

#### Amendments to recommendations concerning venlafaxine

On 31 May 2006 the MHRA issued revised prescribing advice for venlafaxine\*. This amendment brings the guideline into line with the new advice but does not cover other areas where new evidence may be available. NICE expects to make a decision on a full update later in 2007.

Revised sections are in *italics*.

\*See:

[http://www.mhra.gov.uk/home/idcplg?IdcService=SS\\_GET\\_PAGE&useSecondary=true&ssDocName=CON2023843&ssTargetNodeId=389](http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&useSecondary=true&ssDocName=CON2023843&ssTargetNodeId=389)

Issue date: April 2007

## **Depression (amended)**

### **Management of depression in primary and secondary care**

**Clinical Guideline 23 (amended)****Depression: management of depression in primary and secondary care**

**Issue date:** April 2007

This document, which contains the Institute's full guidance on the management of depression in primary and secondary care, is available from the NICE website ([www.nice.org.uk/CG023NICEguideline](http://www.nice.org.uk/CG023NICEguideline)).

An abridged version of this guidance (a 'quick reference guide') is also available from the NICE website ([www.nice.org.uk/CG023quickrefguide](http://www.nice.org.uk/CG023quickrefguide)). Printed copies of the quick reference guide can be obtained from the NHS Response Line: telephone 0870 1555 455 and quote reference number N1237.

Information for the Public is available from the NICE website or from the NHS Response Line; quote reference number N1238 for a version in English. A version in Welsh is available from the NICE website ([www.nice.org.uk/CG022](http://www.nice.org.uk/CG022)).

**This guidance is written in the following context:**

This guidance represents the view of the Institute, which was arrived at after careful consideration of the evidence available. Health professionals are expected to take it fully into account when exercising their clinical judgement. The guidance does not, however, override the individual responsibility of health professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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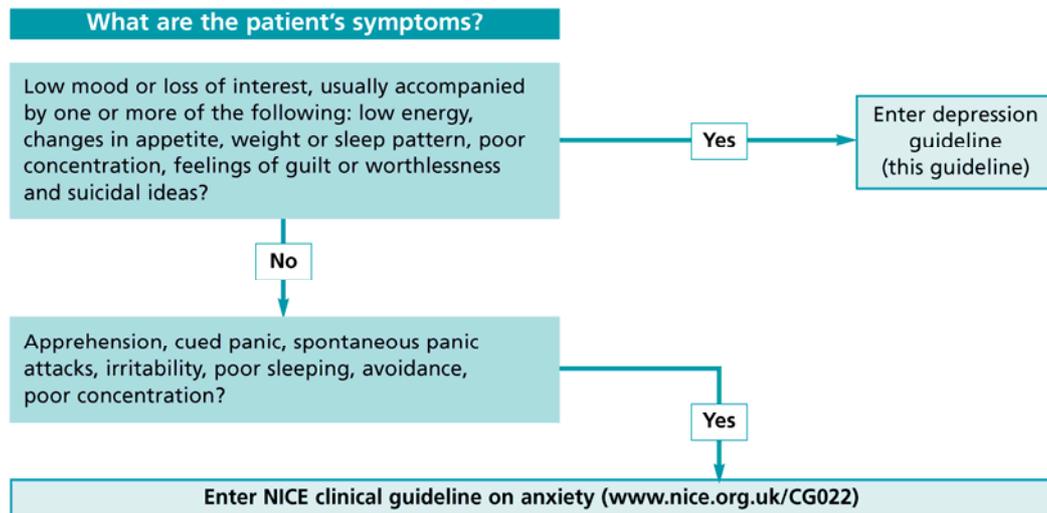
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## Which NICE guideline?



## **Key priorities for implementation**

### **Screening in primary care and general hospital settings**

- Screening should be undertaken in primary care and general hospital settings for depression in high-risk groups – for example, those with a past history of depression, significant physical illnesses causing disability, or other mental health problems, such as dementia.

### **Watchful waiting**

- For patients with mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, a further assessment should be arranged, normally within 2 weeks ('watchful waiting').

### **Antidepressants in mild depression**

- Antidepressants are not recommended for the initial treatment of mild depression, because the risk–benefit ratio is poor.

