

Anxiety Disorders: A Narrative Review

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Received: November 12, 2024; **Accepted:** November 18, 2024; **Published:** November 25, 2024

ABSTRACT

The prevalence of anxiety disorders in the U.S. has varied between 34 and 38%. Surprisingly, this rate has only increased 1% across the last three decades. Emotional sensitivity and worrying are the only negative effects that have appeared in this recent literature. Also, only two studies have focused on risk factors including anxiety sensitivity and avoidance behavior. Most of the recent research has explored potential underlying biological mechanisms and interventions. The underlying mechanisms have included low heart rate variability, abnormal EEG patterns, altered cytokines, dysregulated neurolipids, neuroinflammation, low hippocampal volume and gray matter and a low connection between cranial hemispheres. The interventions have included metacognition, cognitive behavioral therapy, internet delivery of cognitive behavioral therapy, coloring, acupuncture, exercise, cannabidiol and pharmacology in general. Although this is an informative literature, it is unclear why limited attention has been directed at negative effects and risk factors for anxiety disorders.

Introduction

Anxiety disorders are defined as common psychiatric conditions that are characterized by general apprehension and excessive worrying [1]. Non-specific physical and psychological symptoms include restlessness, fatigue, difficulty concentrating, irritability, muscle tension, palpitations, shortness of breath, dizziness and sleep disturbances. Individuals with anxiety disorders have an increased risk for suicide and cardiovascular disease. Effective therapies have included cognitive behavior therapy, SSRIs and SNRIs.

Methodology

In this narrative review, 37 papers on anxiety disorders in adults are summarized. The papers were derived from a search on PubMed and PsycINFO entering the terms anxiety disorders in adults and the years 2019-2024. Exclusion criteria for this review included papers on proposed protocols, case studies and non-English language papers. The publications can be categorized as the prevalence of anxiety disorders, negative effects of anxiety disorders, predictors/risk factors, potential underlying biological mechanisms for anxiety disorders and interventions. Accordingly, this review is divided into sections that correspond to those categories. Although some papers can

be grouped in more than one category, 3 papers are focused on the prevalence of anxiety disorders, 2 papers on the negative effects, 1 paper on predictors/risk factors for anxiety disorders, 11 on potential underlying biological mechanisms and 20 papers on interventions. A discussion of methodological limitations of this literature appears after those sections.

Prevalence of Anxiety Disorders

The prevalence of anxiety disorders has narrowly ranged between 34 and 38% in the U.S. [2,3]. According to a paper entitled "Global trends in the incidence of anxiety disorders from 1990 to 2019", the prevalence has only increased by one percent in both sexes, although the increase was notably greater in male adults [4].

Negative Effects of Anxiety Disorders

Surprisingly, only a couple studies in this recent literature focused on negative effects of anxiety disorders. The negative effects were emotional sensitivity and worrying

In the study on **emotional sensitivity**, recognition of emotional facial expressions (happiness, anger, and fear) was assessed in a sample of web-based respondents (N=7,176) [5]. Those

individuals with anxiety disorders showed less recognition of those emotional facial expressions. Lower emotional sensitivity scores and anxiety scores were reported for the older age participants.

Table 1: Prevalence, negative effects and predictors/risk factors for anxiety disorders (and first authors).

Prevalence	First authors
34-38% in the U.S.	Herring
1% increase in global trend 1990 to 2019	Cao
Negative effects	
Emotional sensitivity	Rutter
Worrying	Nordahl
Predictors/Risk Factors	
Panic attacks, personality disorders, avoidance behavior, etc.	Hovenkamp-Hermelink

In research on worrying, questionnaires were given on anxiety, depression, and metacognition (N=312 participants) [6]. Not surprisingly, worrying, meta-worry (worry about worry), and cognitive beliefs about worry were associated with greater anxiety [6].

