

Economic Plan

This document identifies the priorities for economic analysis and the proposed methods for addressing these questions as described in section 7.1.3 of the Guidelines Manual (2009).

1 Guideline

Title of guideline: Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults: management in primary, secondary and community care (update)

2 Process for agreement

The economic plan was prepared by the guideline economist in consultation with the rest of the NCC technical team and GDG. It was discussed and agreed on 14/9/09 by the following people ^a:

For the NCC and GDG:

NCC economist: Ifigeneia Mavranezouli

NCC representative(s) ^b: Tim Kendall, Esther Flanagan, Nick Meader, Jennie Robertson

GDG representative(s) ^c: John Cape, Judy Leibowitz, Jan Scott

For NICE:

CCP lead ^d: Chris Carson

Commissioning manager: Claire Turner

Economic lead ^e: Francis Ruiz, Stefanie Kinsley

Costing lead: Mark Minchin

^a This may be done by face-to-face meeting, teleconference, or email as convenient.

^b May be the project manager, a systematic reviewer or research fellow and/or the centre director or manager, as appropriate for the NCC and guideline.

^c May be GDG chair, clinical lead and/or other members as appropriate.

^d CCP Director or Associate Director who is taking the lead for the guideline.

^e One of the CCP health economic Technical Advisors.

Proposals for any substantive changes will be circulated by email to this group. If revisions are agreed, they will be listed as addenda to this document (section 5 below).

3 Proposed economic plan

3.1 Complete one row for each clinical question in the guideline:

<i>Clinical question (in PICO format if possible)</i>		<i>Requires analysis?</i>	<i>Comment and explanation</i>
Service level interventions			
1	In the treatment of GAD, which models of care produce the best outcomes? - collaborative care - stepped care - case management - stratified (matched) care - attached professional model - chronic disease (disease management) model	Low priority for analysis	Identifying and promoting models of care that improve outcomes in people with GAD have important resource implications. However, it is unlikely that there will be sufficient quantitative evidence to inform economic modelling (especially in terms of resource use, definition of settings, and so on). It is expected that implementation of any models of care that improve outcomes will increase the cost effectiveness of treatments for people with GAD, by providing the most effective treatments to the 'right' sub-populations, thus reducing unnecessary resource use and directing more intensive treatments to those in need. The GDG will consider resource implications and implementation issues when making relevant recommendations.
2	What methods are effective in identifying people with GAD?	Low priority for analysis	Although identification of people with GAD is a determinant of the cost effectiveness of interventions addressed to this population, this issue is not of high priority for economic modelling since no great differences in healthcare resource use are expected for the various methods currently available for identification of people with GAD.
Pharmacological and physical interventions for GAD			
3a	In the treatment of GAD, what are the risks and benefits associated with the following drugs compared with other drugs, psychological interventions and with placebo? - SSRIs - venlafaxine - duloxetine	High priority for analysis	Use of pharmacological interventions in the treatment of GAD is likely to have a significant impact on use of NHS resources. There is some existing economic evidence which will be presented to the GDG. An economic model will be developed to assess the cost effectiveness of effective pharmacological treatments for GAD, according to the guideline systematic literature review and meta-analysis. Comparators will include, depending on available evidence:

