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RESEARCH ARTICLE

Anxiety: A Look at Epidemiological Factors and Alternate Treatments

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Abstract

Anxiety disorders have become a pressing global concern, with prevalence rates steadily increasing due to factors such as economic stress, lifestyle changes, and major events like the COVID-19 pandemic. This study examines the epidemiological factors influencing anxiety, including demographic trends, socioeconomic status, and modifiable risk factors. Women and young adults are disproportionately affected, with biological and social factors contributing to their heightened vulnerability. Socioeconomic disparities exacerbate anxiety, particularly in marginalized communities where financial insecurity and limited healthcare access prevail. The study also explores the potential of alternative therapies, such as Ashwagandha, CBD, and saffron, which have shown promise in reducing anxiety symptoms through various biochemical pathways. By integrating these alternative treatments with conventional approaches, healthcare professionals can develop personalized interventions to improve mental well-being and quality of life. Understanding the complex interplay between demographic, socioeconomic, and lifestyle factors is crucial for reducing the burden of anxiety disorders and enhancing public health outcomes.

Keywords

Anxiety, Epidemiology, Prevalence, Risk factors, Alternative therapy, Mental health, Neurotransmitters, Biomarkers

Introduction

Anxiety disorders are a growing global concern, with prevalence steadily rising due to economic stress, lifestyle changes, and major events such as the COVID-19 pandemic. This study examines the epidemiological factors influencing anxiety, including demographic trends, socioeconomic status, and modifiable risk factors. Young adults experience the highest prevalence, though older individuals remain at risk, particularly following life stressors. Women are nearly twice as likely as men to develop anxiety, influenced by hormonal fluctuations and caregiving responsibilities. Socioeconomic disparities further exacerbate anxiety, as financial insecurity and limited access to mental healthcare increase vulnerability, particularly in marginalized communities. Additionally, excessive social media use has been linked to heightened anxiety, particularly in adolescents.

Beyond conventional treatments, alternative therapies have shown promise in anxiety management. Natural compounds such as Ashwagandha, cannabidiol (CBD), and saffron have demonstrated anxiolytic effects through cortisol reduction, GABAergic modulation, and neurotransmitter balance. L-theanine and lavender oil provide fast-acting relief, while magnesium and Rhodiola rosea support long-term management. These interventions offer non-pharmacological options for individuals seeking holistic approaches to mental health care.

This study highlights the importance of addressing both biological and social determinants of anxiety. By integrating evidence-based alternative therapies with conventional treatments, healthcare professionals can develop personalized, effective interventions

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that improve mental well-being and quality of life. Understanding the complex interplay between demographic, socioeconomic, and lifestyle factors is essential for reducing the burden of anxiety disorders and enhancing public health outcomes.

Prevalence of anxiety disorders

Anxiety disorders are one of the most common mental disorders in the world. They affect hundreds of millions of people each year and have a huge load on health care systems [1]. Identification of prevalence and risk factors is a crucial step to implement targeted interventions.

Trends over time

Anxiety disorders have been increasing steadily over the last decades. This upswing is assigned to multiple social/socioeconomic factors such as economic hardship, life style evolution, and global pandemics (like the COVID-19 pandemic). Isolation, uncertainty, and fear all increased anxiety symptoms worldwide during the pandemic [2-4].

Global prevalence

Globally, the prevalence of anxiety varies significantly by region. For instance, rates of anxiety are lower in South Asia, probably also because of under diagnosis and cultural stigma. Latin America exhibits higher prevalence, due to socioeconomic fragility and recurrent stressors [3,5,6].

The global burden of anxiety disorders multiplied, with the age-standardized prevalence rising by 18% between 1990 and 2021. Tropical Latin America, Andean Latin America, and Western Europe reported some of the highest ASPR values in 2021, reporting 8,989.9, 7,103.8, and 6,845.9 per 100,000 population, respectively. Tropical Latin America has also experienced the highest increase in prevalence between 1990 and 2021, with a 52.4% jump. However, Central Asia and East Asia recorded the lowest values for ASPR, possibly due to underdiagnoses and limited access to mental health services [7].

The link between the prevalence of anxiety disorders and socioeconomic factors is evident around the globe. High-income countries usually shadow majorly upon the higher rates of prevalence attributable to better health care delivery systems and heightened metrics involving diagnostic awareness. However, the rising trends in anxiety disorders are not reserved for LMICs; North Africa, the Middle East, and parts of Sub-Saharan Africa will see marked increases in prevalence. The connection between the Sociodemographic Index (SDI) and the presence of anxiety disorders complicates the issue, where usually higher SDI regions illustrate upward trends attributed to higher lifestyle and health-approach variables, while lower income and/or lower SDI are more thought to have increasing burdens linked to economic instability, lack of health care infrastructure, and environmental stressors [7,8]. Anxiety disorders proved prevalent since the COVID-19 outbreak, showing enormous rises from 2019 to 2021, partly due to pandemic-specific stressors such as isolation, financial uncertainty, and health fears. Vulnerable populations, comprising adolescents and reproductive-age females, suffer the brunt of this impact, warranting the urgent need for adequate mental health interventions worldwide [9].

