



Limited research
supports yoga, exercise,
bibliotherapy, and
dietary supplements



CAM

for your anxious patient: What the evidence says

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The number of people with psychiatric disorders who use complementary and alternative medicine (CAM) is on the rise. In surveys of patients seeking psychiatric care, estimates of CAM use range from 8% to 57%; the most frequent uses are for depression and anxiety disorders. A population-based study in the United States found that 9% of respondents had anxiety attacks and 57% of these individuals had used CAM.¹ Similarly, in a Finnish population-based study (N=5,987) 35% of subjects reported some form of CAM use in the previous year; those with comorbid anxiety and depressive disorders used CAM most frequently.²

Unfortunately, a MEDLINE search shows that the number of studies examining psychotropic medications dwarfs the number of studies on even the most common CAM treatments used for psychiatric disorders. Far more patients with diagnosed mental disorders are studied in trials of standard treatments than CAM treatments. Because very few studies evaluate the cost-effectiveness of CAM treatments for psychiatric disorders, the risk-to-benefit ratio is difficult to calculate. Although several CAM treatments for depressive disorders have enough support to be considered options,³ CAM options for anxiety disorders are fewer and have less evidence of efficacy.

For these reasons, it is hard to recommend any CAM treatment as first line. Despite the relative lack of high quality research on CAM treatment outcomes, high rates of CAM use make it critical for clinicians to understand what treatments are available—or at least which treatments should be favored if patients are intent on trying them. We review the current research for yoga, exercise, bibliotherapy, and the dietary supplements kava and inositol for treating anxiety disorders



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Despite a lack of quality research, some CAM treatments warrant consideration for patients who don't fully respond to SSRIs or benzodiazepines

Table 1

Evidence on the effectiveness of yoga for anxiety disorders

Study	Design	Results
Vahia et al, 1973 ⁷	36 patients with psychoneurosis randomly assigned to yoga (N=15) or a control intervention of relaxation, postures, breathing, and writing (N=12)	Significant difference between groups in TAS scores after but not before treatment. Reduction in mean TAS score for yoga group but not control group
Vahia et al, 1973 ⁸	39 patients received 6 weeks of yoga (N=21) or medication (amitriptyline and chlordiazepoxide on a variable dosage schedule) (N=18)	Yoga showed significantly greater reductions in TAS in this non-randomized sample
Sahasi et al, 1989 ⁹	91 patients randomly assigned to yoga practiced daily for 40 minutes (N=38) or diazepam at unspecified frequency or doses (N=53) for 3 months	Mean reduction in IPAT with yoga (3.39, $P < .05$) vs control group (0.36, $P > .05$). Attrition rate was 21.1% in yoga group and 66% in controls
Sharma et al, 1991 ¹⁰	71 patients with anxiety neurosis randomly assigned to 1-week yoga training, then daily practice (N=41) or control (N=30, placebo capsule)	HAM-A measured at 3 weekly intervals for 12 weeks. Significant between group mean difference at 3 weeks (greater improvement in yoga group compared with controls). Significant improvement in yoga group between 3 and 6 weeks but not for controls
Shannahoff-Khalsa et al, 1999 ¹¹	21 OCD patients randomly assigned to kundalini yoga (N=11) or relaxation and mindfulness meditation (N=10). Multiple outcome measures; Y-BOCS was primary	Seven in each group completed 3 months; patients who practiced yoga demonstrated greater improvements on Y-BOCS. Intent-to-treat analysis (Y-BOCS) for the baseline and 3-month tests showed that only the yoga group improved. Groups were merged for an additional year of yoga; at 15 months, the final group (N=11) improved 71% on the Y-BOCS

HAM-A: Hamilton Anxiety Rating scale; IPAT: Institute for Personality and Ability Testing, Anxiety Scale; OCD: obsessive-compulsive disorder; TAS: Taylor's Anxiety Scale; Y-BOCS: Yale-Brown Obsessive Compulsive Scale

and suggest those that warrant consideration for patients who do not respond, respond partially, or suffer from side effects from selective serotonin reuptake inhibitors (SSRIs) or benzodiazepines.

Limitations of CAM research

There are several limitations to the research literature on CAM approaches for anxiety disorders.⁴ First, there is a wide diversity of practices considered alternative or complementary and various ways in which these methods are applied across cultures. Some authors consider complementary medicines to be only herbal remedies, whereas others include individual therapies such as acupuncture, aromatherapy, herbal therapy, homeopathy, iridology, naturopathy, and reflexology.⁵ This article defines "alterna-

tive" treatments as those other than a form of psychotherapy or an FDA-approved medication that substitute for standard psychiatric treatment, and "complementary" approaches as those used to augment standard psychiatric treatments.

