Generalised anxiety disorder in adults: Evidence Update September 2012

A summary of selected new evidence relevant to NICE clinical guideline 113 'Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults: management in primary, secondary and community care' (2011)

Evidence Update 22

Evidence Updates provide a summary of selected new evidence published since the literature search was last conducted for the accredited guidance they relate to. They reduce the need for individuals, managers and commissioners to search for new evidence. Evidence Updates highlight key points from the new evidence and provide a commentary describing its strengths and weaknesses. They also indicate whether the new evidence may have a potential impact on current guidance. For contextual information, this Evidence Update should be read in conjunction with the relevant clinical guideline, available from the NHS Evidence topic page for anxiety.

Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.

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National Institute for Health and Clinical Excellence

Level 1A
City Tower
Piccadilly Plaza
Manchester M1 4BT
www.nice.org.uk

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Introduction

This Evidence Update identifies new evidence that is relevant to, and may have a potential impact on, the following reference guidance:

[1] **Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. NICE clinical guideline 113 (2011).**

A search was conducted for new evidence from 1 July 2010 to 02 April 2012. A total of 3207 pieces of evidence were identified and assessed, of which 5 were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An Evidence Update Advisory Group, comprised of topic experts, reviewed the prioritised evidence and provided a commentary.

The evidence covered in an Evidence Update should reflect the scope of that covered by the reference guidance; because the scope of the 2011 update of NICE's generalised anxiety disorder and panic disorder guideline did not include panic disorder, this topic was removed from the scope of the Evidence Update.

Although the process of updating NICE guidance is distinct from the process of an Evidence Update, the relevant NICE guidance development centres have been made aware of the new evidence, which will be considered when guidance is reviewed.

Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

[1] NICE-accredited guidance is denoted by the Accreditation Mark

Key points

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key points for this Evidence Update. It also indicates the EUAG's opinion on whether the new evidence may have a potential impact on the current guidance listed in the introduction. For further details of the evidence behind these key points, please see the full commentaries.

The section headings used in the table below are taken from the guidance.

	Potential impact on guidance	
Key point	**Yes**	**No**
Step 2: Diagnosed generalised anxiety disorder (GAD) that has not improved after step 1 interventions ***Low-intensity psychological interventions for GAD*** • Internet-based cognitive behavioural therapy (CBT) may be effective for treating GAD whether support is given by clinicians or non-clinicians.		✓
Step 3: GAD with marked functional impairment or that has not improved after step 2 interventions ***Meta-cognitive therapy and intolerance of uncertainty therapy*** • Meta-cognitive therapy and intolerance of uncertainty therapy may be effective methods of CBT in GAD. ***Treatments for GAD in older people*** • Psychotherapy and drug treatment may both have a higher likelihood of being effective for treating GAD in older people compared with control; however, the effect size of CBT may not be significantly larger than control.		✓ ✓
Step 4: Complex, treatment-refractory GAD and very marked functional impairment or high risk of self-harm ***Collaborative care*** • Collaborative care with patient's choice of drug treatment, CBT or both drug treatment and CBT may be effective in treating GAD.		✓

1 Commentary on new evidence

These commentaries analyse the key references identified specifically for the Evidence Update. The commentaries focus on the 'key references' (those identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update), which are identified in bold text. Supporting references provide context or additional information to the commentary. Section headings are taken from the guidance.

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

No new key evidence was found for this section.

1.2 Stepped care for people with GAD

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

Low-intensity psychological interventions for GAD

NICE CG113 recommends low-intensity psychological interventions for step 2 treatment of GAD, with a choice of individual non-facilitated self-help, individual guided self-help or psychoeducational groups.

Robinson et al. (2010) reported on an Australian study of an internet-based cognitive behavioural therapy (CBT) tool (the worry programme) that compared clinician assistance with technician assistance and with a delayed-treatment control group. Participants (n=150) were recruited via a website, on which they completed several screening questionnaires to determine presence and severity of symptoms of anxiety. Reasons for exclusion from the study included: age younger than 18 years, no regular access to a computer, the internet and a printer and current participation in cognitive behavioural therapy.

