NERVOUS SYSTEM

Stress/mild anxiety

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<th>Practice points</th>
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<tr>
<td>• B complex vitamins may support stress and mood, and are well tolerated</td>
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<td>• Kava may be beneficial for anxiety and stress states. Long-term use should be monitored</td>
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<td>• Passionflower and chamomile may have mild anxiolytic activity however clinical data are limited</td>
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<td>• The role of fish oil in anxiety is unclear, although omega-3s are known to have multiple roles in cognitive health</td>
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<td>• Anxiety is a group of conditions characterised by excessive fears and worries that may be difficult to control. It may be accompanied by other overlapping comorbidities such as depression. Stress is a normal human response to a threat, however, when associated with high levels of autonomic arousal, erroneous cognitions, and dysfunctional coping strategies, the effects of stress can significantly impact day-to-day living. Around 14% of the Australian population (16–85 years) experience anxiety or stress-related disorders each year: - 9–12% experience mild disorders - Women experience higher rates than men (18% and 11% respectively) - The highest rate of anxiety is experienced in the 35–44 y bracket (18%)</td>
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<td>• Psychoeducation (education about the nature of anxiety, its purpose and presentation)</td>
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<td>• Psychological treatments: - Refer patient to psychologist and/or online resource for assessment/treatment - Cognitive behavioural therapy (CBT) may be at least as effective as medication for many anxiety disorders - Online programs may be as effective as face-to-face therapy - Mindfulness-based meditation may decrease anxiety with benefits still present after 3 years</td>
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<tr>
<td>• Pharmacological treatments: selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenaline reuptake inhibitors (SNRIs) and benzodiazepines, however patients tend to prefer CBT and see it as more likely to be effective in the long term</td>
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Complementary medicines

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<th>Primary recommendations</th>
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<tr>
<td><strong>B-COMPLEX VITAMINS</strong></td>
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<td><strong>Mechanism of action</strong></td>
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<td>• Folate, B6 and B12 have a role in neural health and energy metabolism. They are also involved in the metabolism of the potentially toxic amino acid homocysteine (Hcy) to methionine. High Hcy and low B vitamins may be associated with poorer cognitive function and neurodegenerative disorders. Chronic stress depletes B6. Several B vitamins are integral to the synthesis of neurotransmitters and catecholamines that are essential for psychological wellbeing, including serotonin and dopamine</td>
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<td>• 2 double-blind randomised controlled trials (RCTs) assessing effects of B complex-containing multivitamins on mood, psychological strain and cognitive effects reported: - Significantly reduced personal strain, confusion and dejected / depressed moods associated with chronic work stress after 12 weeks of supplementation - Significant improvements in scales of mood and stress states and performance trend toward reduced mental fatigue during intense mental processing</td>
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<td>• A meta-analysis (8 trials) found that multivitamin/mineral supplementation for at least 28 days reduced levels of perceived stress, mild psychiatric symptoms, and anxiety</td>
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Adverse effects
• High doses of vitamin B6 taken over a long period of time may cause peripheral neuropathy.\textsuperscript{11} This is unlikely to occur at doses <200 mg/d\textsuperscript{12}

Interactions
• Folic acid may decrease the activity of phenytoin and methotrexate\textsuperscript{13}
• Folic acid may increase the toxicity of fluorouracil\textsuperscript{13}
• Riboflavin (B2) may increase effect of migraine drugs\textsuperscript{13}

Dosage: Recommended dietary intake for adults\textsuperscript{24}

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<tr>
<th></th>
<th>B1 mg/d</th>
<th>B2 mg/d</th>
<th>B3 mg/d</th>
<th>B5 mg/d</th>
<th>B6 mg/d</th>
<th>B12 ug/d</th>
<th>Folate ug/d</th>
<th>Biotin ug/d</th>
<th>Choline mg/d</th>
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<tr>
<td>mg/d</td>
<td>1.1</td>
<td>1.1</td>
<td>14-35</td>
<td>4-6</td>
<td>1.3-50</td>
<td>2.4</td>
<td>400-1000</td>
<td>25</td>
<td>425-3500</td>
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KAVA (Piper methysticum)

