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**FILE: ■ Complementary and Alternative Medicine  
■ Anxiety Disorders**

**HC 110566-333**

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**RE: Complementary and Alternative Medicine Self-treatment in Anxiety Disorders;  
Kava Appears to be the Best Botanical Treatment**

Jorm AF, Christensen H, Griffiths KM, Parslow RA, Rodgers B, Blewitt KA. Effectiveness of complementary and self-help treatments for anxiety disorders. *Med J Aust.* October 4, 2004;181(7 Suppl):S29-S46.

Anxiety disorders are one of the most common types of mental disorders. Many people use complementary and self-help treatments to alleviate anxiety. The public needs to be informed about which treatments are effective and which have not been adequately evaluated. The purpose of this review article is to provide guidance to general practitioners. The authors define complementary treatment as one that is not generally upheld by Western countries and self-help is defined as a treatment that can be used without consulting a health professional.

The authors searched clinical practice guidelines, brochures, books, review articles, and websites and located 108 types of complementary and self-help treatments. Next they searched electronic databases (such as PubMed) for evidence of the use of the treatments for anxiety. They searched databases through the year 2003 (the study was published in 2004). The evidence was evaluated using the National Health and Medical Research Council (NHMRC) levels of evidence. NHMRC rates the evidence on four levels (I-IV) with level I: evidence from systematic review of all randomized controlled trials, level II: evidence from at least one properly designed randomized controlled trial, level III-1: evidence from well-designed randomized controlled trials, level III-2: evidence from comparative studies with concurrent controls, level III-3: evidence from comparative studies with historical controls, level IV: evidence from case-series, and level V: (added by the authors) no or minimal evidence. For at least 70 of the treatments there was no evidence in the medical literature. The authors claim to have excluded clinical trials using undiagnosed subjects with "anxiety symptoms" yet they did in fact include these trials in some cases. An obvious weakness in the design was the failure to account for preclinical or animal studies that suggest anxiolytic effects. This would have been a much more appropriate "Level V".

*Medicines and homeopathic remedies*

Bach flower remedies: Dilute tinctures of flowers produced by Dr. Bach. Level of evidence II. The authors conclude that Bach flower remedies are not an effective treatment for test anxiety. There was no evidence regarding efficacy for other anxiety disorders.

Berocca: Berocca<sup>®</sup> (Bayer Healthcare) is a multivitamin preparation containing vitamin B complex, vitamin C, calcium, and magnesium. Level of evidence II. The authors conclude that there is no current evidence for an effect of Berocca on anxiety disorders.

Ginger (*Zingiber officinale*): Level of evidence: V. The authors conclude that there is no reliable evidence supporting the efficacy of ginger for treating anxiety disorders.

Gotu kola (*Centella asiatica*): Level of evidence: V. The authors conclude that there is no evidence supporting the use of gotu kola for anxiety. (Note: the authors have reported one randomized clinical trial with gotu kola as an "animal study". This is interesting since no "animal studies" were included in the search criteria.)

Inositol: Level of evidence: II. The authors conclude that there is some evidence that inositol is effective for treating panic disorder and obsessive-compulsive disorder. Longer-term studies are needed to make firm conclusions. There are several positive controlled clinical trials with inositol, so their conclusions are puzzling.

Kava (*Piper methysticum*): Level of evidence: I. A Cochrane review of 11 randomized controlled trials concluded that kava is superior to placebo for treating generalized anxiety. The authors warn against liver toxicity and add that long-term safety data is needed.

Abafado: Abafado is a tea made from dried leaves of lemongrass leaves (*Cymbopogon citratus*). Level of evidence: II. Abafado does not have acute anxiolytic properties, according to the authors.

Licorice (*Glycyrrhiza glabra*): Level of evidence: IV. The authors conclude that there is no good quality evidence showing that licorice is effective in reducing anxiety.

Magnesium: Level of evidence: II. The authors conclude that there is little evidence that demonstrates that magnesium is effective for anxiety.

Passionflower (*Passiflora incarnata*): Level of evidence: II. A small trial showed passionflower was as effective as an anxiolytic when compared with oxazepam. However, there is no evidence using a placebo control. The authors conclude that there is not enough evidence to draw any conclusion.

St. John's wort (SJW, *Hypericum perforatum*): Level of evidence: IV. There are no randomized controlled studies in anxiety. There is only weak, uncontrolled evidence supporting the efficacy of SJW for anxiety, according to the authors.

Valerian (*Valeriana officinalis*): Level of evidence: II. The authors conclude that there is little evidence regarding the treatment of anxiety disorders with valerian.

Vitamin C (ascorbic acid): Level of evidence: V. There is only one study and it is a case study of obsessive-compulsive disorder. The authors conclude that there is insufficient evidence to evaluate the effects of ascorbic acid on anxiety.

5-hydroxy-L-tryptophan (5-HTP): Level of evidence: II. The authors conclude that there is evidence that 5-HTP might be effective for treating anxiety disorders. They state that until the risk of eosinophilia-myalgia syndrome is clarified, 5-HTP should not be recommended for anxiety.

Homeopathy: Homeopathy uses highly dilute concentrations so that the molecules of the substance may not be detectable. Level of evidence: II. The authors conclude that there is no convincing evidence that homeopathy is effective for anxiety.

### *Physical Treatments*

Acupuncture: Level of evidence: II. The authors conclude that there is promising evidence that acupuncture can reduce symptoms of anxiety in patients with anxiety neuroses.

Aromatherapy: Level of evidence: II. The authors conclude that there is no evidence that aromatherapy is an effective treatment for anxiety. However, it may be beneficial for patients in a hospital.

Hydrotherapy: Level of evidence: II. The authors conclude that there is very little evidence in support of hydrotherapy for anxiety.

Massage/touch therapy: Level of evidence: II. The authors conclude that there is some evidence that massage is effective for alleviating post-traumatic stress in children. The efficacy in adults or for treating other anxiety disorders is limited.

### *Lifestyle*

Autogenic training: Autogenic training is a self-relaxation procedure where the patient concentrates on body perceptions (i.e., warmth, weight, breathing). Level of evidence: I. The authors conclude that there is some evidence that autogenic training is effective and other evidence that it is not effective. Additional research is needed.

Bibliotherapy: Bibliotherapy uses material to help the person solve problems relevant to their needs. Level of evidence: I. The authors conclude that bibliotherapy may be effective for reducing symptoms of anxiety associated with specific phobias. Additional research is needed to determine which self-help tools are most effective.

Dance and movement therapy: Level of evidence: II. The authors conclude that there is evidence that structured movement therapy may be helpful in reducing test anxiety and in people with self-identified anxiety or in group therapy. Conventional dance classes may be more effective than physical exercise—this finding requires additional research.

Exercise: Level of evidence: I. The authors conclude that there is strong evidence that exercise is effective for mild to moderate anxiety, but studies are needed to determine its effects on specific anxiety syndromes. Exercise is a highly promising treatment for anxiety.

Humor: Level of evidence: V. The authors conclude that there is some evidence that humor can work in a laboratory setting, there is no evidence that it works in anxiety disorders.

Meditation: Level of evidence: II. The authors conclude that meditation may be effective for high trait anxiety and generalized anxiety disorder. Its effectiveness has not been established in treating other forms of anxiety.

Music: Level of evidence: II. Music has only been evaluated in people with high levels of anxiety symptoms, not in people diagnosed with anxiety disorders.

Prayer: Level of evidence: II. As of 2003, there was no evidence to support prayer alone as a treatment of anxiety.

Relaxation: Relaxation therapy involves a series of techniques to elicit the relaxation response. Level of evidence: I or II. The authors conclude that relaxation is an effective therapy for dental phobia, test anxiety, panic disorder, and generalized anxiety disorder. There is no strong evidence that validated exposure-based or efficacious drug treatments are more effective than relaxation. Relaxation may be less effective than other behavioral treatments for small-animal and specific phobias, social phobia, post-traumatic stress disorder, and obsessive-compulsive disorder.

Yoga: Level of evidence: II. There are no well-conducted studies so it cannot be determined if yoga is effective.

#### *Dietary Changes*

Alcohol: Level of evidence: II. There is some evidence that alcohol has a short-term anxiety-reducing effect. For people with alcohol-use disorders, eliminating alcohol may be an effective way of reducing anxiety.

Caffeine reduction: Level of evidence for caffeine reduction: IV. Level of evidence for caffeine challenges: II. The authors conclude that there is some evidence that caffeine increases anxiety levels and precipitates panic attacks in people with anxiety disorders. Long-term, well-designed randomized controlled trials are needed.

Carbohydrate-rich, protein-poor diet: Level of evidence: V. The authors conclude additional research is needed.

Nicotine avoidance: Level of evidence: V. As of 2003, there was no evidence that abstinence from nicotine benefits people with anxiety disorders.

Of the treatments described above, those with the best evidence of effectiveness are: kava for generalized anxiety; exercise for generalized anxiety; relaxation training for generalized anxiety, panic disorder, dental phobia, and test anxiety; and bibliotherapy for specific phobias.

Note: This paper did not receive a proper peer review, since critical errors were found. The most egregious was not using their own criteria for selecting trials to include. These results should be taken with a large grain of salt. The loose usage of evidence categories, where each level includes a wide variety of appropriate and inappropriate clinical trials is really not meaningful.