Eligible participants were then telephoned for a diagnostic interview to determine whether they met criteria for GAD as defined in the Diagnostic and statistical manual of mental disorders, 4th edition (DSM-IV). People were randomly assigned to clinician-assisted internet CBT, technician-assisted internet CBT or to delayed treatment (control) by computerised randomisation before the diagnostic telephone call. The authors stated that blinding was not possible because the outcomes were self-reported.

The internet CBT programme consisted of 6 sessions to be completed within 10 weeks at a rate of 1 every 7–10 days. Participants in the clinician-assisted group (n=47) had weekly email or telephone contact and access to an online forum where they could ask questions. The clinician was encouraged to engage with participants including in goal setting, problem solving and strategies to overcome barriers to progress. People in the technician-assisted group (n=50) had weekly email or telephone contact with the technician, but no access to a forum because the technician could not offer clinical advice. The clinician and the technician were instructed to limit their contact with individual participants to 10 minutes per week. The technician was supervised by the clinician, and reported any perceived deterioration in participants' mental health or concerns about their wellbeing to the clinician. People in the control group (n=48) received no treatment for 11 weeks, and then began clinician-assisted treatment 1 week after the intervention groups completed treatment.

The primary outcome was change in the Penn State Worry Questionnaire (PSWQ) and the GAD-7 assessment tool. Analyses were by intention-to-treat and used the last observation carried forward method to account for missing data. At week 11, post-treatment data were

collected for 45 of 50 participants (90%) in the technician-assisted group, 46 of 47 people (98%) in the clinician-assisted group and 47 of 48 people (98%) in the control group.

Significant differences were seen in PSWQ and GAD-7 scores at the end of treatment after controlling for the pre-treatment scores (both $p<0.001$). Mean difference in scores from baseline for both the clinician-assisted (PSWQ=−12.57, GAD-7=−6.89) and the technician-assisted groups (PSWQ=−10.84, GAD-7=−5.88) differed significantly from the control group (PSWQ=−1.40, GAD-7=−1.69, $p<0.001$), but did not differ significantly from each other.

The authors recognised potential limitations of this study including the small size and the use of delayed treatment control rather than using a placebo based on attention control to simulate therapy. Use of the last observation carried forward to account for missing data is also a potential source of bias.

The study provides some evidence that an internet-based method of CBT is effective with support from either clinicians or trained non-clinicians with clinician support. This particular method of internet-based CBT appears to be available only in Australia (via an organisation called 'This Way Up'), so the direct application of this method in UK practice is limited. However, the evidence is generally consistent with the option of individual guided self-help as recommended in NICE CG113.

Key reference

Robinson E, Titov N, Andrews G et al. (2010) Internet treatment for generalized anxiety disorder: a randomized controlled trial comparing clinician vs. technician assistance. PloS One 5: e10942

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

Meta-cognitive therapy and intolerance of uncertainty therapy

NICE CG113 recommends a high-intensity psychological intervention as an option for treating GAD that has not improved after step 2 treatment. CBT or applied relaxation are particular strategies recommended in the guideline. However, the guideline does not make recommendations on choosing a particular method of CBT.

Van der Heiden et al. (2012) did a single-centre randomised controlled trial in people aged 18–65 years in the Netherlands with a primary diagnosis of GAD (n=126) as defined in the DSM-IV. The interventions assessed were meta-cognitive therapy (n=54), intolerance of uncertainty therapy (n=52) and delayed therapy (n=20).

Patients were either not receiving drug treatment, or were on stable drug treatment and had to agree to no changes in drug treatment during the study. Exclusion criteria were mainly related to patients having other serious mental health disorders such as severe major depressive disorder or psychotic disorder, substance abuse needing treatment, mental impairments or organic brain disorders.

Meta-cognitive therapy focused on the patient's beliefs about worry, not worry itself, using verbal cognitive restructuring strategies, behavioural experiments (for example, postponed worry in which worrying is delayed until a specified time) and worry enhancement experiments (in which patients increase worrying to determine whether positive events occur).