Mechanism of action
• Kava’s key active constituents, the kavalactones, may modulate calcium and sodium channels, modify binding of ligands to GABA receptors, inhibit noradrenaline and dopamine reuptake, and reverse inhibition of monoamine oxidase\textsuperscript{6,15}

Research
Kava may have benefit in general anxiety disorder (GAD), general anxiety-related disorders, and when tapering off benzodiazepines\textsuperscript{6,15}
• A 2003 Cochrane review (12 RCTS; n=700) found kava extract had a significant effect in reducing anxiety scores and is an effective symptomatic treatment for anxiety\textsuperscript{16}
• A 2005 meta-analysis (6 RCTs; n=345) found kava extract was effective in patients with non-psychotic anxiety disorders\textsuperscript{17}
• A 2013 RCT (n=75) found an aqueous extract of kava (120/240 mg/d kavalactones) significantly reduced anxiety in patients with GAD. With patients with moderate-severe GAD, the effect size was larger\textsuperscript{18}
• 3 randomised controlled trials have found kava decreases anxiety associated with menopause both for women with concomitant HRT or without\textsuperscript{19}
• There is contradictory evidence for kava being comparable to pharmaceutical anti-anxiety agents. One clinical trial found kava was as effective as buspirone in the acute treatment of out-patients suffering from GAD.\textsuperscript{20} Another trial compared effects of kava and oxazepam on anxiety after a cognitive battery. Kava did not reduce anxiety compared to oxazepam, however, it did not affect cognition whereas oxazepam reduced alertness. The placebo group had an increase in anxiety\textsuperscript{21}
• A randomised controlled trial comparing kava, oxazepam and placebo found a medicinal dose of kava containing 180 mg of kavalactones did not impair driving ability, whereas 30 mg of oxazepam caused some impairment\textsuperscript{22}

Adverse effects
• Well tolerated short term (1–24 weeks)\textsuperscript{16}
• Adverse effects unlikely at recommended dosage\textsuperscript{19}
• Kava has been implicated in several idiosyncratic, rare cases of liver damage. Aqueous extracts are likely to be safer in this context\textsuperscript{19}
• May cause GI upset and headache\textsuperscript{11}
• Not recommended during pregnancy and lactation\textsuperscript{19}

Interactions
• Concomitant use with alcohol, barbiturates, benzodiazepines, or other CNS depressants may increase risk of drowsiness and motor reflex depression\textsuperscript{11}

Dosage
• Typically found in tablet/capsule form
Dosage range: ~300 mg/d kava extract (providing 105–250 mg kavalactones)\textsuperscript{11}


| Secondary recommendations |

**PASSIONFLOWER (Passiflora incarnata)**

- Preliminary evidence suggests that passionflower may modulate the GABA system and may bind to central benzodiazepine receptors\(^{23,24}\).
- Widely used traditionally as a mild sedative and for anxiety and restlessness. Often in combination with other herbs\(^{24}\).
- Limited evidence in human trials indicates passionflower may be comparable to oxazepam for reducing anxiety in patients with GAD and may reduce anxiety related to surgery\(^{6}\).
- However, a 2009 Cochrane review (2 studies; n=198) concluded that despite some positive findings no firm conclusions could be drawn based on insufficient evidence\(^{25}\).
- **Dosage range**: dried herb 0.5–2 g 3–4 times/d\(^{11,24}\).

| Diet and lifestyle recommendations |

- Adopt a diet rich in complex carbohydrates, (wholegrains, fruits, vegetables), lean protein and omega-3 rich foods. Decrease refined carbohydrates, saturated fats, and processed foods\(^{6}\).
- Moderate-graded physical activity may decrease the risk of anxiety\(^{6}\).
- Encourage withdrawal of alcohol, caffeine and nicotine which may exacerbate\(^{6}\).
- Meditation techniques (mindfulness and other forms of meditation) may reduce anxiety and stress-related symptoms\(^{6}\).

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**REFERENCES**