	<ul style="list-style-type: none"> - mirtazapine - bupropion - TCAs - benzodiazepines - antipsychotics - pregabalin - beta-blockers - antihistamines - azapirones (for example, buspirone) 		<ul style="list-style-type: none"> • effective drugs with acceptable risk profiles, licensed or commonly used out-of-patent drugs for GAD and appropriate as first-line treatments • placebo / standard care • effective psychosocial interventions (including CCBT and self help) • combination therapies. <p>Psychosocial interventions and combination therapies will be considered in the economic analysis if appropriate clinical data allow direct or indirect comparisons between pharmacological, psychosocial and combination therapies (see questions 5a and 7 below).</p>
3b	In the treatment of GAD, what are the risks and benefits associated with different doses of pharmacological interventions?	Low priority for analysis	Using different doses of pharmacological interventions has resource implications. However, these are not that significant and therefore the topic is low priority for analysis. Optimal doses as suggested by the clinical literature are going to be considered in the economic analysis for 3a.
4	In the treatment of GAD, what are the risks and benefits associated with the following interventions? <ul style="list-style-type: none"> - hypnotherapy - valerian - acupuncture - aromatherapy - homeopathy 	Low priority for analysis	Provision of complementary therapies by the NHS is likely to have important resource implications. However, this topic was considered as a low priority for analysis as it is unlikely that there will be sufficient quantitative clinical evidence and resource use / cost data to inform economic modelling.
Psychosocial interventions for GAD			
5a	In the treatment of GAD, what are the risks and benefits associated with the following interventions compared with other interventions (including treatment as usual): <ul style="list-style-type: none"> - CBT (individual or group) - cognitive therapy - CCBT (with or without support) - IPT 	Moderate priority for <u>separate</u> analysis	<p>Effective psychosocial interventions will be included in the economic analysis for question 3a, if appropriate clinical data allow direct or indirect comparisons between psychosocial and pharmacological interventions for this population.</p> <p>If data do not allow comparison between psychosocial and pharmacological interventions, then comparisons of the cost effectiveness between different psychological interventions or versus</p>

	<ul style="list-style-type: none"> - behavioural therapy/behavioural activation - counselling/person-centred therapy - problem solving - relaxation training - short-term/long-term psychodynamic psychotherapy - family interventions/couples therapy - acceptance and commitment therapy - systemic interventions - psychoeducation - cognitive analytic therapy - self-help (bibliotherapy, guided self-help, help-lines, self-help groups, etherapy, psychosocial support) - physical activity - mindfulness - group psychotherapy - dialetical behaviour therapy - creative arts/performance arts therapies 		<p>standard care will be made, always depending on availability of relevant data and time constraints.</p> <p>If this is not possible, then the GDG will consider undertaking simple cost analyses to assess costs and potential savings associated with certain interventions that are judged by the GDG to be associated with important resource implications.</p> <p>For all interventions, resource implications as well as implementation issues (for example, availability of appropriately trained staff in the NHS) will be considered by the GDG when making recommendations.</p> <p>Economic analysis of CCBT for people with GAD will be prioritised, since the guideline is updating the NICE TA 97 [1]. However, it must be noted that no clinical evidence on cCBT packages designed specifically for people with GAD has been identified so far in the literature.</p>
5b	In people with GAD, do competence, support and/or training of the therapist conducting the psychosocial intervention predict outcomes?	Low priority for <u>separate</u> analysis	Competence and/or training of the therapist significantly affects the cost effectiveness of psychosocial interventions. This issue will not be examined in a separate economic analysis, but the analysis undertaken for 3a, 5a and 7 will consider the cost effectiveness of interventions provided by adequately competent/trained therapists.
5c	In people with GAD, are the following sub-groups of people less likely to benefit from psychosocial interventions? <ul style="list-style-type: none"> - people with learning disabilities - people with English as a second language - older adults - people with visual or hearing impairments 	Not relevant	This issue has important resource implications and may affect the cost effectiveness of CCBT for certain subgroups of people. However, this is not a suitable topic for separate economic analysis as no relevant quantitative data are available in the literautre. Nevertheless, the GDG will consider resource implications relating to provision of psychosocial interventions to these sub-groups, when making recommendations.
6a	In people with panic disorder with or without agoraphobia, does CCBT (with or without support) improve outcomes compared with other interventions (including treatment as usual)?	High priority for analysis	Use of CCBT in the treatment of panic disorder is likely to have a significant impact on use of NHS resources. An economic model will be developed to update the economic analysis undertaken for the NICE TA 97 on CCBT [1]. The analysis will take into account new RCTs conducted in this area. CCBT packages considered in the guideline