Intolerance of uncertainty therapy focused on helping patients to tolerate, cope with and accept uncertainty in their lives. Patients learnt to distinguish between worries that were amenable to problem solving and those that were not, and then had problem solving training to deal with worries that may have a solution. The final stage of intolerance of uncertainty therapy modified positive beliefs about worry by cognitive therapeutic interventions.

Randomisation was done by the principal investigator rolling a die. The principal investigator also provided training to the therapists administering the therapy sessions, and regularly

supervised the group sessions for both meta-cognitive and intolerance of uncertainty therapy. This indicates no allocation concealment or blinding and was recognised by the authors as a limitation of the study, but the nature of the interventions may have precluded any attempt at allocation concealment or blinding.

The primary outcome measures were the PSWQ and the trait version of the State-Trait Anxiety Inventory (STAI-T), and process measures were made using the Meta Cognitions Questionnaire. Intention-to-treat analyses used the last observation carried forward method to account for dropouts.

In the intention-to-treat population, there were significant pre-treatment differences in scores on both the STAI-T and the negative beliefs about worry section of the Meta Cognitions Questionnaire. Both scores were higher in the meta-cognitive therapy group than in the delayed treatment group (STAI-T=61.10 for meta-cognitive therapy, STAI-T=59.02 for delayed therapy, Meta Cognitions Questionnaire data not reported; between-group difference in scores $p<0.05$ for both instruments).

The intention-to-treat analysis showed significant reductions for both intervention groups compared with delayed treatment in PSWQ score (meta-cognitive therapy=−19.96, intolerance of uncertainty therapy=−10.72, delayed therapy=−0.40) and STAI-T (meta-cognitive therapy=−16.28, intolerance of uncertainty therapy=−10.72, delayed therapy=−2.66; differences between intervention groups and delayed therapy $p<0.05$ for both instruments).

The authors noted that use of self-report measures could be a limitation of this study, and postulated that use of a clinician rating scale (such as the Hamilton Anxiety Rating Scale [HAM-A]) could have been included. The size of the trial may be an additional limitation.

The results of this study suggest that psychological therapy is useful in GAD, which is consistent with recommendations in NICE CG113.

Key reference

van der Heiden C, Muris P, van der Molen HT (2012) Randomized controlled trial on the effectiveness of metacognitive therapy and intolerance-of-uncertainty therapy for generalized anxiety disorder. Behaviour Research and Therapy: 50 100–9

Antipsychotics

NICE CG113 states ‘do not offer an antipsychotic for the treatment of GAD in primary care’.

The search and sift process for the Evidence Update found new evidence examining atypical (also known as second generation) antipsychotics in GAD, specifically olanzapine, risperidone and quetiapine. At the time of publication of this Evidence Update, olanzapine, risperidone and quetiapine did not have UK marketing authorisation for GAD.

During the development of NICE CG113, evidence was considered for antipsychotics in GAD, including olanzapine and risperidone. However, evidence for quetiapine was not assessed by the guideline because a NICE technology appraisal was expected. The technology appraisal was subsequently suspended when the manufacturer of the extended release formulation of quetiapine withdrew a marketing application for GAD. Therefore, NICE has not formally appraised the evidence for quetiapine in GAD, and consequently any formal review by NICE of the evidence base for all atypical antipsychotics in GAD is currently incomplete.

Because of the additional issue that these drugs are unlicensed in this indication, it has been decided that atypical antipsychotics in GAD (in isolation or as adjuvant therapy) would benefit from a more wide-ranging review elsewhere within NICE’s work programme, at which time further information may be made available.

Supporting references

National Institute for Health and Clinical Excellence. Generalised anxiety disorder - quetiapine [ID347]. [online; accessed 13 July 2012]

Treatments for GAD in older people

NICE CG113 recommends CBT as a step 3 treatment option, but has no recommendations specific to use of CBT in older people.

