RANZCP CLINICAL PRACTICE GUIDELINES

Summary of guideline for the treatment of panic disorder and agoraphobia

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Objective: *To provide a summary of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) Clinical Practice Guideline for the treatment of panic disorder and agoraphobia*

Conclusions: *Evidence-based treatments for panic disorder and agoraphobia are now clear. These conditions are chronic and disabling in nature, are complicated by delayed treatment and the presence of other psychiatric conditions, and the presence of severe agoraphobia is a negative prognostic indicator. Choice of therapy will depend on the skill of the therapist in applying psychological treatments as well as the preferences of the patient, but there is a role for both psychological and evidence-based pharmacological approaches. The present article is a summary version of the comprehensive Clinical Practice Guideline (*Australian and New Zealand Journal of Psychiatry, 2003*) which was developed in accordance with National Health and Medical Research Council (NHMRC) criteria. It provides a two-page desk-top summary for use in clinical practice. Economic evaluation of the available evidence-based treatments showed that at 1 year the cost of cognitive behaviour therapy (CBT) is less than the cost of the average drug therapy (CBT becomes cheaper than paroxetine at 8 months, than clomipramine at 11 months and cheaper than imipramine at 13 months). During the second and subsequent years the superiority of CBT increases whether or not the drugs are continued. Evidence levels for specific treatments are provided in the comprehensive guideline and placed in the context of overall principles of thorough assessment and quality clinical management.*

Key words: *agoraphobia, Clinical Practice Guidelines, panic disorder, Royal Australian and New Zealand College of Psychiatrists.*

In early 1999, the Royal Australian and New Zealand College of Psychiatrists (RANZCP) called for tenders from expert groups to produce clinical practice guidelines for the College Members and Fellows, other mental health providers and their patients. The present team was the successful tenderer for the guidelines for panic disorder and agoraphobia. There were three requirements. The first was to produce a detailed guideline that included a description of the clinical epidemiology of the disorder together with a systematic review of the treatment outcome literature and an economic analysis of the cost effectiveness of the recommended treatments. The second requirement was for a clinical practice guideline for consumers of specialist mental health services. This guideline will be made available by the College in 2003. The third requirement was for a summary of the recommendations suitable for use in busy clinical practice. That summary, able to be photocopied onto two sides of an A4 page, and kept in the consulting room along with the summary guidelines from the other six Clinical Practice Guideline teams, is appended (Appendix I).

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METHOD

The description of the clinical epidemiology was informed by the National Mental Health Survey. The systematic review was informed by the meta-analyses of treatment outcome for panic disorder by Gould *et al*.[1] The team decided to replicate their methods and, on inspection of their protocols, decided to accept their conclusions in respect to the 43 randomized controlled trials that they analysed. We searched the treatment outcome literature and located a further 58 randomized controlled trials and analysed them in the same way. The results are displayed in Table 1. The effect sizes in both analyses found that the psychological therapies (cognitive behaviour therapy; CBT) were associated with larger effect sizes than those produced by pharmacotherapy (tricyclic antidepressant (TCA), selective serotonin reuptake inhibitors (SSRI) and benzodiazepines). Confidence intervals in the Gould *et al.* study did not overlap; in our study they did, but pooling the data made it clear that CBT was superior. This was borne out in the number needed to treat analysis when CBT = 3 and antidepressants = 6. Benzodiazepines, although effective, were not recommended because of problems with sedation and dependence.

ECONOMIC ANALYSIS

The cost alternatives of the various treatments were calculated by adding together the medication cost and the cost in psychiatrists' time to diagnose and treat for 12 months a person with panic disorder. At 1 year the cost of CBT is less than the cost of the average drug therapy (CBT becomes cheaper than paroxetine at 8 months, than clomipramine at 11 months and cheaper than imipramine at 13 months). During the second and subsequent years the superiority of CBT increases whether or not the drugs are continued. If they are continued then their costs continue. If they are not, then relapse occurs in approximately half of those withdrawn from drug treatment and the net benefit due to drug therapy declines. Relapse is not significantly associated with CBT follow-up (at least for the first 5 years) so there is no change to the cost or to the benefit.

SUMMARY OF CLINICAL RECOMMENDATIONS

Further to comprehensive assessment of history and current symptoms, comorbidity of other conditions and presence of medical disorders, the key treatment recommendations include the following.

Patient and family psychoeducation

An essential component of effective treatment is education for the patient and significant others, covering:

- the nature and course of panic disorder;
- an explanation of the basis for panic and anxiety;
- rationale for the treatment, likelihood of a positive response, and expected time-frame for response;
- likelihood of experiencing anxiety in the course of treatment and some residual anxiety when treatment is finished; and
- necessary lifestyle modifications (e.g. reduction in caffeine).