Predictors/Risk Factors for Anxiety Disorders

Papers on predictors/risk factors were also hard to find in this recent literature on anxiety disorders. Only one literature review appeared on predictors/risk factors for anxiety disorders. In this review entitled “Predictors of persistence of anxiety disorders across the lifespan”, 48 studies were included (N =29,690 patients) [7]. Not surprisingly, many predictors appeared in this review on 48 studies including **having panic attacks, personality disorders, treatment-seeking, poor clinical status following treatment, severe avoidance behavior, low extraversion, and greater anxiety sensitivity leading to behavioral inhibition.**

Potential Underlying Biological Mechanisms for Anxiety Disorders

Several potential underlying biological mechanisms have been suggested for anxiety disorders in this recent literature. These include low heart rate variability, abnormal EEG patterns, altered cytokines, dysregulated neurolipids, low hippocampal volume, low gray matter and low connection between hemispheres in the brain. Some of these could also be considered negative effects as well as risk factors given that these are cross-sectional studies, suggesting that directionality or causality cannot be determined. The categories for these appear to be arbitrarily dependent on the researchers’ interests, and it is surprising that the researchers haven’t referred to them as reciprocal or interdependent variables.

Low heart rate variability, for example, could be considered a negative effect, a risk variable or an underlying biological mechanism. In a systematic review and meta-analysis on 99 studies (N=4897 anxiety disorder patients and 5559 controls), heart rate variability was assessed [8]. Low heart rate variability was more frequently noted in the anxiety disorder patients during a resting state but, surprisingly, not following a stressor.

Abnormal EEG patterns have also been reported for individuals with anxiety disorders. In a paper entitled “Linear and nonlinear

EEG-based functional networks in anxiety disorders”, enhanced network complexity and theta network efficiency at rest were characteristic of those with anxiety disorders [9].

Pro-inflammatory cytokines have also been noted in those with anxiety disorders. In two papers from the same research group but different first authors, different cytokines were discussed. In this sample (N= 50 adults with anxiety disorder and 38 healthy adults), the pro-inflammatory cytokine IL-2 was elevated, and the anti-inflammatory cytokine IL-10 was reduced [10].

Table 2: Potential underlying biological mechanisms for anxiety disorders (and first authors).

Mechanisms	First authors
Low heartrate variability	Cheng
Elevated Pro-inflammatory cytokines	Sarmin
Elevated Anti-inflammatory cytokines	Mamun-Or-Rashid
Neuroinflammation	Won
Reduced gray matter volume	Ou, Liu
Decreased connection between the two hemispheres	Mou

In the same database, this research group suggested that interleukin -17A and interleukin- 23A levels were elevated in those with anxiety disorders [11]. These interleukins have played a pro-inflammatory role in many diseases, especially autoimmune diseases including rheumatoid arthritis, multiple sclerosis, irritable bowel syndrome, Alzheimer's and traumatic brain injury.

Other abnormal cytokine patterns have been noted in other samples as well. In one sample TNF-alpha was elevated (a pro-inflammatory cytokine) and IL-4 and IL-10 (anti-inflammatory cytokines) were reduced, consistent with the pattern just reported [8].

Neuroinflammation has been associated with alterations of the brain. As one research group has noted, hypothalamic-pituitary-adrenal axis activity leads to inflammation in prefrontal and limbic structures [12]. Neurolipids, as they relate to neuroinflammation, have been implicated for their influence on various neural activities, for example, neurotransmission.

Other changes in the brain have involved **reduced gray matter volume**. In a review of 11 studies on adults with anxiety disorders, gray matter volume reduction was significantly correlated with anxiety severity scores [13]. In a systematic review and meta-analysis on a larger group of studies (N=24 studies, 906 patients with anxiety disorders and 1000 healthy controls), lower gray matter volume was particularly noted in the insula, which is overactivated in those with anxiety disorders [14]. Further impairment in brain function has been related to the **decreased connection between** the two hemispheres of the brain noted in adults with anxiety disorders (n=34) [15].

Interventions for Anxiety Disorders

Most of the recent literature on anxiety disorders has been focused on interventions. The interventions can be categorized

as psychological, physical and pharmacological interventions. Cognitive behavioral therapy (CBT) and the Internet delivery of CBT have been the most popular psychological interventions. The physical interventions have included a few alternative therapies including acupuncture, coloring and exercise. The pharmacological interventions have included cannabidiol, ketamine, and oxytocin.

Table 3: Interventions for anxiety disorders (and first authors).