—Heather S. Oliff, PhD

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# Effectiveness of complementary and self-help treatments for anxiety disorders

Anthony F Jorm, Helen Christensen, Kathleen M Griffiths, Ruth A Parslow, Bryan Rodgers and Kelly A Blewitt

Anxiety disorders are among the most common mental disorders. They are estimated to affect 7% of men and 12% of women in Australia each year.<sup>1</sup> Anxiety disorders are also a major cause of disability: they account for around 2.7 million person-days out of role per month among Australian adults<sup>1</sup> and 6.5% of disability in the total population.<sup>2</sup>

In psychiatric classification systems, categorically distinct types of anxiety disorders are distinguished, such as panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder and phobias. However, these anxiety disorders often occur together, and there is substantial comorbidity with depression and substance-use disorders.<sup>1</sup> While a categorical view of anxiety disorders may be useful for clinicians, community studies show a continuous dimension of anxiety severity, which is highly correlated with a dimension of depression severity.<sup>3</sup> Disability increases as people move along this continuum.

There are effective medications and cognitive-behaviour treatments for anxiety disorders.<sup>4</sup> However, only a fifth of people with anxiety as their principal complaint are estimated to have consulted a health professional in the previous 12 months.<sup>5</sup> Furthermore, only half of these people received an intervention known to be effective for anxiety disorders.<sup>5</sup> One reason people with anxiety disorders commonly give for not seeking professional help is that they prefer to manage the condition themselves.<sup>5</sup> Indeed, people with a high level of anxiety and depression symptoms more commonly report using self-help methods than professional help.<sup>6</sup>

Australians also commonly use complementary therapies: an estimated 52% of Australian adults used complementary medicines in the year 2000, and 23% consulted complementary practitioners. These percentages have increased since 1993.<sup>7</sup> Although we do not know how much of this use is for anxiety disorders, many of the complementary medicines available are marketed for "stress" or anxiety.

Given their frequent use, complementary and self-help treatments warrant the same level of evaluation as conventional treatments. The public needs to be informed about which treatments are effective, which are not, and which have not been adequately evaluated. General practitioners can play an important role in providing guidance. The purpose of our review is to provide GPs with an overview of the evidence on complementary

## ABSTRACT

**Objectives:** To review the evidence for the effectiveness of complementary and self-help treatments for anxiety disorders.

**Data sources:** Systematic literature search using PubMed, PsycLit, and the Cochrane Library.

**Data synthesis:** 108 treatments were identified and grouped under the categories of medicines and homoeopathic remedies, physical treatments, lifestyle, and dietary changes. We give a description of the 34 treatments (for which evidence was found in the literature searched), the rationale behind the treatments, a review of studies on effectiveness, and the level of evidence for the effectiveness studies.

**Conclusions:** The treatments with the best evidence of effectiveness are kava (for generalised anxiety), exercise (for generalised anxiety), relaxation training (for generalised anxiety, panic disorder, dental phobia and test anxiety) and bibliotherapy (for specific phobias). There is more limited evidence to support the effectiveness of acupuncture, music, autogenic training and meditation for generalised anxiety; for inositol in the treatment of panic disorder and obsessive-compulsive disorder; and for alcohol avoidance by people with alcohol-use disorders to reduce a range of anxiety disorders.

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and self-help treatments for anxiety disorders. We have previously reviewed the evidence on such treatments for depression.<sup>8</sup>

We distinguish between complementary treatment and self-help treatment:

- a complementary treatment is one involving practices and beliefs that are not generally upheld by the dominant health system in Western countries; and
- a self-help treatment is one that can be used by the public without necessarily consulting a health professional.
- While some self-help treatments are also complementary, others would be accepted by many practitioners in the dominant health system (eg, bibliotherapy, exercise). Each treatment is reviewed for its effectiveness in reducing generalised anxiety disorder or high levels of anxiety symptoms, as well as specific anxiety disorders (phobias, panic disorder/agoraphobia, obsessive-compulsive disorder, acute stress disorder, post-traumatic stress disorder).

## METHODS

Our searches of the following sources identified 108 types of complementary and self-help treatments:

- clinical practice guidelines;<sup>4,9-19</sup>
- brochures from health food shops;
- books and review articles on the topic;<sup>20-24</sup> and
- key web sites — the top eight search engines, as rated by *searchenginewatch*, were used to compile a list of the top 20 Internet sites for each of the key search terms (given below),

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**1 Modified\* National Health and Medical Research Council (NHMRC) levels of evidence**

Level	Description
I	Evidence obtained from a systematic review of all relevant randomised controlled trials.
II	Evidence obtained from at least one properly designed randomised controlled trial.
III-1	Evidence obtained from well-designed pseudorandomised controlled trials (alternate allocation or some other method).
III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a parallel control group.
III-3	Evidence obtained from comparative studies with historical control, two or more single-arm studies, or interrupted time series without a parallel control group.
IV	Evidence obtained from case-series, either post-test or pre-test/post-test.
V	No evidence, minimal evidence such as testimonials, single case studies, controlled studies of non-clinical samples only.

\* The NHMRC evidence levels have been modified by adding a Level V to include even weaker types of evidence.

resulting in a list of about 110 sites, which were browsed to identify treatment recommendations.

Once the treatments were identified, PubMed, PsycLit and the Cochrane Library were searched using the following terms: name of treatment AND (anxiety OR panic OR phobic OR phobia OR agoraphobia OR post traumatic stress OR posttraumatic stress OR acute stress OR obsessive compulsive). The list of treatment terms used in the searches is available on request. The medical literature was searched up to 2 December 2002 for the earliest searches and 29 April 2003 for the latest ones. Articles were included if they reported treatment of individuals selected as having an anxiety disorder or a high level of anxiety symptoms. Articles on anxiety in normal samples were excluded. Occasionally, articles on anxiety symptoms in non-clinical samples (not selected for anxiety disorder or a high level of symptoms) are mentioned in the reviews below if they form an important part of the literature. However, they were not used in rating the effectiveness of treatments.

The evidence was evaluated using the National Health and Medical Research Council (NHMRC) levels of evidence modified by adding a Level V, as shown in Box 1.<sup>25</sup> We added a Level V to allow for even weaker types of evidence. It should be noted that these levels relate to the quality of the evidence, not the effectiveness of the intervention. A treatment could have been evaluated by rigorous methodologies and found to be ineffective or, conversely, evaluated by weaker methodologies, but found to be highly effective.

**RESULTS**

Treatments have been grouped under the following categories: medicines and homoeopathic remedies, physical treatments, lifestyle, and dietary changes. Most of the evidence relates to general-

ised anxiety disorder or high levels of anxiety symptoms, but when there is evidence relating to other anxiety disorders we flag this for each treatment. Information on safety is provided if available, but for many treatments there was none. For many treatments identified as being used for anxiety disorders, no evidence was found in the literature search. These treatments are listed in Box 2.

**Medicines and homoeopathic remedies**

**Bach flower remedies**

*Description:* Highly dilute tinctures of flowers are produced by adding particular flowers to spring water and preserving with alcohol.

*Rationale:* The Bach flower remedies are said to operate by transmitting energy from the flowers to the tincture.

*Level of evidence:* II.

*Review of effectiveness:* There have been two randomised double-blind, placebo-controlled studies of the effect of these remedies on test anxiety. In the first study, students who reported test anxiety were either administered the Bach "rescue remedy" or a placebo.<sup>26</sup> There was no consistent pattern to suggest that the rescue remedy reduced anxiety levels more than the placebo. The second study was a partial cross-over trial in which students were administered a mixture of 10 Bach flower remedies (impatiens, mimulus, gentian, chestnut bud, rock rose, larch, cherry plum, white chestnut, scleranthus and elm) or placebo.<sup>27</sup> There was no difference in anxiety reduction between the treatment and placebo groups.

*Conclusion:* Bach flower remedies do not appear to be an effective treatment for test anxiety. There is no evidence regarding the efficacy of these remedies for other anxiety disorders.

**Berocca**

*Description:* Berocca is a multivitamin preparation produced by Roche containing vitamin B complex, vitamin C, calcium and magnesium.

*Rationale:* This vitamin and mineral supplement may have stress-reducing effects.

*Level of evidence:* Level II.

*Review of effectiveness:* One randomised controlled trial (RCT) in healthy young adults<sup>28</sup> demonstrated reduced anxiety levels and improved psychological well-being in the intervention group relative to the group taking placebo, but there are no trials of individuals with high levels of anxiety or anxiety disorders.

*Conclusion:* There is no current evidence for an effect of Berocca on anxiety disorders.

**Ginger (Zingiber officinale)**

*Description:* A herbal remedy derived from a root and taken as tea or drink, or used as a tincture, in crystallised or tablet form.

*Rationale:* A traditional treatment for anxiety, it is now thought that ginger might reduce anxiety through antagonistic effects of its constituents (eg, gingerols) at the 5-HT<sub>3</sub> receptor.<sup>29</sup>

*Level of evidence:* V.

