NICE National Institute for Health and Care Excellence

NICE guideline

Generalised anxiety disorder and panic disorder in adults: management

Clinical guideline
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www.nice.org.uk/guidance/cg113

Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guideline replaces CG22 and ESUOM12.

This guideline partially replaces CG123.

This guideline is the basis of QS53.

Overview

This guideline covers the care and treatment of people aged 18 and over with generalised anxiety disorder (chronic anxiety) or panic disorder (with or without agoraphobia or panic attacks). It aims to help people achieve complete relief of symptoms (remission), which is associated with better functioning and a lower likelihood of relapse.

Who is it for?

- Healthcare professionals
- Adults with a working diagnosis of generalised anxiety disorder or panic disorder (with or without agoraphobia), and their families and carers

Recommendations

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the guidance.

People have the right to be involved in discussions and make informed decisions about their care, as described in making decisions about your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

Healthcare professionals should follow our general guidelines for people delivering care:

- service user experience in adult mental health
- shared decision making
- medicines adherence
- medicines optimisation
- multimorbidity
- decision-making and mental capacity.

1.1 Principles of care for people with generalised anxiety disorder (GAD)

Learning disabilities and cognitive impairment

1.1.1 For people with GAD who have a mild learning disability or mild acquired cognitive

impairment, offer the same interventions as for other people with GAD, adjusting the method of delivery or duration of the intervention if necessary to take account of the disability or impairment. **[2011]**

1.1.2 When assessing or offering an intervention to people with GAD and a moderate to severe learning disability or moderate to severe acquired cognitive impairment, consider consulting with a relevant specialist. **[2011]**

1.2 Stepped care for people with GAD

A stepped-care model (shown below) is used to organise the provision of services and to help people with GAD, their families, carers and practitioners to choose the most effective interventions.

1.2.1 Follow the stepped-care model, offering the least intrusive, most effective intervention first. **[2011]**

The stepped-care model

Focus of the intervention	Nature of the intervention
STEP 4: Complex treatment-refractory generalised anxiety disorder (GAD) and very marked functional impairment, such as self-neglect or a high risk of self-harm	Highly specialist treatment, such as complex drug and/or psychological treatment regimens; input from multi-agency teams, crisis services, day hospitals or inpatient care
STEP 3: GAD with an inadequate response to step 2 interventions or marked functional impairment	Choice of a high-intensity psychological intervention (cognitive behavioural therapy [CBT]/applied relaxation) or a drug treatment
STEP 2: Diagnosed GAD that has not improved after education and active monitoring in primary care	Low-intensity psychological interventions: individual non-facilitated self-help, individual guided self-help and psychoeducational groups
STEP 1: All known and suspected presentations of GAD	Identification and assessment; education about GAD and treatment options; active monitoring

Individual non-facilitated self-help: this is a self-administered intervention intended to treat GAD involving written or electronic self-help materials (usually a book or workbook). It is similar to individual guided self-help but usually with minimal therapist contact, for example an occasional short telephone call of no more than 5 minutes.

Step 1: All known and suspected presentations of GAD

Identification

1.2.2 Be alert to possible anxiety disorders (particularly in people with a past history of an anxiety disorder, possible somatic symptoms of an anxiety disorder or in those who have experienced a recent traumatic event). Consider asking the person about their feelings of anxiety and their ability to stop or control worry, using the 2-item Generalized Anxiety Disorder scale (GAD-2). **[2011]**

1.2.3 Identify and communicate the diagnosis of GAD as early as possible to help people understand the disorder and start effective treatment promptly. **[2011]**

1.2.4 Consider the diagnosis of GAD in people presenting with anxiety or significant worry, and in people who attend primary care frequently who:

- have a chronic physical health problem **or**
- do not have a physical health problem but are seeking reassurance about somatic symptoms (particularly older people and people from minority ethnic groups) **or**
- are repeatedly worrying about a wide range of different issues. **[2011]**

1.2.5 When a person with known or suspected GAD attends primary care seeking reassurance about a chronic physical health problem or somatic symptoms and/or repeated worrying, consider with the person whether some of their symptoms may be due to GAD. **[2011]**

Assessment and education

1.2.6 For people who may have GAD, conduct a comprehensive assessment that does

not rely solely on the number, severity and duration of symptoms, but also considers the degree of distress and functional impairment. **[2011]**

1.2.7 As part of the comprehensive assessment, consider how the following factors might have affected the development, course and severity of the person's GAD:

- any comorbid depressive disorder or other anxiety disorder
- any comorbid substance misuse
- any comorbid medical condition
- a history of mental health disorders
- past experience of, and response to, treatments.

  Be aware when prescribing selective serotonin reuptake inhibitors (SSRIs) of the need to ask about cocaine use when considering drug–drug interactions, and the need to avoid concurrent use of multiple serotonergic drugs. Follow the Medicines and Healthcare products Regulatory Agency (MHRA) safety advice on citalopram. **[2011, amended 2020]**

1.2.8 For people with GAD and a comorbid depressive or other anxiety disorder, treat the primary disorder first (that is, the 1 that is more severe and in which it is more likely that treatment will improve overall functioning).

For guidance on depression, obsessive–compulsive disorder and post-traumatic stress disorder see our guidelines on mental health and behavioural conditions. **[2011, amended 2020]**

1.2.9 For people with GAD who misuse substances, be aware that:

- substance misuse can be a complication of GAD
- non-harmful substance use should not be a contraindication to the treatment of GAD
- harmful and dependent substance misuse should be treated first as this may lead to significant improvement in the symptoms of GAD (see our guidelines on drug misuse and alcohol-use disorders).