			systematic review of clinical evidence will be evaluated against all comparators identified in this literature, provided that appropriate and adequate data are available. Where evidence for certain CCBT packages has not changed since the development of the TA economic model, the results of the TA economic analysis will be presented to the GDG.
6b	In people with panic disorder, are the following sub-groups of people less likely to benefit from CCBT? - people with learning disabilities - people with English as a second language - older adults - people with visual or hearing impairments	Not relevant	As in 5c
Combination treatment			
7	In people with GAD, are combined pharmacological and psychosocial interventions associated with improved outcomes compared with pharmacological or psychosocial interventions alone?	High priority for analysis	Combination therapy has significant resource implications for the NHS. Combination therapies will be examined in economic analysis for question 3a, if appropriate clinical data allow this. Resource implications as well as implementation issues (for example availability of appropriately trained staff in the NHS) will be considered by the GDG when making recommendations.
Sequencing of treatment			
8	In people with GAD whose anxiety does not respond, or responds inadequately, to treatment - for those receiving pharmacological treatment, is increasing the dose effective? - are strategies for switching pharmacological interventions effective? - are augmentation strategies effective? - which psychosocial interventions are appropriate?	Low priority for <u>separate</u> analysis	Inadequate or no response to treatment has significant resource implications as it requires extra healthcare resources. However, it is unlikely that there will be adequate clinical evidence on people with GAD not responding (or partially responding) to treatment, covering all alternative treatment options, to inform a <u>separate</u> economic model. Nevertheless, strategies for non-responders such as dose increasing, sequencing of drugs, augmentation and provision of psychological treatments will be considered in the economic analysis described in 3a, if adequate data are available.

Relapse prevention			
9	In people with GAD, whose anxiety has responded to treatment, what strategies are effective in preventing relapse (including maintenance treatment)? For how long should maintenance treatment be provided?	Medium priority for analysis	<p>Strategies aiming at relapse prevention are likely to have a great impact on the use of NHS resources, especially if they are expected to be provided on a long-term basis. However, it is anticipated that relevant clinical data covering a wide range of alternative treatment options will be limited, thus not allowing for meaningful modelling that can lead to robust conclusions. If, however, sufficient data of acceptable quality are available, then an economic analysis may be undertaken (depending also on time constraints) to assess the cost effectiveness of effective strategies in relapse prevention. The analysis will consider all options for which adequate evidence exists. In any case, the GDG will consider resource implications when making relevant recommendations.</p> <p>Regarding optimal duration of maintenance treatment, this is going to be factored in the economic analysis for 3a, depending on availability of clinical data.</p>

3.2 For each question where economic analysis is proposed:

Question number(s) ^f	Outline proposed method of analysis ^g
3a, 5a, 7	<p>Pharmacological, psychosocial and combination therapies for people with GAD</p> <p>An economic model, most likely in the form of a decision tree, will be developed to assess the cost effectiveness of strategies for the treatment of people with GAD.</p> <p>The comparators considered for analysis will ideally be effective drugs with acceptable risk profiles, licensed or commonly used out-of-patent drugs for GAD and appropriate as first-line treatments, placebo/standard care, effective psychosocial interventions, as well as combination therapies.</p> <p>The comparators will be determined by availability of clinical data. Psychosocial interventions and combination therapies will be considered if appropriate clinical data allow direct or indirect comparisons between these and pharmacological interventions.</p> <p>Ideally, combination therapies will be compared with specific pharmacological and psychosocial interventions, possibly the most cost-effective ones (as demonstrated by guideline modelling) or those most commonly used in clinical practice. However, if available data do not allow such comparisons, then adding psychosocial treatments to any (not specified) medication may be the only option for modelling. At this point, the expected (by the GDG) comparison will be CBT plus specific drugs versus the drugs alone.</p> <p>The dose/frequency/duration of treatment will be modelled based on the dosage protocols reported in the clinical trials from which efficacy data will be taken, considering also optimal standards recommended in the guideline.</p> <p>The study population will be people with GAD.</p> <p>The main health states in the model are expected to be response / no response to treatment and possibly remission or relapse. Other issues that may be considered (depending on availability of data) include:</p> <ul style="list-style-type: none"> • Compliance with treatment • Strategies for non-responders such as dose increasing, augmentation, sequencing of drugs, switching of therapies • The presence of side effects from medication and their optimal management

^f Two or more questions may be addressed by a single analysis if appropriate.

^g Give a brief description of the type of analysis that is proposed, as far as is known at this stage. Consider the type of economic evaluation (CEA, CUA, CCA,...); how outcomes will be measured (QALYs, LYs,...); the type of modelling (decision tree, Markov, simulation...); proposed comparators and population subgroups to be considered; potential sources of information and assumptions; and whether analysis could be based on an existing model. Follow methods advised in the Guidelines Manual whenever possible. Note that this is not expected to be a full project protocol, and that the methods of analysis may change.

