Depression: the treatment and management of depression in adults (update)

NICE guideline
Draft for consultation, February 2009

If you wish to comment on this version of the guideline, please be aware that all the supporting information and evidence is contained in the full version.
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This guidance is a partial update of NICE CG23 (published December 2004, revised July 2006) and will replace it. The original NICE guideline and supporting documents are available from www.nice.org.uk/CG23

Where recommendations are shaded in grey the evidence has not been updated since the original guideline. Yellow shading in these recommendations indicates where wording changes have been made for the purposes of clarification only.

Introduction

This guideline makes recommendations for the identification, treatment and management of depression in adults aged 18 years and over, in primary and secondary care.

Depression is a broad and heterogeneous diagnostic grouping. Central to it is depressed mood and/or loss of pleasure in most activities. Symptoms occur on a continuum of severity and there is no natural threshold when depression becomes clinically important. A diagnosis of depression in ICD-10 requires at least four out of ten depressive symptoms whereas DSM-IV (major depression) requires at least five out of nine. Symptoms should be present for at least 2 weeks and every symptom should be present at sufficient severity for most of every day. Both diagnostic symptoms require at least one (DSM-IV) or two (ICD-10) core symptoms to be present (low mood, loss of enjoyment and interest in both ICD-10 and DSM- and, in ICD-10, loss of energy). Severity is determined both by symptom number and severity as well as degree of impairment. It is now increasingly recognised that depression below the thresholds in DSM-IV and ICD-10 can be distressing and disabling, particularly if persistent. Therefore this updated guideline covers ‘subthreshold’ or ‘minor’ depression (requiring at least one core symptom of depression with insufficient other symptoms and/or impairment to meet the full diagnosis). It should be noted that classificatory systems are agreed conventions that seek to define different severities of Depression in adults: NICE updated guideline DRAFT (February 2009)
depression in order to guide description and treatment, with their value
determined by how useful they are in practice.

After careful review of the diagnostic criteria and the evidence, the Guideline
Development Group decided to adopt DSM-IV criteria for this update rather than
ICD-10 which had been used in the previous guideline. This is because DSM-IV
criteria are used in nearly all the evidence reviewed and DSM-IV provides
definitions for minor depression, atypical symptoms and seasonal depression. Its
definition of severity also makes it less likely that a diagnosis of depression will
be based solely on symptom counting. In practical terms the change will not
affect clinical practice except at the margins where it is intended to better target
the use of specific interventions such as antidepressants for more severe
degrees of depression. The term ‘depression’ in this guideline refers to DSM-IV
major depression, unless qualified by ‘minor’ when it refers to depression below
the threshold for major depression.

A wide range of biological, psychological and social factors have a significant
impact on the course of the disorder and response to treatment and are not
captured well by the current diagnostic systems. Therefore family and previous
history as well as the degree of associated disability are important when
undertaking a diagnostic assessment of depression (see appendix C for further
details).

For the purposes of this guideline the diagnosis of depression requires
assessment of a) severity, b) duration of episode and c) course of illness. This
guideline uses the following categories of severity, drawing on the classification
of depression as set out in DSM-IV:

- minor depression (2 to 4 symptoms with maintained function).
- mild (major) depression (few, if any, symptoms in excess of those required to
  make the diagnosis and resulting in only minor functional impairment)
- moderate (major) depression (symptoms or functional impairment between
  mild and severe)

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• severe (major) depression (several symptoms in excess of those required to make the diagnosis and markedly interfering with functioning).

The guideline draws on the best current available evidence for the treatment and management of depression. However, there are some significant limitations to the current evidence base, which have implications for this guideline. These include limited data on both long-term outcomes for most, if not all, interventions, and outcomes generally for severe depression.

The guideline will assume that prescribers will use a drug’s summary of product characteristics (SPC) to inform their decisions for individual patients. The guideline recommends some drugs for indications for which they do not have UK marketing authorisation at the date of publication, if they are already in use in the NHS for that indication, and there is evidence to support that use. Drugs are marked with an asterisk if they do not have UK marketing authorisation for the indication in question at the time of publication.

This guideline has updated NICE technology appraisal guidance 59 on electroconvulsive therapy (ECT)\(^1\) and NICE technology appraisal guidance 97 on computerised cognitive behavioural therapy for depression and anxiety.\(^2\)

\(^1\) Available from: www.nice.org.uk/TA59.
Person-centred care

This guideline offers best practice advice on the care of adults with depression.

Treatment and care should take into account patients’ needs and preferences. People with depression should have the opportunity to make informed decisions about their care and treatment, in partnership with their practitioners. If patients do not have the capacity to make decisions, practitioners should follow the Department of Health guidelines – ‘Reference guide to consent for examination or treatment’ (2001) (available from www.dh.gov.uk). Practitioners should also follow the code of practice that accompanies the Mental Capacity Act (summary available from www.publicguardian.gov.uk).

Good communication between practitioners and patients is essential. It should be supported by evidence-based written information tailored to the patient’s needs. Treatment and care, and the information patients are given about it, should be culturally appropriate. It should also be accessible to people with additional needs such as physical, sensory or learning disabilities, and to people who do not speak or read English.

If the patient agrees, families and carers should have the opportunity to be involved in decisions about treatment and care.

Families and carers should also be given the information and support they need.
Key priorities for implementation

- Practitioners should be alert to possible depression (particularly in those with a past history of depression or a chronic physical illness with associated functional impairment) and consider asking patients they suspect may have depression two questions, specifically:
  - During the last month, have you often been bothered by feeling down, depressed or hopeless?
  - During the last month, have you often been bothered by having little interest or pleasure in doing things? [1.3.1.1]

- When assessing a person who may be depressed, practitioners should conduct a comprehensive assessment which takes into account the degree of impairment and/or disability associated with the possible depression, the duration of the episode, and does not rely simply on a symptom count. [1.1.4.1]

- For people with persistent minor and mild to moderate depression practitioners should consider:
  - a structured physical activity programme
  - individual guided self-help based on cognitive behavioural therapy principles
  - computerised cognitive behavioural therapy (CCBT).

  The choice of intervention should be guided by the person’s preference. [1.4.2.1]

- Antidepressants are not recommended for the routine treatment of recent-onset minor depression and mild depression because the risk–benefit ratio is poor, but should be considered for people with:
  - minor and mild depression which persists after other interventions

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- initial presentation of persistent minor depression
- a past history of moderate or severe depression. [1.4.5.1]

- Practitioners should be aware of the need to support and encourage people who are taking antidepressants to continue medication for at least 6 months after remission of an episode. In addition, they should discuss with the person:
  - that this greatly reduces the risk of relapse
  - that antidepressants are not associated with physical dependence.