Be aware when prescribing SSRIs of the need to ask about cocaine use when considering drug–drug interactions, and the need to avoid concurrent use of multiple serotonergic drugs. Follow the MHRA safety advice on citalopram. **[2011, amended 2020]**

1.2.10 Following assessment and diagnosis of GAD:

- provide education about the nature of GAD and the options for treatment, including NICE's information for the public
- monitor the person's symptoms and functioning (known as active monitoring).

  This is because education and active monitoring may improve less severe presentations and avoid the need for further interventions. **[2011]**

1.2.11 Discuss the use of over-the-counter medications and preparations with people with GAD. Explain the potential for interactions with other prescribed and over-the-counter medications and the lack of evidence to support their safe use. **[2011]**

Step 2: Diagnosed GAD that has not improved after step 1 interventions

Low-intensity psychological interventions for GAD

1.2.12 For people with GAD whose symptoms have not improved after education and active monitoring in step 1, offer 1 or more of the following as a first-line intervention, guided by the person's preference:

- individual non-facilitated self-help
- individual guided self-help
- psychoeducational groups. **[2011]**

1.2.13 Individual non-facilitated self-help for people with GAD should:

- include written or electronic materials of a suitable reading age (or alternative media)
- be based on the treatment principles of cognitive behavioural therapy (CBT)
- include instructions for the person to work systematically through the materials over a period of at least 6 weeks
- usually involve minimal therapist contact, for example an occasional short telephone call of no more than 5 minutes. **[2011]**

1.2.14 Individual guided self-help for people with GAD should:

- be based on the treatment principles of CBT
- include written or electronic materials of a suitable reading age (or alternative media)
- be supported by a trained practitioner, who facilitates the self-help programme and reviews progress and outcome
- usually consist of 5 to 7 weekly or fortnightly face-to-face or telephone sessions, each lasting 20 to 30 minutes. **[2011, amended 2018]**

1.2.15 Psychoeducational groups for people with GAD should:

- be based on CBT principles, have an interactive design and encourage observational learning
- include presentations and self-help manuals
- be conducted by trained practitioners
- have a ratio of 1 therapist to about 12 participants
- usually consist of 6 weekly sessions, each lasting 2 hours. **[2011]**

1.2.16 Practitioners providing guided self-help and/or psychoeducational groups should:

- receive regular high-quality supervision

- use routine outcome measures and ensure that the person with GAD is involved in reviewing the efficacy of the treatment. **[2011]**

Step 3: GAD with marked functional impairment or that has not improved after step 2 interventions

Treatment options

1.2.17 For people with GAD and marked functional impairment, or those whose symptoms have not responded adequately to step 2 interventions:

- Offer either
  - an individual high-intensity psychological intervention (see recommendations 1.2.18 to 1.2.22) **or**
  - drug treatment (see recommendations 1.2.23 to 1.2.33).
- Provide verbal and written information on the likely benefits and disadvantages of each mode of treatment, including the tendency of drug treatments to be associated with side effects and withdrawal syndromes.
- Base the choice of treatment on the person's preference as there is no evidence that either mode of treatment (individual high-intensity psychological intervention or drug treatment) is better. **[2011]**

High-intensity psychological interventions

1.2.18 If a person with GAD chooses a high-intensity psychological intervention, offer either CBT or applied relaxation. **[2011]**

1.2.19 CBT for people with GAD should:

- be based on the treatment manuals used in the clinical trials of CBT for GAD
- be delivered by trained and competent practitioners

- usually consist of 12 to 15 weekly sessions (fewer if the person recovers sooner; more if clinically required), each lasting 1 hour. **[2011]**

1.2.20 Applied relaxation for people with GAD should:

- be based on the treatment manuals used in the clinical trials of applied relaxation for GAD
- be delivered by trained and competent practitioners
- usually consist of 12 to 15 weekly sessions (fewer if the person recovers sooner; more if clinically required), each lasting 1 hour. **[2011]**

1.2.21 Practitioners providing high-intensity psychological interventions for GAD should:

- have regular supervision to monitor fidelity to the treatment model, using audio or video recording of treatment sessions if possible and if the person consents
- use routine outcome measures and ensure that the person with GAD is involved in reviewing the efficacy of the treatment. **[2011]**

1.2.22 Consider providing all interventions in the preferred language of the person with GAD if possible. **[2011]**

Drug treatment

1.2.23 If a person with GAD chooses drug treatment, offer a selective serotonin reuptake inhibitor (SSRI). Consider offering sertraline first because it is the most cost-effective drug, but note that at the time of publication (January 2011) sertraline did not have UK marketing authorisation for this indication. Informed consent should be obtained and documented. Monitor the person carefully for adverse reactions.

Note that this is an off-label use for some SSRIs. See NICE's information on prescribing medicines. **[2011, amended 2020]**

1.2.24 If sertraline is ineffective, offer an alternative SSRI or a serotonin–noradrenaline reuptake inhibitor (SNRI), taking into account the following factors:

- tendency to produce a withdrawal syndrome (especially with paroxetine and venlafaxine)
- the side-effect profile and the potential for drug interactions
- the risk of suicide and likelihood of toxicity in overdose (especially with venlafaxine)
- the person's prior experience of treatment with individual drugs (particularly adherence, effectiveness, side effects, experience of withdrawal syndrome and the person's preference).

