Appendix 7: Review protocols

Review question	In the treatment of GAD, what are the risks and benefits associated with the following interventions compared with other interventions (including treatment as usual)?
Sub-questions	
Chapter	6, 7
Sub-section	
Topic Group	
Sub-section lead	
Search strategy	**Databases:** CINAHL, CENTRAL, EMBASE, MEDLINE, PsycINFO **Additional sources:** Reference lists of included studies, systematic reviews
Existing reviews	
• Updated	
• Not updated	
Search filters used	Anxiety update [RCT, mainstream]
Question specific search filter	N/A
Amendments to filter/ search strategy	
Eligibility criteria	
• Intervention	**Cognitive behavioural interventions** ***CBT*** Discrete, time-limited, structured psychological interventions, derived from the cognitive behavioural model of affective disorders and where the patient: • works collaboratively with the therapist to identify the types and effects of thoughts, beliefs and interpretations on current symptoms, feelings states and/or problem areas • develops skills to identify, monitor and then counteract problematic thoughts, beliefs and interpretations related to the target symptoms/problems • learns a repertoire of coping skills appropriate to the target thoughts, beliefs and/or problem areas. ***Problem solving*** A psychological intervention that focuses on learning to cope with specific problems areas and where therapist and patient work collaboratively to identify and prioritise key problem areas, to break problems down into specific, manageable tasks, problem solve, and develop appropriate coping behaviours for problems. ***Behaviour therapy / behavioural activation*** A discrete, time-limited, structured psychological intervention, derived from the behavioural model of affective disorders and where the therapist and patient: • work collaboratively to identify the effects of behaviours on current symptoms, feelings states and/or problem areas. • seek to reduce symptoms and problematic behaviours through behavioural tasks related to: reducing avoidance,

	graded exposure, activity scheduling, reducing avoidance and initiating positively reinforced behaviours. ***Cognitive analytic therapy*** An integrative and relational approach that combines CBT methods with attention to the therapeutic relationship as the vehicle of change, through understanding how problematic, harsh and punitive relationship patterns (reciprocal roles) have been learned and continue to be re-enacted, both with others and in the person's relationship with him or herself. ***Guided self-help*** A self-administered intervention designed to treat depression, which makes use of a range of books or a self-help manual that is based on an evidence-based intervention and designed specifically for the purpose. A healthcare professional (or paraprofessional) facilitates the use of this material by introducing, monitoring and reviewing the outcome of such treatment. This intervention would have no other therapeutic goal, and would be limited in nature to usually no more than three contacts. ***CCBT*** A form of CBT, which is delivered using a computer (including CD-ROM and the internet). It can be used as the primary treatment intervention, with minimal therapist involvement or as augmentation to a therapist-delivered programme where the introduction of CCBT supplements the work of the therapist. **Interpersonal therapy (IPT)** A discrete, time-limited, structured psychological intervention, derived from the interpersonal model of affective disorders that focuses on interpersonal issues and where therapist and patient: • work collaboratively to identify the effects of key problematic areas related to interpersonal conflicts, role transitions, grief and loss, and social skills, and their effects on current symptoms, feelings states and/or problems • seek to reduce symptoms by learning to cope with or resolve these interpersonal problem areas. **Counselling** A discrete, usually time-limited, psychological intervention. • The intervention may have a facilitative approach often with a strong focus on the therapeutic relationship but may also be structured and at times directive. • An intervention was classified as counselling if the intervention(s) offered in the study did not fulfil all the criteria for any other psychological intervention. If a study using counsellors identified a single approach, such as cognitive behavioural or interpersonal, it was analysed in that category. **Psychodynamic psychotherapy** A psychological intervention derived from a psychodynamic/ psychoanalytic model, and where: • Therapist and patient explore and gain insight into conflicts and how these are represented in current situations and