	<p>The time horizon of the analysis will depend on availability of data (endpoints of relevant RCTs), but will ideally be long enough to assess costs and effects associated with remission following treatment.</p> <p>The perspective of the analysis will be that of the NHS plus Personal Social Services (PSS). Resource use of the various treatment pathways will be based on clinical studies (clinical trials or observational studies) reporting relevant data, the Hospital Episode Statistics for England, other published literature, and, where evidence is lacking, the GDG expert opinion. Unit costs will be based on national sources (BNF, NHS reference costs, PSSRU Health and Social Care Costs) where possible.</p> <p>Outcomes will be expressed in the form of QALYs. Two studies have reported utility scores for health states experienced by people with GAD [2,3]. Both of them have generated QALYs using the methods recommended by the NICE Guidelines Manual. These studies will be reviewed and the results will be presented to the group in order to decide which set of utility scores is more appropriate for use in the economic analysis.</p> <p>Costs and outcomes will be discounted at a 3.5% rate, unless the model has a time horizon of up to a year.</p> <p>Deterministic and probabilistic sensitivity analyses will be used to explore the impact of uncertainty in key parameters on the results of the analysis.</p> <p>A number of studies have assessed the cost effectiveness of pharmacological treatments for people with GAD [4-7]. These are going to be reviewed and their summary will be presented to the GDG. Studies of adequate quality and relevance will be included in economic evidence profiles, accompanying respective GRADE clinical evidence profiles.</p>
6a	<p>CCBT for people with panic disorder</p> <p>An economic model will be developed to assess the cost effectiveness of strategies for the treatment of people with panic disorder. The model (regarding structure / health states, as well as time horizon) is likely to be an adaptation of the model developed for this purpose in the NICE TA 97 [1]. However, it will be attempted to 'improve' model characteristics (for example, extend the time horizon) if more up-to-date data allow this.</p> <p>CCBT packages for panic disorder will be compared with all relevant comparators for which appropriate clinical data are available.</p> <p>The study population will be people with panic disorder, with or without agoraphobia.</p> <p>The perspective of the analysis will be that of the NHS plus PSS. Resource use and unit cost data will be estimated as described above.</p> <p>Outcomes will be expressed in the form of QALYs. Only two studies have reported utility scores for people with panic disorder, but not for distinct health states <i>within</i> panic disorder [13,14]. One of the studies [13] was used in the NICE TA 97 for derivation of utility scores for panic disorder, but limitations of the study's methodology and applicability were clearly stated. The results of both utility studies for panic disorder will be presented to the GDG in order to decide whether they are appropriate to use in the economic analysis. Secondary outcomes, such as the number of people responding to treatment or the number of people in remission</p>

	<p>at endpoint of analysis may be considered, too, if available utility scores are considered to be inappropriate for the economic model.</p> <p>Costs and outcomes will be discounted at a 3.5% rate, unless a time horizon of up to a year is considered.</p> <p>Deterministic and probabilistic sensitivity analyses will be used to explore the impact of uncertainty in key parameters on the results of the analysis.</p> <p>A few studies have assessed the cost effectiveness of CCBT for people with panic disorder [8-12]. These are going to be reviewed and their summary will be presented to the GDG. Studies of adequate quality and relevance will be included in economic evidence profiles, accompanying respective GRADE clinical evidence profiles.</p>
9	<p>Relapse prevention for people with GAD</p> <p>An economic Markov model may be developed to assess the cost effectiveness of pharmacological treatments aiming at relapse prevention for people with GAD. The development of this model will depend on availability of data as well as time constraints.</p> <p>The comparators will be all interventions/strategies for which there is evidence of effectiveness in relapse prevention. The dose/frequency/duration of treatment will be modelled based on the protocols reported in the clinical trials from which efficacy data will be taken, considering also optimal standards recommended in the guideline.</p> <p>The main health states of the model are likely to be ‘no GAD symptoms’ (“well”) and ‘GAD symptoms’ (relapse). In addition, a number of issues that affect cost effectiveness of long-term treatments will be considered when developing the model structure:</p> <ul style="list-style-type: none"> • Compliance / withdrawal from treatment • The presence of side effects from medication and their optimal management <p>The time horizon of the analysis will be long enough to assess long-term costs and outcomes of treatments, but will depend on availability of appropriate data.</p> <p>The perspective of the analysis will be that of the NHS plus PSS. Resource use and unit cost data will be estimated as described above.</p> <p>Outcomes will be expressed in the form of QALYs. Utility scores will be derived from a relevant literature for people with GAD as discussed above [2,3].</p> <p>Costs and outcomes will be discounted at a 3.5% rate.</p> <p>Deterministic and probabilistic sensitivity analyses will be used to explore the impact of uncertainty in key parameters on the results of the analysis.</p>