### **Guided self-help**

- For patients with mild depression, healthcare professionals should consider recommending a guided self-help programme based on cognitive behavioural therapy (CBT).

### **Short-term psychological treatment**

- In both mild and moderate depression, psychological treatment specifically focused on depression (such as problem-solving therapy, brief CBT and counselling) of 6 to 8 sessions over 10 to 12 weeks should be considered.

### **Prescription of an SSRI**

- When an antidepressant is to be prescribed in routine care, it should be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are as

effective as tricyclic antidepressants and are less likely to be discontinued because of side effects.

### **Tolerance and craving, discontinuation/withdrawal symptoms**

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

### **Initial presentation of severe depression**

- When patients present initially with severe depression, a combination of antidepressants and individual CBT should be considered as the combination is more cost-effective than either treatment on its own.

### **Maintenance treatment with antidepressants**

- Patients who have had two or more depressive episodes in the recent past, and who have experienced significant functional impairment during the episodes, should be advised to continue antidepressants for 2 years.

### **Combined treatment for treatment-resistant depression**

- For patients whose depression is treatment resistant, the combination of antidepressant medication with CBT should be considered.

### **CBT for recurrent depression**

- CBT should be considered for patients with recurrent depression who have relapsed despite antidepressant treatment, or who express a preference for psychological interventions.

The following guidance is evidence based. The grading scheme used for the recommendations (A, B, C, Good Practice Points [GPP] or NICE) is described in appendix A; a summary of the evidence on which the guidance is based is provided in the full guideline (see section 5).

## 1 Guidance

This guideline makes recommendations for the identification, treatment and management of depression for adults aged 18 years and over, in primary and secondary care. Depression is a broad and heterogeneous diagnostic grouping, central to which is depressed mood or loss of pleasure in most activities. Depressive symptoms are frequently accompanied by symptoms of anxiety, but may also occur on their own. ICD-10 uses an agreed list of ten depressive symptoms, and divides the common form of major depressive episode into four groups: not depressed (fewer than four symptoms), mild depression (four symptoms), moderate depression (five to six symptoms), and severe depression (seven or more symptoms, with or without psychotic symptoms). Symptoms should be present for a month or more and every symptom should be present for most of every day.

For the purposes of this guideline, the treatment and management of depression has been divided into the following descriptions as defined by ICD-10:

- mild depression
- moderate depression
- severe depression
- severe depression with psychotic symptoms.

However, it is doubtful whether the severity of the depressive illness can realistically be captured in a single symptom count. Clinicians will wish to consider family and previous history as well as the degree of associated disability in making this assessment (see appendix E).

We also make recommendations using the following descriptions, which are defined in the text:

- recurrent depression
- treatment-resistant depression
- chronic depression.

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 considerable implications for this guideline. These include very limited data on both long-term outcomes for most, if not all, interventions, and outcomes generally for the type of severe depression that often presents major challenges in secondary care mental health services. In part, these limitations arise from the problems associated with the randomised control trial methodology for all interventions, but particularly for psychological and service interventions.

However, the most significant limitation is with the concept of depression itself. The view of the Guideline Development Group is that it is too broad and heterogeneous a category, and has limited validity as a basis for effective treatment plans. A focus on symptoms alone is not sufficient because a wide range of biological, psychological and social factors have a significant impact on response to treatment and are not captured by the current diagnostic systems.

The guideline makes good practice points and evidence-based recommendations for the psychological, pharmacological, service-level and self-help interventions appropriate to each section.

## **1.1 Good practice points relevant to the care of all people with depression**

### **1.1.1 Depression and anxiety**

1.1.1.1 When depressive symptoms are accompanied by anxious symptoms, the first priority should usually be to treat the depression. Psychological treatment for depression often reduces anxiety, and many antidepressants also have sedative/anxiolytic effects. When the patient has anxiety without depression, the NICE guideline on management of anxiety should be followed (see section 6 and 'Which NICE guideline?' on page 4). **GPP**

### **1.1.2 Providing good information, informed consent and mutual support**

The provision of information and support is important in promoting understanding and collaboration between patients, their families and carers and healthcare professionals.