	relationships including the therapy relationship (for example, transference and counter-transference). • This leads to patients being given an opportunity to explore feelings, and conscious and unconscious conflicts, originating in the past, with a technical focus on interpreting and working though conflicts. • Therapy is non-directive and recipients are not taught specific skills (for example, thought monitoring, re-evaluating, or problem solving). **Dialectical behaviour therapy** A multi-modal treatment programme first developed for women who self-harm, and has since been applied to other populations. Five stages of treatment are described: pre-treatment, achieving behavioural control, emotionally processing the past, resolving ordinary problems in living and capacity to experience sustained joy. Solutions from four sets of cognitive behavioural procedures are used: skills training, contingency management, exposure and cognitive modification. Dialectical strategies, which encompass aspects of both acceptance and change (for example, use of metaphor and paradox), are an integral feature of the treatment. **Creative arts or performance arts therapies** Complex interventions that combine psychotherapeutic techniques with activities aimed at promoting creative expression. These interventions are underpinned by the belief that creative processes encourage self-expression, promote self-awareness and increase insight, in the context of a reparative therapeutic relationship, thereby enhancing a person's psychological well-being. In all arts therapies: • the creative process is used to facilitate self-expression within a specific therapeutic framework • the aesthetic form is used to 'contain' and give meaning to the patient's experience • the artistic medium is used as a bridge to verbal dialogue and insight-based psychological development if appropriate • the aim is to enable the patient to experience him/herself differently and develop new ways of relating to others. **Mindfulness-based cognitive therapy (MBCT)** A form of cognitive behavioural therapy that develops a person's ability to be attentive and aware of their negative thoughts but not react to them. It is derived from mindfulness-based stress reduction programme. MBCT may enable people to learn to become more aware of the bodily sensations, thoughts and feelings associated with episodes of panic or anxiety and to relate constructively to these experiences. **Couple-focused therapies** Time-limited, psychological interventions derived from a model of the interactional processes in relationships where: • Interventions are aimed to help participants understand the effects of their interactions on each other as factors in the development and/or maintenance of symptoms and

	problems. • The aim is to change the nature of the interactions so that people may develop more supportive and less conflictual relationships. The style of the therapy can vary and reflect different approaches, for example cognitive behavioural or psychodynamic. **Family intervention** Family sessions with a specific supportive or treatment function based on systemic, cognitive behavioural or psychoanalytic principles, which must contain at least one of the following: • psychoeducational intervention, and/or • problem solving/crisis management work, and/or • intervention with the identified service user. Studies included were also required to use an intervention that was at least of 6 weeks' duration. **Relaxation therapy** Relaxation therapy refers to a number of techniques that are designed to teach an individual to relax, usually through reducing muscle tension and breathing exercises, and hence reduce stress or anxiety. Numerous relaxation techniques exist (underpinned by a range of different philosophical perspectives) and include deep relaxation methods such as progressive relaxation and guided imagery relaxation, briefer methods including diaphragmatic breathing, refocusing and applied relaxation. **Psychoeducation** Psychoeducation (or 'patient teaching,' 'patient instruction' and 'patient education') was defined according to the following criteria: • any group or individual programme involving an explicitly described educational interaction between the information provider and the service user/carer as the prime focus of the study was included • programmes had to address the illness from a multidimensional viewpoint, including familial, social, biological and pharmacological perspectives • studies in which service users/carers were provided with information, support and different management strategies (characteristic of most programmes) were included • programmes of 10 or fewer sessions were classified as 'brief', and 11 or more as 'standard' for this review • interventions including elements of behavioural training, such as social skills or life skills training, were excluded • educational programmes performed by service user peers, and staff education studies were excluded. **Exercise** For the purposes of the guideline, exercise was defined as a structured, achievable physical activity characterised by frequency, intensity and duration and used as a treatment for GAD. It could be undertaken individually or in a group. Exercise may be divided into aerobic forms (training of cardio-respiratory capacity) and anaerobic forms (training of muscular strength/endurance and flexibility/co-ordination/relaxation).

<table>
<tr><td></td><td>The aerobic forms of exercise, especially jogging or running, have been most frequently investigated. In addition to the type of exercise, the frequency, duration and intensity should be described.

Non-statutory support
A range of community-based interventions often not provided by healthcare professionals, which provide support, activities and social contact in order to improve the outcome of GAD.</td></tr>
<tr><td>• Comparator</td><td>Treatment as usual control groups

Sub-question: Alternative psychosocial/pharmacological/ combined management strategies</td></tr>
<tr><td>• Population (including age, gender etc)</td><td>Adults >18 years old with a working primary diagnosis of GAD

Populations excluded:
- Children and young people (<18 years old)
- Panic disorder (will not be updated)