Review with the patient the need for continued antidepressant treatment beyond 6 months, taking into account the number of previous episodes, the presence of residual symptoms, and concurrent physical health problems and psychosocial difficulties. [1.8.2.1]

- When people with depression present initially with severe depression, combining antidepressants with individual CBT should be considered as this combination is more cost effective than either treatment on its own. Individual CBT should be offered for those who did not take or cannot tolerate antidepressants or who declined antidepressants. [1.5.4.3]

- All interventions for depression should be delivered by practitioners who are competent to deliver the intervention. Psychological and psychosocial interventions should be based on the relevant treatment manual(s), which practitioners should follow with regard to the structure and duration of the intervention. Staff should:
  - use competence frameworks developed from the relevant treatment manuals
  - receive regular high quality supervision
  - use routine outcome measures and ensure that the person with depression is involved in reviewing the efficacy of the treatment
monitor and evaluate adherence and competence, for example, through the use of video and audio tapes and external audit and scrutiny where appropriate. [1.1.5.1]

- People with depression considered to be at significant risk of relapse (including those who have relapsed despite with antidepressant treatment and who are unable or unwilling to continue with antidepressant treatment) or who have residual symptoms, should be offered the following psychological treatments:
  - individual or group CBT for those with residual symptoms
  - mindfulness-based CBT for those who are currently well but have experienced three or more previous episodes of depression. [1.8.2.7]
1 Guidance

The following guidance is based on the best available evidence. The full guideline (www.nice.org.uk/CGXXXfullguideline) gives details of the methods and the evidence used to develop the guidance.

1.1 Care of people with depression

1.1.1 Providing information and informed consent, and ensuring continuity of care

1.1.1.1 When working with people with depression and their families and carers practitioners should:

- build a trusting relationship and work in an open, engaging and non-judgemental manner
- explore treatment options in an atmosphere of hope and optimism, explaining the different courses of depression and that recovery is possible
- be aware that stigma and discrimination can be associated with a diagnosis of depression.

1.1.1.2 When working with people with depression and their carers practitioners should:

- avoid clinical language without adequate explanation
- ensure that comprehensive written information is available in the appropriate language and in audio format if possible
- provide and work proficiently with independent interpreters where needed.
1.1.3 Practitioners should be aware of, and inform people with depression and their families and carers about, self-help groups, support groups and other local resources.

1.1.4 Practitioners should make all efforts necessary to ensure that a person with depression can give meaningful and informed consent before treatment is initiated. This is especially important when a person with depression has a more severe depression or is subject to the Mental Health Act.

1.1.2 Advance directives

1.1.2.1 Although there are limitations with advance directives about the choice of treatment for people who are depressed, it is recommended that they are developed and documented in care plans, especially for people who have recurrent severe or psychotic depression, and for those who have been treated under the Mental Health Act.

1.1.3 Supporting families and carers

1.1.3.1 When families and carers are involved in supporting a person with severe or persistent depression, practitioners should consider offering:

- written and verbal information on depression and its management, including how families and carers can support the person
- a carers’ assessment of their caring, physical and mental health needs where necessary
- information about and facilitate access to local carer and family support groups and relevant voluntary organizations.

They should be able to negotiate confidentiality and the sharing of information between the person with depression and their carers.
1.1.4 Principles for assessment, coordination of care, and choosing treatments

The effective assessment of a person with depression (including where appropriate, a comprehensive review of physical, psychological and social needs and a risk assessment) and the subsequent coordination of his or her care may contribute significantly to improved outcomes.

1.1.4.1 When assessing a person who may be depressed, practitioners should conduct a comprehensive assessment which takes into account the degree of impairment and/or disability associated with the possible depression, the duration of the episode, and does not rely simply on a symptom count. [KP]

1.1.4.2 When assessing need, practitioners should seek to understand how the factors set out below may have affected the development, course and severity of a person’s depression:

- the quality of interpersonal relationships
- the history of depression and other comorbid mental or physical disorders
- the past experience of, and response to, treatments
- the living conditions and degree of social isolation
- a review of any past history of mood elevation to determine if the depression may be part of a bipolar disorder (in which case they should refer to ‘Bipolar Disorder’, NICE clinical guideline 38).

Along with the person’s preferences, this assessment should guide the content of any treatment.

1.1.4.3 Practitioners should be aware that some people with depression find discussion of their problems difficult because of shame or stigma. Care should be taken to ensure that discussion takes place in settings in which confidentiality, privacy and dignity can be respected.
1.1.4.4 Practitioners working with people with depression from diverse ethnic and cultural backgrounds should ensure they are competent in:

- culturally appropriate assessment skills
- using different explanatory models of depression
- addressing cultural and ethnic differences in the formulation of treatment plans and the expectations of and adherence to treatment
- working with families from diverse ethnic and cultural backgrounds.

1.1.4.5 Practitioners should always ask a person with depression directly about suicidal ideas and intent. Where the risk of self harm or suicide is present practitioners should assess whether the person has adequate social support and is aware of sources of help. They should arrange help appropriate to the level of risk and advise the person to seek further help if the situation deteriorates.

1.1.4.6 Practitioners should advise a person with depression and their carers to be vigilant for changes in mood, negativity and hopelessness, and suicidal ideas, particularly during high-risk periods, such as during initiation of, and changes to, any treatment plan and increased personal stress. They should be advised to contact the appropriate healthcare practitioner if concerned.

1.1.5 **Effective delivery of interventions for depression**

1.1.5.1 All interventions for depression should be delivered by practitioners who are competent to deliver the intervention. Psychological and psychosocial interventions should be based on the relevant treatment manual(s), which practitioners should follow with regard to the structure and duration of the intervention. Staff should:

- use competence frameworks developed from the relevant treatment manual(s)
• receive regular high quality supervision
• use routine outcome measures and ensure that the person with depression is involved in reviewing the efficacy of the treatment
• monitor and evaluate adherence and competence, for example, through the use of video and audio tapes and external audit and scrutiny where appropriate. [KP]

1.1.5.2 Where available, consideration should be given to providing all interventions in the preferred language of the person with depression.

1.2 Stepped care

The stepped-care model of depression draws attention to the different needs that people with depression have – depending on the characteristics of their depression and their personal and social circumstances – and the responses that are required from services. It provides a framework in which to organise the provision of services supporting both patients and carers, and practitioners in identifying and accessing the most effective interventions (see Figure 1). The aim of a stepped care programme is to provide the least intrusive, most effective intervention first and to promote the organisation and delivery of care in a way which is understandable to patients and carers, and professionals.
**Figure 1. The stepped care model**

<table>
<thead>
<tr>
<th>Focus of the intervention</th>
<th>Nature of the intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STEP 1</strong>: All known and suspected presentations of depression</td>
<td>Assessment, referral, psychoeducation, active monitoring and support</td>
</tr>
<tr>
<td><strong>STEP 2</strong>: Minor, mild to moderate depression</td>
<td>Low intensity psychological and psychosocial interventions, medication, referral</td>
</tr>
<tr>
<td><strong>STEP 3</strong>: Mild to moderate depression with limited response to initial interventions, moderate and severe depression</td>
<td>Medication, high intensity psychological interventions, combined treatments, referral</td>
</tr>
<tr>
<td><strong>STEP 4</strong>: Severe and complex* depression, risk to life, severe self-neglect</td>
<td>Medication, high intensity psychological interventions, ECT, crisis service, combined treatments, multi-professional and in-patient care.</td>
</tr>
</tbody>
</table>

* Complex includes depression with a poor response to multiple treatments, complicated by psychosis, and/or significant psychiatric comorbidity or psychosocial factors

### 1.3  Step 1: recognition, assessment and initial management

1.3.1.1  Practitioners should be alert to possible depression (particularly in those with a past history of depression or a chronic physical illness with associated functional impairment) and consider asking patients they suspect may have depression two questions, specifically:

- During the last month, have you often been bothered by feeling down, depressed or hopeless?
- During the last month, have you often been bothered by having little interest or pleasure in doing things? [KP]

1.3.1.2  If a person answers ‘yes’ to either of the depression identification questions, a healthcare professional, who is competent in basic
mental health assessment, should undertake a mental health assessment. If the healthcare professional is not competent in basic mental health assessment, a referral should be made to an appropriate professional. Where this is not the person's GP, the GP should be informed of the referral.