Interventions	First authors
<u>Psychological Interventions</u>	
Cognitive behavioral therapy	Strand, Popa, VanDis
Internet cognitive behavioral therapy	Ritola, Basile, VanLoenen, Dogsn, Domhardt
Metacognitive therapy	Kennair
Dialectical behavior therapy	Afshari
Interpretation training	Hirsch
<u>Physical Interventions</u>	
Coloring therapy	Samuel
Acupuncture	Li
Exercise	Herring, Gordon
<u>Pharmacological Interventions</u>	
Escitalopram, ketamine, oxytocin	Fagan
Cannabidiol	Shelley

Psychological Interventions

In the **metacognitive model** of anxiety disorders, interpersonal problems are common in individuals with anxiety disorders [16]. Meta-worry, which is worry about worry, is uniquely related to interpersonal problems in this model.

In a study that used **cognitive behavioral therapy** to change cognitive beliefs (N=56 patients with anxiety disorders), the change in cognitive beliefs predicted a reduction in trait worry and trait anxiety [17]. A change in interpersonal problems also predicted a decrease in trait anxiety.

Metacognitive therapy has been compared to cognitive behavior therapy [18]. In this research, individuals with anxiety disorders were assigned to a CBT or a metacognitive therapy group (N= 60 patients). Those who had an anxiety disorder were noted to have high neuroticism and low extroversion and openness personality traits. Both treatments reduced neuroticism and increased extroversion and open-ness, but the metacognitive therapy effects were reputedly greater than those of cognitive behavior therapy. This finding was surprising inasmuch as cognitive behavioral therapy has been the treatment of choice for anxiety disorders and metacognitive therapy is relatively new.

Cognitive behavioral therapy according to some represents the gold standard psychotherapy approach for anxiety disorders [19]. Standard CBT targets worries, dysfunctional beliefs and intolerance of uncertainty. In this study, a group of individuals with anxiety disorders (N= 66) were randomly assigned to a CBT group or an “integrative and multimodal CBT assisted by virtual reality” group. Ten weekly sessions were given on

cognitive restructuring, problem-solving, behavioral exposure and relaxation techniques. Several assessments were given including the Hamilton Anxiety Rating Scale, the Penn State Worry Questionnaire, the Automatic Thoughts Questionnaire, the Dysfunctional Attitudes Scale and the Unconditional Self-Acceptance Questionnaire. Both forms of therapy were effective, but CBT was more effective at reducing anxiety. Decreased anxiety and worry scores were significantly correlated with decreases in dysfunctional cognitive processes.

CBT has also been compared with **dialectical behavior therapy** (DBT) which is based on cognitive behavioral therapy but focuses specifically on mindfulness, distress tolerance, emotion regulation and interpersonal effectiveness [20]. In this research, those with anxiety disorders were randomly assigned to a CBT or a DBT group (N= 72). Depression and anxiety were decreased in the CBT group and executive function was increased in the DBT group.

In one of the only longitudinal studies in this literature entitled “Long-term outcomes of CBT for anxiety - related disorders: a systematic review and meta-analysis”, 69 randomized controlled trials were reviewed (N= 4118 patients) [21]. Even low-quality CBT reduced anxiety disorders at 1 to 6 months, at 6 to 12 months and after 12 months. The relapse rates at 3 to 12 months were extremely low, ranging from 0 to 14%.

Cognitive behavioral therapy (CBT) has also been effectively delivered via internet. For example, CBT was given across 8 to 12 free sessions (N= 894 participants) [22]. Effect sizes were large on changes in the GAD - 7 and the Penn State Worry Questionnaire. Of those with extremely high scores on the GAD - 7, 47% achieved reliable recovery.

In a review on 10 studies on the **remote delivery of CBT** (N= 1071 participants), large effect sizes were noted from pre to post the 12 sessions [23]. In a review on “virtual reality exposure - based CBT” for those with severe anxiety disorders, 16 trials were reviewed (N=817 participants) [24]. A medium effect size was noted for the comparison between the virtual CBT versus the waitlist groups and no differences were noted between the virtual reality CBT group versus a standard CBT group. The absence of differences between these in person and online CBT groups is promising as the latter would be less expensive and available to more individuals who need therapy for anxiety disorders.