  Note that this is an off-label use for some SSRIs. See NICE's information on prescribing medicines. **[2011, amended 2020]**

1.2.25 If the person cannot tolerate SSRIs or SNRIs, consider offering pregabalin.

As of 1 April 2019, pregabalin is a Class C controlled substance (under the Misuse of Drugs Act 1971) and scheduled under the Misuse of Drugs Regulations 2001 as Schedule 3. Evaluate patients carefully for a history of drug abuse before prescribing and observe patients for development of signs of abuse and dependence (MHRA, Drug Safety Update April 2019). Follow the MHRA safety advice on pregabalin in pregnancy. **[2011, amended 2022]**

1.2.26 Do not offer a benzodiazepine for the treatment of GAD in primary or secondary care except as a short-term measure during crises. Follow the advice in the BNF on the use of a benzodiazepine in this context. **[2011]**

1.2.27 Do not offer an antipsychotic for the treatment of GAD in primary care. **[2011, amended 2018]**

1.2.28 Before prescribing any medication, discuss the treatment options and any concerns the person with GAD has about taking medication. Explain fully the reasons for prescribing and provide written and verbal information on:

- the likely benefits of different treatments

- the different propensities of each drug for side effects, withdrawal syndromes and drug interactions (consult the interactions section of the BNF)
- the risk of activation with SSRIs and SNRIs, with symptoms such as increased anxiety, agitation and problems sleeping
- the gradual development, over 1 week or more, of the full anxiolytic effect
- the importance of taking medication as prescribed and the need to continue treatment after remission to avoid relapse. **[2011, amended 2020]**

1.2.29 Take into account the increased risk of bleeding associated with SSRIs, particularly for older people or people taking other drugs that can damage the gastrointestinal mucosa or interfere with clotting (for example, non-steroidal anti-inflammatory drugs [NSAIDS] or aspirin). Consider prescribing a gastroprotective drug in these circumstances. **[2011]**

1.2.30 For people aged under 30 who are offered an SSRI or SNRI:

- warn them that these drugs are associated with an increased risk of suicidal thinking and self-harm in a minority of people under 30 **and**
- see them within 1 week of first prescribing **and**
- monitor the risk of suicidal thinking and self-harm weekly for the first month. **[2011]**

1.2.31 For people who develop side effects soon after starting drug treatment, provide information and consider 1 of the following strategies:

- monitoring the person's symptoms closely (if the side effects are mild and acceptable to the person) **or**
- reducing the dose of the drug **or**
- stopping the drug and, according to the person's preference, offering either
  - an alternative drug (see recommendations 1.2.24 to 1.2.25) **or**
  - a high-intensity psychological intervention (see recommendations 1.2.18

to 1.2.22). **[2011]**

1.2.32 Review the effectiveness and side effects of the drug every 2 to 4 weeks during the first 3 months of treatment and every 3 months thereafter. **[2011]**

1.2.33 If the drug is effective, advise the person to continue taking it for at least a year as the likelihood of relapse is high. **[2011]**

Inadequate response to step 3 interventions

1.2.34 If a person's GAD has not responded to a full course of a high-intensity psychological intervention, offer a drug treatment (see recommendations 1.2.23 to 1.2.33). **[2011]**

1.2.35 If a person's GAD has not responded to drug treatment, offer either a high-intensity psychological intervention (see recommendations 1.2.18 to 1.2.22) or an alternative drug treatment (see recommendations 1.2.24 to 1.2.25). **[2011]**

1.2.36 If a person's GAD has partially responded to drug treatment, consider offering a high-intensity psychological intervention in addition to drug treatment. **[2011]**

1.2.37 Consider referral to step 4 if the person with GAD has severe anxiety with marked functional impairment in conjunction with:

- a risk of self-harm or suicide **or**
- significant comorbidity, such as substance misuse, personality disorder or complex physical health problems **or**
- self-neglect **or**
- an inadequate response to step 3 interventions. **[2011]**

Step 4: Complex, treatment-refractory GAD and very marked functional impairment or high risk of self-harm

(Step 4 normally refers to community mental health teams but may include specialist

services and specialist practitioners in primary care.)

Assessment

1.2.38 Offer the person with GAD a specialist assessment of needs and risks, including:

- duration and severity of symptoms, functional impairment, comorbidities, risk to self and self-neglect
- a formal review of current and past treatments, including adherence to previously prescribed drug treatments and the fidelity of prior psychological interventions, and their impact on symptoms and functional impairment
- home environment
- support in the community
- relationships with and impact on families and carers. **[2011]**

1.2.39 Develop a comprehensive care plan in collaboration with the person with GAD that addresses needs, risks and functional impairment and has a clear treatment plan. **[2011]**

Treatment

1.2.40 Inform people with GAD who have not been offered or have refused the interventions in steps 1 to 3 about the potential benefits of these interventions, and offer them any they have not tried. **[2011]**

1.2.41 Consider offering combinations of psychological and drug treatments, combinations of antidepressants or augmentation of antidepressants with other drugs, but exercise caution and be aware that:

- evidence for the effectiveness of combination treatments is lacking **and**
- side effects and interactions are more likely when combining and augmenting antidepressants. **[2011]**

1.2.42 Combination treatments should be undertaken only by practitioners with

expertise in the psychological and drug treatment of complex, treatment-refractory anxiety disorders and after full discussion with the person about the likely advantages and disadvantages of the treatments suggested. **[2011]**

1.2.43 When treating people with complex and treatment-refractory GAD, inform them of relevant clinical research in which they may wish to participate, working within local and national ethical guidelines at all times. **[2011]**

1.2.44 To facilitate shared decision making, evidence-based information about treatments should be available and discussion of the possible options should take place. **[2004]**

1.2.45 People's preference and the experience and outcome of previous treatment(s) should be considered in determining the choice of treatment. **[2004]**

1.2.46 Common concerns about taking medication, such as fears of addiction, should be addressed. **[2004]**

Language

1.2.47 Where available, consideration should be given to providing psychotherapies in the person's own language if this is not English. **[2004]**

Treatment and referral advice to help prevent relapse

1.2.48 For people with a common mental health disorder who are at significant risk of relapse or have a history of recurrent problems, discuss with the person the treatments that might reduce the risk of recurrence. The choice of treatment or referral for treatment should be informed by the response to previous treatment, including residual symptoms, the consequences of relapse, any discontinuation symptoms when stopping medication, and the person's preference. **[2011]**

1.3 Stepped care for people with panic disorder

The guideline provides recommendations for care at different stages of the person's journey, represented as different steps:

- Step 1 – recognition and diagnosis
- Step 2 – treatment in primary care
- Step 3 – review and consideration of alternative treatments
- Step 4 – review and referral to specialist mental health services
- Step 5 – care in specialist mental health services.