1.3.1.3 When undertaking an assessment of someone with suspected depression, practitioners should consider the use of a validated measure (for example, for symptoms, functions and/or disability) in order to inform and evaluate treatment.

1.3.1.4 For people with significant language or communication difficulties, for example those with sensory impairments, practitioners should consider the use of the Distress Thermometer\(^3\) and/or asking a family member or carer about the person’s possible depressive symptoms to identify depression.

1.3.2 Risk assessment and monitoring

1.3.2.1 Where a person with depression presents considerable immediate risk to self or others, urgent referral to a specialist mental health service should be arranged.

1.3.2.2 Practitioners should advise patients of the potential for increased agitation, anxiety, suicidal ideation (and for people taking antidepressants, akathisia) in the initial stages of treatment. They should actively seek out these symptoms and ensure that the person with depression knows how to seek help promptly if these are at all distressing. In the event that a patient develops marked and/or

\(^3\) Distress thermometer is a single-item question screen, which will identify distress coming from any source. The patient places a mark on the scale answering: “How distressed have you been during the past week on a scale of 0 to 10?”. Scores of 4 or more indicate a significant level of distress that should be investigated further. (Roth AJ, et al 1998. Rapid screening for psychological distress in men with prostate carcinoma. Cancer 82: 904-1908.)
prolonged agitation (or akathisia while taking an antidepressant), the treatment should be reviewed.

1.3.2.3 When a person with depression is assessed to be at risk of suicide, practitioners should consider:

- toxicity in overdose where an antidepressant is prescribed and when determining the quantity supplied at any one time; where necessary, implement strategies to limit the amount of drug available
- the use of additional support such as more frequent direct or telephone contacts
- referral to specialist mental health services.

1.4 Step 2: recognised depression – persistent minor and mild to moderate depression

1.4.1 General measures

Depression with anxiety

1.4.1.1 When depression is accompanied by symptoms of anxiety, the first priority should usually be to treat the depression. Treatment for depression often reduces anxiety symptoms. When the patient has an anxiety disorder without depression, the NICE guideline for the relevant anxiety disorder should be followed.

Sleep hygiene

1.4.1.2 Patients with depression may benefit from advice on sleep hygiene including:

- establishing regular sleep and wake times
- avoiding excess eating, smoking or drinking before sleep
- creating a proper environment for sleep.
Active monitoring

1.4.1.3 For people with persistent minor and mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, practitioners should:

- discuss the presenting problem(s) and any concerns that the person may have about them
- provide information about the nature and course of depression
- arrange a further assessment, normally within 2 weeks
- make contact with people who do not attend follow-up appointments.

1.4.2 Low intensity psychosocial interventions

1.4.2.1 For people with persistent minor and mild to moderate depression practitioners should consider:

- a structured physical activity programme
- individual guided self-help based on cognitive behavioural therapy principles
- computerised cognitive behavioural therapy (CCBT).

The choice of intervention should be guided by the person’s preference. [KP]

Delivery of low intensity psychosocial interventions

1.4.2.2 Individual guided self-help programmes based on cognitive behavioural principles for people with persistent minor and mild to moderate depression should consist of:

- the provision of appropriate written materials (or alternative media to support access)
• support from a trained practitioner, who typically facilitates the self-help programme and reviews progress and outcome
• treatment sessions normally taking place over 9 to 12 weeks, including follow up.

1.4.2.3 Physical activity programmes for people with persistent minor and mild to moderate depression should normally:

• be delivered individually or in structured groups (according to patient preference) with the support of a competent practitioner
• provide an average of 3 sessions per week of moderate duration (45 minutes to 1 hour) over 10 to 14 weeks (average 12 weeks) tailored to the individual to maximise adherence.

1.4.2.4 For people with persistent minor and mild to moderate depression, CCBT based on cognitive behavioural therapy (CBT) should be provided via a stand-alone computer or a web-based programme. Programmes should run for 9 to 12 weeks, including follow-up and should:

• include an explanation of the CBT model, encourage tasks between sessions, use thought challenging, active monitoring of behaviour, thought patterns and outcomes
• be supported by an appropriately trained practitioner, who typically provides limited facilitation of the programme and reviews progress and outcome.

1.4.3 Group CBT

1.4.3.1 For people with persistent minor and mild to moderate depression, practitioners should consider group-based CBT for those people who decline an individual low intensity intervention or express a preference for a group-based intervention.
1.4.3.2 Group-based CBT for people with persistent minor and mild to moderate depression should:

- consist of 10 to 12 meetings of 8 to 10 participants
- normally take place over 12 to 16 weeks, including follow up
- be based on a structured model such as ‘Coping with Depression’
- be delivered by two trained and competent practitioners.

1.4.4 **Counselling**

1.4.4.1 For people with persistent minor and mild to moderate depression who have declined a low intensity intervention or group CBT, counselling may be considered. However, practitioners should take care to explain the uncertainty about the effectiveness of counselling for people with depression.

1.4.4.2 Counselling for people with persistent minor and mild to moderate depression should be:

- based on a non-directive person-centred model
- typically in the range of 6 to 10 sessions over 8 to 12 weeks.

1.4.5 **Drug treatment**

1.4.5.1 Antidepressants are not recommended for the routine treatment of recent-onset minor depression and mild depression because the risk–benefit ratio is poor, but should be considered for people with:

- minor and mild depression which persists after other interventions
- initial presentation of persistent minor depression
- a past history of moderate or severe depression. [KP]

1.4.5.2 Although there is evidence that St John’s wort may be of benefit in mild or moderate depression, practitioners should:
not prescribe or advise its use by people with depression because of uncertainty about appropriate doses, persistence of effect, variation in the nature of preparations and potential serious interactions with other drugs (including oral contraceptives, anticoagulants and anticonvulsants)

advise people with depression of the different potencies of the preparations available and of the potential serious interactions of St John’s wort with other drugs.

1.5 Step 3: recognised depression – mild to moderate depression with poor response to initial interventions, moderate and severe depression

1.5.1.1 For people with persistent minor and mild to moderate depression who have not benefited from a low intensity psychosocial intervention, and those with moderate and severe depression, practitioners should consider a high intensity psychological treatment or initiation or review of antidepressant medication. The choice of intervention should be influenced by:

- the person’s treatment preference
- the duration of the episode and the trajectory of symptoms
- the previous illness course and response to treatment.