4 Key references

1. National Institute for Health and Clinical Excellence. Computerised cognitive behavioural therapy for depression and anxiety (CCBT). NICE technology appraisal guidance 97. NICE, 2006. Available from www.nice.org.uk/TA97.
2. Revicki DA, Brandenburg N, Matza L, Hornbrook MC, Feeny D. Health-related quality of life and utilities in primary-care patients with generalized anxiety disorder. *Qual Life Res* 2008; 17(10): 1285-94.
3. Allgulander C, Jorgensen T, Wade A, Francois C, Despiegel N, Auquier P, Toumi M. Health-related quality of life (HRQOL) among patients with generalised anxiety disorder: evaluation conducted alongside an escitalopram relapse prevention trial. *Current Medical Research and Opinion* 2007; 23: 2543-2549.
4. Guest JF, Russ J, Lenox SA. Cost-effectiveness of venlafaxine XL compared with diazepam in the treatment of generalised anxiety disorder in the United Kingdom. *European Journal of Health Economics* 2005; 6: 136-145
5. Heuzenroeder L, Donnelly M, Haby MM, Mihalopoulos C, Rossell R, Carter R, Andrews G, Vos T. Cost-effectiveness of psychological and pharmacological interventions for generalized anxiety disorder and panic disorder. *Australian and New Zealand Journal of Psychiatry* 2004; 38: 602-612
6. Iskedjian M, Walker JH, Bereza BG, Le M, Einarson TR. Cost-effectiveness of escitalopram for generalized anxiety disorder in Canada. *Current Medical Research and Opinion* 2008; 24 (5): 1539-48.
7. Jorgensen TR, Stein DJ, Despiegel N, Drost PB, Hemels ME, Baldwin DS. Cost-effectiveness analysis of escitalopram compared with paroxetine in treatment of generalized anxiety disorder in the United Kingdom. *Annals of Pharmacotherapy* 2006; 40: 1752-1758
8. Kaltenthaler E, Brazier J, De NE, Tumor I, Ferriter M, Beverley C, Parry G, Rooney G, Sutcliffe P. Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation. *Health Technology Assessment* 2006; 10 (33): 1-186.
9. Klein B, Richards JC, Austin DW. Efficacy of internet therapy for panic disorder. *Journal of Behavioural Therapy* 2006; 37, 213-238.
10. McCrone P, Knapp M, Proudfoot J, Ryden C, Cavanagh K, Shapiro DA, Ilson S, Gray JA, Goldberg D, Mann A, Marks I, Everitt B, Tylee A. Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *British Journal of Psychiatry* 2004; 185: 55-62
11. McCrone P, Marks IM, Mataix-Cols D, Kenwright M, McDonough M. Computer-aided self-exposure therapy for phobia/panic disorder: a pilot economic evaluation. *Cogn Behav Ther* 2009; 18:1-9.
12. Mihalopoulos C, Kiropoulos L, Shih S-TF, Gunn J, Blashki G, Meadows G. Exploratory economic analyses of two primary care mental health projects: implications for sustainability. *Medical Journal of Australia* 2005; 183: S73-S76.
13. Alonso J, Angermeyer MC, Bernert S, Bruffaerts R, Brugha TS, Bryson H, et al. Disability and quality of life impact of mental disorders in Europe: results from the

- European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatr Scand* 2004; 109 (Suppl 420): 38–46.
14. Rubin HC, Rapaport MH, Levine B, Gadsjo JK, Rabin A, Auerbach M et al. Quality of well being in panic disorder: the assessment of psychiatric and general disability. *Journal of Affective Disorders* 2000; 57(1-3): 217-221.