Gould et al. (2012) did a meta-analysis of randomised controlled trials of CBT in anxiety disorders in people older than 55 years (including trials of wider age groups that reported age-specific results). Anxiety disorders included GAD, panic disorder, agoraphobia, post-traumatic stress disorder, obsessive-compulsive disorder and 'anxiety not otherwise specified'.

Eligible studies had either active control (other treatment: drug treatment, social support or attention control placebo) or non-active control (treatment as usual or waiting list). 12 studies were included in the meta-analysis (n=658): 7 studies were of GAD only, 4 were in a range of anxiety disorders (including GAD) and 1 was in panic disorder. The mean proportion of participants with a comorbid psychiatric disorder was 41.5%, and the mean number of CBT sessions was 12. Most studies included components of cognitive therapy, psychoeducation, relaxation training, and graded exposure.

Potential sources of bias that were most adequately addressed by the included studies were incomplete outcome data (10 studies), selective outcome reporting (8 studies) and blinding of outcome assessors (8 studies). Randomisation was less well adequately addressed (only 6 studies reported sequence generation adequately and no studies clearly reported allocation concealment). Potential confounding factors included use of concurrent drug treatment, demographically unrepresentative samples, and self-referral. Effect sizes were calculated across anxiety outcome measures; 9 studies used the PSWQ as the anxiety outcome measure.

Immediately after the intervention compared with baseline, CBT was not significantly different from active controls (effect size difference=−0.20 in favour of CBT, p=0.06). However, the difference between CBT and non-active controls was significant (effect size difference=−0.66 in favour of CBT, p<0.001).

For follow-up, meta-analysis was done only for active controls because non-active controls did not have these data because of ethical limitations preventing withholding of treatment. At 3 months, CBT was not significantly different from active control (effect size difference=−0.40 in favour of CBT, p=0.13). A significant difference was seen at 6 months (effect size difference= 0.29 in favour of CBT, p=0.04). However, at 12 months the difference was again non-significant (effect size difference=−0.21 in favour of CBT, p =0.47).

The authors noted that the significant result seen at 6-month follow-up may be due to a larger number of studies reporting outcomes at this time than reported 3-month and 12-month outcomes. However, they recognised that the main limitation to the meta-analysis was the small number of studies, especially those reporting follow-up.

NICE CG113 does not make specific recommendations for treatment of GAD in older people. However, the results of this study suggest that CBT may be more effective than non-active controls, but no better than active controls for treating anxiety in older people. The authors stated that the effect size was 'small to moderate in older people compared with moderate to large in working-age adults'. However no data were given to quantify the effect sizes seen in working-age adults. A direct comparison of outcomes of CBT in working age people versus older people is needed to address this uncertainty.

Gonçalves and Byrne (2012) did a systematic review and meta-analysis of established interventions for the treatment of GAD (drugs, psychological, or lifestyle interventions) in older people. Studies were included if participants were older than 55 years with a mean or median age of 60 years or older and at least 75% were diagnosed with GAD as primary disorder. Outcome was defined as response to intervention, as defined in the individual studies. This differed between studies, with some defining response as a 25% reduction in anxiety from

baseline, some needing a reduction of 50%, and others relying on clinician ratings of improvement or a combination of clinician rating and change in anxiety score from baseline. 25 articles reporting on a total of 27 trials were included (n= 2374).

For all drug treatments versus control (2 studies of benzodiazepines, 5 studies of antidepressants, 1 study of quetiapine and 1 study of pregabalin) the odds ratio (OR) for response was 0.32 in favour of intervention (95% CI 0.18 to 0.54, p<0.001). Benzodiazepines had an OR of 0.19 (95% CI 0.08 to 0.46, p<0.001), antidepressants had an OR of 0.46 (0.29 to 0.73, p<0.001) and 'other' drugs (pregabalin and quetiapine) had an OR of 0.30 (95% CI 0.07 to 1.25, p value not stated), all in favour of the intervention. The confidence intervals suggested that the effect of 'other' drugs was not significant.