1.5.2 Treatment options

1.5.2.1 Discuss the relative merits of different interventions with the person with depression and offer:

- antidepressant drugs (normally SSRIs)
- psychological interventions (normally CBT and interpersonal therapy)
- a combination of antidepressants and CBT.
The choice should be based on patient preference, the likelihood of adherence to the treatment, and the likely side effects.

1.5.3 Antidepressant drugs

The choice of antidepressants

1.5.3.1 Discuss antidepressant treatment options with the person with depression, including the following:

- their perception of the efficacy and tolerability of individual drugs if they have previously received antidepressants
- the choice of antidepressants including discussion of the anticipated side-effect profile and potential interactions with concomitant medication or physical illness.

1.5.3.2 When an antidepressant is to be prescribed, it should normally be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are equally effective as other antidepressants, are better tolerated, have a favourable risk-benefit ratio and are less likely to be discontinued because of side effects.

1.5.3.3 When prescribing an SSRI, practitioners should consider using a product in a generic form. It should be noted that:

- fluoxetine, fluvoxamine and paroxetine are associated with a higher propensity for drug interactions than other SSRIs. Practitioners should consult appendix 1 of the BNF for information on drug interactions
- paroxetine is associated with a higher incidence of discontinuation symptoms.

1.5.3.4 Consider toxicity in overdose when choosing an antidepressant for people at significant risk of suicide. Be aware of the greater risk of death from overdose with tricyclic antidepressants (with the exception Depression in adults: NICE updated guideline DRAFT (February 2009)
of lofepramine) and venlafaxine, than other equally effective drugs recommended for routine use in primary care.

1.5.3.5 When prescribing drugs other than SSRIs, practitioners should take into account:

- the increased likelihood of the person with depression stopping treatment because of side effects, and with venlafaxine and TCAs, the consequent need to increase the dose gradually
- the specific cautions, contraindications, and monitoring requirements for some drugs. For example, the possibility of exacerbation of hypertension with venlafaxine and duloxetine; the risk of hypokalaemia with reboxetine; the need for haematological monitoring with mianserin. Consult the BNF for detailed information.
- that non-reversible MAOIs, such as phenelzine, should normally be prescribed only by specialist mental health professionals
- that dosulepin should not be initiated.

Starting and initial phase of treatment

1.5.3.6 When prescribing antidepressant medication prescribers should explore any concerns the person may have about taking medication, and provide a full explanation of the reasons for prescribing, including:

- the delay in development of the full antidepressant effect
- the importance of taking medication as prescribed and the need to continue treatment after remission
- information on any potential side effects
- the potential for interactions with other medications
- the risk of discontinuation symptoms and how these can be minimised, particularly with shorter half-life drugs, such as paroxetine and venlafaxine
• the fact that physical dependence does not occur with antidepressants.

Written information appropriate to the person's needs should be made available.

1.5.3.7 People started on antidepressants who are not considered to be at increased risk of suicide should normally be seen after 2 weeks. Thereafter they should be seen on an appropriate and regular basis, for example, at intervals of 2 to 4 weeks in the first 3 months and at longer intervals thereafter, if response is good.

1.5.3.8 A person with depression started on antidepressants who is considered to present an increased suicide risk or is younger than 30 years (because of the potential increased prevalence of suicidal thoughts in the early stages of antidepressant treatment for this group) should normally be seen after 1 week and frequently thereafter as appropriate until the risk is no longer considered clinically significant.

1.5.3.9 If a person with depression experiences side effects following prescription of an antidepressant early in treatment, the prescriber should, in discussion with the person:

• monitor symptoms closely where side effects are mild and acceptable to the person
• stop or change to a different antidepressant if the person with depression prefers
• consider short-term concomitant treatment with a benzodiazepine (not normally for more than 2 weeks) where anxiety, agitation and/or insomnia are problematic.
1.5.3.10 People who start on low-dose tricyclic antidepressants and who have a clear clinical response can be maintained on that dose with careful monitoring.

1.5.3.11 When improvement is not occurring on the first antidepressant the prescriber should check that the drug has been taken regularly and in the prescribed dose.

1.5.3.12 If, after 4 weeks of treatment with a therapeutic dose of an antidepressant, response is minimal:

- consider increasing the dose in line with the schedule suggested by the Summary of Product Characteristics if there are no significant side effects
- consider switching to another antidepressant as described in section 1.8 (Sequencing treatment) if there are side effects or the person expresses a preference for changing treatment.

1.5.3.13 If the person’s depression shows some improvement, continue treatment for another 2 to 4 weeks and, then, if response is still not adequate, if there are side effects or the person expresses a preference for changing treatment, consider switching to another antidepressant as described in section 1.8 (Sequencing treatment).

1.5.4 Psychological treatments

Cognitive and behavioural therapies, interpersonal therapy and couples therapy

The following recommendations focus primarily on the provision of cognitive and behavioural therapy. However, interpersonal therapy (IPT) and couples therapy are also effective treatments for depression.

Choice of psychological treatment

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1.5.4.1 For people with moderate depression who are offered psychological interventions the choice of treatment should include:

- Individual cognitive behavioural therapies
- IPT if the person expresses a preference for it or if, in the view of the healthcare professional, the person with depression may benefit from it.

1.5.4.2 Couple-focused therapy may be considered for people with depression who have a regular partner and:

- have not benefited from a low intensity intervention or pharmacological treatment, and
- where in the opinion of the person with depression or the clinician, the current relationship may either contribute to the development or maintenance of depression or the involvement of the partner is considered to be of potential therapeutic benefit.

1.5.4.3 When people with depression present initially with severe depression, combining antidepressants with individual CBT should be considered as this combination is more cost effective than either treatment on its own. Individual CBT should be offered for those who did not take or cannot tolerate antidepressants or who declined antidepressants. [KP]

1.5.4.4 If people do not show adequate improvement, consider aspects of the treatment which could be improved (for example, therapist alliance, conceptualisation of the problem, competence of the treatment delivery), or consider an alternative treatment.

**Delivering high intensity psychological interventions**

1.5.4.5 For all psychological interventions the duration of treatment should normally be within the limits indicated in this guideline. As the aim of treatment is to obtain significant improvement or remission:
• the duration of treatment may be shorter if remission has been achieved
• the duration of treatment may be longer if progress is being made, and there is agreement between the practitioner and the person with depression that further sessions would be beneficial, for example if there is comorbid personality disorder or psychosocial factors.

1.5.4.6 For all people with depression receiving individual CBT, the duration of treatment should typically be in the range of 16 to 20 sessions over 6 to 9 months.

• For people with moderate and severe depression consideration should be given to providing 2 sessions per week for the first 2 to 3 weeks of treatment.
• For all people with depression consideration should be given to follow-up sessions, which typically consist of 2 to 4 sessions over 12 months.

1.5.4.7 For all people with depression receiving IPT the duration of treatment should typically be in the range of 16 to 20 sessions over 6 to 9 months.

• For people with severe depression consideration should be given to providing 2 sessions per week for the first 2 to 3 weeks of treatment.

1.5.4.8 Couple-focused therapy for depression should normally be based on behavioural principles and an adequate course of therapy should be 15 to 20 sessions over 5 to 6 months.
1.5.5 **Short-term psychodynamic psychotherapy**

1.5.5.1 For people with moderate depression who have declined or have not benefited from CBT or IPT, short-term psychodynamic psychotherapy may be considered. However, practitioners should take care to explain the uncertainty about the efficacy of short-term psychodynamic psychotherapy in the treatment of depression.