Step 1: Recognition and diagnosis of panic disorder

Consultation skills

1.3.1 All healthcare professionals involved in diagnosis and management should have a demonstrably high standard of consultation skills so that a structured approach can be taken to the diagnosis and subsequent management plan for panic disorder. The standards required for Membership of the Royal College of General Practitioners are a good example of standards for consulting skills. **[2004, amended 2020]**

Diagnosis

The accurate diagnosis of panic disorder is central to the effective management of this condition. It is acknowledged that frequently there are other conditions present, such as depression, that can make the presentation and diagnosis confusing.

1.3.2 The diagnostic process should elicit necessary relevant information such as personal history, any self-medication, and cultural or other individual characteristics that may be important considerations in subsequent care. **[2004]**

1.3.3 There is insufficient evidence on which to recommend a well-validated, self-

reporting screening instrument to use in the diagnostic process, and so consultation skills should be relied upon to elicit all necessary information. **[2004]**

Comorbidities

1.3.4 The clinician should be alert to the common clinical situation of comorbidity, in particular, panic disorder with depression and panic disorder with substance misuse.

Be aware when prescribing SSRIs of the need to ask about cocaine use when considering drug–drug interactions, and the need to avoid concurrent use of multiple serotonergic drugs. Follow the MHRA safety advice on citalopram. **[2004, amended 2020]**

1.3.5 The main problem(s) to be treated should be identified through a process of discussion with the person. In determining the priorities of the comorbidities, the sequencing of the problems should be clarified. This can be helped by drawing up a timeline to identify when the various problems developed. By understanding when the symptoms developed, a better understanding of the relative priorities of the comorbidities can be achieved, and there is a better opportunity of developing an effective intervention that fits the needs of the individual. **[2004]**

Presentation in A&E with panic attacks

It is important to remember that a panic attack does not necessarily constitute a panic disorder and appropriate treatment of a panic attack may limit the development of panic disorder. For people who present with chest pain at A&E services, there appears to be a greater likelihood of the cause being panic disorder if coronary artery disease is not present or the person is female or relatively young. Two other variables, atypical chest pain and self-reported anxiety, may also be associated with panic disorder presentations, but there is insufficient evidence to establish a relationship.

1.3.6 If a person presents in A&E, or other settings, with a panic attack, they should:

- be asked if they are already receiving treatment for panic disorder

- undergo the minimum investigations necessary to exclude acute physical problems
- not usually be admitted to a medical or psychiatric bed
- be referred to primary care for subsequent care, even if assessment has been undertaken in A&E
- be given appropriate written information about panic attacks and why they are being referred to primary care
- be offered appropriate written information about sources of support, including local and national voluntary and self-help groups. **[2004]**

Step 2 for people with panic disorder: offer treatment in primary care

The recommended treatment options have an evidence base: psychological therapy, medication and self-help have all been shown to be effective. The choice of treatment will be a consequence of the assessment process and shared decision making.

1.3.7 The treatment option of choice should be available promptly. **[2004]**

1.3.8 There are positive advantages of services based in primary care (for example, lower rates of people who do not attend) and these services are often preferred by people. **[2004]**

1.3.9 For people with mild to moderate panic disorder, offer or refer for 1 of the following low-intensity interventions:

- individual non-facilitated self-help
- individual facilitated self-help. **[2011]**

1.3.10 Information about support groups, where they are available, should be offered. (Support groups may provide face-to-face meetings, telephone conference support groups [which can be based on CBT principles], or additional information

on all aspects of anxiety disorders plus other sources of help.) **[2004]**

1.3.11 The benefits of exercise as part of good general health should be discussed with all people with panic disorder as appropriate. **[2004]**

Step 3 for people with panic disorder: review and offer alternative treatment if appropriate

1.3.12 For people with moderate to severe panic disorder (with or without agoraphobia), consider referral for:

- CBT **or**
- an antidepressant if the disorder is long-standing or the person has not benefitted from or has declined psychological intervention. **[2011]**

Psychological interventions

1.3.13 CBT should be used. **[2004]**

1.3.14 CBT should be delivered only by suitably trained and supervised people who can demonstrate that they adhere closely to empirically grounded treatment protocols. **[2004]**

1.3.15 CBT in the optimal range of duration (7 to 14 hours in total) should be offered. **[2004]**

1.3.16 For most people, CBT should take the form of weekly sessions of 1 to 2 hours and should be completed within a maximum of 4 months of commencement. **[2004]**

1.3.17 Briefer CBT should be supplemented with appropriate focused information and tasks. **[2004]**

1.3.18 Where briefer CBT is used, it should be around 7 hours and designed to integrate with structured self-help materials. **[2004]**

1.3.19 For a few people, more intensive CBT over a very short period of time might be appropriate. **[2004]**

Pharmacological interventions

General

1.3.20 Benzodiazepines are associated with a less good outcome in the long term and should not be prescribed for the treatment of individuals with panic disorder. **[2004]**

1.3.21 Sedating antihistamines or antipsychotics should not be prescribed for the treatment of panic disorder. **[2004]**

Antidepressant medication

Antidepressants should be the only pharmacological intervention used in the longer-term management of panic disorder. The classes of antidepressants that have an evidence base for effectiveness are the selective serotonin reuptake inhibitors (SSRIs), serotonin-noradrenaline reuptake inhibitors (SNRIs) and tricyclic antidepressants (TCAs). At the time of this amendment (June 2020) escitalopram, sertraline, citalopram, paroxetine and venlafaxine are licensed for the treatment of panic disorder.