Psychotherapy trials (12 of the 13 psychotherapy trials were of CBT) had an overall OR of 0.33 (95% CI 0.17 to 0.66, p<0.01) for response in favour of intervention. The psychotherapy studies were subdivided by type of control. For waiting list control, the OR for response was significantly in favour of intervention 0.12 (95% CI 0.04 to 0.38, p<0.001); for usual care control the OR was 0.24 (95% CI 0.08 to 0.65, p<0.01). But differences between control and intervention were not significant for active control, with an OR of 0.75 (95% CI 0.30 to 1.89, p=0.54); and for psychotherapy in both arms of a trial, with an OR of 0.76 (95% CI 0.04 to 13.35, p=0.85). The interventions were not significantly different from controls in the active control (such as discussion groups and enhanced usual care) and psychotherapy control groups.

Although significant results were seen overall for psychotherapy trials, the outcome measures here (odds ratios of response) are different from those of the meta-analysis by Gould et al. (2012) reported above (effect size), so they are not directly comparable. This uncertainty means that further research is needed to assess the effectiveness of psychotherapy including CBT in older adults.

The authors identified publication bias for drug trials but not for psychotherapy. Meta-regression analyses showed no significant differences for year of study, mean age of participants, length of intervention, presence of comorbid depression, study quality score or individual versus group psychotherapy.

Author-recognised limitations included heterogeneity of available clinical trials and analyses done and assessment of cognitive impairment. The authors also recognised the uncertainty around evidence of combination treatments compared with single interventions in older people.

The results of this study suggest that both drug treatment and psychotherapy are effective for treating GAD in older people, so management strategies do not seem to need to differ between age groups. This is consistent with the recommendations in NICE CG113, which do not make specific recommendations for older people. However, this meta-analysis included benzodiazepines, which NICE CG113 recommends for short-term use only in crises, because of associated tolerance and dependence.

Key references

Gonçalves DC, Byrne GJ (2012) Interventions for generalized anxiety disorder in older adults: Systematic review and meta-analysis. Journal of Anxiety Disorders 26: 1–11

Gould RL, Coulson MC, Howard RJ (2012) Efficacy of cognitive behavioural therapy for anxiety disorders in older people: a meta-analysis and meta-regression of randomized controlled trials. Journal of the American Geriatrics Society 60: 218– 229

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

Collaborative care

NICE CG113 recommends offering a high-intensity psychological intervention (CBT or applied relaxation) or drug treatment as step 3 treatment for GAD. CBT should consist of 12–15 weekly sessions. Drug treatment should begin with a selective serotonin reuptake inhibitor (SSRI), with an alternative SSRI or a serotonin-norepinephrine reuptake inhibitor (SNRI) offered if the first drug is ineffective. Benzodiazepines should not be offered except for short-term use during crises. If step 3 treatment fails, step 4 treatments include combined drug and psychological treatments. Combination treatments should only be undertaken by practitioners with expertise in treating complex treatment-refractory anxiety disorders.

Craske et al. (2011) reported on a randomised controlled trial in the USA, of a collaborative care intervention compared with usual care in 1004 adults aged 18–75 years with various anxiety disorders (of whom 549 had GAD). Participants in the intervention group (including 270 people with GAD) could choose computer-assisted CBT designed to guide both the mental-health professional and the patient or pharmacotherapy (with drug treatment advice given by psychiatrists to the primary care doctor), or both. The CBT addressed the 4 most common anxiety disorders in primary care (GAD, panic disorder, social anxiety disorder and post-traumatic stress disorder). The outcome of the study was remission (defined as an overall anxiety severity impairment score of less than 5), improvement meaning the participant did not want further treatment or improvement with residual symptoms needing a type of treatment not offered in the study.