Other forms of therapy have also been delivered via the Internet. For example, **interpretation training** was delivered via Internet to reduce worry and anxiety in individuals with anxiety disorders [25]. A cognitive bias modification group was compared to a control group (N =230). The Interpretation training reduced interpretation bias, negative thought intrusions and anxiety symptoms at the completion of the treatment and at a follow-up assessment three months later.

In a review entitled “Science-based mobile apps for reducing anxiety”, 16 experimental studies were entered into a meta-analysis [26]. The results suggested that **mindfulness, cognitive restructuring, and psychoeducation** were effectively delivered via mobile apps.

In still another review on Internet and mobile - based interventions for anxiety disorders, 34 randomized controlled trials were reviewed (N= 3724 participants) [27]. The analysis revealed a large effect suggesting the reduction of the severity of anxiety symptoms.

Physical Interventions

The results of three physical interventions have been reported in this literature including coloring, acupuncture, and exercise. In a study that the authors referred to as **coloring therapy**, coloring sessions (30-120 minutes per session) were given five times a week for three weeks [28]. For this intervention a 32-page coloring book and 24 coloring pencils were provided to 88 patients with anxiety disorders. The patients were randomly assigned to a group that included coloring therapy plus conventional therapy plus anti-anxiety medication plus physical therapy versus a group that only received conventional therapy. Not surprisingly, the group that received multiple therapies including the coloring therapy had reduced anxiety, depression, and negative emotions and an increase in positive emotions. Unfortunately, the coloring therapy results were confounded by being coupled with conventional therapy, anti-anxiety medication and physical therapy.

Acupuncture is another example of a physical intervention that has been effective for anxiety disorders. A systematic review and a meta-analysis were conducted on 27 studies on acupuncture (N=1782 participants) [29]. Lower scores on the Hamilton Anxiety Scale and the Self -Rating Anxiety Scale were noted across the 27 studies.

Exercise effects on anxiety disorders have been noted in three studies in this recent literature. In the first study, a treadmill running group was compared to a group that were seated quietly at rest (N=35) [2]. The treadmill running group reported less state anxiety and feelings of greater energy following the session. The effects were greater for females.

In another study by the same research group, but with a different first author, a group receiving eight weeks of resistance exercise training was compared to a waitlist control group (N=44) [30]. The anxiety disorders were determined by the Psychiatric Diagnostic Screening Questionnaire and the GAD - 7 Scale. The resistance exercise training led to a reduction in anxiety and worry and an increase in strength.

Physical activity has also been noted to decrease anxiety disorder symptoms in a group that was also experiencing social physique anxiety (N=470) [31]. The anxiety symptoms were lower in the Individuals who engaged in more physical activity. An indirect effect of the social physique anxiety accounted for 58% of the effect of physical activity on anxiety disorder symptoms. Apparently, social physique anxiety has been appearing frequently enough in this literature for the creation of a social physique anxiety scale.

The positive effects of these physical interventions may relate to the stimulation of pressure receptors under the skin that then leads to reduced anxiety and stress hormones [32]. Acupuncture and exercise have been noted for these effects. Surprisingly, massage therapy which involves more direct pressure of the

skin receptors has not been explored for its effects on anxiety disorders in this literature.

Pharmacological Interventions

Several pharmacological therapies have been notably effective for reducing anxiety disorders. In a review of the literature, duloxetine, **escitalopram**, **ketamine**, **oxytocin** and agents modulating the orexin, endocannabinoid and immune systems have been notably effective [33].

In another review entitled "Use of **cannabidiol** in anxiety and anxiety - related disorders" eight studies including six randomized controlled trials were reviewed [34]. Cannabidiol medication was well tolerated with minimal adverse effects including fatigue and sedation. The authors of the review suggested that improved clinical outcomes may have derived from decreased cytokines and/or increased activity. The problem is that the doses varied widely from 6 mg to 400 mg per dose across the studies, making the data difficult to interpret or inform pharmacological therapy for anxiety disorders.