*Review of effectiveness:* There are no studies of ginger administered alone for anxiety. Administration of *kampo* (ie, traditional Japanese) herbal preparations containing ginger was associated with reduced anxiety levels in four patients diagnosed as suffering from panic attacks with agoraphobia.<sup>30</sup> However, given the methodological limitations of case studies, and that the contribution of ginger

2 Treatments identified as being used for anxiety, but for which no evidence was found in the literature searched	
Broad category	Treatments with no evidence
Medicines and homoeopathic remedies	American ginseng ( <i>Panax quinquefolius</i> ), ashwaganda ( <i>Withania somnifera</i> ), astragalus ( <i>Astragalus membranaceus</i> ), B vitamins, biotin, black cohosh ( <i>Actaea racemosa</i> and <i>Cimicifuga racemosa</i> ), borage ( <i>Borago officinalis</i> ), brahmi ( <i>Bacopa monniera</i> ), Californian poppy ( <i>Eschscholtzia californica</i> ), cat's claw ( <i>Uncaria tomentosa</i> ), catnip ( <i>Nepeta cataria</i> ), chamomile ( <i>Anthemis nobilis</i> ), chaste tree berry ( <i>Vitex agnus castus</i> ), Chinese medicinal mushrooms (reishi) ( <i>Ganoderma lucidum</i> ), choline, chromium, coenzyme Q10, cowslip ( <i>Primula veris</i> ), damiana ( <i>Turnera aphrodisiaca</i> ), dandelion ( <i>Taraxacum officinale</i> ), flax seeds (linseed) ( <i>Linum usitatissimum</i> ), GABA ( $\gamma$ -aminobutyric acid), ginkgo ( <i>Gingko biloba</i> ), ginseng ( <i>Panax ginseng</i> ), hawthorn ( <i>Crataegus oxyacantha</i> ), hops ( <i>Humulus lupulus</i> ), hyssop ( <i>Hyssopus officinalis</i> ), lecithin, lemon balm ( <i>Melissa officinalis</i> ), L-glutamine, L-tyrosine, melatonin, milk thistle ( <i>Silybum marianum</i> ), mistletoe ( <i>Viscum album</i> ), motherwort ( <i>Leonurus cardiaca</i> ), nettles ( <i>Urtica dioica</i> ), nicotinamide, oats ( <i>Avena sativa</i> ), omega 3 fatty acids, para-aminobenzoic acid (PABA), pantothenic acid, peppermint ( <i>Mentha piperita</i> ), phenylalanine, potassium, rehmannia ( <i>Rehmannia glutinosa</i> ), SAM-e, schizandra ( <i>Schizandra chinensis</i> ), selenium, Siberian ginseng ( <i>Eleutherococcus senticosus</i> ), skullcap ( <i>Scutellaria lateriflora</i> ), spirulina ( <i>Spirulina maxima</i> and <i>S. platensis</i> ), St Ignatius bean ( <i>Ignatia amara</i> ), taurine, tension tamer, tissue salts, vervain ( <i>Verbena officinalis</i> ), wild yam ( <i>Dioscorea villosa</i> ), wood betony ( <i>Stachys officinalis</i> ; <i>Betonica officinalis</i> ), yeast, zinc, zizyphus ( <i>Zizyphus spinosa</i> ).
Lifestyle	Adequate sleep, distraction techniques, marijuana (avoidance), pleasant activities, t'ai chi.
Dietary changes	Avoiding certain foods (barley, rye, wheat, dairy foods), sugar avoidance, ketogenic diet.

to the effects of the preparation is unknown, this study provides little useful information about ginger. It has been suggested that ginger might interact with warfarin to increase bleeding time,<sup>31</sup> but a recent systematic review failed to confirm this potential interaction.<sup>32</sup>

**Conclusion:** There is no scientifically reliable evidence as to the efficacy of ginger in the treatment of anxiety disorders.

**Gotu kola (Centella asiatica)**

**Description:** A traditional multipurpose herbal remedy used for anxiety and administered in the form of capsules, teas and tinctures.

**Rationale:** The constituents of gotu kola bind to cholecystokinin (CCK) receptors, which have been implicated in panic anxiety.<sup>33</sup> The herb may also affect anxiety through the GABA ( $\gamma$ -aminobutyric acid) system.<sup>33</sup> Gotu kola has been reported to decrease anxiety indicators (eg, acoustic startle response) in animals.<sup>33</sup>

**Level of evidence:** V.

**Review of effectiveness:** There are no published studies of the effectiveness of gotu kola in the treatment of human anxiety disorders or symptoms of elevated anxiety. However, there is one study of the effect of gotu kola on anxiety symptoms in healthy participants. This small randomised double-blind, placebo-controlled study (n=20 per group) showed no change in self-rated anxiety half an hour to 2 hours after the administration of gotu kola, but acoustic startle response was attenuated at 60 and 90 minutes. The trial focused on the period immediately after a single administration of a large dose of gotu kola and did not use a standard measure of anxiety.

**Conclusion:** There is no evidence that gotu kola is useful for patients with anxiety disorders.

**Combined preparations**

**Description:** We defined combined preparations as mixtures containing a number of substances, including herbs. Combined preparations claiming to reduce anxiety include the Chinese medicine suanzaorentang, Worry Free (Maharishi Ayurvedic Prod-

ucts International, Colorado Springs, USA), Sedariston (a combination of St John's wort and valerian), and euphytose, a preparation commonly used in France.

**Rationale:** Claims of efficacy are based on traditional practice.

**Level of evidence:** II.

**Review of effectiveness:** Suanzaorentang has been tested in a time-series design in which a placebo was alternated with the herbal preparation in 30 individuals with reported high anxiety scores.<sup>34</sup> Anxiety scores decreased significantly after the week of active treatment and returned to previous high levels when taking the placebo. Worry Free has been tested in a pilot RCT in individuals with generalised anxiety disorder.<sup>35</sup> Ten patients were randomised to either Worry Free or placebo. After the 3-month trial period, those in the herbal preparation group had reduced symptoms and fewer had a diagnosis of anxiety disorder. Sedariston was compared with diazepam in a double-blind RCT of 100 outpatients with moderately severe anxiety disorders.<sup>36</sup> After 2 weeks, the group treated with Sedariston showed significantly larger decrements in trait anxiety scores than the group treated with diazepam. The effectiveness of euphytose has been tested on 182 outpatients with acute anxiety reactions, who were randomly assigned to euphytose or to placebo.<sup>37</sup> After 28 days, those taking euphytose had significantly reduced anxiety levels. It was well tolerated, and there were no differences in adverse events between the placebo and euphytose groups. However, it is thought that euphytose may potentiate an interaction effect with digoxin.<sup>31</sup>

**Conclusion:** There are too few studies to recommend the use of herbal preparations for treating anxiety. Suanzaorentang may be effective in anxiety, but it has not been evaluated in clinical groups or in RCTs. The pilot RCT of Worry Free produced good outcomes, but the number in each group was very small and the findings would need to be replicated. The one trial of Sedariston found that, compared with diazepam, it produced a greater reduction in anxiety. Euphytose may be effective in acute anxiety reactions, although its use in other anxiety disorders has not been evaluated.

### Homoeopathy

*Description:* Homoeopathy uses preparations with highly dilute concentrations of a substance so that the molecules of the substance are not detectable.

*Rationale:* Homoeopathy assumes that symptoms reflect the body's attempt to heal itself. It is assumed that a substance that makes a well person ill with a particular set of symptoms will, in highly diluted form, promote recovery in an ill person who is suffering from the same set of symptoms.<sup>38</sup> Many theories have been proposed as to how homoeopathy might act on the body, including explanations based on quantum physics and information theory.<sup>39</sup> However, the precise mechanism is unknown.

*Level of evidence:* II.

*Review of effectiveness:* There have been two randomised double-blind, placebo-controlled studies of the effect of homoeopathy on anxiety. One study of primary care patients in whom either homoeopathy or a placebo was substituted for benzodiazepines reported no difference in anxiety between the homoeopathic-treated and placebo groups.<sup>40</sup> Another study of students with above-average anxiety levels reported less sleep loss but similar anxiety levels among a homoeopathic-treated group compared with a placebo group.<sup>41</sup> However, given the multiple statistical comparisons involved, the positive result may have been achieved by chance.

*Conclusion:* There is no convincing evidence that homoeopathy is effective in treating anxiety.

### Inositol

*Description:* Inositol is an isomer of glucose. Large amounts are present in the human body. It occurs in the normal human diet, with around 1 g/day being consumed.

*Rationale:* Inositol is involved in the phosphatidylinositol cycle, a second messenger system used by some serotonin and noradrenalin receptors.<sup>42</sup>

*Level of evidence:* II.

*Review of effectiveness:* There have been five randomised double-blind trials of inositol at doses of 12–18 g/day. In panic disorder, inositol was found to be superior to placebo<sup>43</sup> and as effective as fluvoxamine.<sup>44</sup> In obsessive-compulsive disorder, it was found to be superior to placebo,<sup>45</sup> but did not augment the effects of selective serotonin reuptake inhibitors (SSRIs).<sup>46</sup> In post-traumatic stress disorder, however, inositol did not differ from placebo.<sup>47</sup> The size of these studies was small (13–21 patients) and treatment duration was short (4–6 weeks). In all studies, side effects were minimal.

*Conclusion:* There is some evidence for the effectiveness of inositol in treating panic disorder and obsessive-compulsive disorder. However, larger longer-term trials are needed.