1.5.5.2 For all people with depression receiving short-term psychodynamic psychotherapy the duration of treatment should typically be in the range of 16 to 20 sessions over 4 to 6 months.

1.6 **Treatment choice based on depression sub-types and personal characteristics**

There is little evidence to guide prescribing in relation to a range of depression sub-types or personal characteristics. The main issue concerns the impact of other physical disorders on the treatment of depression. Refer to the guideline on the treatment of depression in chronic physical health problems for further information.

1.6.1.1 Practitioners should not routinely vary the treatment strategies for depression described in this guideline either by depression sub-type (for example, atypical depression or seasonal depression) or personal characteristics (for example, sex or ethnicity) as there is no convincing evidence to support such action.

1.6.1.2 Practitioners should advise people with winter depression that follows a seasonal pattern and who wish to try light treatment in preference to antidepressant or psychological treatment that the evidence for the efficacy of light therapy is uncertain.

1.6.1.3 When prescribing antidepressants for older adults practitioners should:
• prescribe at an age-appropriate dose taking into account the impact of age, general physical health and concomitant medication on pharmokinetics and pharmodynamics
• carefully monitor for side effects.

1.6.1.4 People with severe depression who have not been in receipt of any effective intervention, should initially be offered a combination of CBT and antidepressant medication.

1.6.1.5 For people with long-standing moderate or severe depression who would benefit from additional social or vocational support consideration should be given to:

• befriending as an adjunct to pharmacological or psychological treatments. Befriending should be by trained volunteers providing, typically, at least weekly contact for between 2 and 6 months
• a rehabilitation programme where a person’s depression has resulted in loss of work or disengagement from other social activities over a longer term.

1.7 Enhanced care for depression

1.7.1.1 Medication management as a discrete intervention for people with depression should not be routinely provided by services. It is likely to be effective only when provided as part of a more complex intervention.

1.7.1.2 For people with severe depression and those with moderate depression and complex problems practitioners should consider:

• referral to specialist mental health services for a programme of co-ordinated multi-professional care
• the provision of collaborative care where the depression is in the context of a chronic physical health problem with associated functional impairment.  

1.8 Sequencing treatments after initial inadequate response

Some people with depression do not respond well to initial treatment; this section describes the strategies to be adopted when this arises.

1.8.1 Drug treatments

1.8.1.1 When initiating or revising a pharmacological treatment for a person with depression whose symptoms have not adequately responded to initial pharmacological interventions practitioners should:

• increase the frequency of appointments using outcome monitoring with a validated outcome measure
• be aware that the use of a single agent rather than combination medication or augmentation causes a lower side-effect burden
• consider re-introducing previous treatments that have been inadequately delivered or adhered to including increasing dose or switching to an alternative antidepressant.

Switching antidepressants

1.8.1.2 When switching to another antidepressant, practitioners should be aware that the evidence for the relative advantage of switching either within a class or between classes is weak. Reasonable choices for a second antidepressant include:

• initially a different SSRI or better tolerated newer generation antidepressant

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4 See the NICE guideline on depression in chronic health problems for the evidence base for this.
• subsequently switching to an antidepressant of a different pharmacological class that may be less well tolerated, for example, venlafaxine, a TCA or an MAOI.

1.8.1.3 When switching to another antidepressant, which can normally be achieved within a week when switching from drugs with a short half-life, prescribers should consider the potential for interactions in determining the choice of new drug and the nature and duration of the transition. Exercise caution particularly when switching:

• from fluoxetine or paroxetine to a TCA, as these drugs inhibit the metabolism of TCAs. A lower starting dose of the TCA will be required, particularly with fluoxetine because of its long half-life
• to a new serotonergic antidepressant or MAOI, because of the risk of serotonin syndrome. Features of serotonin syndrome include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus
• from a non-reversible MAOI; a 2-week washout period is required. Other antidepressants should not routinely be prescribed during this 2 week period.

**Combining medications**

Combining medications is usually called 'augmentation treatment' when an antidepressant is used with a non-antidepressant drug and 'combination treatment' when two antidepressants are used together.

1.8.1.4 When using combinations of medications, the healthcare professional should:

• ensure they select medications that are known to be safe when used together
• be aware of the increased side effect burden this causes
• discuss the rationale for any combination with the person with depression, inform them if off-label medication is prescribed, and monitor carefully for adverse effects
• when using unusual combinations, familiarise themselves with the primary evidence and consider obtaining a second opinion.

1.8.1.5 Where a person with depression is informed about and prepared to tolerate the increased side-effect burdens consider augmenting an existing antidepressant with:

- lithium
- an antipsychotic – there is some evidence for aripiprazole, olanzapine, quetiapine and risperidone*
- another antidepressant – there is some evidence for mianserin, and mirtazepine in augmenting SSRIs.

1.8.1.6 When prescribing lithium, ensure that renal and thyroid function are monitored before and during treatment, and consider using ECG monitoring in high-risk people with depression. Serum lithium levels must be monitored.

1.8.1.7 When prescribing antipsychotics monitor weight, lipid and glucose levels, and side effects relevant to the chosen drug (for example, extrapyramidal side effects and prolactin-related side effects with risperidone).

1.8.1.8 When augmenting an antidepressant with another drug or using a combination of antidepressants, practitioners should document the rationale for the chosen combination and consider seeking a second opinion where evidence for the efficacy of a chosen strategy is limited or where the risk-benefit ratio is unclear.

* None of these drugs has UK marketing authorisation for the treatment of depression.
1.8.1.9 The following strategies are not recommended for routine use as there is insufficient evidence for their use:

- augmentation of an antidepressant with a benzodiazepine for more than 2 weeks
- augmentation of an antidepressant with buspirone, carbamazepine, lamotrigine, pindolol, valproate or thyroid hormones
- dosulepin, which should not be initiated because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.

**Combined psychological and drug treatment**

1.8.1.10 For a person whose depression has not responded to either pharmacological or psychological interventions, the combination of antidepressant medication with CBT should be considered.

**Referral**

1.8.1.11 For a person whose depression has failed to respond to various strategies for augmentation and combination treatments, referral to a clinician with a specialist interest in treating depression or a specialist service should be considered.

**1.8.2 Continuation and relapse prevention**

1.8.2.1 Practitioners should be aware of the need to support and encourage people who are taking antidepressants to continue medication for at least 6 months after remission of an episode. In addition, they should discuss with the person:

- that this greatly reduces the risk of relapse
- that antidepressants are not associated with physical dependence.

Review with the patient the need for continued antidepressant treatment beyond 6 months, taking into account the number of Depression in adults: NICE updated guideline DRAFT (February 2009)
previous episodes, the presence of residual symptoms, and concurrent physical health problems and psychosocial difficulties. [KP]

1.8.2.2 For people with depression who are at significant risk of relapse or have a history of recurrent depression, practitioners should discuss the choice of treatments to reduce the risk of recurrence. The choice of treatment should be influenced by:

- preference of the person
- previous treatment history including the consequences of a relapse, residual symptoms, the response to previous treatment and problems with side effects of discontinuation of treatment.