Anxiety and stress are ubiquitous, perhaps motivating interest in CAM options and prompting research on heterogeneous groups of individuals with poorly defined clinical syndromes or with isolated symptoms of anxiety or subjective distress. Few studies examine well-defined patient groups with diagnosed anxiety disorders. There are also multiple research design problems, including poorly specified treatments, poorly chosen placebos, and interpreting nonsignificant differences from established treatments as equivalence in underpowered studies.

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Table 2

Exercise for anxiety: More research is needed

Study	Design	Results
Broocks et al, 1999 ¹⁵	46 patients with panic disorder randomly assigned to 10 weeks of running, clomipramine, or wplacebo pills	Both exercise and clomipramine resulted in significant decreases in symptoms but clomipramine improved symptoms earlier and more effectively
Merom et al, 2008 ¹⁶	21 patients with panic disorder, GAD, or social phobia randomly assigned to GCBT and either a home-based walking program or educational sessions	GCBT plus walking had a significant effect on depression, anxiety, and stress compared with GCBT plus educational sessions
Abrantes et al, 2009 ¹⁷	15 patients with OCD assigned to a 12-week exercise intervention that was added to their standard behavioral and/or pharmacologic treatment	Subjects reported improved mood, anxiety, obsessions, and compulsions after each exercise session

GAD: generalized anxiety disorder; GCBT: group cognitive-behavioral therapy

The CAM treatments reviewed in this article have ≥ 2 randomized controlled trials (RCTs) that support their use for patients with diagnosed anxiety disorders, and ≥ 1 study that shows that the treatment can induce remission.

Yoga

In 2005 Kirkwood et al carried out the first systematic review of research evidence for the effectiveness of yoga in anxiety treatment.⁶ Of 19 studies identified, 4 RCTs and 1 nonrandomized trial met their inclusion criteria, which were an anxiety disorder diagnosis, use of yoga or yoga-based exercises alone, and anxiety rating scales used as outcome measures. Most found significant improvement in anxiety symptoms with yoga compared with placebo. Details of the 5 trials evaluated in Kirkwood's review are summarized in *Table 1 (page 44)*.⁷⁻¹¹

Since the 2005 review, 3 additional studies of yoga and anxiety have been published, but none would meet Kirkwood's inclusion criteria. One that evaluated a heterogeneous group of patients using an intervention with multiple components—only 1 of which was yoga—found the intervention significantly reduced anxiety scores.¹² A second study comparing yoga with relaxation in 131 patients with mild-to-moderate stress but no anxiety disorder diagnosis showed yoga was as effective as relaxation

in improving anxiety symptoms as measured by the anxiety subscale of the State Trait Personality Inventory.¹³ In a study of 183 nonrandomized survivors of the 2004 southeast Asia tsunami with posttraumatic stress disorder (PTSD) symptoms, yoga-based breathing either alone or paired with trauma reduction exposure techniques significantly reduced PTSD symptoms compared with wait-list controls.¹⁴

Conclusion. Few controlled studies evaluated yoga for anxiety disorders, and all have significant methodologic limitations and/or poor methodology reporting. The diagnostic conditions treated and both yoga interventions and control conditions varied. However, these limited results are encouraging, particularly for treatment of obsessive-compulsive disorder (OCD). There is little information regarding safety or contraindications of yoga. Reported attrition rates were high in most studies, which may raise concerns about patient motivation and compliance.

Exercise

The literature examining the relationship between exercise and depression is extensive, but much less has been published about exercise in patients with anxiety disorders (*Table 2*).¹⁵⁻¹⁷ In a 10-week trial, Broocks and colleagues compared clomip-

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Several RCTs found significant improvement in anxiety symptoms with yoga compared with placebo



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Results from small trials suggest exercise may help improve anxiety symptoms

Table 3

Preliminary evidence supports bibliotherapy for select anxiety disorders

Study	Design	Results
Lidren et al, 1994 ¹⁸	36 adults with panic disorder randomly assigned to bibliotherapy, bibliotherapy plus group therapy, or wait-list control	Both bibliotherapy and bibliotherapy plus group therapy were more effective than wait-listing in reducing the frequency of panic attacks and severity of physical panic symptoms
Rapee et al, 2006 ¹⁹	267 children with anxiety disorders randomly assigned to bibliotherapy (parents treating their children in the home with written materials with no therapist contact), 9 sessions of group CBT, or wait-list control	Parent-delivered bibliotherapy was beneficial compared with wait-listing but was not as efficacious as group CBT
Abramowitz et al, 2009 ²⁰	21 patients with mild-to-moderate social phobia underwent an 8-week self-directed CBT program with minimal therapist involvement	Bibliotherapy was superior to wait-listing. One-third of patients experienced clinically significant change

CBT: cognitive-behavioral therapy

ramine, exercise (running), and placebo in 46 outpatients with panic disorder.¹⁵ Both exercise and clomipramine, 112.5 mg/d, significantly reduced panic symptoms compared with placebo, but clomipramine was more effective and faster-acting.

