiety disorder in older adults. *Am J Psychiatry* 2013; 170:782.
- ¹⁰⁷ Norton PJ, Price EC. A meta-analytic review of adult cognitive-behavioral treatment outcome across the anxiety disorders. *J Nerv Ment Dis*. 2007;195(6):521-31.
- ¹⁰⁸ Twomey C, O'reilly G, Byrne M. Effectiveness of cognitive behavioural therapy for anxiety and depression in primary care: a meta-analysis. *Fam Pract*. 2014; 00(00): 1-13
- ¹⁰⁹ Hofmann SG, Smits JA. Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *J Clin Psychiatry*. 2008;69(4):621-32.
- ¹¹⁰ Cognitive-behavioral therapy for generalized anxiety. Borza L. *Dialogues Clin Neurosci*. 2017 Jun;19(2):203-208. doi: 10.31887/DCNS.2017.19.2/lborza.PMID: 28867944
- ¹¹¹ Clond M. Emotional Freedom Techniques for Anxiety: A Systematic Review With Meta-analysis. *J Nerv Ment Dis*. 2016;204(5):388-95.
- ¹¹² Thabrew H, Ruppeldt P, Sollers JJ. Systematic Review of Biofeedback Interventions for Addressing Anxiety and Depression in Children and Adolescents with Long-Term Physical Conditions. *Appl Psychophysiol Biofeedback*. 2018;43(3):179-192.
- ¹¹³ Goessl VC, Curtiss JE, Hofmann SG. The effect of heart rate variability biofeedback training on stress and anxiety: a meta-analysis. *Psychol Med*. 2017;47(15):2578-2586.
- ¹¹⁴ Kühlmann AYR, De rooij A, Kroese LF, Van dijk M, Hunink MGM, Jeekel J. Meta-analysis evaluating music interventions for anxiety and pain in surgery. *Br J Surg*. 2018;105(7):773-783.

-
- ¹¹⁵ Klainin-yobas P, Oo WN, Suzanne yew PY, Lau Y. Effects of relaxation interventions on depression and anxiety among older adults: a systematic review. *Aging Ment Health*. 2015;19(12):1043-55
- ¹¹⁶ Nunns M, Mayhew D, Ford T, et al. Effectiveness of nonpharmacological interventions to reduce procedural anxiety in children and adolescents undergoing treatment for cancer: A systematic review and meta-analysis. *Psychooncology*. 2018;27(8):1889-1899.
- ¹¹⁷ Felix MMDS, Ferreira MBG, Oliveira LF, Barichello E, Pires PDS, Barbosa MH. Guided imagery relaxation therapy on preoperative anxiety: a randomized clinical trial. *Rev Lat Am Enfermagem*. 2018;26:e3101.
- ¹¹⁸ Mcpherson F, McGraw L. Treating generalized anxiety disorder using complementary and alternative medicine. *Altern Ther Health Med*. 2013; 19(5): 45-50.
- ¹¹⁹ Yang, J.M., et al., Effects of Web-Based Mindfulness-Based Interventions on Anxiety, Depression, and Stress Among Frontline Health Care Workers During the COVID-19 Pandemic: Systematic Review and Meta-Analysis. *J Med Internet Res*, 2023. 25: p. e44000.
- ¹²⁰ Mansor, M., et al., Effect of mindfulness intervention on anxiety, distress, and depression for chronic diseases: a scoping review. *Psychol Health Med*, 2023. 28(6): p. 1549-1561.
- ¹²¹ Ekor M, Adeyemi OS, Otuechere CA. Management of anxiety and sleep disorders: role of complementary and alternative medicine and challenges of integration with conventional orthodox care. *Chin J Integr Med*. 2013;19(1):5-14.
- ¹²² Antonacci D. CAM for your anxious patient: What the evidence says. *Current Psychiatry*. 2010 October;9(10):43-52.