

Clinical Evidence Handbook

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Generalized Anxiety Disorder

CHRISTOPHER K. GALE and JANE MILLICHAMP, *Dunedin School of Medicine, University of Otago, Dunedin, New Zealand*

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Generalized anxiety disorder (GAD) is excessive worry and tension about everyday events, on most days for at least six months, to the extent that there is distress or difficulty in performing day-to-day tasks. However, diagnosing GAD accurately can be difficult.

- Up to one in 20 persons may have GAD at any one time, and most have additional health problems. Less than one-half of persons with GAD have full remission after five years.

- GAD may have a genetic component, and has been linked to previous psychological or other trauma.

IN ADULTS

Cognitive behavior therapy (CBT; including exposure, relaxation, and cognitive restructuring) improves anxiety compared with wait-list control, treatment as usual, or enhanced usual care.

- It is unclear whether CBT is more effective than supportive therapy.

Applied relaxation may be as effective as CBT, but we found insufficient evidence from randomized controlled trials (RCTs) about applied relaxation compared with no treatment.

Various drug treatments, such as benzodiazepines, buspirone, hydroxyzine, antidepressants, and pregabalin, may reduce symptoms of anxiety in persons with GAD, but they can have unpleasant adverse effects, and most trials have been short term.

- Benzodiazepines increase the risk of dependence, sedation, and accidents, and can cause adverse effects in neonates if used during pregnancy.

- Buspirone may be less effective if used in persons who have recently been taking benzodiazepines.

- Antidepressants (imipramine, paroxetine, sertraline, escitalopram, venlafaxine,

and opipramol) have been shown to reduce symptoms compared with placebo, but antidepressants can cause a variety of adverse effects, including sedation, dizziness, falls, nausea, and sexual dysfunction.

- In general, comparisons between different antidepressants have shown similar effectiveness in reducing anxiety, although one RCT found limited evidence of an increased benefit with escitalopram compared with paroxetine.

Antipsychotic drugs may reduce anxiety in persons who have not responded to other treatments, but these drugs may have adverse effects, including drowsiness and movement disorders.

We do not know whether abecarnil reduces anxiety because the RCTs we found reported inconsistent results.

IN CHILDREN AND ADOLESCENTS

CBT improves symptoms compared with wait-list control or active control.

- Most RCTs of CBT in children and adolescents have included other anxiety disorders.

We found limited RCT evidence regarding the effectiveness of antidepressants for childhood GAD. Selective serotonin reuptake inhibitors (fluvoxamine, fluoxetine, sertraline) have shown some promise, but antidepressants are associated with abdominal pain and nausea, and other well-documented adverse effects.

We found no RCT evidence on the effects of applied relaxation, benzodiazepines, buspirone, hydroxyzine, abecarnil, pregabalin, or antipsychotics.

Definition

GAD is defined as excessive worry and tension about everyday events and problems,

on most days for at least six months, to the point that the person experiences distress or has marked difficulty in performing day-to-day tasks. It may be characterized by the following symptoms and signs: increased motor tension (fatigability, trembling, restlessness, and muscle tension); autonomic hyperactivity (shortness of breath, rapid heart rate, dry mouth, cold hands, and dizziness); and increased vigilance and scanning (feeling “keyed up,” increased startling, and impaired concentration), but not because of panic attacks. One nonsystematic review of epidemiologic and clinical studies found marked reductions in quality of life and psychosocial functioning in persons with anxiety disorders, including GAD. It also found that persons with GAD had low overall life satisfaction and some impairment in the ability to fulfill roles, social tasks, or both.

Incidence and Prevalence

The most recent community surveys have used a newer version of the Composite International Diagnostic Interview, which allows direct comparisons among different surveys. One observational survey in Europe completed in 2003, which included persons from Belgium, France, Germany, Italy, the Netherlands, and Spain, estimated the 12-month prevalence of GAD at 1.0 percent (0.5 percent men, 1.3 percent women).

An observational survey in New Zealand (12,800 persons) estimated the 12-month prevalence of GAD at 2.0 percent; 95% confidence interval (CI), 1.7 to 2.3 percent (men: 1.4 percent; 95% CI, 1.1 to 1.8 percent; women: 2.6 percent; 95% CI, 2.2 to 3.1 percent). In this survey, persons older than 65 years had a markedly lower 12-month prevalence of GAD at 1.0 percent (95% CI, 0.6 to 1.5 percent). The lifetime prevalence of GAD was estimated at 6.0 percent (95% CI, 5.5 to 6.6 percent).