### Kava (*Piper methysticum*)

*Description:* The kava plant is a member of the pepper family. The root of the plant is used traditionally by Pacific Islanders to make a beverage that has social, ceremonial and medicinal uses. In Western countries, medicines containing kava extracts are marketed for the treatment of anxiety.

*Rationale:* The active ingredients, known as kava lactones, affect a range of neurotransmitter systems. Kava lactones are associated with the modulation of serotonergic and glutamatergic systems,

dopamine antagonism, and enhancement of the binding capacity of GABA receptors.<sup>48</sup>

*Level of evidence:* I.

*Review of effectiveness:* A Cochrane review of 11 RCTs concluded that kava is superior to placebo for treating generalised anxiety.<sup>49</sup> Adverse events reported in these trials were mild, transient and infrequent. Kava is also non-addictive at therapeutic doses.<sup>50</sup> However, there have been reports of rare cases of liver failure in people taking high doses.<sup>50</sup> This has prompted authorities in some countries to take action — ranging from warnings to consumers to removing kava products from the market. The Australian Therapeutic Goods Administration has issued a voluntary recall of kava products, and consumers have been advised to discontinue use (for further information see <[www.tga.health.gov.au/cm/kavafs0402.htm](http://www.tga.health.gov.au/cm/kavafs0402.htm)>).

*Conclusion:* Despite evidence of effectiveness of kava in treating general anxiety, rare cases of liver toxicity have led to advice against its use. Further data on its long-term safety are needed.

### Lemongrass leaves (*Cymbopogon citratus*)

*Description:* Abafado is a herbal tea prepared from the dried leaves of lemongrass. It is used in Brazil.

*Rationale:* Lemongrass is believed to contain ingredients that reduce anxiety.

*Level of evidence:* II.

*Review of effectiveness:* One RCT of 18 individuals with high trait anxiety has been completed.<sup>51</sup> Participants were provided with abafado or placebo, under double-blind conditions. Effects were observed 30 minutes later under mildly stressful conditions (the administration of a cognitive test). No differences in state anxiety scores were reported between the two groups.

*Conclusion:* Lemongrass in this form does not appear to have acute anxiolytic properties.

### Licorice (*Glycyrrhiza glabra*)

*Description:* Licorice is extracted from the roots of this plant.

*Rationale:* Licorice contains compounds that inhibit monoamine oxidase.<sup>52</sup>

*Level of evidence:* IV.

*Review of effectiveness:* The only evidence is from a small number of case studies claiming effectiveness.<sup>53</sup> Licorice should be used with caution, as excessive use can lead to hypertension, oedema and, in pregnancy, preterm birth.<sup>54,55</sup>

*Conclusion:* There is no good quality evidence supporting licorice as effective in reducing anxiety.

### Magnesium

*Description:* Magnesium supplements are available as tablets or an oral solution.

*Rationale:* It has been proposed that stress in people suffering from mental disorders can lead to marginal magnesium deficiency, which exacerbates symptoms such as anxiety.<sup>56</sup>

*Level of evidence:* II.

*Review of effectiveness:* There have been no RCTs comparing magnesium with placebo in anxiety disorders. However, one RCT examined the effects of combining magnesium supplements with an anxiolytic medication over 10 days in women with mixed anxiety and depression.<sup>57</sup> Those receiving the anxiolytics plus



magnesium showed more rapid reduction in anxiety than a group receiving anxiolytics plus placebo.

**Conclusion:** There is little evidence at present on whether magnesium supplements are effective.

#### **Passionflower (*Passiflora incarnata*)**

**Description:** Passionflower is a plant native to North America. It is sold as a powder, a capsule, tablet or drops, and marketed as a treatment for sleep disorders, nervous tension and anxiety.

**Rationale:** Passionflower is a traditional remedy to treat anxiety. It is not known which constituents have sedative effects.<sup>58</sup>

**Level of evidence:** II.

**Review of effectiveness:** A double-blind RCT in 32 outpatients with generalised anxiety disorder compared treatments of 45 drops of passionflower and 30 mg of oxazepam per day.<sup>59</sup> Four days after the trial began, there were no significant differences between the two treatments. Those taking passionflower reported fewer side effects than those taking oxazepam. There are no trials comparing passionflower with placebo.

**Conclusion:** While a small trial showed passionflower to be as effective as an anxiolytic, there is no evidence using placebo controls. From the evidence available it is not possible to say whether passionflower helps in the treatment of anxiety disorders.

#### **St John's wort (*Hypericum perforatum*)**

**Description:** St John's wort is a herb available as tablets, capsules or drops from supermarkets and health food shops.

**Rationale:** St John's wort is a traditional herbal remedy in Europe. Its mode of action is not fully understood, but it appears to inhibit the synaptic reuptake of serotonin, norepinephrine and dopamine.<sup>60</sup>

**Level of evidence:** IV.

**Review of effectiveness:** While there is evidence supporting St John's wort as effective for depression,<sup>8</sup> there are no RCTs in patients with anxiety disorders. The only evidence comes from an uncontrolled trial of patients with obsessive-compulsive disorder<sup>61</sup> and case reports of patients with generalised anxiety disorder.<sup>62</sup> The Therapeutic Goods Administration has warned that St John's wort may interact with a number of prescription medicines, leading to a loss of their therapeutic effect. Medicines affected include HIV protease inhibitors, HIV non-nucleoside reverse transcriptase inhibitors, cyclosporin, tacrolimus, warfarin, digoxin, theophylline, anticonvulsants, oral contraceptives, SSRIs and related drugs, and triptans. An information sheet for healthcare professionals is available at <[www.tga.gov.au/docs/html/info.htm](http://www.tga.gov.au/docs/html/info.htm)>.

**Conclusion:** There is only weak, uncontrolled evidence for the efficacy of St John's wort for treating anxiety disorders.

#### **Valerian (*Valeriana officinalis*)**

**Description:** The dried root of the valerian plant is a traditional herbal remedy, particularly in Hispanic cultures. Extracts are also available that contain some of the many ingredients. There are many species (probably over 200) of valerian, but the one most commonly used is *Valeriana officinalis*.

**Rationale:** Valerian is primarily used to treat sleep problems, but is also reported to have sedative properties. Many ingredients could contribute to this, including monoterpenes and sesquiterpenes, iridoids, alkaloids and amino acids.<sup>63</sup> Possible mechanisms include effects on the GABA system.

**Level of evidence:** II.

**Review of effectiveness:** One double-blind RCT allocated outpatients with generalised anxiety disorder to treatment with diazepam (2.5–7.5 mg/day), valerian (50–150 mg valerian extract per day) and placebo with 12 participants in each group.<sup>64</sup> Patients with comorbid anxiety and depressive disorders were excluded. All three groups showed significant decrements in rated and self-reported anxiety over the 4-week duration of the trial, but there were no significant differences between the three groups. The small number of participants and the relatively low doses of both diazepam and valerian extract were important limitations of the study. While the study had negative results, there is a report of valerian reducing psychic strain and feelings of somatic arousal in healthy subjects under stressful conditions, suggesting that further investigation is justified.<sup>65</sup> Valerian appears to have few side effects. There is one case report of an overdose,<sup>66</sup> and one report of a possible hazardous interaction with fluoxetine.<sup>67</sup> The reported hepatotoxicity may be due to other substances used in combination with valerian.<sup>68</sup> Some warnings have been given that valerian should not be used during pregnancy or lactation, and there have been more general recommendations not to use preparations based on Mexican (*Valeriana edulis*) or Indian (*Valeriana wallichii*) valerian.<sup>69</sup>

**Conclusion:** There is little evidence regarding the treatment of anxiety disorders with valerian.

#### **Vitamin C (ascorbic acid)**

**Description of treatment:** Vitamin C is a water-soluble vitamin that is important in the formation of collagen and the absorption of iron.

**Rationale:** Ascorbic acid is said to modulate catecholaminergic activity and decrease stress reactions.

**Level of evidence:** V.

**Review of effectiveness:** The only evidence is from a case study in which vitamin C was used to treat obsessive-compulsive disorder.<sup>70</sup>

**Conclusion:** There is insufficient evidence to evaluate the effects of ascorbic acid on anxiety symptoms.

#### **5-hydroxy-L-tryptophan (5-HTP)**

**Description:** This amino acid is naturally produced by the body and also available as a dietary supplement extracted from the plant *Griffonia simplicifolia*.

**Rationale:** A dysfunctional serotonergic system has been implicated in the development of some anxiety disorders. Since 5-HTP is the precursor of serotonin, treatment with 5-HTP could increase the level of serotonin production.