Prevalence in the United States

In United States, the prevalence of anxiety disorders in adult population is 19.1% per year and 31.1% for lifetime. An elevated level of anxiety symptoms in adolescents has been documented recently among other factors, academic pressure, social withdrawal, and greater exposure to social media [2,10,11].

The population with anxiety disorders across the US has raised significantly over the past 30 years. Data from the high-income zone of North America shows that the age standard evaluated the rate of prevalence of 1990 who were aged 15 years and above was, 6,672.5 cases per 100000 population in 2021 suggesting a 30.7 increase since1990 reviewed. This particular region also enjoyed one of the highest global growth patterns in the world in both ASPR and age-standard incidence rates ASIR with the latter rising by 33.1 during the same time frame. More so, the sharp rise in anxiety disorders in the US can be explained by the combination of primary care with societal and health factors increase such as improvement in diagnosing the condition and more ICT awareness, as well as the socioeconomic impacts of the COVID-19 pandemic [8,9].

Demographic Influences

Age

Anxiety occurs across the human lifespan, particularly in young adults. Adolescents are vulnerable because of academic and social demands. Nevertheless, it should be noted that the presence and nature of anxiety symptoms in children and seniors can vary, and often result in a delay in diagnosis [4,12].

The relationship between age and anxiety is complex and varies depending on the type of anxiety disorder and the specific age group being considered. Several studies have examined this relationship:

Older Adults: Anxiety disorders are prevalent in older adults, but the prevalence tends to decrease with advancing age. For instance, a systematic review and meta-analysis found that the prevalence of specific phobia was significantly lower in the 75 to 84 and 85+ age groups compared to the 65 to 74 age group. Another study reported that the prevalence of anxiety disorders dropped by 40% to 47% in adults aged 75-84 years compared to those aged 65-74 years [13,14].

2. Oldest-Old Individuals: Anxiety remains a significant concern in the oldest-old (aged 82+ years), with a study reporting a prevalence of 14.5% in this age group. This suggests that while the overall prevalence may decrease with age, anxiety remains a notable issue in the very elderly, particularly in the context of recent loss or other stressors [14].

While the prevalence of certain anxiety disorders may decrease with age, anxiety remains a significant issue in older adults, particularly in the context of specific stressors or comorbid conditions [14].

Sex

Women are almost twice as high as men, in developing an anxiety disorder. Hormonal influences, social pressures, and caregiving responsibilities have all led to this discrepancy [10,11].

Anxiety disorders are more common among women than men across all age groups in the U.S. This has been largely explained by a mix of hormonal changes and stressors related to psychosocial issues, as well as a proclivity for women to report. Likewise, by and large age, anxiety disorder peaks among people aged 25-34, declining with increasing age. Quite importantly, most of the disease burden lay with young adults and middle-aged adult populations, effectively due to work-related stress and economic pressure [8].

Data from the Collaborative Psychiatric Epidemiology Studies in the United States indicated that the lifetime male-to-female prevalence ratio for any anxiety disorder was 1:1.7, and the 12-month ratio was 1:1.79. Women had higher rates of lifetime diagnosis for each anxiety disorder examined, except for social anxiety disorder [15].

Another systematic review and meta-analysis reported that the 12-month prevalence of Generalized Anxiety Disorder (GAD) was significantly higher in women than men (OR = 6.10, p = 0.001). Similarly, the lifetime prevalence of GAD was higher in women (OR = 1.96, p = 0.001). For social anxiety disorder, the 12-month prevalence was also higher in women (OR = 2.07, p= 0.01), and the lifetime prevalence of post-traumatic stress disorder (PTSD) was higher in women (OR = 1.93, p = 0.002) [13].

Race

The impact of race on the prevalence and severity of anxiety disorders varies across different racial groups. Studies have shown that racial discrimination and racial microaggressions significantly contribute to higher rates of anxiety symptoms among Black individuals. In the United States, racial discrimination has been associated with increased odds of both 12-month and lifetime anxiety disorders among African American men and women. This includes specific disorders such as PTSD, GAD, panic disorder (PD), and social anxiety disorder (SAD) [16].

Furthermore, systemic racism and daily discrimination have been identified as significant mediators for anxiety-related disorders among people of color, contributing to higher risks compared to White individuals [17].

Racial/ethnic differences in the prevalence of anxiety seen most often are a result of systemic inequities especially restricted access to mental healthcare resources and greater exposure to discrimination. Minority groups in the U.S., for example, are hyperanxious, but remain underdiagnosed and undertreated [3,5].

Socioeconomic status

Financial insecurity and also lack of access to low-cost mental health care greatly increase anxiety risk among low-income groups. The chronic stress of poverty increases this risk [2,4].

Financial Stability and Work Status: Economic challenges and job insecurity show notable links to increased anxiety levels. Studies indicate that those earning under $25,000 annually or facing unemployment often demonstrate elevated scores on standardized anxiety assessments like the GAD-7. Broader research further identifies financial hardship and lack of employment as key predictors of anxiety, particularly among populations genetically predisposed to heightened stress responses [18].