Treatment choices include continuing current medication, augmentation with additional medication or the provision of psychological treatment (CBT).

Use of medication for relapse prevention

1.8.2.3 People with depression should be advised to continue antidepressants for at least 2 years if they are at risk of relapse, maintaining the level of medication at which acute treatment was effective unless there is good reason to reduce the dose (such as unacceptable adverse effects), if:

- they have had two or more depressive episodes in the recent past, during which they experienced significant functional impairment
- they have other risk factors for relapse such as residual symptoms, multiple previous episodes, history of severe or prolonged episodes or of poor response
- the consequences of relapse are likely to be severe (for example, suicide attempts, loss of functioning, severe life disruption, and inability to work).
1.8.2.4 When deciding whether to continue maintenance treatment beyond 2 years, re-evaluate in conjunction with the person with depression taking into account age, comorbid conditions and other risk factors.

1.8.2.5 People with depression on long-term maintenance treatment should be regularly re-evaluated, with frequency of contact determined by the following:

- comorbid conditions
- risk factors for relapse
- severity and frequency of episodes of depression.

1.8.2.6 For people with depression who have had multiple episodes of depression, and who have had a good response to treatment with an antidepressant and an augmenting agent, they should remain on this combination after remission if the side effects are tolerable and acceptable to the person with depression. If one medication is stopped it should usually be the augmenting agent. Lithium should not be used as a sole agent to prevent recurrence.

Psychological treatment for relapse prevention

1.8.2.7 People with depression considered to be at significant risk of relapse (including those who have relapsed despite with antidepressant treatment and who are unable or unwilling to continue with antidepressant treatment) or who have residual symptoms, should be offered the following psychological treatments:

- individual or group CBT for those with residual symptoms
- mindfulness-based CBT for those who are currently well but have experienced three or more previous episodes of depression. [KP]
1.8.2.8 CBT should be considered for people with depression with recurrent depression who have relapsed despite antidepressant treatment, including those who:

- have had a limited response to other interventions
- express a preference for psychological interventions
- are unable or unwilling to continue with that intervention, and are assessed as being at significant risk of relapse.

**Psychological treatment delivery**

1.8.2.9 Where there remains a risk of relapse following individual CBT, maintenance CBT or IPT sessions should be considered.

1.8.2.10 Mindfulness-based CBT should normally be delivered in groups of 8 to 15 participants and consist of eight 2-hourly weekly meetings and four further follow-up sessions in the 12 months after the end of treatment.

**1.8.3 Stopping or reducing antidepressants**

1.8.3.1 Discontinuation/withdrawal symptoms may occur on stopping, missing doses or, occasionally, on reducing the dose of the drug but are usually mild and self-limiting but can occasionally be severe, particularly if the drug is stopped abruptly.

1.8.3.2 Practitioners should normally gradually reduce the doses of the drug over a 4-week period although some people may require longer periods. This is not required with fluoxetine because of its long half-life.

1.8.3.3 If discontinuation/withdrawal symptoms occur, practitioners should:

- monitor symptoms and reassure the person if symptoms are mild
• inform the person that they should seek advice from their medical practitioner if they experience significant discontinuation/withdrawal symptoms
• consider reintroducing the original antidepressant at the dose that was effective (or another antidepressant with a longer half-life from the same class) and reduce gradually while monitoring symptoms if symptoms are severe.

1.9 Step 4: complex and severe depression

Referral to specialist mental health services should normally be for people with depression who are at significant risk of self-harm, have psychotic symptoms, require complex multi-professional care, or where an expert opinion on treatment and management is required.

1.9.1.1 The assessment of a person with depression referred to specialist mental health services should include a full assessment of:

• their symptom profile and suicide risk and, where appropriate, previous treatment history
• associated psychosocial stressors, personality factors and significant relationship difficulties, particularly where the depression is chronic or recurrent
• associated comorbidities including alcohol and substance misuse, and personality disorders.

1.9.1.2 In specialist mental health services, after a thorough review of previous treatments for depression has been undertaken, consideration should be given to re-introducing previous treatments that have been inadequately delivered or adhered to.

1.9.1.3 Crisis resolution and home treatment teams should be used as a means of managing crises for people with severe depression who are assessed as presenting significant risk, and as a means of delivering...
high-quality acute care. In this context, teams should pay particular attention to risk monitoring as a high-priority routine activity in a way that allows people to continue their normal lives without disruption.

1.9.1.4 Medication in secondary-care mental health services should be initiated under the supervision of a consultant psychiatrist.

1.9.1.5 Teams working with people with complex and severe depression should develop comprehensive multidisciplinary care plans in collaboration with the person with depression (and their family or carer, where agreed with the person). The care plan should:

- identify clearly the roles and responsibilities of all health and social care professionals involved
- develop a crisis plan that identifies potential triggers that could lead to a crisis
- be shared with the GP and the person with depression and other relevant people involved in the person’s care.

1.9.2 Inpatient care and crisis resolution and home treatment teams

1.9.2.1 Inpatient treatment should be considered for people with depression who are at significant risk of suicide, self-harm or self neglect.

1.9.2.2 The full range of high intensity psychological therapies should normally be offered in inpatient settings. However, consideration should be given to increasing the intensity and duration of the treatments and ensuring that they can be provided effectively and efficiently on discharge.

1.9.2.3 Crisis resolution and home treatment teams should be considered for people with depression who might benefit from early discharge from hospital after a period of inpatient care.
1.9.3 The pharmacological management of psychotic depression

1.9.3.1 For people with psychotic depression, augmenting the current treatment plan with antipsychotic medication should be considered, although the optimum dose and duration of treatment are unknown.

1.9.4 Electroconvulsive therapy (ECT)

1.9.4.1 ECT should be considered for severe depression which is life-threatening and when a rapid response is required, or when other treatments have failed. ECT should not be routinely used for people with moderate depression but may be considered for those whose depression has not responded to multiple treatments. For those who have not responded well to a previous course of ECT, consider a repeat trial of ECT only after all other options have been considered and following discussion of the risks and benefits with the individual and/or where appropriate their carer/advocate.

1.9.4.2 When considering ECT as a treatment choice, ensure the person with depression is fully informed of the risks associated with ECT, and with the risks and benefits specific to them. The assessment should be documented and consider the following:

- the risks associated with a general anaesthetic
- current medical comorbidities
- potential adverse events, notably cognitive impairment
- the risks associated with not receiving ECT.

The risks associated with ECT may be enhanced in older people and therefore clinicians should exercise particular caution when considering ECT treatment in this group.

1.9.4.3 A decision to use ECT should be made jointly with the person as far as possible, taking into account the following factors:
• valid informed consent should be obtained where the person has the capacity to grant or refuse consent, without pressure or coercion, which may occur as a result of the circumstances and clinical setting
• the person should be reminded of their right to withdraw consent at any point
• there should be strict adherence to recognised guidelines about consent and the involvement of patient advocates and/or carers to facilitate informed discussion is strongly encouraged
• if informed consent is not possible, ECT should only be given where it does not conflict with a valid advance directive and the individual’s advocate and/or carer should be consulted.