**Level of evidence:** II.

**Review of effectiveness:** One randomised, 8-week, double-blind, placebo-controlled trial compared the effect of 5-HTP (plus carbidopa), clomipramine and placebo in psychiatric outpatients with anxiety disorders without depression.<sup>71,72</sup> The anxiety disorders included generalised anxiety disorder, agoraphobia and/or panic disorder, and obsessive-compulsive disorder. Compared with placebo, 5-HTP reduced anxiety levels. However, five participants dropped out due to increased anxiety, and results were only reported for those who completed the study.<sup>72</sup> Another controlled study provided evidence that 5-HTP might prevent panic attacks. A double-blind placebo-controlled study of patients with panic disorder, challenged with CO<sub>2</sub> to induce anxiety, reported that

patients who had previously received a dose of 5-HTP developed fewer panic and anxiety symptoms than patients who had received placebo.<sup>73</sup> There have also been two small, open, uncontrolled studies of 5-HTP with long-standing anxiety disorders. In the first, nine of 10 patients with anxiety disorder (generalised anxiety disorder, or agoraphobia and/or panic disorder) showed improvement with the introduction of 5-HTP and carbidopa.<sup>74</sup> In the second study, five treatment-refractory patients with obsessive-compulsive disorder showed no reduction in obsessive-compulsive symptoms after an SSRI and pindolol were augmented with 5-HTP. The further addition of carbidopa to increase the uptake of 5-HTP in the brain created unacceptable side effects.<sup>75</sup> Elsewhere, it has been noted that 5-HTP should not be taken with SSRIs or monoamine oxidase inhibitors (MAOIs).<sup>76</sup> 5-HTP has also been found to contain contaminants associated with the eosinophilia-myalgia syndrome,<sup>77</sup> and the US Food and Drug Administration (2001) has raised concerns about the safety of "uncontaminated" 5-HTP in individuals who may be susceptible to eosinophilia-myalgia syndrome.<sup>78</sup>

*Conclusion:* There is some evidence that 5-HTP might be effective in the treatment of anxiety disorders. However, until the risk of the eosinophilia-myalgia syndrome is clarified, 5-HTP cannot be recommended as a treatment for anxiety.

## Physical treatments

### Acupuncture

*Description:* Acupuncture is performed by stimulating designated points of the body through the insertion of needles, finger pressure, application of heat, or a combination of these treatments.

*Rationale:* According to traditional Chinese medicine, there is a network of energy (chi) that flows through the body in different channels. Any imbalance in this flow of energy creates a disease process, and acupuncture can correct such imbalances.

*Level of evidence:* II.

*Conclusion:* There is promising evidence that acupuncture can effectively reduce symptoms of anxiety in individuals with anxiety neuroses.

*Review of effectiveness:* One RCT has been conducted in which three groups, each comprising 80 individuals with confirmed anxiety neuroses, were treated with acupuncture only, behavioural desensitisation (including insight and supportive psychotherapy) only, or a combination of these treatments.<sup>79</sup> Those who received a combination of acupuncture and desensitisation showed significantly higher cure rates (52%) than those given either acupuncture only (20%) or desensitisation only (26%). For 60 of the 240 subjects followed up 1 year after treatment, the cure rates were 48%, 22% and 18%, respectively. Other studies reporting benefits of acupuncture have included only small numbers of patients receiving this treatment (fewer than 20).

### Aromatherapy

*Description:* Aromatherapy involves exposure to the fragrances of essential oils from plants to promote healing. It is often delivered through skin massage or by means of a vaporiser.

*Rationale:* It is thought that aromas facilitate relaxation and exert a calming effect.

*Level of evidence:* II.

*Review of effectiveness:* There are no controlled studies of the effect of aromatherapy on patients with a clinical diagnosis of anxiety. One RCT of aromatherapy in men with speech anxiety found no difference in the anxiety reduction of men treated with aromatherapy and men in a control group.<sup>80</sup> A systematic review of RCTs of aromatherapy delivered through massage found that the intervention resulted in significantly lower anxiety levels than a control intervention in hospitalised cancer, cardiac and intensive care patients.<sup>81</sup> However, participants were not specifically selected for anxiety, the reduction in anxiety was reported to be transient, and the trials contained methodological flaws.<sup>81</sup>

*Conclusion:* There is currently no evidence that aromatherapy is an effective treatment for anxiety disorders. However, it may provide short-term relief of anxiety symptoms in medical patients in hospital settings.

### Hydrotherapy

*Description:* Hydrotherapy typically involves immersion in warm (close to body temperature) moving water.

*Rationale:* Hydrotherapy assists physical relaxation, but the exact mechanism for influencing anxiety is unknown.

*Level of evidence:* IV.

*Review of effectiveness:* One study of 14 patients with a range of anxiety disorders found a significant decrease in subjective anxiety and electromyograph readings from the frontalis muscles after 15 minutes of hydrotherapy with four water jets in a 38°C hot tub.<sup>82</sup> No attempt was made to determine how lasting these changes were.

*Conclusion:* There is very little evidence for the effectiveness of hydrotherapy in treating anxiety disorders.

### Massage/touch therapy

*Description:* Massage involves the smooth manual rubbing of muscle and other soft tissue, especially the back, shoulders and neck, usually by a trained masseuse or physiotherapist.

*Rationale:* Massage reduces cortisol, and possibly catecholamine, levels, although the precise mechanism behind this is not fully understood. Touch, itself, may be important, the therapy may promote a sense of being cared for, and physiological effects (eg, on vagal activity and on electroencephalogram recordings) may also be involved.<sup>83,84</sup>

*Level of evidence:* II.

*Review of effectiveness:* One RCT of 60 children referred for signs of post-traumatic stress (in the aftermath of a hurricane) compared the effects of eight 30-minute sessions of back massage over a 1-month period with the effect of a similar number of control sessions of watching relaxing video movies.<sup>85</sup> Over the eight sessions, massage therapy was superior on several measures of anxiety. Other trials have examined effectiveness at reducing anxiety levels in other adolescent and adult patient groups (eg, with depression, bulimia and physical illnesses) and in non-patient samples.<sup>83,86-89</sup>

*Conclusion:* There is some evidence that massage is effective in alleviating post-traumatic stress in children, but there is only very limited evidence for its effectiveness in adults or for treating other disorders. More studies of groups with anxiety disorders are warranted.

## Lifestyle

### Autogenic training

*Description:* Autogenic training is a self-relaxation procedure based on passive concentration on bodily perceptions (eg, heaviness and warmth of arms, legs and abdomen; rhythm of breathing and heartbeat).

*Level of evidence:* I.

*Review of effectiveness:* A meta-analysis of clinical outcome studies of autogenic training identified seven controlled studies that assessed the effectiveness of this treatment in reducing anxiety.<sup>90</sup> Three studies found that, compared with control groups, autogenic training significantly reduced anxiety for individuals with a diagnosed anxiety disorder, and those who described themselves as being anxious or having high levels of stress. One study found that student nurses given autogenic training for 6 weeks to reduce their risk of stress took significantly fewer days off compared with a control group. Two other studies found that autogenic training alone or autogenic training with other treatments had no significant effect on individuals' levels of test anxiety. The remaining study found that study participants who experienced "tension" reported that their levels of tension reduced by similar amounts after receiving no treatment, after receiving autogenic training only, or after receiving autogenic training and other treatments.

*Conclusion:* There is some evidence that autogenic training reduces levels of stress and anxiety symptoms. However, findings concerning autogenic training are mixed and further research needs to be undertaken.

### Bibliotherapy

*Description:* Bibliotherapy is the use of written materials or computer programs, or listening to or viewing audiotapes or videotapes, for the purpose of gaining understanding or solving problems relevant to a person's developmental or therapeutic needs.

*Level of evidence:* I.

*Review of effectiveness:* A number of meta-analyses of the effectiveness of bibliotherapy in treating anxiety have been undertaken, the most recent being in 2003.<sup>91-94</sup> In these studies, bibliotherapy has been found to be most effective in reducing anxiety when the problem is circumscribed in its nature (eg, specific phobias), and when the individual is highly motivated to undertake treatment.<sup>94</sup> Bibliotherapy, by itself, had little effect on symptoms of panic disorder or obsessive-compulsive disorder.<sup>94</sup> Also, for most of these studies, the materials used were developed specifically for the research. The effectiveness of the many self-help materials that can be obtained by individuals in the community remains untested.

*Conclusion:* Bibliotherapy is most likely to reduce symptoms of anxiety associated with specific phobias. Further research is needed to determine which types of self-help tools are most effective and the conditions under which they are effective.

### Dance and movement therapy

*Description:* Dance and movement therapies embrace a diverse range of treatments and activities, including professional help by trained therapists through to self-help forms of dance and movement. The therapy may be directly concerned with the individual's psychological problems or may take a form that has no overt link

to these problems. In some instances (eg, aerobic dance), dance is a medium for physical exercise (this is dealt with in the section on exercise (see page S36).

*Rationale:* Theories of movement therapy emphasise the importance of mind-body integration; the influence of physical movement on cognition, emotions and other behaviour; and the development of self-efficacy. Additional features include promotion of communication with others and reduction of feelings of isolation, although these are more relevant to treatment in residential settings.<sup>95</sup>

*Level of evidence:* II.