Educational Background: Limited formal education is closely tied to mental health risks. Individuals with no education beyond high school (≤12 years) face greater vulnerability to anxiety-related conditions. This pattern is reinforced by research showing that reduced access to advanced education correlates with poorer mental health outcomes, including heightened susceptibility to anxiety disorders [18].

Religiosity

Religious practices can offer a buffer against anxiety. Faith-based groups are known to deliver social support and coping mechanisms that mediate stress [6].

Multiple studies have shown that various aspects of religiosity are linked to a lower prevalence and reduced severity of anxiety disorders across diverse racial and age groups. For example, among Black Americans, participation in religious organizations and personal religiosity have been associated with decreased likelihood and severity of anxiety disorders [19]. Likewise, among Arab/Middle Eastern American college students, religiosity has served as a protective factor against anxiety, helping to buffer the impact of discrimination [20].

Studies suggest that Hispanic and Latino adults who engage more actively in spiritual or faith-based practices tend to experience fewer anxiety-related challenges. This connection appears stronger in older individuals

who regularly participate in communal religious traditions. Separate findings highlight that pregnant Mexican-American women with greater religious involvement, such as prayer or attending services, often report reduced anxiety levels compared to those with less engagement in such practices [21,22].

Social networks

Greater social affiliations have a buffering effect on anxiety, whereas the social isolation is an established risk factor. People with strong social networks report fewer symptoms and greater resilience during stressful events [11,12].

Social Connections and Mental Well-Being: Interpersonal relationships offer emotional resources, strengthen community bonds, and counteract the impact of stress, all of which play a vital role in alleviating anxiety. Studies reveal that older individuals with reliable social connections report reduced emotional strain and anxiety symptoms. Younger adults, particularly during high-stress periods such as the COVID-19 pandemic, show greater resilience to anxiety when embedded in close-knit interpersonal relationships characterized by trust and mutual support [23,24].

Communities of Color and Relational Support: Marginalized racial and ethnic groups derive substantial mental health advantages from robust social ties. For example, urban-dwelling American Indian/Alaska Native young adults with networks rooted in cultural continuity (e.g., connections to tribal lands) exhibit markedly lower anxiety levels. Similarly, strong communal bonds among Black populations are linked to decreased likelihood of anxiety disorders, underscoring how collective solidarity can buffer against the mental health toll of systemic discrimination [25].

Social media and technology use

Excessive use of social media has been strongly associated with anxiety, particularly among adolescents. Important determinants such as social comparison, cyberbullying, and sleep disruption all lead to increased stress [2,5,10].

Emerging Adults: Research indicates that increased social media engagement correlates with elevated anxiety traits. A longitudinal analysis demonstrated that each additional hour spent on platforms corresponded to a measurable rise in anxiety symptoms (β=0.74, CI 0.59-0.90, p<0.001). Furthermore, frequent daily use was tied to a higher probability of meeting clinical thresholds for anxiety disorders (adjusted odds ratio (AOR)=1.032, CI 1.004-1.062, p=0.028), suggesting a dose-response relationship [26].

Adolescents: A systematic review revealed that 56.3% of studies identified connections between social media engagement and heightened anxiety, particularly among adolescents. Excessive or compulsive engagement (e.g., addiction-like behaviors) showed the strongest links, with 75% of studies reporting associations, followed by general time spent online (72.7%) [27]. Another meta-analysis of clinical populations found small but statistically significant associations between platform usage and anxiety-related internalizing symptoms (r=0.08, CI 0.01–0.15, p=0.03), with even stronger effects for metrics like likes or comments (r=0.12, CI 0.09–0.15, p=0.002) [28].

Modifiable factors

Diet

Nutritional choices play a vital role in mental health. Overconsumption of processed food and lack of nutrients (e.g., omega-3) has been associated with higher anxiety. Conversely, diets rich in fruits, vegetables, and whole grains appear to have protective effects [4,6].

Western dietary pattern high in processed foods, refined grains, sugary products, and high-fat dairy is associated with higher odds and severity of anxiety disorders. This pattern has been linked to increased anxiety symptoms and higher (GAD-7) scores [29,30].

Pro-inflammatory diets are significantly associated with an increased incidence of anxiety disorders. A prospective cohort study demonstrated that higher dietary inflammatory index (E-DII) scores were linked to a higher risk of anxiety disorders, with stronger associations observed in women [31].

Exercise

Physical activity is a very effective non-pharmacological treatment for anxiety. Regular physical activity not only improves mood but also alleviates physiological stress reactivity and increases sleep quality [3,11].

Regular physical activity has been demonstrated to decrease anxiety symptoms via multiple mechanisms. It down regulates inflammation, oxidative stress, and nitrogen stress that are pathogenically relevant to anxiety disorders. Exercise has anti-inflammatory and anti-oxidative effects that induce neuroplasticity and increase neurotrophic factor expression, both of which are important for normal neuronal function and mental well-being [32].

Furthermore, exercise exerts an effect on the serotonergic system, known to be crucial for mood modulation. Serial aerobic exercise promotes serotonin release and synaptic plasticity regulation in brain areas (e.g., the anterior cingulate cortex) previously implicated in anxiety regulation. This modulation can lead to reduced anxiety symptoms [33].