A more recent RCT compared group cognitive-behavioral therapy (GCBT) plus a home-based walking program vs GCBT and in 21 patients with panic disorder, generalized anxiety disorder (GAD), or social phobia.¹⁶ Compared with GCBT plus educational sessions, GCBT plus walking had a significant effect on self-reported depression, anxiety, and stress. Results differed by diagnosis; the most marked effects occurred in individuals with social phobia, whereas benefits for those with panic disorder or GAD were questionable.

Fifteen patients with OCD were recruited to participate in a 12-week, moderate-intensity aerobic exercise program added to their standard behavioral and/or pharmacologic treatment.¹⁷ Subjects demonstrated improvement in negative mood, anxiety, obsessions, and compulsions after each exercise session. Changes after each session persisted over the 12-week intervention, although the magnitude attenuated over the duration of the intervention.

Conclusion. Although initial results from small trials suggest exercise may help improve anxiety symptoms, further studies

are needed to determine how to best use exercise training to treat anxious patients, specifically regarding dose-response relationship, differences in effectiveness between aerobic and resistance training, and the mechanisms by which exercise improves psychiatric symptoms.

Bibliotherapy

Investigation of bibliotherapy for treatment of anxiety disorders has been limited (*Table 3*).¹⁸⁻²⁰ A 2009 RCT demonstrated that for 21 patients with mild-to-moderate social phobia, bibliotherapy—in the form of an 8-week self-directed CBT program with minimal therapist involvement—was superior to a wait-list control and induced clinically significant change in approximately one-third of patients.²⁰

Rapee et al randomly assigned 267 children age 6 to 12 with anxiety disorders to bibliotherapy that consisted of parents treating their children in the home with written materials, 9 sessions of GCBT, or a wait-list control condition.¹⁹ Bibliotherapy provided by parents demonstrated benefit compared with wait-listing but was not as efficacious as GCBT at post-treatment and 3-month follow-up.

Lidren and colleagues randomly assigned 36 adult patients with panic disorder to bibliotherapy, group therapy combined with bibliotherapy, or a wait-

Table 4

Dietary supplements for anxiety disorders

Study	Design	Results
Kava		
Pittler et al, 2003 ²²	Meta-analysis of 11 RCTs with a total of 645 GAD patients	Compared with placebo, kava significantly reduced anxiety as measured by total HAM-A score
Witte et al, 2005 ²³	Meta-analysis of 6 RCTs using kava extract WS1490 in patients with nonpsychotic anxiety disorders	Kava reduced HAM-A score more than placebo and seemed to be more effective in women and younger adults
Sarris et al, 2009 ²⁴	60 adults with ≥ 1 month of elevated generalized anxiety randomly assigned to an aqueous extract of kava	Aqueous-extract kava was significantly more effective than placebo in reducing HAM-A score
Inositol		
Benjamin et al, 1995 ²⁵	21 patients with panic disorder with or without agoraphobia randomly assigned to inositol, 12 g/d, or placebo	Inositol significantly reduced frequency and severity of panic attacks and severity of agoraphobia compared with placebo
Fux et al, 1996 ²⁶	13 OCD patients randomly assigned to inositol, 18 g/d, or placebo for 6 weeks	Patients taking inositol had significantly lower Y-BOCS scores compared with those receiving placebo
Fux et al, 1999 ²⁷	10 OCD patients receiving an SSRI randomly assigned to augmentation with inositol, 18 g/d, or placebo for 6 weeks	No significant differences between treatments
Palatnik et al, 2001 ²⁸	In a crossover trial, 20 panic disorder patients completed 1 month of inositol, up to 18 g/d, and 1 month of fluvoxamine, up to 150 mg/d	Improvements in HAM-A, CGI, and agoraphobia scores were similar for both treatments
<small>CGI: Clinical Global Impression scale; GAD: generalized anxiety disorder; HAM-A: Hamilton Anxiety Rating scale; OCD: obsessive-compulsive disorder; RCTs: randomized controlled trials; SSRI: selective serotonin reuptake inhibitor; Y-BOCS: Yale-Brown Obsessive Compulsive Scale</small>		

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Preliminary evidence supports bibliotherapy for social anxiety disorder, childhood anxiety disorders, and panic disorder

list.¹⁸ Both treatments were more effective than wait-listing in reducing the frequency of panic attacks, severity of physical panic symptoms, catastrophic cognitions, agoraphobic avoidance, and depression. Both interventions maintained their effects at 3- and 6-month follow-up and produced clinically significant change in most patients.