*Review of effectiveness:* A small trial with severely disabled psychiatric outpatients (who had a variety of unreported diagnoses) compared changes in six patients who received movement therapy over 16 weeks with those in four control patients. Both groups also received medication and group therapy. Patients in the experimental group showed a significantly greater decrease in muscular tension and trait anxiety measures, but not in state anxiety. The report does not describe the method of allocating patients to the experimental and control groups.<sup>96</sup> A second trial, using randomised allocation, evaluated short-term changes in anxiety and depression after a single session of dance therapy for groups of hospitalised psychiatric patients ( $n = 20$ ) and individuals drawn from the neighbourhood community ( $n = 20$ ). The experimental groups (10 subjects in each) showed significantly greater decrements in anxiety and depression scores than the control group over the 1-hour period. The degree of change between the patient and community participants was not significantly different.<sup>97</sup> A further RCT of volunteer students with self-identified problems of test anxiety found that four 35-minute movement sessions over 2 consecutive weeks led to a significantly greater reduction in total scores for the Test Attitude Inventory in the experimental group ( $n = 11$ ) compared with the control group ( $n = 10$ ).<sup>98</sup> The sessions were described as "quasi-educational in nature, with a cognitive/behavioural and psychoeducational emphasis", and the content specifically addressed test anxiety. There are also five case reports of the effectiveness of Dosa therapy (a Japanese form of movement therapy) in reducing anxiety levels in female graduate students with anxiety problems.<sup>99</sup> Short- and long-term changes in anxiety associated with dance therapy and dance classes have also been studied in groups unselected for anxiety levels or disorders. One report found significantly greater reductions in questionnaire measures of anxiety in student psychiatric nurses who received a single session of dance therapy compared with those in the control group. This applied in one study in which 17 students were randomly allocated to dance therapy or to no intervention, and also in a second study in which 46 students were randomly allocated to dance therapy or verbal therapy.<sup>100</sup> An observational study of student classes in colleges of further education found a significant decrement of almost 1 SD in state anxiety scores over a term of study for 23 modern dance students.<sup>101</sup> The change was greater than that found for students in sport, music and mathematics classes (all non-significant).

*Conclusion:* There is some evidence that structured movement therapy is helpful in reducing test anxiety, and it may also be helpful for managing other anxiety problems in clinical groups and in people with self-identified anxiety. The suggestion that conventional dance classes may alleviate state anxiety (more so than other physical exercise) is worthy of further study.

**Exercise**

*Description:* Exercise is physical activity, which may be aerobic (eg, running), with the aim of increasing cardiovascular fitness and stamina, or anaerobic (involving weight training), with the aim of increasing strength and endurance.

*Rationale:* Possible mechanisms include that exercise acts as a buffer for stress; that exercise engages the same processes as those elicited by meditation; that exercise might act to put people with agoraphobia into unsafe environments, and thereby offer "exposure therapy"; or that exercise might produce more monoamine neurotransmitters, which may reduce anxiety.<sup>102</sup> Some authors have suggested that exercise is potentially more likely to be effective for some anxiety conditions, such as generalised anxiety disorder and panic disorder, but not for others, such as phobias and post-traumatic stress disorder (given that these conditions are associated with responses to specific situation cues or experiences).<sup>103</sup> It has also been suggested that there may be multiple and synergistic causes of exercise's effectiveness, given that exercise affects biological and psychological processes.

*Level of evidence:* I.

*Review of effectiveness:* There have been numerous meta-analyses of the effect of exercise on anxiety symptoms. However, only two have examined the effects of exercise on individuals with elevated anxiety levels. In one meta-analysis of 104 studies, there were 11 that yielded data on trait anxiety for individuals who had been specifically identified as highly anxious.<sup>104</sup> The mean effect size from these comparisons was 0.47 SD units, indicating that, relative to results in comparison groups, exercise was associated with a moderate reduction in anxiety. The second meta-analysis examined the effect of aerobic and non-aerobic physical exercise on symptoms of anxiety and depression.<sup>105</sup> Individual controlled and randomised controlled trials were included if groups had anxiety scores above the 50th percentile. The latter meta-analysis identified 11 studies that compared an exercise group with a control group of patients waiting for treatment (wait-list controls) and revealed an effect size of 0.94. Within these comparisons, seven studies included individuals with a formal anxiety diagnosis, while the remainder consisted of individuals with higher than average anxiety. Studies of individuals with a diagnosis were associated with an effect size of 0.99, and those undiagnosed with an effect size of 0.85. The major limitation of this meta-analysis from our perspective is the inclusion of individuals with mild to moderate anxiety (50th percentile or above) who did not meet anxiety diagnostic criteria, and the lack of outcome data for different types of anxiety disorders. Moreover, of the studies with "a strictly defined group of participants with diagnoses of anxiety disorders", there were none that compared the effect of exercise with a placebo control or with the effect of psychotherapy or medication.

However, outcomes for specific types of anxiety conditions have been reported for generalised anxiety disorder and high trait anxiety, with two controlled trials indicating aerobic exercise to be superior to strength and mobility exercises,<sup>106</sup> and a 6-week jogging intervention to be as effective as cognitive behaviour therapy and more effective than no treatment.<sup>107</sup> For panic disorder, Broocks et al compared a 10-week running program with either treatment with clomipramine or with a placebo.<sup>108</sup> At the end of the intervention, both active treatments were more effective than placebo, but clomipramine had an earlier effect, a stronger effect on three of the five outcome measures, and was associated with a lower drop-out rate (zero, compared with 31% for the

exercise group). Panic disorder has been reported to respond to both aerobic and non-aerobic interventions.<sup>109</sup> Finally, Manger examined the performance of 26 volunteers who met criteria for post-traumatic stress disorder.<sup>110</sup> The intervention was 6–10 weeks of treadmill exercise for 30 minutes, two to three times a week. Only nine subjects remained after the intervention. Despite methodological problems, the authors suggested that the effects of exercise on post-traumatic stress disorder were promising.

*Conclusion:* Exercise has demonstrated strong effects for mild to moderate anxiety, but further studies are required to determine its effects on specific anxiety conditions. There is one trial that shows exercise to be as effective in the longer term as standard use of highly effective anti-anxiety medication (clomipramine) in panic disorder. Clearly, there is a need to investigate the potentially strong therapeutic effects of exercise on specific anxiety conditions, and further RCTs are required. Exercise is a highly promising treatment for anxiety.

**Humour**

*Description:* Humour allows us to see as amusing or ridiculous aspects of both everyday life and the unusual events that confront us.

*Rationale:* Laughter is claimed to be beneficial to the autonomic system. It can also provide a physical release for accumulated tension, and hence may moderate the effects of stressful life events on physical and psychological feelings.

*Level of evidence:* V.

*Review of effectiveness:* There have been a number of RCTs, all with undergraduate students, that have tested the effects of humour on symptoms of anxiety. Students treated for arachnophobia with either systematic desensitisation or humour-based desensitisation reported the same degree of reduction in their phobia. However, humour alone was not used in this study.<sup>111</sup> Others have examined the effects of humour on healthy students placed in anxiety-provoking situations. One such study found that having a sense of humour reduces the likelihood that experiences of stress will cause anxiety, but this occurred in men only.<sup>112</sup> In another trial, students who expected that they would soon experience an unpleasant event showed fewer signs of stress when they listened to a humorous tape while waiting compared with those who listened to a non-humorous tape or no tape.<sup>113,114</sup> Similarly, those with a good sense of humour showed fewer symptoms of stress in such circumstances compared with those with a poor sense of humour.<sup>113</sup>

*Conclusion:* There is some indication that humour can reduce anxiety in undergraduate students in laboratory settings. However, there is no evidence on the use of humour in anxiety disorders.

**Meditation**

*Description:* Meditation involves focusing the mind on an object or word combined with a passive attitude and a comfortable physical position.

*Rationale:* Meditation is believed to produce a state of relaxation that is incompatible with feelings of anxiety to induce a "trance state" that elicits positive mood and/or to provide a period of "rest".

*Level of evidence:* II.

*Review of effectiveness:* Five RCTs have examined the effect of meditation in generalised anxiety disorder or high trait anxiety.

Four of the five trials found that meditation produced equivalent effects to other forms of relaxation, including applied relaxation, progressive muscular relaxation and biofeedback,<sup>115-118</sup> and these effects were superior compared with those in a control group (wait-list controls) but not superior to "sitting meditation".<sup>116,118</sup> By contrast, another study reported no difference between meditation, relaxation, an "anti-relaxation" control and no treatment control.<sup>119</sup> Another trial compared meditation to relaxation, skills acquisition and practice-only for test anxiety and found that meditation was more effective than practice-only, but less effective on test performance than skills acquisition.<sup>120</sup> Shannahoff-Khalsa reported that a yogic meditation technique (based on kundalini yoga) was more effective than a standard relaxation procedure in the treatment of obsessive-compulsive disorder.<sup>121</sup> There have also been case studies of the effects of meditation on dental fear.<sup>122,123</sup>

**Conclusion:** Meditation may be an effective intervention for high trait anxiety and generalised anxiety disorder. Its effectiveness in treating other forms of anxiety disorder has not been established.

### Music

**Description:** Music is widely used by the public for reducing anxiety, but also by music therapists, who may combine it with other therapeutic elements.

**Rationale:** Music is a traditional intervention.

**Level of evidence:** II.

**Conclusion:** There is some evidence to support the anxiety-reducing effects of music. However, music has only been evaluated in people with high levels of anxiety symptoms, not with diagnosed anxiety disorders.

**Review of effectiveness:** There have been three RCTs comparing music interventions with no treatment in people with high levels of anxiety symptoms. One study involved a single session and produced no improvement;<sup>124</sup> another involved three sessions and produced improvement at the end of treatment that was not maintained 6 months later;<sup>125</sup> the third trial involved 10 sessions and produced an improvement which was maintained 2 months later.<sup>126</sup> Music has also been shown to have the same degree of anxiety-reducing effect as muscle relaxation<sup>127</sup> and to boost the effect of a brief cognitive reframing intervention.<sup>128</sup>

### Prayer

**Description:** Prayer can be used to promote healing of oneself or of someone else (intercessory prayer). It can also be used as an adjunct to psychotherapy.