Populations primarily diagnosed with the following mental health problems will be excluded (but maybe comorbid with GAD):
- major depression
- bipolar depression
- seasonal affective disorder
- PTSD
- anxiety disorders associated with dementia</td></tr>
<tr><td>• Outcomes</td><td>• Anxiety symptoms (mean anxiety rating scale score, response [>50% reduction in mean anxiety rating scale score], remission) at end of treatment and follow up. Measures: Hamilton Anxiety Rating Scale (HAM-A)/ Clinical Anxiety Scale (CAS); Beck Anxiety Inventory (BAI); Penn State Worry Questionnaire (PSWQ); Spielberger State-Trait Anxiety Inventory (STAI-T); Hospital Depression and Anxiety Scale (HADS) (anxiety subscale); Leeds Anxiety Scale; Zung Self-Rating of Anxiety Scale.
• Quality of life (for example, SF-36, EQ-5D) at end of treatment and follow-up
• Tolerability (leaving the study early for any reason, leaving the study early due to lack of efficacy, leaving the study early due to adverse events)
• Adverse events (for example gastrointestinal symptoms, weight gain/loss, mortality)</td></tr>
<tr><td>• Study design</td><td>RCT</td></tr>
<tr><td>• Publication status</td><td>[Published and unpublished (if criteria met)]</td></tr>
<tr><td>• Year of study</td><td>Pre DSM-III-R (1987) to present</td></tr>
<tr><td>• Duration</td><td>All durations considered at present</td></tr>
<tr><td>• Minimum sample size</td><td>Sample sizes of 10 or more participants
Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data)</td></tr>
</table>

• Study setting	Primary care, hospital, residential and nursing, tertiary care, an so on (both inpatient and non-inpatient settings)
Additional assessments	Studies were categorised as short-term (<12 weeks), medium-term (12-51 weeks) and long-term (>52 weeks)

Review question	**In the treatment of GAD, what are the risks and benefits associated with drugs compared with other drugs, psychological interventions and with placebo?**
Sub-questions	
Chapter	8
Sub-section	
Sub-section lead	
Search strategy	**Databases:** CINAHL, CENTRAL, EMBASE, MEDLINE, PsycINFO **Additional sources:** Reference lists of included studies, systematic reviews
Existing reviews	
• **Updated**	N/A
• **Not updated**	N/A
Search filters used	Anxiety update [RCT, mainstream]
Question specific search filter	N/A
Amendments to filter/ search strategy	N/A
Eligibility criteria	
• Intervention	SSRIs, venlafaxine, duloxetine, mirtazapine, bupropion, TCAs, benzodiazepines, antipsychotics, pregabalin, beta-blockers, antihistamines, azapirones (for example, buspirone)
• Comparator	Placebo Sub-question: Alternative psychosocial/pharmacological/ combined management strategies
• Population (including age, gender etc)	Adults >18 years old with a working primary diagnosis of GAD Populations excluded: - Children and young people (<18 years old) - Panic disorder (will not be updated) Populations *primarily* diagnosed with the following mental health problems will be excluded (but maybe comorbid with GAD): - major depression - bipolar depression - seasonal affective disorder - PTSD - anxiety disorders associated with dementia
• Outcomes	• Anxiety symptoms (mean anxiety rating scale score, response [>50% reduction in mean anxiety rating scale score], remission) at end of treatment and follow-up. Measures: Hamilton Anxiety Rating Scale (HAM-A)/

	Clinical Anxiety Scale (CAS); Beck Anxiety Inventory (BAI); Penn State Worry Questionnaire (PSWQ); Spielberger State-Trait Anxiety Inventory (STAI-T); Hospital Depression and Anxiety Scale (HADS) (anxiety subscale); Leeds Anxiety Scale; Zung Self-Rating of Anxiety Scale. • Quality of life (for example, SF-36, EQ-5D) at end of treatment and follow-up • Tolerability (leaving the study early for any reason, leaving the study early due to lack of efficacy, leaving the study early due to adverse events) • Adverse events (for example gastrointestinal symptoms, weight gain/loss, mortality)
• Study design	RCT
• Publication status	[Published and unpublished (if criteria met)]
• Year of study	Pre DSM-III-R (1987) to present
• Duration	All durations considered at present
• Minimum sample size	Sample sizes of 10 or more participants Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	Primary care, hospital, residential and nursing, tertiary care and so on (both inpatient and non-inpatient settings)
Additional assessments	N/A

Review question	**In the treatment of GAD, what are the risks and benefits associated with complementary therapies compared with other drugs, psychological interventions and with placebo?**
Sub-questions	
Chapter	8
Sub-section	
Topic Group	
Sub-section lead	
Search strategy	**Databases:** CINAHL, CENTRAL, EMBASE, MEDLINE, PsycINFO **Additional sources:** Reference lists of included studies, systematic reviews
Existing reviews	
• **Updated**	N/A
• **Not updated**	N/A
Search filters used	Anxiety update [RCT, mainstream]
Question specific search filter	N/A
Amendments to filter/ search strategy	N/A
Eligibility criteria	
• Intervention	Hypnotherapy, valerian, acupuncture, aromatherapy, homeopathy,
• Comparator	Placebo Sub-question: Alternative psychosocial/pharmacological/combined