In a meta-analysis of 79 randomized controlled trials (11,002 participants with anxiety disorders), **psychological and pharmacological** treatments were compared [35]. Psychotherapy studies had medium to large effect sizes while the medication studies had small effect sizes. The methodological limitation is that the medication studies had placebo controls while very few psychotherapy studies had active controls for reliable group comparisons.

Methodological Limitations of this Literature

This recent literature on anxiety disorders has several methodological limitations that relate to the variety of sampling, measures and data analytic methods used by the different research groups. The samples have varied from being groups of individuals who have been diagnosed with an anxiety disorder to those who have received high scores on various anxiety scales. Those diagnostic and self-report groups have not been compared nor have individuals with different severity levels been compared within those two groups. In addition, some researchers have sampled individuals with a variety of anxiety disorders and others have limited their samples to generalized anxiety disorder. Duration or chronicity of the disorder would presumably have differential effects, but duration and chronicity were typically not measured and longitudinal studies were missing from this recent literature.

Results typically did not vary by demographic factors like age and gender, which was also surprising. Age differences might be expected on the severity of anxiety, but age effects were typically not reported. Although gender differences were noted in a couple studies, gender differences were infrequently reported.

Surprisingly, only a couple studies focused on negative effects of anxiety disorders and only a few studies focused on risk factors. The negative effects included emotional sensitivity and worrying which are characteristics included in the diagnosing of anxiety disorders and also two of the risk factors noted for anxiety disorders, raising the question of directionality. Most of the studies have been cross-sectional rather than longitudinal. As a result, the directionality of the risk factors and negative effects could not be

determined. They are likely bi-directional or reciprocal, but that possibility has rarely been mentioned. The metacognition studies suggest that worry can lead to the diagnosis of anxiety disorder and then meta-worry (worry about worry) exacerbates the anxiety disorder. Surprisingly, depression was rarely mentioned, although it is often comorbid with anxiety disorders.

The research on potential underlying biological mechanisms highlights many physiological and neurological problems including low heart rate variability, abnormal EEG patterns, neuroinflammation and low gray matter volume. These were typically interpreted as causal factors or at least contributory to anxiety disorders. These same problems could also result from anxiety disorders. Again, directionality cannot be determined from the typically cross-sectional studies. Surprisingly, gene studies were not found, as they have been, for example, in the recent literature on the related post-traumatic stress disorder [32].

Many of the intervention studies were systematic reviews and meta-analyses of the most frequently used and reputedly most effective therapies for anxiety disorders. These included meta-analyses of cognitive behavioral therapy studies, internet/mobile app delivered cognitive behavioral therapy and pharmacology studies. The reviews on behavioral therapy studies would have been more informative if they had compared the efficacy of the different specific CBT techniques. In the reviews on pharmacology studies, several different SSRIs and SSNRIs were reportedly effective just as they have been for depression and other affective disorders rather than uniquely effective for anxiety disorders, but that lack of specificity was not mentioned. The comparisons that reported greater effects for CBT than for medications were also surprising. If the underlying mechanisms of anxiety disorders are physiological and neurological, it is not clear how behavioral/psychological therapies would be more effective. Invariably, both the psychological and pharmacological studies measured the change in symptoms of anxiety disorders, not the remission of the disorders which would be the ultimate measure of therapy efficacy.

Conclusion

Despite these methodological limitations, this literature has highlighted the severity of anxiety disorders. The relative absence of recent research on the negative effects and risk factors for anxiety disorders highlights the need for longitudinal studies on individuals experiencing anxiety disorders. Further research on predictors/risk factors would seemingly help identify those who may need therapy. Future research is also needed to specify the relative significance of the predictors/risk factor variables for identifying those who need intervention and the specific intervention techniques that are effective in reducing anxiety disorders.