An observational survey of persons 16 to 74 years of age in the United Kingdom in 2000 used the Clinical Interview Schedule-Revised, followed by a Schedules for Clinical Assessment in Neuropsychiatry interview of a stratified sample. The survey estimated that 4.7 percent of persons had GAD (men: 4.6 percent; women: 4.8 percent). A survey of children and adolescents five to 16 years of age in the United Kingdom in 2004, which used a similar methodology, estimated that 0.7 percent of persons had GAD (boys: 0.6 percent; girls: 0.8 percent).

In the European survey of adults, 76 percent of persons who had more than one mental disorder for 12 months had GAD. Those persons who had GAD were significantly more likely to have other mental disorders, including: major depression (odds ratio [OR] to have the disorder = 37.1; 95% CI, 23.2 to 59.1), social phobia (OR = 13.5; 95% CI, 7.8 to 23.6), specific phobia

Clinical Questions

What are the effects of treatments for generalized anxiety disorder in adults?

Beneficial	Antidepressants (imipramine, duloxetine, paroxetine, sertraline, escitalopram, venlafaxine, opipramol)
	Cognitive behavior therapy
Likely to be beneficial	Applied relaxation
	Buspirone
	Hydroxyzine
	Pregabalin
Trade-off between benefits and harms	Antipsychotics
	Benzodiazepines
Unknown effectiveness	Abecarnil

What are the effects of treatments for generalized anxiety disorder in children and adolescents?

Beneficial	Cognitive behavior therapy
Trade-off between benefits and harms	Antidepressants in children (sertraline, fluvoxamine, fluoxetine, paroxetine, venlafaxine)
Unknown effectiveness	Abecarnil
	Antipsychotics
	Applied relaxation
	Benzodiazepines
	Buspirone
	Hydroxyzine
	Pregabalin

(OR = 7.4; 95% CI, 4.6 to 12.0), posttraumatic stress disorder (OR = 16.4; 95% CI, 9.1 to 29.8), agoraphobia (OR = 26.6; 95% CI, 10.8 to 65.1), panic disorder (OR = 21.8; 95% CI, 11.5 to 41.2), and alcohol dependence (OR = 18.9; 95% CI, 4.8 to 74.4).

Another observational survey in 2004 found that persons with GAD were also more likely to have physical health problems. In one systematic review (search date 2006), persons with GAD had a significantly decreased quality of life (effect size: six studies, 248 persons, *P* < .01). A nonsystematic review (20 observational studies in younger and older adults) suggested that autonomic arousal to stressful tasks was decreased in older persons, and that older persons became accustomed to stressful tasks more quickly than younger persons.

Etiology and Risk Factors

GAD is believed to be associated with an increase in the number of minor life events, independent of

demographic factors; however, this finding is also common in patients with other diagnoses. One nonsystematic review (five case-control studies) of psychological sequelae from civilian trauma found that rates of GAD reported in four of the five studies were significantly increased compared with a control population (risk ratio [RR] = 3.3; 95% CI, 2.0 to 5.5). One systematic review (search date 1997) of cross-sectional studies found that bullying (or peer victimization) was associated with a significant increase in the incidence of GAD (effect size: 0.21; CI not reported). One systematic review (search date not reported, two family studies, 45 index cases, 225 first-degree relatives) found a significant association between GAD in the index patients and in their first-degree relatives (OR = 6.1; 95% CI, 2.5 to 14.9). One systematic review of twin and family studies (search date 2003, 23 twin studies, 12 family studies) found an association among GAD, other anxiety disorders, and depression, and postulated that a common genetic factor was implicated.

Prognosis

One systematic review found that 25 percent of adults with GAD will be in full remission after two years, and 38 percent will have a remission after five years. The Harvard/Brown Anxiety Research Program reported on the five-year follow-up of 167 persons with GAD. During this period, the weighted probability was 38 percent for full remission, 47 percent for at least partial remission, 27 percent for relapse from full remission, and 39 percent for relapse from partial remission.

EDITOR'S NOTE: Abecarnil and opipramol are not available in the United States.

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