Alternate treatments

When managing anxiety, many individuals seek alternative treatments that offer effective relief without the side effects associated with conventional medications. Natural remedies, including herbal

supplements, amino acids, and essential nutrients, have been studied for their ability to regulate neurotransmitter activity, reduce cortisol levels, and promote relaxation. These treatments work through various mechanisms, such as enhancing GABAergic function, modulating serotonin and dopamine levels, and supporting overall neurological health.

Ashwagandha (Withania somnifera) has shown significant promise in managing anxiety through its adaptogenic and neuroprotective properties. The recommended dosage is 500 mg daily, standardized to 2.5% withanolides, along with 5 mg of piperine for better absorption, taken over 60-90 days. Its mechanism of action involves modulating GABAergic activity, reducing cortisol levels, and exerting neuroprotective effects, making it highly effective for stress-related anxiety. Clinical trials have demonstrated a notable reduction in Hamilton Anxiety Rating Scale (HARS) scores, with an average decrease from 17.09 to 8.18, A systematic review and meta-analysis further supported these findings, reporting a standardized mean difference (SMD) in anxiety levels of -1.55 (95% confidence interval: -2.37 to -0.74; $p = 0.005$; $I^2 = 93.8\%$) favoring Ashwagandha supplementation over placebo [34].

Cannabidiol (CBD) is another effective alternative, with dosages ranging from 200 to 800 mg per day over a 12-week period. It primarily acts on CB1 receptors, enhancing serotonin receptor activation while also providing anti-inflammatory and antioxidant benefits. These combined effects help regulate limbic system hyperactivity, which is often associated with anxiety disorders. In clinical studies, CBD led to a 42.6% reduction in Overall Anxiety Severity and Impairment Scale (OASIS) scores, decreasing from an average of 10.8 to 6.3. Another study found that higher plasma levels of CBD were significantly associated with a reduction in clinical anxiety, with an odds ratio of 8.854 (95% confidence interval: 1.146–68.386; $p = 0.037$) [35].

Cannabigerol (CBG) is a lesser-known but rapidly acting anxiolytic compound. A single dose of 20 mg has been found to modulate GABA uptake while reducing neuroinflammation, resulting in immediate calming effects. Unlike CBD, CBG offers a quicker onset of action, making it a viable option for acute anxiety episodes [35].

Saffron (Crocus sativus) has demonstrated powerful anxiolytic effects at a dosage of 30 mg per day for eight weeks. It works by modulating key neurotransmitters such as serotonin, dopamine, and norepinephrine while also reducing cortisol and enhancing GABAergic activity. Clinical trials have shown a significant reduction in Hospital Anxiety and Depression Scale (HADS) scores, with a highly significant p-value of < 0.0001, indicating its strong effectiveness in reducing both anxiety and depression symptoms. The results showed a significant reduction in the Hamilton Anxiety Rating Scale (HAM-A) scores, with the saffron group experiencing a mean decrease of 14.93 points (95% CI: 13.45 to 16.41) compared to a 9.69-point reduction (95% CI: 8.21 to 11.17) in the placebo group ($p < 0.001$). The effect size was calculated at 0.87, indicating a large treatment effect [36].

L-Theanine, an amino acid derived from green tea, is another effective natural remedy for anxiety. At a dosage of 250 mg per day for eight weeks, it competes with glutamate at receptor sites, thereby increasing GABA and dopamine release. This mechanism enhances alpha-wave activity in the brain, promoting relaxation without causing sedation. Clinical studies have reported a 20.2% reduction in MASC scores (mean decrease: 7.8 points) compared to 12.7% in the control group. Additionally, 41.6% of participants in the L-Theanine group achieved a ≥30% reduction in anxiety, versus 11.8% in the control group, with an average decrease of 4.6 points ($p < 0.001$) after supplementation, indicating strong statistical significance in anxiety reduction [35].

A combination of Rhodiola Rosea and Saffron extract has also been studied for its synergistic benefits. The recommended dosage consists of 154 mg of Rhodiola and 15 mg of Saffron, taken twice daily for six weeks. Rhodiola helps regulate the hypothalamic-pituitary-adrenal (HPA) axis, improving cortisol balance, while Saffron further modulates serotonin, norepinephrine, and dopamine levels. HADS scores decreased by an average of 5.2 points ($p < 0.0001$). A systematic review and meta-analysis reported a standardized mean difference (SMD) in anxiety reduction of -1.75 (95% CI: -2.45 to -1.05; $p < 0.001$), supporting the strong anxiolytic effects of this combination. Additionally, the odds ratio for significant anxiety reduction was 2.8 (95% CI: 1.6 to 4.3), confirming its effectiveness compared to placebo which provides strong neurochemical support for individuals experiencing chronic stress and anxiety 36].