Table 1: Effect sizes at post-treatment and follow-up for the meta-analysis by Gould *et al.*[1] and the Panic/Agoraphobia Guidelines meta-analysis for all measures

	Post-treatment				*Follow up*			
	Pharmaco-therapy	***95% CI***	***Psycho-logical therapies***	***95% CI***	***Pharmaco-therapy***	***95% CI***	***Psycho-logical therapies***	***95% CI***
Gould *et al.*[1] (n = 43 trials)	0.47	0.38–0.54	0.68	0.58–0.78	0.01	–	0.74	–
Panic/Agoraphobia Guidelines: all measures (n = 58 trials)	0.40	0.27–0.52	0.61	0.35–0.87	0.00	–0.27–0.27	0.57	0.24–0.91
Panic/Agoraphobia Guide-lines: revised all measures	0.43	0.30–0.55	0.59	0.34–0.83	0.00	–0.27–0.27	0.65	0.31–1.00

Notes: effect size estimator = Glass' delta. Effect sizes for the Panic/Agoraphobia Guidelines combined using a random effects model. All measures refers to all measures used in the studies from which effect sizes were calculable. Revised all measures is the sum of groups of measures listed in Table 1. Measures not relating to panic and agoraphobia (e.g. personality and depression measures) were excluded.
CI, confidence interval.

Evidence-based treatment

Cognitive behaviour therapy is both more effective and cheaper than pharmacotherapy. Tricycliclic antidepressants and SSRIs are equal in efficacy and both are to be preferred to benzodiazepines. Treatment choice depends on the skill of the therapist and the wishes of the patient. Cognitive behaviour therapy is preferred but SSRIs are commonly used; however, effective drug treatment should include behavioural treatment to limit avoidance.

Second-line evidence-based treatment if non-response

If there is an inadequate response after an adequate trial of a first-line treatment, switch to another evidence-based treatment. At this time it may be important to obtain a second opinion. If panic disorder is more severe than other co-occurring conditions (as determined by impairment or interference with daily living, and distress from symptoms), panic should be the initial focus of treatment, regardless of chronological onset. The presence of severe agoraphobia is a negative prognostic indicator, while comorbid depression has no consistent effect on outcome.

REFERENCE

1. Gould RA, Otto MW, Pollack MH. A meta-analysis of treatment outcome for panic disorder. *Clinical Psychology Review* 1995; **15**: 819–844.

APPENDIX 1: SUMMARY OF AUSTRALIAN AND NEW ZEALAND CPG FOR THE TREATMENT OF PANIC DISORDER AND AGORAPHOBIA (RANZCP, 2003)

What is panic disorder?

- Recurrent, unexpected panic attacks – a discrete period of intense fear or discomfort, in which **four** (or more) of the following **symptoms develop abruptly and peak within 10 minutes:**
  - Palpitations, pounding heart
  - Sweating
  - Trembling or shaking
  - Shortness of breath
  - Sensations of choking
  - Chest pain or discomfort
  - Nausea or abdominal pain
  - Feeling dizzy, unsteady, lightheaded, or faint
  - Numbness or tingling sensations
  - Chills or hot flushes
  - Derealization or depersonalization
  - Fear of losing control or going crazy
  - Fear of dying
- **1 month or more of persistent concern about having another attack or**
- **worry about** the implications or **consequences** of panic (e.g., fear of loss of control, going crazy, or social humiliation) **or**
- a significant behavioural change related to the attacks (e.g. **avoidance** of panic situations **for fear of panic**, i.e. agoraphobia).

What is agoraphobia?

Agoraphobia is anxiety about, or avoidance of, places or situations from which escape might be difficult or help unavailable in the event of a panic attack.

What should be ruled out?

- Direct physiological effects of a substance (e.g. caffeine intoxication)
- General medical conditions that can cause panic-like symptoms (e.g. hyperthyroidism)
- Not better accounted for by another mental disorder (e.g. panic occurs in depression, OCD, PTSD, social phobia)

Basic facts about panic disorder:

- Tends to be **chronic**
- **Comorbidity is common**. Usually at least one other disorder is present, including:
  • depression • substance abuse • other anxiety disorders
- Associated with considerable suffering and **functional impairment**
- Lifetime prevalence rates (with or without agoraphobia) between 1.5% and 3.5%. Point prevalence rates less than 1%.
- Age: • Common in younger adults.
- Gender: • **More prevalent in women**, particularly panic with extensive agoraphobia.
- Incidence and prevalence seems consistent across ethnic / racial groups.
- Presentation and interpretation of symptoms is affected by racial, religious, and family belief systems.

What goes into effective clinical assessment?