References

- DeMartini J, Patel G, Fancher TL. Generalized Anxiety Disorder. *Ann Intern Med.* 2019. 170: ITC49-ITC64.
- Herring MP, Monroe DC, Gordon BR, Hallgren M, Campbell MJ. Acute Exercise Effects among Young Adults with Analogue Generalized Anxiety Disorder. *Med Sci Sports Exerc.* 2019. 51: 962-969.
- Szuhany KL, Simon NM. Anxiety Disorders: A Review. *JAMA.* 2022. 328: 2431-2445.
- Cao H, Wu Y, Yin H, Sun Y, Yuan H, et al. Global Trends in the Incidence of Anxiety Disorders From 1990 to 2019: Joinpoint and Age-Period-Cohort Analysis Study. *JMIR Public Health Surveill.* 2024. 10: e49609.
- Rutter LA, Scheuer L, Vahia IV, Forester BP, Smoller JW, et al. Emotion sensitivity and self-reported symptoms of generalized anxiety disorder across the lifespan: A population-based sample approach. *Brain Behav.* 2019. 9: e01282.
- Nordahl H, Vollset T, Hjemdal O. An empirical test of the metacognitive model of generalized anxiety disorder. *Scand J Psychol.* 2023. 64: 263-267.
- Hovenkamp-Hermelink JHM, Jeronimus BF, Myroniuk S, Riese H, Schoevers RA. Predictors of persistence of anxiety disorders across the lifespan: a systematic review. *Lancet Psychiatry.* 2021. 8: 428-443.
- Cheng YC, Su MI, Liu CW, Huang YC, Huang WL. Heart rate variability in patients with anxiety disorders: A systematic review and meta-analysis. *Psychiatry Clin Neurosci.* 2022. 76: 292-302.
- Schoenberg PLA. Linear and Nonlinear EEG-Based Functional Networks in Anxiety Disorders. *Adv Exp Med Biol.* 2020. 1191: 35-59.
- Sarmin N, Roknuzzaman ASM, Sarker R, -Or-Rashid M, Qusar MS, et al. Association of interleukin-2 and interleukin-10 with the pathophysiology and development of generalized anxiety disorder: a case-control study. *BMC Psychiatry.* 2024. 24: 462.
- Mamun-Or-Rashid, Roknuzzaman ASM, Sarker R, Nayem J, Bhuiyan MA, et al. Altered serum interleukin-17A and interleukin-23A levels may be associated with the pathophysiology and development of generalized anxiety disorder. *Sci Rep.* 2024. 14: 15097.
- Won E, Kim YK. Neuroinflammation-Associated Alterations of the Brain as Potential Neural Biomarkers in Anxiety Disorders. *Int J Mol Sci.* 2020. 21: 6546.
- Ou CH, Cheng CS, Lin PL, Lee CL. Grey matter alterations in generalized anxiety disorder: A voxel-wise meta-analysis of voxel-based morphometry studies. *Int J Dev Neurosci.* 2024. 84: 281-292.
- Liu H, Hao Z, Qiu S, Wang Q, Zhan L, et al. Grey matter structural alterations in anxiety disorders: a voxel-based meta-analysis. *Brain Imaging Behav.* 2024. 18: 456-474.
- Mou S, Yan S, Shen S, Shuai Y, Li G, et al. Prolonged Disease Course Leads to Impaired Brain Function in Anxiety Disorder: A Resting State EEG Study. *Neuropsychiatr Dis Treat.* 2024. 20: 1409-1419.
- Nordahl H, Strand ER, Hjemdal O, Nordahl HM. Is meta-worry relevant to interpersonal problems? Testing the metacognitive model of generalized anxiety disorder in an analogue- and a clinical sample of GAD. *Cogn Behav Ther.* 2024. 53: 455-466.
- Strand ER, Hjemdal O, Anyan F, Nordahl H, Nordahl HM. Change in interpersonal problems and metacognitive beliefs as predictors of improvement in patients with generalized anxiety disorder. *Clin Psychol Psychother.* 2023. 30: 842-851.
- Kennair LEO, Solem S, Hagen R, Havnen A, Nysaeter TE, et al. Change in personality traits and facets (Revised NEO Personality Inventory) following metacognitive therapy or cognitive behaviour therapy for generalized anxiety