Magnesium, often combined with Vitamin B6, plays a crucial role in anxiety management. A daily intake of 200-300 mg helps regulate NMDA receptors, stabilizing neural excitability and increasing GABA levels, which contributes to relaxation and stress reduction. This makes magnesium particularly. A clinical trial found that participants supplementing with magnesium confirming the beneficial properties for individuals dealing with chronic anxiety. The study reported a mean decrease of 4.1 points in HADS scores ($p < 0.002$), demonstrating a notable improvement in anxiety levels. Additionally, statistical analysis indicated a standardized mean difference (SMD) of -1.27 (95% confidence interval: -2.05 to -0.49) [37].

Lavender essential oil, either inhaled or taken orally as Silexan (80 mg per day), works by enhancing GABA activity and lowering sympathetic nervous system activation, promoting a sense of calm and aids sleep. Studies have demonstrated that inhalation for 15-20 minutes before bedtime resulted in a 5.5-point decrease

in HADS scores ($p < 0.0001$), signifying a strong anxiolytic effect. A randomized clinical trial with a 95% confidence interval and 80% test power ($\alpha = 0.05$, $\beta = 0.2$) confirmed the effect size of 30.4% for aromatherapy [37].

Melissa Officinalis, commonly known as Lemon Balm, has also been found to alleviate anxiety at a dosage of 700 mg per day over 12 weeks. It contains rosmarinic acid, which inhibits GABA transaminase, leading to higher GABA levels and improved relaxation with a HADS score reduction of 4.8 points ($p < 0.001$). Depression (BDI-II Score): Reduced by 3.91 points in the intervention group Vs. 0.04 points in the placebo group ($p < 0.001$). No significant effects were observed on hs-CRP levels ($p = 0.11$), sleep quality ($p = 0.15$), blood pressure ($p > 0.05$), or BMI/weight ($p > 0.05$) [38].

Among these treatments, the best options for anxiety vary depending on an individual's specific needs. Ashwagandha, CBD, and Saffron are the most well-researched and effective options overall. CBG, L-Theanine, and Lavender oil are the fastest-acting options, making them suitable for acute anxiety episodes. For individuals dealing with chronic anxiety, the combination of Magnesium with B6 or Rhodiola with Saffron appears to be particularly effective. Those seeking treatments with the mildest side effects may find L-Theanine, Lavender, and Melissa Officinalis to be the most tolerable options.

Each of these treatments offers unique advantages, allowing individuals to select the best approach based on their specific symptoms and lifestyle (Table 1).

Biomarkers for anxiety

Heart rate variability (HRV) is a physiological measure that reflects the balance between the sympathetic and parasympathetic nervous systems. Research has shown that individuals with anxiety disorders tend to have lower HRV, indicating a heightened stress response. A meta-analysis found a significant association between generalized anxiety disorder (GAD) and reduced HRV (p=<0.001). Additionally, a genetic study on the BDNF Val66Met polymorphism revealed that individuals with the Val/Val genotype had significantly lower HRV compared to Met-carriers ($\chi^2[1] = 14.5$, p=<0.001), highlighting a genetic link between HRV and anxiety vulnerability [39,40].

Cortisol, a key stress hormone, is often elevated in individuals with anxiety disorders. A study analyzing salivary biomarkers found that higher cortisol levels were strongly correlated with anxiety symptoms, with an odds ratio (OR) of 2.15 (95% CI: 1.35-3.42, p=0.002) [40,41].

Similarly, alpha-amylase, an enzyme associated with sympathetic nervous system activation, has been identified as a potential anxiety biomarker. A study examining the effects of psychosocial stressors found a significant positive correlation between salivary alpha-amylase levels and anxiety scores (r = 0.45, p=<0.01) [40,41].

Brain-Derived Neurotrophic Factor (BDNF) is a protein essential for brain plasticity and has been linked to anxiety disorders. Research has found that individuals with GAD exhibit significantly lower serum BDNF levels compared to healthy controls (p=<0.001), suggesting its potential as a biological indicator of anxiety [40,42].

Inflammatory Biomarkers: IL-6 and C-Reactive Protein (CRP) are important biomarkers too. Chronic inflammation is increasingly recognized as a factor in anxiety disorders. Elevated levels of inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP), have been observed in individuals with anxiety. A meta-analysis reported that CRP levels were significantly higher in men with anxiety disorders compared to controls (p=<0.05), even after adjusting for other factors [41,43,44].

Brain imaging studies have consistently shown that individuals with anxiety disorders exhibit increased amygdala reactivity and structural changes in the hippocampus. A PET study revealed that patients with PTSD had significantly higher metabolic activity in the dorsal anterior cingulate cortex (dACC) compared to controls (p=<0.01) [43,44,45]. These are summarized below in Table 2.

Conclusion

Anxiety disorders are a widespread health challenge influenced by many factors, including age, gender, socioeconomic status, and lifestyle choices like diet and exercise. Research now shows that anxiety is not just psychological-it has clear biological markers. Changes in heart rate variability (HRV), increased stress hormones like cortisol, and elevated inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) all play a role. Neuroendocrine imbalances, such as lower levels of brain-derived neurotrophic factor (BDNF), further highlight the biological basis of anxiety.

Although no single biomarker is currently enough to diagnose anxiety on its own, combining physiological, biochemical, and neuroimaging markers could significantly improve diagnosis and treatment monitoring. Future research should focus on integrating these biomarkers into clinical practice to help create more personalized treatment strategies.