1.9.4.4 The choice of electrode placement and stimulus dose related to seizure threshold should balance efficacy against the risk of cognitive impairment. It should be noted that:

• bilateral ECT is more effective than unilateral ECT but may cause more cognitive impairment
• with unilateral ECT, higher stimulus dose is associated with greater efficacy, but also increased cognitive impairment compared with lower stimulus dose.

1.9.4.5 Clinical status should be assessed after each ECT treatment using a formal valid outcome measure, and treatment should be stopped when an adequate response has been achieved, or sooner if side effects outweigh the potential benefits.

1.9.4.6 Cognitive function should be assessed before the first treatment and monitored at least every 2-4 treatments, and at the end of a course of treatment. Assessment should include:

• orientation and time to reorientation after each treatment
• measures of new learning, retrograde amnesia and subjective memory impairment carried at least 24 hours after a treatment.

If there is evidence of significant cognitive impairment at any stage, in discussion with the patient, consideration should be given to changing from bilateral to unilateral electrode placement, reducing the dose, or stopping treatment depending on the balance of risks and benefits.

1.9.4.7 When a person with depression has responded to a course of ECT, medication should be continued or initiated to prevent relapse. Lithium augmentation of antidepressants should be considered.

1.9.4.8 Maintenance ECT for relapse prevention should not be routinely used in the treatment of depression because the longer-term benefits and risks of ECT have not been clearly established. If maintenance ECT is undertaken:

• cognitive assessment, consisting of at a minimum, measures of new learning, retrograde amnesia and subjective memory impairment, should be conducted at initiation of treatment and during follow up together with assessment of clinical status using standardised outcome measures
• the data on the outcome of the treatment and the cognitive assessment should be submitted to a national audit of the use of maintenance ECT.

1.10 Other physical treatments for depression

1.10.1.1 Vagus nerve stimulation should only be undertaken as part of research studies carried out in specialist centres with expertise in the techniques.

1.10.1.2 Current evidence suggests that there are no major safety concerns associated with transcranial magnetic stimulation (TMS) for severe Depression in adults: NICE updated guideline DRAFT (February 2009)
depression. There is uncertainty about the procedure’s clinical efficacy, which may depend on higher intensity, greater frequency, bilateral application and/or longer treatment durations than have appeared in the evidence to date. TMS should therefore be performed only in research studies designed to investigate these factors.\textsuperscript{6}

1.10.1.3 Future research should aim to address patient selection criteria, the optimal use of this procedure in relation to other treatments, and the duration of any treatment effect. Clinicians should collaborate to ensure that studies are sufficiently large to be adequately powered. The Institute may review the procedure upon publication of further evidence.\textsuperscript{7}

\textsuperscript{5-6} Recommendations taken from ‘Transcranial magnetic stimulation for severe depression’ (NICE interventional procedure guidance 242).
2 Notes on the scope of the guidance

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover. The scope of this guideline is available from http://www.nice.org.uk/guidance/index.jsp?action=download&o=42260.

How this guideline was developed

NICE commissioned the National Collaborating Centre for Mental Health to develop this guideline. The Centre established a Guideline Development Group (see appendix A), which reviewed the evidence and developed the recommendations. An independent Guideline Review Panel oversaw the development of the guideline (see appendix B).

There is more information in the booklet: ‘The guideline development process: an overview for stakeholders, the public and the NHS’ (third edition, published April 2007), which is available from www.nice.org.uk/guidelinesprocess or from NICE publications (phone 0845 003 7783 or email publications@nice.org.uk and quote reference N1233).

3 Implementation

The Healthcare Commission assesses how well NHS organisations meet core and developmental standards set by the Department of Health in ‘Standards for better health’ (available from www.dh.gov.uk). Implementation of clinical guidelines forms part of the developmental standard D2. Core standard C5 says that NHS organisations should take into account national agreed guidance when planning and delivering care.

NICE has developed tools to help organisations implement this guidance (listed below). These are available on our website (www.nice.org.uk/CGXXX). [NICE to amend list as needed at time of publication]

- Slides highlighting key messages for local discussion.

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Costing tools:
- costing report to estimate the national savings and costs associated with implementation
- costing template to estimate the local costs and savings involved.

Implementation advice on how to put the guidance into practice and national initiatives that support this locally.

Audit support for monitoring local practice.

4 Research recommendations

The 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 research recommendations is detailed in the full guideline (see section 6).

4.1 Sequencing antidepressant treatment after inadequate initial response

What is the best medication strategy for people with depression who have not had sufficient response to a first SSRI antidepressant after 6-8 weeks of adequate treatment?

This question should be addressed using a randomised controlled trial design and compare the effects of continuing on the same drug treatment (with dose increase if appropriate) and switching to another SSRI or to an antidepressant of another class. Built into the design should be an assessment of the effect of increased frequency of follow-up and monitoring alone on improvement. The outcomes chosen should reflect both observer and patient-rated assessments of improvement and an assessment of the acceptability of the treatment options. The study needs to be large enough to determine the presence or absence of clinically important effects using a non-inferiority design and mediators and moderators of response should be investigated.
Why this is important
Inadequate response to a first antidepressant is a frequent problem but the best way of sequencing treatments is not clear from the available evidence. There is good evidence that the likelihood of eventual response decreases with the duration of depression and number of failed treatment attempts so that maximising the response at an early stage may be an important factor in final outcome. The results of this study will be generalisable to a large number of people with depression and will inform the choice of treatment.

4.2 The efficacy of short-term psychodynamic psychotherapy compared with cognitive behaviour therapy (CBT) in the treatment of mild to moderate depression.

In well-defined depression of mild to moderate severity, what is the relative efficacy of short-term psychodynamic psychotherapy compared with cognitive behaviour therapy (CBT)?

This question should be answered using a randomised controlled design which reports short and medium-term outcomes (including cost effectiveness outcomes) of at least 18 months’ duration. There should be particular attention paid to the reproducibility of the treatment model and training and supervision of those providing interventions in order to ensure that the treatments are both robust and generalisable. The outcomes chosen should reflect both observer and patient-rated assessments of improvement and an assessment of the acceptability of the treatment options. The study needs to be large enough to determine the presence or absence of clinically important effects using a non-inferiority design and mediators and moderators of response should be investigated.

Why this is important
Psychological treatments are an important therapeutic option for people with depression. CBT has the best evidence base for efficacy but it is not effective for Depression in adults: NICE updated guideline DRAFT (February 2009)
everyone. The availability of alternatives drawing from a different theoretical model is therefore important. Psychotherapy based on psychodynamic principles has historically been provided in the NHS but the provision is patchy and there is a lack of a good evidence-base. It is therefore important to establish whether short-term psychodynamic psychotherapy is an effective alternative treatment to CBT and one that should be provided. The results of this study will have important implications for the provision of psychological treatment in the NHS.

4.3 **The cost effectiveness of combined medication and cognitive behaviour therapy (CBT) compared with sequenced treatment for moderate to severe depression**

What is the cost-effectiveness of combined medication and cognitive behaviour therapy (CBT) compared with sequenced medication then CBT and vice versa for moderate to severe depression?