**Rationale:** Prayer has traditionally been used in time of illness and is often used by the public to help in coping with mental health problems.

**Level of evidence:** II.

**Review of effectiveness:** There have been no controlled trials of either personal or intercessory prayer in anxiety disorders. However, there has been one RCT adding a religious component, including prayer, to standard treatment for generalised anxiety disorder in religious patients.<sup>129</sup> This trial found that including a religious component produced greater improvement after 3 months' treatment, but no difference after 6 months.

**Conclusion:** There is currently no evidence to support prayer alone as a treatment for anxiety disorders.

### Relaxation

**Description:** Relaxation therapy involves a family of techniques to elicit the relaxation response.<sup>130</sup> A variety of types are distinguished, including progressive relaxation, release-only relaxation, cue-controlled relaxation, differential relaxation, rapid relaxation and applied relaxation. Progressive relaxation, probably the most common form, teaches individuals to systematically identify and relax specific muscle groups.

**Rationale:** Relaxation induces a state that is incompatible with the physiological and psychological arousal associated with anxiety. Relaxation teaches individuals to recognise symptoms of anxiety and respond to them with a technique that reduces arousal.

**Level of evidence:** I or II.

**Review of effectiveness**

**Generalised anxiety disorder and high trait anxiety:** A meta-analysis reported relaxation to be superior by an average of 0.60 SD units relative to non-active interventions (for example, waitlist control).<sup>131</sup> We identified 26 controlled trials<sup>116-118,127,132-153</sup> in which relaxation was found to be generally superior to the control conditions, and to be as effective as a range of psychological treatments, including cognitive behaviour therapy, meditation, autogenic training and biofeedback. Anxiety management<sup>136</sup> and muscle stretching<sup>139</sup> were reported to be superior in one study each.

**Panic disorder and agoraphobia:** A meta-analysis identified relaxation to be as effective as non-active interventions, with an effect size of about 0.58.<sup>154</sup> Drug treatments were compared in two studies. These indicated an effect size of 0.22 in favour of the drug treatments. Five studies compared relaxation with other forms of behavioural therapy, including exposure therapy. These yielded an effect size of 0.08 in favour of behavioural therapies. These findings are consistent with our review of 11 controlled trials of relaxation therapy.<sup>155-165</sup> In four, with a wait-list control group or placebo control, relaxation was better; relaxation was as effective as behavioural interventions, such as cognitive behaviour therapy or cognitive therapy (as effective in four of five studies, less effective in one), it was more effective than paradoxical intention (one study), as effective or almost as effective as exposure-based therapies in the short term (five studies, with one finding it was not as effective),<sup>157</sup> and roughly equivalent to drug treatments (two studies).

**Post-traumatic stress disorder:** A meta-analysis of treatments for post-traumatic stress disorder identified one study in which relaxation (effect size, 0.45) was inferior to behavioural therapies for this disorder (effect size, 1.27).<sup>166</sup> Our review of six studies<sup>167-172</sup> indicated that, although relaxation may be superior to no intervention (wait-list controls), it appears to be less effective than cognitive restructuring, social skills training, exposure therapy and combined treatments.

**Obsessive-compulsive disorder:** There have been four trials of relaxation therapies in obsessive-compulsive disorder.<sup>173-176</sup> One involved students diagnosed with obsessive-compulsive disorder.<sup>173</sup> Relaxation was found to be inferior to behavioural therapy and in-vivo exposure therapy, respectively.<sup>174,175</sup> Greist et al reported that relaxation was inferior to both computer-assisted and clinician-assisted behaviour therapy.<sup>176</sup>

**Social phobia:** There have been two studies of social phobia.<sup>177,178</sup> In one study with a wait-list control group, relaxation was reported to be superior; it was as effective as self-instructional training,<sup>178</sup>

and less effective than social skills training.<sup>177</sup> These studies yielded a combined pre–post effect size of 0.51 (95% CI, 0.45–0.57), which was of smaller magnitude than effect sizes reported for benzodiazepines and SSRIs (effect sizes, 1.5) in a meta-analysis reported by Fedoroff and Taylor.<sup>179</sup>

**Dental phobia:** Five controlled trials have identified that relaxation is as effective as other behavioural and drug interventions in dental phobia.<sup>180-184</sup>

**Small-animal phobia and specific phobias:** Seven trials have indicated that, for snake or spider phobias, there is little evidence that relaxation is more effective than control, but that exposure-based therapies are effective.<sup>185-191</sup> One study has indicated that both relaxation and stress inoculation treatment (a technique involving the reconstruction of negative thoughts while physically present in the feared situation) produce pre–post change in people with fear of flying. For claustrophobia, Ost et al reported that both applied relaxation and exposure produced change.<sup>192</sup> Two studies of blood phobia indicated that applied relaxation provided a slight advantage which did not persist at follow-up.<sup>193,194</sup>

**Speech anxiety:** Of eight RCTs, three (using wait-list controls or placebo) found relaxation to be more effective than, and three found it to be as effective as, other behavioural therapies such as biofeedback, systematic desensitisation, and speech practice.<sup>195-202</sup> Rational emotive therapy has been found to be more effective,<sup>197</sup> but relaxation has been found to be superior to aromatherapy.<sup>200</sup>

**Test anxiety:** Of 29 RCTs, those using wait-list controls or other controls found that relaxation is more effective, and the rest found it to be as effective as other behavioural therapies for test anxiety, such as systematic desensitisation, rational emotive therapy, biofeedback, rehearsal and skills acquisition, and meditation.<sup>203-231</sup>

**Conclusion:** Relaxation is an effective therapy for dental phobia, test anxiety, panic disorder and generalised anxiety disorder. In particular, there is no strong evidence to indicate that validated exposure-based or efficacious drug treatments are more effective than relaxation. However, although relaxation lowers symptoms relative to those in wait-list controls, it may be less effective than other behavioural treatments for small-animal and specific phobias, social phobia, post-traumatic stress disorder and obsessive-compulsive disorder.

## Yoga

**Description:** Yoga includes exercises for attaining bodily and mental control and wellbeing.

**Rationale:** Yoga is often used for relief of stress and anxiety.

**Level of evidence:** II.

**Review of effectiveness:** One study showed that yoga was superior to diazepam for generalised anxiety, but patients were assigned to yoga treatment based on preference rather than random assignment.<sup>232</sup> In another randomised trial, test anxiety was treated with a set of yoga exercises combined with one of the following — autosuggestion, progressive muscle relaxation or a control talking session.<sup>227</sup> Yoga treatment was found to be superior to both relaxation and control treatments on one outcome measure, but not on another. However, the results were not fully described and the outcome measures were of unknown validity.

**Conclusion:** In the absence of any well-conducted studies, it is impossible to say whether yoga is effective.

## Dietary changes

### Alcohol

**Description:** Alcohol is commonly used to reduce anxiety in the short term, but prolonged use may lead to greater anxiety. For this reason, it has been recommended that people with anxiety or other psychiatric disorders should avoid alcohol altogether.<sup>233</sup>

**Rationale:** Heavy drinkers have an increased risk of suffering from anxiety disorders. There are two main ways in which heavy drinking might lead to increased anxiety. Firstly, while acute alcohol intoxication affects GABA receptors in a similar way to benzodiazepines, chronic alcohol use leads to decreased GABA tone and generates anxiety.<sup>234</sup> Secondly, heavy alcohol consumption leads to problems (eg, financial, occupational, relationship and health problems) which may increase anxiety.

**Level of evidence:** II (for the short-term anxiety-reducing properties of alcohol); IV (for the benefits of abstinence in heavy drinkers).

**Review of effectiveness:** There have been a number of controlled trials examining the short-term effects of alcohol on anxiety. In these trials, people with a range of anxiety disorders have been given alcohol or a placebo drink and then exposed to a stressful situation. Many of these studies show that alcohol reduces anxiety in response to the stressor,<sup>235-243</sup> but there are negative studies as well.<sup>240-243</sup> There have been no controlled trials of heavy drinkers with anxiety disorders abstaining from alcohol. However, uncontrolled studies of patients admitted to alcohol detoxification programs show very high levels of anxiety initially and a very rapid decline in anxiety symptoms after cessation of alcohol.<sup>244-249</sup> The rapidity of the response suggests that alcohol cessation is producing this effect.

**Conclusion:** There is some evidence that use of alcohol has a short-term anxiety-reducing effect. However, for those with alcohol-use disorders, eliminating alcohol use may be an effective way of reducing anxiety.

### Caffeine reduction

**Description:** Caffeine occurs naturally in the leaves, seeds and nuts of some plants. It is found in coffee, tea, soft drinks (eg, cola), chocolate, cocoa and some medications.