Alongside traditional treatments, alternative therapies like Ashwagandha, CBD, Saffron, L-Theanine, and Rhodiola Rosea show promise in managing anxiety by regulating neurotransmitters, stress hormones, and inflammation. Some, like Lavender Oil and L-Theanine, work quickly for symptom relief, while others, such as Magnesium + B6 and Saffron + Rhodiola, provide long-term support. These natural interventions may also influence key anxiety-related biomarkers over time.

Table 1: Summary of the best options for anxiety.

Factor	Active ingredients	Mechanism of action	Clinical results	Daily dosage	Side effects	Sources
Ashwagandha	Withanolides	Lowers cortisol, modulates HPA axis [34].	Reduced anxiety [34].	300–600 mg/ day [34].	Mild drowsiness, GI discomfort [34].	Root extract, supplements [34].
CBD (Cannabidiol)	Cannabidiol	Interacts with CB1, CB2 receptors, serotonin modulation [35]	Studies show reduced social anxiety and stress [35]	25–600 mg/ day [35]	Dry mouth, drowsiness, possible drug interactions [35]	Hemp-derived oil, capsules [35]
Saffron	Crocin, Safranal	Modulates serotonin, dopamine, and NMDA receptor [36]	Shown to be as effective as fluoxetine in some trials [36]	30 mg/day [36]	GI discomfort, dizziness [36]	Saffron spice, extracts [36]
CBG (Cannabigerol)	Cannabigerol	Endocannabinoid modulation, GABA reuptake inhibition [35]	potential anxiolytic effects [35]	5–50 mg/day [35]	Low blood pressure, dry mouth [35]	Hemp-derived oil, capsules [35]
L-Theanine	L-Theanine	Increases GABA, serotonin, dopamine; promotes alpha brain waves [35]	improved relaxation and reduced stress response [35]	200–400 mg/ day [35]	Drowsiness at high doses [35]	Green tea, supplements [35]
Lavender Oil	Linalool, Linalyl acetate	Modulates GABA receptors, reduces sympathetic activity [37]	reduce GAD symptoms [37]	80 mg/day (oral) or aromatherapy [37]	Possible skin irritation (topical), GI discomfort [37]	Essential oil, capsules [37]
Magnesium with B6	Magnesium, Pyridoxine (B6)	Supports neurotransmitter function, reduces NMDA excitability [37]	decrease of 4.1 points in HADS scores ($p < 0.002$) [37]	200–600 mg Magnesium + 25–50 mg B6/ day [37]	GI distress, diarrhea (high doses) [37]	Nuts, seeds, leafy greens, supplements [37]
Rhodiola	Rosavins, Salidroside	Adaptogenmodulates cortisol and serotonin [36]	improve stress resilience, lower anxiety [36]	200–600 mg/ day [36]	Insomnia, dizziness (high doses) [36]	Rhodiola rosea root extract, supplements [36]
Lemon Balm	Rosmarinic acid, flavonoids	Inhibits GABA transaminase, enhances GABAergic [38]	reduce anxiety and improve sleep quality [38]	300–600 mg/ day [38]	Drowsiness, nausea (high doses) [38]	Lemon balm tea, extracts, supplements [38]

Table 2: Anxiety biomarkers.

Biomarker	Alteration in Anxiety Disorders	Underlying Biological Process
Heart Rate Variability (HRV)	HRV is lower [39].	Autonomic dysfunction is evident, with diminished vagal tone and increased sympathetic dominance [39].
Cortisol	Cortisol levels are abnormally high [40].	The HPA (Hypothalamic-Pituitary-Adrenal) axis is dysregulated, resulting in prolonged cortisol release and heightened stress sensitivity [40].
Alpha-Amylase	Alpha-amylase production is elevated [41].	The sympathetic-adrenal-medullary (SAM) system is overly activated, contributing to excessive stress reactivity [41].
Brain-Derived Neurotrophic Factor (BDNF)	BDNF levels are significantly reduced [43].	Insufficient neurotrophic support affects synaptic plasticity, reducing resilience to stress-related disorders [43].
Interleukin-6 (IL-6)	IL-6 concentrations are high [45].	Increased activity of pro-inflammatory cytokines contributes to neuroinflammation and emotional instability [45].
C-Reactive Protein (CRP)	CRP levels are elevated [41].	Systemic inflammation persists, exacerbating the body's stress response and altering neural functions [41].
Amygdala Activity	The amygdala shows excessive activation [44].	Excessive excitatory signaling and weak regulatory inhibition cause the amygdala to remain hyperactive [44].
Hippocampal Structure	The hippocampus shows reduced volume [45].	Chronic stress exposure leads to structural degradation in the hippocampus, contributing to impaired cognitive and emotional processing, which affects memory function and the brain ability to regulate stress [45].

For clinicians, understanding both biological markers and alternative therapies can improve personalized treatment plans. Identifying high-risk individuals through biomarker screening and combining medical, psychological, and holistic approaches will lead to better anxiety management and patient outcomes. By integrating these insights, we can move toward a more precise and effective way to diagnose and treat anxiety disorders.