- disorder: Results from a randomized controlled trial. *Clin Psychol Psychother*. 2021. 28: 872-881.
19. Popa CO, Sava FA, Muresan S, Schenk A, Cojocaru CM, et al. Standard CBT versus integrative and multimodal CBT assisted by virtual-reality for generalized anxiety disorder. *Front Psychol*. 2022. 13: 1008981.
 20. Afshari B, Jafarian Dehkordi F, Asgharnejad Farid AA, Aramfar B, Balagabri Z, et al. Study of the effects of cognitive behavioral therapy versus dialectical behavior therapy on executive function and reduction of symptoms in generalized anxiety disorder. *Trends Psychiatry Psychother*. 2022. 44: e20200156.
 21. van Dis EAM, van Veen SC, Hagenaars MA, Batelaan NM, Bockting CLH, et al. Long-term Outcomes of Cognitive Behavioral Therapy for Anxiety-Related Disorders: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2020. 77: 265-273.
 22. Ritola V, Lipsanen JO, Pihlaja S, Gummerus EM, Stenberg JH, et al. Internet-Delivered Cognitive Behavioral Therapy for Generalized Anxiety Disorder in Nationwide Routine Care: Effectiveness Study. *J Med Internet Res*. 2022. 24: e29384.
 23. Trenoska Basile V, Newton-John T, Wootton BM. Remote cognitive-behavioral therapy for generalized anxiety disorder: A preliminary meta-analysis. *J Clin Psychol*. 2022. 78: 2381-2395.
 24. van Loenen I, Scholten W, Muntingh A, Smit J, Batelaan N. The Effectiveness of Virtual Reality Exposure-Based Cognitive Behavioral Therapy for Severe Anxiety Disorders, Obsessive-Compulsive Disorder, and Posttraumatic Stress Disorder: Meta-analysis. *J Med Internet Res*. 2022. 24: e26736.
 25. Hirsch CR, Krahé C, Whyte J, Krzyzanowski H, Meeten F, et al. Internet-delivered interpretation training reduces worry and anxiety in individuals with generalized anxiety disorder: A randomized controlled experiment. *J Consult Clin Psychol*. 2021. 89: 575-589.
 26. Doğan T, Koçtürk N, Akın E, Kurnaz MF, Öztürk CD, et al. Science-Based Mobile Apps for Reducing Anxiety: A Systematic Review and Meta-Analysis. *Clin Psychol Psychother*. 2024. 31: e3058.
 27. Domhardt M, Geßlein H, von Rezori RE, Baumeister H. Internet- and mobile-based interventions for anxiety disorders: A meta-analytic review of intervention components. *Depress Anxiety*. 2019. 36: 213-224.
 28. Samuel B, Wang H, Shi C, Pan Y, Yu Y, et al. The effects of coloring therapy on patients with generalized anxiety disorder. *Animal Model Exp Med*. 2022. 5: 502-512.
 29. Li M, Liu X, Ye X, Zhuang L. Efficacy of acupuncture for generalized anxiety disorder: A PRISMA-compliant systematic review and meta-analysis. *Medicine (Baltimore)*. 2022. 101: e30076.
 30. Gordon BR, McDowell CP, Lyons M, Herring MP. Resistance exercise training among young adults with analogue generalized anxiety disorder. *J Affect Disord*. 2021. 281: 153-159.
 31. Herring MP, Gordon BR, McDowell CP, Quinn LM, Lyons M. Physical activity and analogue anxiety disorder symptoms and status: Mediating influence of social physique anxiety. *J Affect Disord*. 2021. 282: 511-516.
 32. Tiffany Field. Seasonal Affective Disorder: A Narrative Review. *J Clin Psychol Neurol*. 2024. 2: 1-8.
 33. Fagan HA, Baldwin DS. Pharmacological Treatment of Generalised Anxiety Disorder: Current Practice and Future Directions. *Expert Rev Neurother*. 2023. 23: 535-548.
 34. Skelley JW, Deas CM, Curren Z, Ennis J. Use of cannabidiol in anxiety and anxiety-related disorders. *J Am Pharm Assoc*. 2020. 60: 253-261.
 35. Carl E, Witcraft SM, Kauffman BY, Gillespie EM, Becker ES, et al. Psychological and pharmacological treatments for generalized anxiety disorder (GAD): a meta-analysis of randomized controlled trials. *Cogn Behav Ther*. 2020. 49: 1-21.