**Rationale:** It has been suggested that caffeine induces anxiety by binding to adenosine receptors and blocking the anxiolytic effects of adenosine.<sup>250</sup>

**Level of evidence:** IV (for caffeine reduction); II (for caffeine challenges).

**Review of effectiveness:** Several researchers have reported case studies or case series where caffeine reduction was associated with decreased anxiety levels among patients with anxiety disorders.<sup>251-254</sup> In addition, in retrospective surveys, people with anxiety disorders have reported high rates of caffeine discontinuation due to perceived anxiety-producing side effects.<sup>255,256</sup> However, there have been no controlled studies of the effect of caffeine abstinence or reduction on anxiety disorders. Clinical recommendations that patients with anxiety disorders should avoid caffeine are primarily based on the results of caffeine challenge studies. These studies measure the immediate effect on anxiety of the short-term administration of caffeine to people with anxiety disorders after a caffeine-free period. Double-blind, randomised, placebo-controlled challenge studies have consistently demonstrated that, compared with placebo, caffeine is associated with a greater increase in

anxiety in people with panic or generalised anxiety disorders.<sup>257-261</sup> Similarly, a double-blind, placebo-controlled challenge study found that caffeine increased anxiety levels in people with social phobia.<sup>262</sup> Evidence for longer-term effects of caffeine on anxiety is weak. Survey studies have demonstrated a significant association between daily caffeine intake and anxiety among people with panic disorder<sup>255,256</sup> or high trait anxiety when under stress.<sup>263</sup> However, another study reported no association between daily caffeine intake and anxiety.<sup>264</sup> There have been no controlled studies of the long-term effects of caffeine in patients with anxiety disorder.

*Conclusion:* There is some evidence that caffeine increases anxiety levels and precipitates panic attacks among people with anxiety disorders. However, there is a need for well designed RCTs of the long-term effect on anxiety of reducing or eliminating caffeine intake in people with anxiety disorders.

#### **Carbohydrate-rich, protein-poor diet**

*Description:* A carbohydrate-rich, protein-poor diet has more cereal products and little or no meat, dairy products or nuts.

*Rationale:* Biochemical imbalances in the brain can mediate or exacerbate the negative effects of stress experienced by individuals. In particular, serotonin activity in the brain occurs as a result of stress. Those with chronic stress may have depleted levels of brain serotonin, which results in their dealing with stress less effectively.<sup>265</sup> A diet which increases levels of serotonin in the brain may assist individuals to cope more effectively with stress. Diets high in carbohydrates and low in protein have been reported to increase serotonin levels in the brain.<sup>266</sup>

*Level of evidence:* V.

*Review of effectiveness:* In one RCT, stress-prone individuals on a high-carbohydrate, low-protein diet performed significantly better on memory scanning tasks after experiencing controllable stress compared with those who had a low-carbohydrate, protein-rich diet.<sup>265</sup> This difference did not occur, however, when they were subjected to uncontrollable stress. The numbers in this study were very small, just 22 stress-prone subjects and 21 controls, and the stress measured was that experienced in a laboratory setting.

*Conclusion:* The effects of this diet in people with anxiety disorders have not been rigorously evaluated.

#### **Nicotine avoidance**

*Description:* Nicotine is found in tobacco and in products to assist tobacco withdrawal.

*Rationale:* Nicotine stimulates the release of various neurotransmitters that can affect anxiety, including nicotinic acetylcholine receptors, glutamate, GABA, dopamine, norepinephrine and serotonin.

*Level of evidence:* V.

*Review of effectiveness:* It is now hypothesised that nicotine use results in smokers having increased levels of anxiety, but that nicotine withdrawal also increases anxiety, which is then relieved in the short term by smoking again.<sup>267</sup> While abrupt withdrawal of cigarettes can often trigger higher levels of anxiety in the short term,<sup>268</sup> these eventually disappear, leaving individuals with fewer symptoms of anxiety than they experienced while regularly smoking.<sup>269,270</sup> In a study of 70 smokers whose abstinence from smoking was carefully monitored over a 4-week period, West and Hajek reported reductions in anxiety levels.<sup>270</sup> However, there are no studies specifically on people with anxiety disorders.

*Conclusion:* There is currently no evidence on whether abstinence from nicotine benefits people with anxiety disorders.

## **DISCUSSION**

For ease of reference, Box 3 gives an overview of the evidence available for each treatment. The treatments with the best evidence of effectiveness are kava (for generalised anxiety), exercise (for generalised anxiety), relaxation training (for generalised anxiety, panic disorder, dental phobia and test anxiety) and bibliotherapy (for specific phobias). However, none of these treatments has as much support as standard treatments recommended in clinical practice guidelines. For example, a meta-analysis of treatments for generalised anxiety included 13 studies of 22 interventions using cognitive behaviour therapy and 24 studies of 39 interventions using pharmacological treatments.<sup>131</sup> By contrast, for generalised anxiety, we found 11 trials of kava, 11 of exercise, 15 of relaxation and four of bibliotherapy.

More limited evidence supports the effectiveness of acupuncture, music, autogenic training and meditation for generalised anxiety; inositol in the treatment of panic disorder and obsessive-compulsive disorder; massage in the treatment of post-traumatic stress in children; and alcohol avoidance by people with alcohol-use disorders to reduce a range of anxiety disorders. Some of these last treatments may well be effective, but they have received very little research attention. Research on the effectiveness of treatments for anxiety disorders has tended to focus on a small number of standard treatments and needs to be broadened, particularly in view of the public's more favourable attitudes to some non-standard treatments.

Since most of the studies reviewed have dealt with generalised anxiety disorder or high levels of anxiety, there is a particular need for work on other anxiety disorders. Future studies also need to pay particular attention to the use of larger sample sizes, and longer follow-up periods, blinding of treatments (where feasible) and use of intention-to-treat analysis. We also know little about how some of these treatments perform in population subgroups, such as children and adolescents, the elderly, and in perinatal women.

We have previously reviewed the evidence on complementary and self-help treatments for depression.<sup>60</sup> Anxiety and depression show considerable comorbidity, and prolonged anxiety appears to be an important factor in the aetiology of depression.<sup>271</sup> Thus, it might be expected that treatments that work for anxiety would also work for depression. However, some treatments that have been reported as effective for anxiety disorders have been largely ignored for depression (eg, kava), and some treatments that have been reported as effective for depression have been largely ignored for anxiety disorders (eg, St John's wort). There is scope for further research extending treatments across the divide between anxiety and depression.

Given the frequent use of complementary and self-help treatments, it would be wise for GPs and others who are treating depressed or anxious patients to routinely enquire about the use of these other treatments. An important reason is to prevent potentially harmful interactions with conventional treatments. There has already been a voluntary recall of kava products and there has been a warning from the Therapeutic Goods Administration about the interaction of St John's wort with prescription medications.

Another reason to enquire about use of complementary and self-help treatments is to educate patients to make better choices. If

**SUPPLEMENT • DEPRESSION: REDUCING THE BURDEN**

**3 Evidence on effectiveness of complementary and self-help treatments for anxiety disorders**

Treatment	Level of evidence	Conclusion
<i>Medicines and homoeopathic remedies</i>		
Bach flower remedies	II	Not effective for test anxiety. No evidence on other anxiety disorders
Berocca	II	No evidence on anxiety disorders
Ginger	V	No evidence on anxiety disorders
Gotu kola	V	No evidence on anxiety disorders
Combined preparations (including herbs)	II	No convincing evidence
Homoeopathy	II	No convincing evidence
Inositol	II	Some evidence for effectiveness with panic disorder and obsessive-compulsive disorder
Kava	I	Effective for generalised anxiety, but may cause liver toxicity in rare cases
Lemongrass leaves	II	Not effective
Licorice	IV	No convincing evidence
Magnesium	II	No convincing evidence
Passionflower	II	No convincing evidence
St John's wort	IV	No convincing evidence
Valerian	II	No convincing evidence
Vitamin C	V	No convincing evidence
5-hydroxy-L-tryptophan	II	Some evidence for effectiveness, but cannot be recommended because of possible risk of eosinophilia–myalgia syndrome
<i>Physical treatments</i>		
Acupuncture	II	Some evidence for effectiveness for generalised anxiety
Aromatherapy	II	No evidence on anxiety disorders
Hydrotherapy	IV	No convincing evidence
Massage/touch therapy	II	Some evidence for effectiveness with post-traumatic stress disorder in children, but no convincing evidence for adults or on other anxiety disorders
<i>Lifestyle</i>		
Autogenic training	I	Some evidence for effectiveness for generalised anxiety
Bibliotherapy	I	Evidence of effectiveness for specific phobias, but not for other anxiety disorders
Dance/movement therapy	II	Some evidence of effectiveness for test anxiety. No convincing evidence on other anxiety disorders
Exercise	I	Evidence for effectiveness for generalised anxiety. More evidence on other anxiety disorders is needed
Humour	V	No convincing evidence
Meditation	II	Some evidence for effectiveness with generalised anxiety. More evidence on other anxiety disorders is needed
Music	II	Some evidence for effectiveness with generalised anxiety. More evidence on other anxiety disorders is needed
Prayer	II	No convincing evidence
Relaxation	I or II	Evidence for effectiveness with generalised anxiety, panic disorder, dental phobia and test anxiety
Yoga	II	No convincing evidence
<i>Dietary and other changes</i>		
Alcohol	IV	Some evidence that eliminating alcohol reduces anxiety in people with alcohol disorders
Caffeine reduction	II or IV	No convincing evidence
Carbohydrate-rich, protein-poor diet	V	No convincing evidence
Nicotine avoidance	V	No evidence on anxiety disorders



patients do wish to use such treatments, it is preferable that they use those most supported by evidence.

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### COMPETING INTERESTS

None identified.

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## SUPPLEMENT • DEPRESSION: REDUCING THE BURDEN

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