This question should be answered using a randomised controlled trial design in which moderately to severely ill people with depression receive either combined treatment from the outset, or single modality treatment with addition of the other modality if there is inadequate response to initial treatment. The outcomes chosen should reflect both observer and patient-rated assessments for acute and medium-term outcomes to at least 6 months, and an assessment of the acceptability and burden of the treatment options. The study needs to be large enough to determine the presence or absence of clinically important effects using a non-inferiority design together with robust health economic measures.

**Why this is important**

There is a reasonable evidence base for the superior effectiveness of combined medication and CBT over either treatment alone in moderate to severe depression. However the practicality, acceptability and cost effectiveness of combined treatment over a sequenced approach is less well-established. The answer has important practical implications for service delivery and resource implications for the NHS.
4.4 The efficacy of light therapy compared with antidepressants for mild to moderate depression with a seasonal pattern

What is the efficacy of light therapy compared with antidepressants for mild to moderate depression with a seasonal pattern?

This question should be answered using a randomised controlled trial design in which mild to moderately ill people suffering from depression with a seasonal pattern (seasonal affective disorder) receive light therapy or an SSRI antidepressant in a partially placebo-controlled design. The doses of both light and SSRI should be at accepted or proposed therapeutic levels and there should be an initial phase over a few weeks in which a plausible placebo treatment is administered followed by randomisation to one of the active treatments. The outcomes chosen should reflect both observer and patient-rated assessments of improvement and an assessment of the acceptability of the treatment options. The study needs to be large enough to determine the presence or absence of clinically important effects and mediators and moderators of response should be investigated.

Why this is important

Although the status of seasonal depression as a separate entity is not entirely clear surveys have consistently reported a high prevalence of seasonal (predominantly winter) depression in the UK. This reflects a considerable degree of morbidity for sufferers predominantly in the winter months. Light therapy has been proposed as a specific treatment for winter depression but only small inconclusive trials have been carried out, from which it is not possible to tell whether either light therapy or antidepressants are effective in its treatment. Clarification of whether and to what degree treatments are effective would help to inform the decisions that people with seasonal depression and healthcare professionals have to make about the treatment of winter depression.
4.5 The efficacy of cognitive behavioural therapy (CBT) compared with antidepressants for persistent minor depression

What is the efficacy of CBT compared with antidepressants for persistent minor depression?

This question should be answered using a randomised controlled design which reports short and medium-term outcomes (including cost effectiveness outcomes) of at least 6 months’ duration. A careful definition of persistence needs to be used which needs to include duration of symptoms and consideration of failure of low-intensity interventions and does not necessarily imply a full diagnosis of dysthymia. The outcomes chosen should reflect both observer and patient-rated assessments of improvement and an assessment of the acceptability of the treatment options. The study needs to be large enough to determine the presence or absence of clinically important effects using a non-inferiority design and mediators and moderators of response should be investigated.

Why this is important
Persistent minor (sub-threshold) depression is increasingly recognised as affecting a considerable number of people and causing significant suffering but the best way to treat it is not known. There are studies of the efficacy of antidepressants for dysthymia (persistent minor depression that has lasted at least 2 years) but a lack of evidence for CBT. Minor depression of recent onset tends to improve but how long one should wait before offering medication or psychological treatment is not known. This research suggestion is aimed at informing the treatment options available for this group of people with minor depression that persists in spite of low-intensity interventions.
5 Other versions of this guideline

5.1 Full guideline
The full guideline, ‘Depression: the treatment and management of depression in adults’ contains details of the methods and evidence used to develop the guideline. It is published by the National Collaborating Centre for Mental Health, and is available from [NCC website details to be added] and our website (www.nice.org.uk/CGXXXfullguideline). [Note: these details will apply to the published full guideline.]

5.2 Quick reference guide
A quick reference guide for practitioners is available from www.nice.org.uk/CGXXXquickrefguide

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

5.3 ‘Understanding NICE guidance’
A summary for patients and carers (‘Understanding NICE guidance’) is available from www.nice.org.uk/CGXXXpublicinfo

For printed copies, phone NICE publications on 0845 003 7783 or email publications@nice.org.uk (quote reference number N1XXX). [Note: these details will apply when the guideline is published.]

We encourage NHS and voluntary sector organisations to use text from this booklet in their own information about depression.
6 Related NICE guidance

Published
Available from www.nice.org.uk/CG028


Under development
NICE is developing the following guidance (details available from www.nice.org.uk):

- Depression: the treatment and management of depression in adults with chronic physical health problems. NICE clinical guideline (publication expected September 2009).

7 Updating the guideline

NICE clinical guidelines are updated so that recommendations take into account new information. New evidence is checked 3 years after publication, and healthcare professionals and patients are asked for their views; we use this information to decide whether all or part of a guideline needs updating. If important new evidence is published at other times, we may decide to do a more rapid update of some recommendations.
Appendix A: The Guideline Development Group

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Appendix B: The Guideline Review Panel

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring adherence to NICE guideline development processes. In particular, the panel ensures that stakeholder comments have been adequately considered and responded to. The panel includes members from the following perspectives: primary care, secondary care, lay, public health and industry.

[NICE to add] [Note: these details will apply when the guideline is published.]

[Name; style = Unnumbered bold heading]
[job title and location; style = NICE normal]
Appendix C: Assessing depression and its severity

Key symptoms:

- persistent sadness or low mood; and/or
- marked loss of interests or pleasure.

At least one of these, most days, most of the time for at least 2 weeks.

If any of above present, ask about associated symptoms:

- disturbed sleep (decreased or increased compared to usual)
- decreased or increased appetite and/or weight
- fatigue or loss of energy
- agitation or slowing of movements
- poor concentration or indecisiveness
- feelings of worthlessness or excessive or inappropriate guilt
- suicidal thoughts or acts.

Then ask about duration and associated disability, past and family history of mood disorders, and availability of social support

1. Factors that favour general advice and active monitoring:

- four or fewer of the above symptoms with little associated disability
- symptoms intermittent, or less than 2 weeks duration
- recent onset with identified stressor
- no past or family history
- social support available
- lack of suicidal thoughts.

2. Factors that favour more active treatment in primary care:

- five or more symptoms with associated disability
- persistent or long-standing symptoms
- personal or family history of depression
• low social support
• occasional suicidal thoughts.

3. Factors that favour referral to mental health professionals:
   • poor or incomplete response to two or more interventions
   • recurrent episode within 1 year of last one
   • history suggestive of bipolar disorder
   • person with depression or relatives request referral
   • more persistent suicidal thoughts
   • self-neglect.

4. Factors that favour urgent referral to specialist mental health services
   • actively suicidal ideas or plans
   • psychotic symptoms
   • severe agitation accompanying severe symptoms
   • severe self-neglect.

Depression definitions

Minor depression: 2-4 symptoms with maintained function

Mild depression: Few, if any, symptoms in excess of 5 with only minor functional impairment

Moderate depression: Symptoms or functional impairment are between 'mild' and 'severe'

Severe depression: Several symptoms in excess of 5 and symptoms markedly interfere with functioning. With or without psychotic features.

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8 These are taken from DSM-IV. ICD-10 is similar but the threshold for mild depression is lower at 4 symptoms.