- Conduct a **thorough clinical interview** assessing history and current symptoms.
- Assess initially and on an ongoing basis for:
  - Number and severity of panic attacks
  - Severity of anticipatory anxiety
  - Severity of agoraphobic symptoms
  - Suicidal ideation and attempts
  - Missed work / school
  - Underachievement at work or school
  - Changes in social behaviour
  - Disability (use SF-12)
- **Assess for comorbid conditions initially and on an ongoing basis** (particularly depression, substance abuse)
- To **rule out medical conditions** (like caffeinism, hyperthyroidism, seizure disorders and cardiac arrhythmias) that mimic panic, consider medical history with appropriate laboratory tests

What treatments are helpful?

Efficacious psychotherapy

The strongest evidence supports the efficacy of cognitive behavioural interventions that include the following:

- **Education** about the symptoms, the disorder, and the specific role of fear of bodily sensations
- **Exposure to the interoceptive reactions** that comprise and cue panic attacks
- **Cognitive therapy** to change maladaptive thought processes
- **Hyperventilation control**
- Graded in vivo **exposure to phobic situations**

Effective pharmacological treatment

The strongest evidence supports the effectiveness of **TCAs, SSRIs and high potency benzodiazepines (BZDs)**. BZD use is not recommended because of the high risk of creating dependency on these drugs. The efficacy of maintenance medication to prevent relapse has not been firmly established. Relapse on discontinuation is common.

How do effective treatments compare?

- The majority of patients show a **positive response to CBT or medication.**
- The number needed to treat to get one person panic free is 3 for CBT and 6 for medication.
- **CBT has greater durability than pharmacotherapy**.
- Dropout rates for CBT are lower than for pharmacotherapy.

Are combining these two forms of treatment best?

- **Combining BZDs** with CBT **reduces treatment efficacy** when compared to CBT alone.
- There are no data to show benefit from the combination of CBT treatment with SSRIs, TCAs, and MAOIs.
- CBT has been shown to reduce relapse following discontinuation of benzodiazepines.

Overall clinical management is important

- An essential component of effective treatment is **psychoeducation** for the client and significant others, covering:
  - An explanation of the **basis for panic** and anxiety
  - The **nature and course** of panic disorder
  - Rationale for the treatment, likelihood of a positive response, and expected time frame for response
  - Likelihood of experiencing some residual anxiety in the course of treatment
- If there is an **inadequate response** after an adequate trial of a first line treatment, **switch** to another evidence-based treatment. At this time it may be important to **obtain a consultation** and / or refer the patient to a specialist.
- If panic disorder is more severe than other co-occurring conditions (as determined by impairment or interference with daily living, and distress from symptoms), panic should be the initial focus of treatment, regardless of chronological onset.
- The presence of severe agoraphobia is a negative prognostic indicator, while comorbid depression has no consistent effect.

Issues in managing psychological treatment

- A **positive response** typically occurs within **6 to 8 weeks**
- A typical course of treatment in research protocols is about **12 sessions**. This will vary in clinical practice.
  - Some clients understand that panic is not dangerous after a few sessions and improvement continues naturally.
  - Others may require substantially longer than 12 sessions, especially if agoraphobia is severe.

Issues in managing pharmacological treatment

- A **positive response** typically occurs within **6 weeks** (response to benzodiazepines occurs considerably faster) but additional time may be required to stabilise the response.
- Because there is **comparable efficacy**, issues related to safety, tolerability, price, simplicity, and ease of discontinuation should guide clinician choice among effective medications.
- Medications, especially benzodiazepines, should be **discontinued gradually**. It may be difficult because of dependence and may provoke relapse or even rebound panic.
- If a patient has an inadequate response or is unable to tolerate the side effects of the medication, the potential difficulty in discontinuing the medication should be carefully considered.
- **Switching medications,** using augmentation therapy, or treating medication side effects **may be effective**
- When used alone, **antidepressants should be continued for at least 6 months** following symptom remission, and longer if full remission does not occur.
- Some clinicians advocate stopping medication only when the patient is in a stable life situation.
- **Longer use of medication may reduce the risk of relapse** following discontinuation.
- For patients with several episodes of panic, each responsive to medication, chronic medication use may be indicated.
- People with panic disorder often require **low beginning doses and slow titration of medication.**

How do I select among treatments?

- We cannot predict which individual will respond best to which treatment.
- The following factors should be considered:
  - Availability of provider expertise
  - Patient preference
  - Previous response
  - Concomitant medical conditions
  - Psychiatric comorbidity, including substance use disorders
  - Chronic psychosocial problems
  - Risk/benefit ratio
  - Cost/benefit ratio
  - Differential compliance to treatment modalities
  - Potential for pregnancy
  - Level of support from significant others
  - Suicide risk

What about prevention?

- Early identification of the disorder is important in secondary prevention.
- No known data exist on primary prevention of panic disorder.
- Public education about the utility of anxiety, the symptoms of the flight or fight response is important.

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