1.3.22 The following must be taken into account when deciding which medication to offer:

- the age of the person
- previous treatment response
- risks
  - the likelihood of accidental overdose by the person being treated and by other family members if appropriate
  - the likelihood of deliberate self-harm, by overdose or otherwise (the

highest risk is with TCAs)

- tolerability
- the possibility of interactions with concomitant medication (consult the interactions section of the BNF)
- the preference of the person being treated
- cost, where equal effectiveness is demonstrated.

Also see recommendation 1.2.30 on SSRIs and SNRIs. **[2004, amended 2020]**

1.3.23 All people who are prescribed antidepressants should be informed, at the time that treatment is initiated, of potential side effects (including transient increase in anxiety at the start of treatment) and of the risk of discontinuation/withdrawal symptoms if the treatment is stopped abruptly or in some instances if a dose is missed or, occasionally, on reducing the dose of the drug.

Also see recommendation 1.2.30 on SSRIs and SNRIs. **[2004, amended 2020]**

1.3.24 People started on antidepressants should be informed about the delay in onset of effect, the time course of treatment, the need to take medication as prescribed, and possible discontinuation/withdrawal symptoms. Written information appropriate to the person's needs should be made available. **[2004]**

1.3.25 Unless otherwise indicated, an SSRI licensed for panic disorder should be offered. **[2004]**

1.3.26 If an SSRI is not suitable or there is no improvement after a 12-week course and if a further medication is appropriate, imipramine or clomipramine may be considered.

Note that this is an off-label use for imipramine and clomipramine. See prescribing medicines for more information. **[2004, amended 2020]**

1.3.27 When prescribing an antidepressant, the healthcare professional should consider

the following.

- Side effects on the initiation of antidepressants may be minimised by starting at a low dose and increasing the dose slowly until a satisfactory therapeutic response is achieved.
- In some instances, doses at the upper end of the indicated dose range may be necessary and should be offered if needed.
- Long-term treatment may be necessary for some people and should be offered if needed.
- If the person is showing improvement on treatment with an antidepressant, the medication should be continued for at least 6 months after the optimal dose is reached, after which the dose can be tapered. **[2004]**

1.3.28 If there is no improvement after a 12-week course, an antidepressant from the alternative class (if another medication is appropriate) or another form of therapy (see recommendation 1.3.8) should be offered. **[2004]**

1.3.29 People should be advised to take their medication as prescribed. This may be particularly important with short half-life medication in order to avoid discontinuation/withdrawal symptoms. **[2004]**

1.3.30 Stopping antidepressants abruptly can cause discontinuation/withdrawal symptoms. To minimise the risk of discontinuation/withdrawal symptoms when stopping antidepressants, the dose should be reduced gradually over an extended period of time. **[2004]**

1.3.31 All people prescribed antidepressants should be informed that, although the drugs are not associated with tolerance and craving, discontinuation/withdrawal symptoms may occur on stopping or missing doses or, occasionally, on reducing the dose of the drug. These symptoms are usually mild and self-limiting but occasionally can be severe, particularly if the drug is stopped abruptly. **[2004]**

1.3.32 Healthcare professionals should inform people that the most commonly experienced discontinuation/withdrawal symptoms are dizziness, numbness and tingling, gastrointestinal disturbances (particularly nausea and vomiting), headache, sweating, anxiety and sleep disturbances. **[2004]**

1.3.33 Healthcare professionals should inform people that they should seek advice from their medical practitioner if they experience significant discontinuation/withdrawal symptoms. **[2004]**

1.3.34 If discontinuation/withdrawal symptoms are mild, the practitioner should reassure the person and monitor symptoms. If severe symptoms are experienced after discontinuing an antidepressant, the practitioner should consider reintroducing it (or prescribing another from the same class that has a longer half-life) and gradually reducing the dose while monitoring symptoms. **[2004]**

Step 4 for people with panic disorder: review and offer referral from primary care if appropriate

1.3.35 In most instances, if there have been 2 interventions provided (any combination of psychological intervention, medication, or bibliotherapy) and the person still has significant symptoms, then referral to specialist mental health services should be offered. **[2004]**

Step 5 for people with panic disorder: care in specialist mental health services

1.3.36 Specialist mental health services should conduct a thorough, holistic reassessment of the individual, their environment and social circumstances. This reassessment should include evaluation of:

- previous treatments, including effectiveness and concordance
- any substance use, including nicotine, alcohol, caffeine and recreational drugs
- comorbidities
- day-to-day functioning
- social networks
- continuing chronic stressors

- the role of agoraphobic and other avoidant symptoms.

  A comprehensive risk assessment should be undertaken and an appropriate risk management plan developed.