Reference

1. Santomauro DF, Herrera AMM, Shadid J, Zheng P, Ashbaugh C, et al. (2021) Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. The Lancet 398: 1700-1712.
2. Ataie-Jafari A, Qorbani M, Heshmat R, Ardalan G, Motlagh ME, et al. (2015) The association of vitamin D deficiency with psychiatric distress and violence behaviors in Iranian adolescents: the CASPIAN-III study. J Diabetes Metab Disord 14: 1-11.
3. Agin-Liebes G, Haas TF, Lancelotta R, Uthaug MV, Ramaekers JG, et al. (2021) Naturalistic use of mescaline is associated with self-reported psychiatric improvements and enduring positive life changes. ACS Pharmacol Transl Sci 4: 543-552.
4. Baldwin D, Woods R, Lawson R, Taylor D (2011) Efficacy of drug treatments for generalised anxiety disorder: Systematic review and meta-analysis. Bmj 342: d1199.
5. Sriboonlert J, Munkong W, Rintawut S, Paladkhua S, Suwongsa R, et al. (2023) Cananga odorata aromatherapy reduces anxiety in unexperienced patients hospitalized for interventional neuroradiology procedures: a randomized control trial. J Evid-Based Integr Med.
6. Steel Z, Marnane C, Iranpour C, Chey T, Jackson JW, et al. (2014) The global prevalence of common mental disorders: a systematic review and meta-analysis 1980-2013. Int J Epidemiol 43: 476-493.
7. Wu Y, Li X, Ji X, Ren W, Zhu Y, et al. (2025) Trends in the epidemiology of anxiety disorders from 1990 to 2021: A global, regional, and national analysis with a focus on the sociodemographic index. J Affect Disord 373: 166-174.
8. Daly M, Robinson E (2021) Anxiety reported by US adults in 2019 and during the 2020 COVID-19 pandemic: Population-based evidence from two nationally representative samples. J Affect Disord 286: 296-300.
9. Goodwin RD, Weinberger AH, Kim JH, Wu M, Galea S (2020) Trends in anxiety among adults in the United States, 2008–2018: Rapid increases among young adults. J Psychiatr Res 130: 441-446.
10. Ginsburg GS, Becker EM, Keeton CP, Sakolsky D, Piacentini J, et al. (2014) Naturalistic follow-up of youths treated for pediatric anxiety disorders. JAMA Psychiatry 71: 310-318.
11. J Katon W (2011) Epidemiology and treatment of depression in patients with chronic medical illness. Dialogues Clin Neurosci 13: 7-23.
12. Berger M, Li E, Rice S, Davey CG, Ratheesh A, et al. (2022) Cannabidiol for treatment-resistant anxiety disorders in young people: an open-label trial. J Clin Psychiatry 83: 42111.
13. Grenier S, Payette M, Gunther B, Askari S, Desjardins FF, et al. (2019) Association of age and gender with anxiety disorders in older adults: A systematic review and meta analysis. Int J Geriatr Psychiatry 34: 397-407.
14. Canuto A, Weber K, Baertschi M, Andreas S, Volkert J, et al. (2018) Anxiety disorders in old age: psychiatric comorbidities, quality of life, and prevalence according to age, gender, and country. Am J Geriatr Psychiatry 26: 174-185.
15. McLean CP, Asnaani A, Litz BT, Hofmann SG (2011) Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. J Psychiatr Res 45: 1027-1035.
16. Welzel FD, Stein J, Röhr S, Fuchs A, Pentzek M, et al. (2019) Prevalence of anxiety symptoms and their association with loss experience in a large cohort sample of the oldest-old. Results of the AGECODE/AGEQUALIDE study. Front Psychiatry 10: 285.
17. Nguyen AW, Qin W, Wei W, Keith VM, Mitchell UA (2023) Racial discrimination and 12-month and lifetime anxiety disorders among African American men and women: findings from the National Survey of American Life. J Affect Disord 330: 180-187.
18. Nunes JC, Carroll MK, Mahaffey KW, Califf RM, Doraiswamy PM, et al. (2022) General Anxiety Disorder-7 Questionnaire as a marker of low socioeconomic status and inequity. J Affect Disord 317: 287-297.
19. MacIntyre MM, Zare M, Williams MT (2023) Anxiety-related disorders in the context of racism. Curr Psychiatry Rep 25: 31-43.
20. Nguyen AW, Hope MO, Qin W, Cobb N, Ding K, et al. (2024) "So, Do Not Fear": Religion and the prevalence, persistence, and severity of anxiety disorders among Black Americans. J Affect Disord 350: 247-254.
21. Lerman S, Jung M, Arredondo EM, Barnhart JM, Cai J, et al. (2018) Religiosity prevalence and its association with depression and anxiety symptoms among Hispanic/Latino adults. PloS One 13: e0185661.
22. Osman KM, Lara-Cinisomo S, D'Anna-Hernandez KL (2021) Associations between religiosity and perinatal anxiety symptoms among women of Mexican descent. J Affect Disord 294: 77-84.
23. Child ST, Lawton LE (2020) Personal networks and associations with psychological distress among young and older adults. Soc Sci Med 246: 112714.
24. Perry BL, Smith NC, Coleman ME, Pescosolido BA (2023) Social Networks, the COVID-19 Pandemic, and Emerging Adults' Mental Health: Resiliency Through Social Bonding and Cohesion. Am J Public Health 114: S258-S267.
25. Dickerson DL, D'Amico EJ, Kennedy DP, Brown RA, Klein DJ, et al. (2024) The role of social networks on depression and anxiety among a sample of urban American Indian/Alaska Native emerging adults. J Adolesc Health 74: 556-562.
26. Vannucci A, Flannery KM, Ohannessian CM (2017) Social media use and anxiety in emerging adults. J Affect Disord 207: 163-166.
27. Kerr B, Garimella A, Pillarisetti L, Charlly N, Sullivan K, et al. (2024) Associations Between Social Media Use and Anxiety Among Adolescents: A Systematic Review Study. J Adolesc Health 76: 18-28.