	management strategies
• Population (including age, gender etc)	Adults >18 years old with a working primary diagnosis of GAD Populations excluded: - Children and young people (<18 years old) - Panic disorder (will not be updated) Populations *primarily* diagnosed with the following mental health problems will be excluded (but maybe comorbid with GAD): - major depression - bipolar depression - seasonal affective disorder - PTSD - anxiety disorders associated with dementia
• Outcomes	• Anxiety symptoms (mean anxiety rating scale score, response [>50% reduction in mean anxiety rating scale score], remission) at end of treatment and follow-up. Measures: Hamilton Anxiety Rating Scale (HAM-A)/ Clinical Anxiety Scale (CAS); Beck Anxiety Inventory (BAI); Penn State Worry Questionnaire (PSWQ); Spielberger State-Trait Anxiety Inventory (STAI-T); Hospital Depression and Anxiety Scale (HADS) (anxiety subscale); Leeds Anxiety Scale; Zung Self-Rating of Anxiety Scale. • Quality of life (for example, SF-36, EQ-5D) at end of treatment and follow-up • Tolerability (leaving the study early for any reason, leaving the study early due to lack of efficacy, leaving the study early due to adverse events) • Adverse events (for example gastrointestinal symptoms, weight gain/loss, mortality)
• Study design	RCT
• Publication status	[Published and unpublished (if criteria met)]
• Year of study	Pre DSM-III-R (1987) to present
• Duration	All durations considered at present
• Minimum sample size	Sample sizes of 10 or more participants Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data).
• Study setting	Primary care, hospital, residential and nursing, tertiary care and so on (both inpatient and non-inpatient settings)
Additional assessments	N/A

Review question	In the treatment of GAD, what are the risks and benefits associated with the following interventions compared with other interventions (including treatment as usual)?
Sub-questions	
Chapter	6, 7, 9
Sub-section	
Topic Group	
Sub-section lead	
Search strategy	**Databases:** CINAHL, CENTRAL, EMBASE, MEDLINE, PsycINFO **Additional sources:** Reference lists of included studies, systematic reviews
Existing reviews	
• **Updated**	N/A
• **Not updated**	N/A
Search filters used	Anxiety update [RCT, mainstream]
Question specific search filter	N/A
Amendments to filter/ search strategy	
Eligibility criteria	
• Intervention	CBT, cognitive therapy, CCBT, IPT, counselling or person-centred therapy, problem-solving therapy, relaxation training, short-term/long-term psychodynamic psychotherapy, family intervention, couples therapy, acceptance and commitment therapy, systemic interventions, psychoeducation, cognitive analytic therapy, self-help (bibliotherapy, guided self-help, helplines, self-help groups, e-therapy, psychosocial support), exercise, mindfulness, group psychotherapy, dialectical behaviour therapy, creative arts/ performance arts therapies
• Comparator	Treatment as usual control groups Sub-question: Alternative psychosocial/pharmacological/ combined management strategies
• Population (including age, gender etc)	Adults >18 years old with a working primary diagnosis of GAD Populations excluded: - Children and young people (<18 years old) - Panic disorder (will not be updated) Populations *primarily* diagnosed with the following mental health problems will be excluded (but maybe comorbid with GAD): - major depression - bipolar depression - seasonal affective disorder - PTSD - anxiety disorders associated with dementia
• Outcomes	• Anxiety symptoms (mean anxiety rating scale score, response [>50% reduction in mean anxiety rating scale score], remission) at end of treatment and follow-up. Measures: Hamilton Anxiety Rating Scale (HAM-A)/

	Clinical Anxiety Scale (CAS); Beck Anxiety Inventory (BAI); Penn State Worry Questionnaire (PSWQ); Spielberger State-Trait Anxiety Inventory (STAI-T); Hospital Depression and Anxiety Scale (HADS) (anxiety subscale); Leeds Anxiety Scale; Zung Self-Rating of Anxiety Scale. • Quality of life (for example, SF-36, EQ-5D) at end of treatment and follow-up • Tolerability (leaving the study early for any reason, leaving the study early due to lack of efficacy, leaving the study early due to adverse events) • Adverse events (for example gastrointestinal symptoms, weight gain/loss, mortality)
• Study design	RCT
• Publication status	[Published and unpublished (if criteria met)]
• Year of study	Pre DSM-III-R (1987) to present
• Duration	All durations considered at present
• Minimum sample size	Sample sizes of 10 or more participants Exclude studies with > 50% attrition from either arm of trial (unless adequate statistical methodology has been applied to account for missing data)
• Study setting	Primary care, hospital, residential and nursing, tertiary care, and so on (both inpatient and non-inpatient settings)
Additional assessments	Studies were categorised as short-term (<12 weeks), medium-term (12-51 weeks) and long-term (>52 weeks)