Across the 4 anxiety disorders studied, 3–11% of participants in the 1-year intervention group opted for drug treatment only; 32–43% opted for CBT only; and 46–65% opted for CBT plus drug treatment (results not reported separately by disorder). For any person choosing drug treatment, an 'anxiety clinical specialist' provided in-person or telephone adherence monitoring and counselling to avoid alcohol and caffeine and optimise sleep hygiene. Drug treatments were prescribed according to an algorithm, with SSRI or SNRI antidepressants as first-line treatment, increasing to the maximum tolerated dose. If the participant did not respond, an alternative antidepressant was prescribed. If improvement was not adequate, another antidepressant or (in selected cases) a benzodiazepine was added. Any further drug treatments were considered after consultation with the expert study psychiatrist. CBT consisted of 6–8 sessions over 10–12 weeks, although flexibility was permitted. Most treatments were completed in the first 6 months.

People in the usual care group continued to be treated by their primary care doctors with drug treatments, counselling or referral to mental health specialists as usual. The only contact with study staff was for assessments.

No power calculation was reported. Missing data were accounted for in a restricted maximum likelihood approach and attrition weights were used to account for participants who missed 1 or more follow-up assessments. At 18 months, 19% of people with GAD had dropped out.

At 18 months, people with GAD in the intervention group had a reduction in GAD Severity Scale (GADSS) from baseline of 6.09 points compared with 4.08 points for usual care (effect size difference of −0.64 [95% CI −0.87 to −0.40]).

The element of patient choice means that this study resembles real-world practice. However, participants in the usual care group received drug treatments (36–42% of the usual care group) and CBT (27–34% of the usual care group), which the authors recognised as potentially lowering the between-group effect size. An additional limitation reported by the authors was that the trial design did not allow comparison of the 3 possible intervention options.

The treatments used in this study span steps 3 and 4 of the care model recommended in NICE CG113, and the interventions were reasonably comparable to those recommended in the guideline. The drug treatment algorithm used in the study resembled the drug treatment strategy of the guideline, with the notable difference that benzodiazepines were allowed as an add-on to antidepressant treatment whereas NICE CG113 recommends that this class of drugs is used only during crises.

Although combination treatment is recommended as a treatment option in the guideline, it also stated that evidence for combination treatments is lacking. The results reported by Craske et al. (2011) are consistent with NICE CG113, and provide some evidence of effectiveness of combination drug and psychological treatment.

Key reference

Craske MG, Stein MB, Sullivan G et al. (2011) Disorder-specific impact of coordinated anxiety learning and management treatment for anxiety disorders in primary care. Archives of General Psychiatry 68: 378–88

1.3 Principles of care for people with panic disorder

Panic disorder was not included in this Evidence Update; see Appendix A: Methodology for further details.

1.4 Stepped care for people with panic disorder

Panic disorder was not included in this Evidence Update; see Appendix A: Methodology for further details.

2 New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the NHS Evidence UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

Stepped care for people with GAD

- Combined pharmacology and psychotherapy for older adults with generalised anxiety disorder
- Interventions for generalised anxiety disorder in older people with cognitive decline
- CBT for generalised anxiety disorder in older people compared to working age adults

Further evidence uncertainties for GAD can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

Appendix A: Methodology

Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. NICE clinical guideline 113 (2011).

The evidence covered in an Evidence Update should reflect the scope of that covered by the reference guidance; because the scope of the 2011 update of NICE's generalised anxiety disorder and panic disorder guideline did not include panic disorder, this topic was removed from the scope of the Evidence Update.

Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 1 July 2010 (the end of the search period of NICE clinical guideline 113) to 2 April 2012:

- AMED (Allied and Complementary Medicine Database)
- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- Embase
- HTA (Health Technology Assessment) database
- MEDLINE
- NHS EED (Economic Evaluation Database)
- PsycINFO

Table 1 provides details of the MEDLINE search strategy used, which was adapted to search the other databases listed above. The search strategy was used in conjunction with validated Scottish Intercollegiate Guidelines Network search filters for RCTs and systematic reviews.