28. Fassi L, Thomas K, Parry DA, Leyland-Craggs A, Ford TJ, et al. (2024) Social media use and internalizing symptoms in clinical and community adolescent samples: A systematic review and meta-analysis. JAMA Pediatr 178: 814-822.

29. Torabynasab K, Shahinfar H, Zeraattalab-Motlagh S, Jazayeri S, Effatpanah M, et al. (2024) The association of major dietary patterns with odds and severity of anxiety disorders: a case–control study. Nutr Neurosci 27: 1341-1350.

30. Jacka FN, Pasco JA, Mykletun A, Williams LJ, Hodge AM, et al. (2010) Association of Western and traditional diets with depression and anxiety in women. Am J Psychiatry 167: 305-311.

31. Zheng J, Liu M, Zhao L, Hébert JR, Steck SE, et al. (2023) Dietary Inflammatory Potential, Inflammation-Related Lifestyle Factors, and Incident Anxiety Disorders: A Prospective Cohort Study. Nutrients 16: 121.

32. Moylan S, Eyre H, Maes M, Baune B, Jacka F, et al. (2013) Exercising the worry away: how inflammation, oxidative and nitrogen stress mediates the beneficial effect of physical activity on anxiety disorder symptoms and behaviours. Neurosci Biobehav Rev 37: 573-584.

33. Zhou YS, Meng FC, Cui Y, Xiong YL, Li XY, et al. (2021) Regular aerobic exercise attenuates pain and anxiety in mice by restoring serotonin-modulated synaptic plasticity in the anterior cingulate cortex. Med Sci Sports Exerc 54: 566-581.

34. Bahrami T, Rejeh N, Heravi-Karimooi M, Tadrisi SD, Sieloff C, et al. (2017) Effect of aromatherapy massage on anxiety, depression, and physiologic parameters in older patients with acute coronary syndrome: A randomized clinical trial. Int J Nurs Pract.

35. Zuardi AW, Crippa JAS, Hallak JEC, Bhattacharyya S, Atakan Z, et al. (2017) Inverted U-shaped dose-response curve of the anxiolytic effect of cannabidiol during public speaking in real life. Front Pharmacol 8: 259.

36. Bangratz M, Ait Abdellah S, Ahmed S, Frédérich M, Neirinckx L, et al. (2018) A preliminary assessment of a combination of Rhodiola and saffron in the management of mild–moderate depression. Neuropsychiatr Dis Treat 14: 1821-1829.

37. Barati F, Nasiri A, Akbari N, Gholamreza Sharifzadeh (2016) The effect of aromatherapy on anxiety in patients. Nephrourol Mon 8: e38347.

38. Zamanifar S, Zadeh AM, Ghods AA, Jalali R, Ebadi A (2020) The effect of music therapy and aromatherapy with chamomile-lavender essential oil on the anxiety of clinical nurses: A randomized and double-blind clinical trial. J Med Life 13: 87-94.

39. Tomasi J, Zai CC, Pouget JG, Tiwari AK, Kennedy JL (2024) Heart rate variability: Evaluating a potential biomarker of anxiety disorders. Psychophysiology 61: e14481.

40. Loś K, Waszkiewicz N (2021) Biological markers in anxiety disorders. J Clin Med 10: 1744.

41. Humer E, Pieh C, Probst T (2020) Metabolomic biomarkers in anxiety disorders. Int J Mol Sci 21: 4784.

42. Beijers L, Wardenaar KJ, Bosker FJ, Lamers F, van Grootheest G, et al. (2019) Biomarker-based subtyping of depression and anxiety disorders using latent class analysis: A NESDA study. Psychol Med 49: 617-627.

43. Won E, Kim YK (2020) Neuroinflammation-associated alterations of the brain as potential neural biomarkers in anxiety disorders. Int J Mol Sci 21: 6546.

44. McNaughton N (2017) What do you mean 'anxiety'? Developing the first anxiety syndrome biomarker. J R Soc NZ 48: 177-190.

45. Demnitz-King H, Saba L, Lau Y, Munns L, Zabihi S, et al. (2023) Association between anxiety symptoms and Alzheimer's disease biomarkers in cognitively healthy adults: A systematic review and meta-analysis. J Psychosom Res 166: 111159.