Conclusion. Some preliminary evidence supports the effectiveness of bibliotherapy for social anxiety disorder, childhood anxiety disorders, and panic disorder.

Dietary supplements

Many dietary and herbal supplements are purported to have therapeutic efficacy for anxiety symptoms. Because of inadequate FDA regulation of manufacturing and marketing of these agents, most of these supplements have not been tested on pa-

tients with anxiety disorders.²¹ Limited evidence supports the use of kava for GAD and inositol for panic disorder (**Table 4**).²²⁻²⁸

Kava. Multiple double-blind RCTs found kava (*Piper methysticum*)—a plant indigenous to South Pacific islands—has effects greater than placebo and comparable to standard treatments for mild to moderately severe GAD. A Cochrane meta-analysis²² of 11 trials with 645 participants concluded that kava is effective for reducing GAD symptoms, with risks comparable to standard treatments for up to 6 months of use.

Case reports of kava-associated liver toxicity led to a marketing ban in Canada in 2000, followed shortly by Germany, Australia, and the United Kingdom. In 2002 the FDA issued a Consumer Advisory²⁹ discouraging kava use. Since then a flurry of research has looked for sources of possible toxicity, including individual

sensitivities,²⁹ excessive dosing, use of toxic parts of the kava plant instead of the roots,^{30,31} interactions with other hepatotoxic substances, and non-water based extraction methods. RCTs demonstrating kava's efficacy and safety were characterized by careful dosing supervision, use of standardized kava extracts, and avoidance of interactions with other hepatotoxic medications or CAM treatments. Doses ≤ 300 mg/d are recommended.²²

RCTs that used the standardized acetone extract WS1490²³ found that women and younger adults show more positive effects from kava, and showed no liver toxicity when used for 1 to 24 weeks. A recent RCT that used kava extracts obtained via water-based methods showed kava had significant anxiolytic effects.²⁴ However, a study of liver toxicity reports found that water-based extractions, acetic extractions, and ethanol extractions all have been associated with toxic hepatic reactions.³² Aqueous extraction does not guarantee safety, and the extraction solvent does not cause toxicity. A recent report of a severe liver reaction to the native drink by a tourist in Samoa³³ suggests that aqueous extractions from the root stock—the type of kava used by South Pacific islanders—also can be unsafe.

Conclusion. Multiple RCTs have found kava relatively safe and effective for treating anxiety symptoms. Caution is necessary, however, because of reports of liver toxicity associated with its use. Physician oversight and monitoring of kava use are appropriate.

Inositol. Evidence from RCTs suggests inositol, a natural isomer of glucose and a precursor in the phosphatidylinositol cycle, can significantly improve panic disorder symptoms.²⁵⁻²⁸ In 1 trial, efficacy and side effects were comparable to fluvoxamine.²⁸ Effective doses ranged from 12 g/d to 18 g/d. Researchers tested inositol as monotherapy or augmentation to SSRIs for patients with mild-to-moderate OCD. In small double-blind crossover RCTs, inositol monotherapy significantly reduced Yale-Brown Obsessive Compulsive Scale scores compared with placebo²⁶ but inositol augmentation added nothing to the effects of SSRIs.²⁷

Related Resources

- National Center for Complementary and Alternative Medicine. <http://nccam.nih.gov>.
- The Journal of Alternative and Complementary Medicine. www.liebertonline.com/loi/acm.
- MedlinePlus: Complementary and Alternative Medicine. www.nlm.nih.gov/medlineplus/complementaryandalternativemedicine.html.

Drug Brand Names

Amitriptyline • Elavil	Diazepam • Valium
Chlordiazepoxide • Librium	Fluvoxamine • Luvox
Clomipramine • Anafranil	

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.

Conclusion. Inositol appears to be effective in improving symptoms of panic disorder. Its use for other anxiety disorders is unproven.

Supervision is recommended

The evidence base for most CAM interventions commonly used for anxiety is relatively poor and recent systematic reviews found few methodologically rigorous studies. This has not, however, diminished CAM treatments' popularity. Despite a paucity of high-quality studies regarding CAM for anxiety disorders, there is enough data supporting yoga, exercise, bibliotherapy, kava, and inositol to allow psychiatrists to collaborate with patients who wish to try these treatments. Advise patients that they may need physician supervision similar to that used with standard psychiatric treatments.

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Multiple RCTs show kava is effective for treating anxiety but case reports of liver toxicity warrant concern



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Evidence from RCTs shows inositol is effective for panic disorder but its use for other anxiety disorders is unproven

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Bottom Line

Yoga, exercise, and bibliotherapy have shown positive effects in patients with anxiety disorders, although not as strong as standard pharmacologic and psychotherapeutic approaches. Advise patients who wish to try complementary and alternative medicine for anxiety to do so with physician supervision.