  Be aware when prescribing SSRIs of the need to ask about cocaine use when considering drug–drug interactions, and the need to avoid concurrent use of multiple serotonergic drugs. Follow the MHRA safety advice on citalopram. **[2004, amended 2020]**

1.3.37 To undertake these evaluations, and to develop and share a full formulation, more than 1 session may be required and should be available. **[2004]**

1.3.38 Care and management should be based on the individual's circumstances and shared decisions made. Options include:

- treatment of comorbid conditions
- CBT with an experienced therapist if not offered already, including home-based CBT if attendance at clinic is difficult
- full exploration of pharmacotherapy
- day support to relieve carers and family members
- referral for advice, assessment or management to tertiary centres. **[2004, amended 2019]**

1.3.39 There should be accurate and effective communication between all healthcare professionals involved in the care of any person with panic disorder, and particularly between primary care clinicians (GP and teams) and secondary care clinicians (community mental health teams) if there are existing physical health conditions that also require active management. **[2004]**

Monitoring and follow-up for individuals with panic disorder

Psychological interventions

1.3.40 There should be a process within each practice to assess the progress of a person undergoing CBT. The nature of that process should be determined on a case-by-case basis. **[2004]**

Pharmacological interventions

1.3.41 When a new medication is started, the efficacy and side-effects should be reviewed within 2 weeks of starting treatment and again at 4, 6 and 12 weeks. Follow the summary of product characteristics with respect to all other monitoring required. **[2004]**

1.3.42 At the end of 12 weeks, an assessment of the effectiveness of the treatment should be made, and a decision made as to whether to continue or consider an alternative intervention. **[2004]**

1.3.43 If medication is to be continued beyond 12 weeks, the individual should be reviewed at 8- to 12-week intervals, depending on clinical progress and individual circumstances. **[2004]**

Self-help

1.3.44 Individuals receiving self-help interventions should be offered contact with primary healthcare professionals, so that progress can be monitored and alternative interventions considered if appropriate. The frequency of such contact should be determined on a case-by-case basis, but is likely to be between every 4 and 8 weeks. **[2004]**

Outcome measures

1.3.45 Short, self-completed questionnaires (such as the panic subscale of the

agoraphobic mobility inventory for individuals with panic disorder) should be used to monitor outcomes wherever possible. **[2004]**

Recommendations for research

The 2011 Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future. The Guideline Development Group's full set of recommendations for research is detailed in the full guideline.

1 A comparison of the clinical and cost effectiveness of sertraline and CBT in people with GAD that has not responded to guided self-help and psychoeducation

What is the relative effectiveness of sertraline compared with cognitive behavioural therapy (CBT) in people with generalised anxiety disorder (GAD) that has not responded to guided self-help and psychoeducation in a stepped-care model?

This question should be addressed using a randomised controlled design in which people with GAD that has not responded to step 2 interventions are allocated openly to treatment with sertraline, CBT or waiting-list control for 12 to 16 weeks. The control group is important to demonstrate that the 2 active treatments produce effects greater than those of natural remission. The period of waiting-list control is the standard length of CBT treatment for GAD and is also commonly the length of time that it would take for specialist CBT to become available in routine practice. After 12 to 16 weeks all participants should receive further treatment chosen in collaboration with their treating clinicians.

The outcomes chosen at 12 to 16 weeks should include both observer- and participant-rated measures of clinical symptoms and functioning specific to GAD, and of quality of life. An economic analysis should also be carried out alongside the trial. The trial needs to be large enough to determine the presence or absence of clinically important effects and of any differences in costs between the treatment options using a non-inferiority design. Mediators and moderators of response should be investigated. Follow-up assessments should continue over the next 2 years to ascertain whether short-term benefits are maintained and, in particular, whether CBT produces a better long-term outcome.

Why this is important

Both sertraline and CBT are efficacious in the treatment of GAD but their relative efficacy has not been compared. In a stepped-care model both CBT and sertraline are treatment options if step 2 interventions (guided self-help and/or psychoeducation) have not resulted in a satisfactory clinical response. At present, however, there are no randomised trial data to help prioritise next-step treatments and no information on how individuals with GAD may be matched to particular therapies. Clarification of the relative short- and longer-term benefits of sertraline and CBT would be helpful in guiding treatment.

2 The clinical and cost effectiveness of 2 CBT-based low-intensity interventions (CCBT and guided bibliotherapy) compared with a waiting-list control for the treatment of GAD

In well-defined GAD, what is the clinical and cost effectiveness of 2 CBT-based low-intensity interventions (computerised cognitive behavioural therapy [CCBT] and guided bibliotherapy) compared with a waiting-list control?

This question should be answered using a 3-armed randomised controlled design using both short- and medium-term outcomes (including cost-effectiveness outcomes). Particular attention should be paid to the reproducibility of the treatment model with regard to content, duration and the training and supervision of those delivering interventions to ensure that the results are both robust and generalisable. The outcomes chosen should include both observer- and participant-rated measures of clinical symptoms and functioning specific to GAD, and an assessment of the acceptability and accessibility of the treatment options.

Why this is important

Psychological treatments are a recommended therapeutic option for people with GAD. CCBT is a promising low-intensity intervention for GAD that does not yet have a substantial evidence base. It is therefore important to establish whether CCBT is an effective and cost-effective treatment that should be provided for GAD, and how it compares with other low-intensity interventions such as guided bibliotherapy. The results of this trial will have important implications for the provision, accessibility and acceptability

of psychological treatment in the NHS.

3 The effectiveness of physical activity compared with waiting-list control for the treatment of GAD

For people with GAD who are ready to start a low-intensity intervention, what is the clinical effectiveness of physical activity compared with waiting-list control?

This question should be answered using a randomised controlled design for people with GAD who have been educated about the disorder (as described in step 1) and are stepping up to a low-intensity intervention. The period of waiting-list control should be 12 weeks. The outcomes chosen should include both observer- and participant-rated measures of clinical symptoms and functioning specific to GAD, and of quality of life.

Why this is important

The evidence base for the effectiveness of physical activity in reducing anxiety symptoms is substantially smaller than that for depression. However, where evidence exists there are signs that physical activity could help to reduce anxiety. As GAD is a commonly experienced mental health disorder the results of this study will have important implications in widening the range of treatment options available in the NHS.