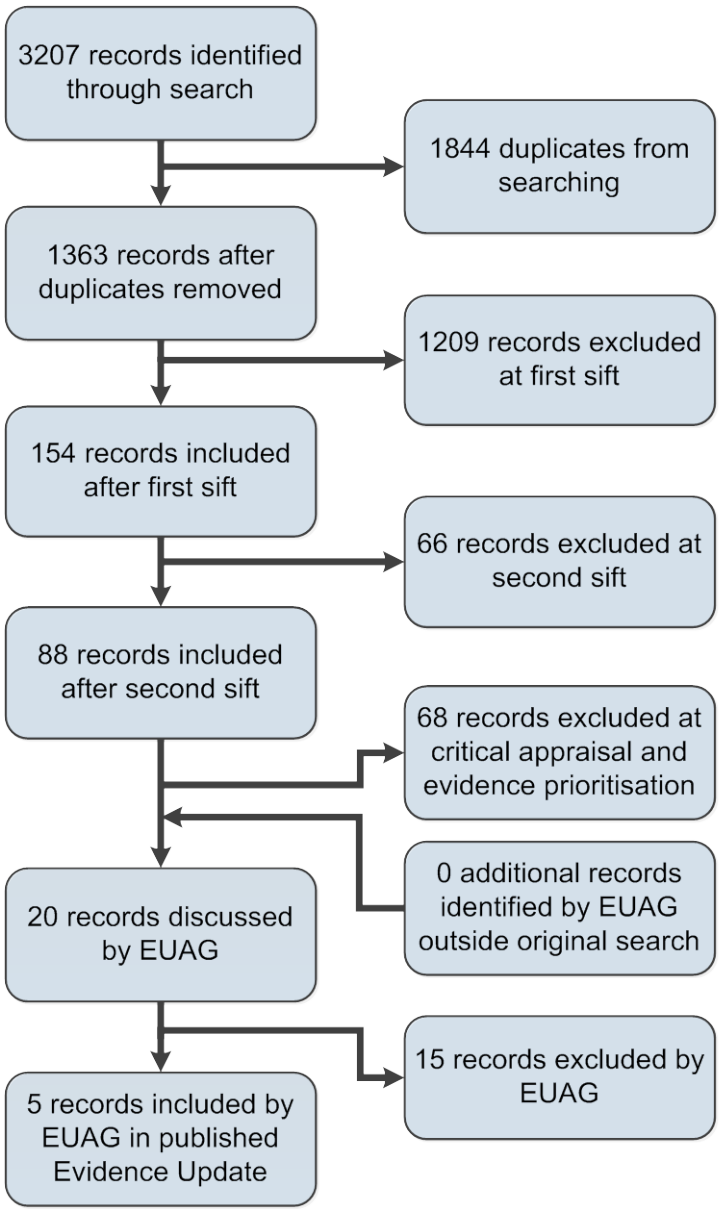
Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

There is more information about how NICE Evidence Updates are developed on the NHS Evidence website.

Table 1 MEDLINE search strategy (adapted for individual databases)
(Although panic disorder was included in the search strategy, evidence for this topic was subsequently excluded during the sift phase.)

1	generalized anxiety disorder.tw.
2	generalised anxiety disorder.tw.
3	Anxiety Disorders/
4	anxiety.ti.
5	Panic Disorder/
6	panic disorder.tw.
7	1 or 2 or 3 or 4 or 5 or 6

Figure 1 Flow chart of the evidence selection process



EUAG – Evidence Update Advisory Group

Appendix B: The Evidence Update Advisory Group and Evidence Update project team

Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

Dr Anna Higgitt – Chair

Consultant Psychiatrist, Central and North West London NHS Foundation Trust

Dr Marta Buszewicz

Senior Lecturer, Research Department of Primary Care and Population Health, University College London

Professor Philip Cowen

Professor of Psychopharmacology, University of Oxford

Professor Karina Lovell

Professor of Mental Health, University of Manchester

Professor Paul Salkovskis

Professor of Clinical Psychology and Applied Science, University of Bath

Professor Jan Scott

Professor of Psychological Medicine, University of Newcastle

Evidence Update project team

Marion Spring

Associate Director

Sian Rees

Clinical Adviser

Professor Tom Quinn

NHS Evidence Clinical Lead

Cath White

Project manager

Lynne Kincaid

Medical Writer

Bazian

Information Specialist support