4 The effectiveness of chamomile and ginkgo biloba in the treatment of GAD

Is chamomile/ginkgo biloba more effective than placebo in increasing response and remission rates and decreasing anxiety ratings for people with GAD?

This question should be addressed using a placebo-controlled, double-blind randomised design to compare the effects of a standardised dose of chamomile (220 mg to 1100 mg) or ginkgo biloba (30 mg to 500 mg) in a readily available form, for example a capsule, with placebo. This should assess outcomes at the end of the trial and at 12-month post-trial follow-up. The outcomes chosen should include both observer- and participant-rated measures of clinical symptoms and functioning specific to GAD, and of side effects. There should be a health economic evaluation included and an assessment of quality of life. The trial should be large enough to determine the presence or absence of clinically important

effects using a non-inferiority design. Mediators and moderators of response should be investigated.

Why this is important

GAD is a common mental health disorder and the results of this study will be generalisable to a large number of people. There is evidence for the efficacy of chamomile and ginkgo biloba in reducing anxiety in people with GAD but the evidence base is small (1 study). However, the scarce literature on the effectiveness of other herbal interventions for treating GAD points to chamomile and ginkgo biloba as 2 of the more effective herbal interventions. Moreover, both these herbal remedies are widely available and relatively inexpensive. Furthermore, at present there is no scientific evidence of side effects or drug–herbal interactions in relation to chamomile or ginkgo biloba. As both these herbal interventions are readily available and have no known side effects, they could be used at an early stage as a means of preventing progression to drug treatments, which are associated with a number of undesirable side effects and dependency.

5 The clinical and cost effectiveness of a primary care-based collaborative care approach to improving the treatment of GAD compared with usual care

What are the benefits of a primary care-based collaborative care approach to improving the treatment of GAD compared with usual care?

This question should be addressed using a cluster randomised controlled design in which the clusters are GP practices and people with GAD are recruited following screening of consecutive attenders at participating GP practices. GPs in intervention practices should receive training in recognising GAD and providing both drug treatment and GP-delivered low-intensity psychological interventions (psychoeducation and non-facilitated self-help). Psychological wellbeing practitioners in intervention practices should provide these low-intensity psychological interventions and support GP-prescribed drug treatment by providing information about side effects, monitoring medication use and liaising about any changes to medication. They should also support the referral for CBT of participants whose symptoms have not improved following low-intensity interventions. Structured, practice-based protocols should define care pathways, the interventions to be provided

by practitioners at each point in the care pathway and the mechanisms they should use to liaise about individual patients. In control practices, participants should receive care as usual from the GP, including referral for primary and secondary care psychological interventions or mental health services.

Outcomes should be evaluated at 6 months with follow-up assessments continuing for up to 2 years to establish whether short-term benefits are maintained in the longer term. The outcomes chosen should include both observer- and participant-rated measures of clinical symptoms and functioning specific to GAD, and of quality of life. An economic analysis should also be carried out alongside the trial. The trial needs to be large enough to determine the presence or absence of clinically important effects and of any differences in costs between collaborative care and usual care.

Why this is important

Most people with GAD in the UK do not receive evidence-based management and poor recognition of GAD by GPs contributes to a lack of appropriate interventions being offered. There is some evidence that complex interventions involving the training of primary care practitioners, together with a collaborative care approach involving GPs, other primary care practitioners and mental health professionals, can improve the uptake of evidence-based interventions and clinical and functional outcomes for people with GAD. However, these approaches have not been evaluated in primary care in the UK. Given the differences between the organisation of primary care in different countries, such as the US, it is important to demonstrate whether these approaches can also be effective in the UK.

6 The clinical and cost effectiveness of 2 CBT-based low-intensity interventions (CCBT and guided bibliotherapy) compared with a waiting-list control for the treatment of panic disorder

In well-defined panic disorder, what is the clinical and cost effectiveness of 2 CBT-based low-intensity interventions (CCBT and guided bibliotherapy) compared with a waiting-list control?

This question should be answered using a 3-armed randomised controlled design using

both short- and medium-term outcomes (including cost-effectiveness outcomes). Particular attention should be paid to the reproducibility of the treatment model with regard to content, duration and the training and supervision of those delivering interventions to ensure that the results are both robust and generalisable. The outcomes chosen should include both observer- and participant-rated measures of clinical symptoms and functioning specific to panic disorder, and an assessment of the acceptability and accessibility of the treatment options.

Why this is important

Psychological treatments are a recommended therapeutic option for people with panic disorder. CCBT is a promising low-intensity intervention for panic disorder that does not yet have a substantial evidence base. It is therefore important to establish whether CCBT is an effective and cost-effective treatment that should be provided for panic disorder, and how it compares with other low-intensity interventions such as guided bibliotherapy. The results of this trial will have important implications for the provision, accessibility and acceptability of psychological treatment in the NHS.

Appendix: Assessing generalised anxiety disorder

The assessment of generalised anxiety disorder (GAD) is based on the criteria in DSM-IV. Assessment should include the number and severity of symptoms, duration of the current episode and course of the disorder.

Key symptoms of GAD

The key symptoms of GAD are:

- excessive anxiety and worry about a number of events or activities
- difficulty controlling the worry.

The worry should occur on a majority of days for at least 6 months. The focus of the worry should not be confined to features of another anxiety disorder (for example, not just about having a panic attack, social embarrassment, a traumatic event, being contaminated or having a serious illness).

If the 2 key symptoms are present, ask about the following associated symptoms:

- restlessness
- being easily fatigued
- difficulty concentrating
- irritability
- muscle tension
- disturbed sleep.

Then ask about duration, distress, impairment of functioning and past history of anxiety and mood disorders.

Factors that favour initial education about GAD and active monitoringonly (step 1) are:

- few symptoms of GAD or symptoms that are intermittent or of less than 6 months' duration (hence subclinical)
- only mild distress and no or limited functional impairment
- no comorbid anxiety or mood disorder
- no past history of anxiety or mood disorders
- individual not interested in any active treatment option.

Factors that favour initial active treatment with low-intensity psychological interventions, including GP-prescribed non-facilitated self-help (step 2) are:

- diagnostic criteria for GAD met
- clinically significant distress and/or impairment in social, occupational or other important areas of functioning
- comorbid anxiety or mood disorder
- individual wishes to pursue active treatment for GAD.

Factors that favour treatment with a high-intensity psychological intervention or a pharmacological intervention (step 3) are:

- marked functional impairment
- less marked but clinically significant functional impairment or distress and inadequate response to a step 2 intervention
- past history of anxiety or mood disorders.

Factors that favour referral for specialist treatment (step 4) are:

- GAD that is refractory to both cognitive behavioural therapy (CBT) and drug treatment
- very severe functional impairment (such as self-neglect)
- persistent suicidal thoughts
- multiple psychiatric comorbidities.

Context

Generalised anxiety disorder (GAD) is 1 of a range of anxiety disorders that includes panic disorder (with and without agoraphobia), post-traumatic stress disorder, obsessive–compulsive disorder, social phobia, specific phobias (for example, of spiders) and acute stress disorder. Anxiety disorders can exist in isolation but more commonly occur with other anxiety and depressive disorders. This guideline covers both 'pure' GAD, in which no comorbidities are present, and the more typical presentation of GAD comorbid with other anxiety and depressive disorders in which GAD is the primary diagnosis.

GAD is a common disorder, of which the central feature is excessive worry about a number of different events associated with heightened tension. A formal diagnosis using the DSM-IV classification system requires 2 major symptoms (excessive anxiety and worry about a number of events and activities, and difficulty controlling the worry) and 3 or more additional symptoms from a list of 6 (see the American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th edition). Symptoms should be present for at least 6 months and should cause clinically significant distress or impairment in social, occupational or other important areas of functioning.

According to the DSM-IV-TR, a fundamental characteristic of panic disorder is the presence of recurring, unforeseen panic attacks followed by at least 1 month of persistent worry about having another panic attack and concern about the consequences of a panic attack, or a significant change in behaviour related to the attacks (see the American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision). At least 2 unexpected panic attacks are necessary for diagnosis and the attacks should not be accounted for by the use of a substance, a general medical condition or another psychological problem. Panic disorder can be diagnosed with or without agoraphobia.

GAD and panic disorder vary in severity and complexity and this has implications for response to treatment. Therefore, it is important to consider symptom severity, duration, degree of distress, functional impairment, personal history and comorbidities when undertaking a diagnostic assessment.

GAD and panic disorder can follow both chronic and remitting courses. Where possible, the goal of an intervention should be complete relief of symptoms (remission), which is associated with better functioning and a lower likelihood of relapse.

The guideline assumes that prescribers will use a drug's summary of product characteristics (SPC) to inform their decisions made with individual service users.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), this is indicated in the recommendation.

New and updated recommendations are included on the management of generalised anxiety disorder in adults.

Finding more information and committee details

To find NICE guidance on related topics, including guidance in development, see the NICE topic page on anxiety.

For full details of the evidence and the guideline committee's discussions, see the full guideline. You can also find information about how the guideline was developed, including details of the committee.

NICE has produced tools and resources to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see resources to help you put guidance into practice.

Update information

June 2020: The information on the classes of antidepressants suitable for longer-term management of panic disorder was updated to include serotonin-noradrenaline reuptake inhibitors (SNRIs), and give details on the medicines licensed for this treatment. Medicines and Healthcare products Regulatory Agency (MHRA) warning advice on citalopram and selective serotonin reuptake inhibitors (SSRIs) prescribing was added to relevant recommendations. SSRIs licensing information was added to relevant recommendations.

July 2019: Because of a risk of abuse and dependence, pregabalin is controlled under the Misuse of Drugs Act 1971 as a class C substance and scheduled under the Misuse of Drugs Regulations 2001 as schedule 3 (as of 1 April 2019). A note has been added in this guideline to reflect this change. Recommendation 1.3.38 was amended to remove structured problem solving as a care and management option, as this had been originally included in error.

Minor changes since publication

May 2024: We have simplified the guideline by removing recommendations on general principles of care that are covered in other NICE guidelines (for example, the NICE guideline on service user experience in adult mental health).

This is a presentational change only, and no changes to practice are intended.

We have also incorporated relevant recommendations from the NICE guideline on common mental health disorders, covering identification (see recommendation 1.2.2) and preventing relapse (see recommendation 1.2.48). These recommendations are marked **[2011]**.

July 2022: We added a link to the MHRA safety advice on pregabalin in pregnancy to recommendation 1.2.25.

June 2018: Recommendation 1.2.14 was amended with advice on cognitive behavioural therapy (CBT) to bring it in line with current best practice and other NICE guidance. Recommendation 1.2.27 was updated with a link to the newest evidence on use of antipsychotics for treatment of generalised anxiety disorder. Recommendation 1.3.10 on low-intensity interventions for mild to moderate panic disorder and 1.3.13 on treatment for moderate to severe panic disorder were added, taken from the NICE guideline on common

mental health problems. Recommendations in section 1.2 on stepped care for people with panic disorder were reordered.

Recommendations marked **[date 1, amended date 2]** had an evidence review in date 1. The amended date means the intent of the recommendation has been changed without an evidence review.

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