1.1.2.1 Patients and, where appropriate, families and carers should be provided with information on the nature, course and treatment of depression including the use and likely side-effect profile of medication. **GPP**

1.1.2.2 Healthcare professionals should make all efforts necessary to ensure that a patient can give meaningful and properly informed consent before treatment is initiated. This is especially important when a patient has a more severe depression or is subject to the Mental Health Act. **GPP**

1.1.2.3 Patients, families and carers should be informed of self-help groups and support groups and be encouraged to participate in such programmes where appropriate. **GPP**

- 1.1.2.4 Primary care trusts and mental health communities should collate information on local self-help groups for practitioners. **GPP**

### **1.1.3 Language**

- 1.1.3.1 When talking to patients and carers, healthcare professionals should use everyday, jargon-free language. If technical terms are used they should be explained to the patient. **GPP**
- 1.1.3.2 Where possible, all services should provide written material in the language of the patient, and independent interpreters should be sought for people whose preferred language is not English. **GPP**
- 1.1.3.3 Where available, consideration should be given to providing psychotherapies and information about medications in the patient's own language if this is not English. **GPP**

### **1.1.4 Advance directives**

- 1.1.4.1 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. **GPP**

### **1.1.5 Patient preference**

- 1.1.5.1 A number of different treatment approaches may be equally effective for patients who are depressed, especially for those with mild and moderate depression who are not considered to be at substantial risk of self-harm. Patient preference and the experience and outcome of previous treatment(s) should be considered when deciding on treatment. **GPP**

### 1.1.6 Assessment and coordination of care

The effective assessment of a patient (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. This is particularly important if the patient receives care in both primary and secondary care. The nature and course of depression are significantly affected by psychological, social and physical characteristics of the patient and his or her environment. These factors can have a significant impact on both the initial choice of intervention and the probability of the patient benefiting from that intervention.

- 1.1.6.1 When assessing a person with depression, healthcare professionals should consider the psychological, social, cultural and physical characteristics of the patient and the quality of interpersonal relationships. They should consider the impact of these on the depression and the implications for choice of treatment and its subsequent monitoring. **GPP**
- 1.1.6.2 In older adults with depression, their physical state, living conditions and social isolation should be assessed. The involvement of more than one agency is recommended where appropriate. **GPP**
- 1.1.6.3 In deciding on a treatment for a depressed patient, the healthcare professional should discuss alternatives with the patient, taking into account other factors such as past or family history of depression, response of any previous episodes to intervention, and the presence of associated problems in social or interpersonal relationships. **GPP**
- 1.1.6.4 Healthcare professionals should always ask patients with depression directly about suicidal ideas and intent. **GPP**
- 1.1.6.5 Healthcare professionals should advise patients and 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 medication and increased personal stress. Patients and carers should be advised to contact the appropriate healthcare practitioner if concerned. **GPP**

1.1.6.6 Healthcare professionals should assess whether patients with suicidal ideas have adequate social support and are aware of sources of help. They should advise them to seek appropriate help if the situation deteriorates. **GPP**

1.1.6.7 Where a patient's management is shared between primary and secondary care, there should be clear agreement between individual healthcare professionals on the responsibility for the monitoring and treatment of that patient, and the treatment plan should be shared with the patient and, where appropriate, with families and carers. **GPP**

1.1.6.8 All healthcare professionals involved in diagnosis and management should have a demonstrably high standard of consultation skills, so that a structured approach can be taken to the diagnosis and subsequent management of depression. **GPP**

1.1.6.9 Healthcare professionals should ensure they maintain their competence in risk assessment and management. **GPP**

## ***1.2 Stepped care***

The stepped-care model of depression draws attention to the different needs that depressed people 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 healthcare professionals in identifying and accessing the most effective interventions (see Figure 2).

<b>Step 5:</b> Inpatient care, crisis teams	Risk to life, severe self-neglect	Medication, combined treatments, ECT
<b>Step 4:</b> Mental health specialists including crisis teams	Treatment-resistant, recurrent, atypical and psychotic depression, and those at significant risk	Medication, complex psychological interventions, combined treatments
<b>Step 3:</b> Primary care team, primary care mental health worker	Moderate or severe depression	Medication, psychological interventions, social support
<b>Step 2:</b> Primary care team, primary care mental health worker	Mild depression	Watchful waiting, guided self-help, computerised CBT, exercise, brief psychological interventions
<b>Step 1:</b> GP, practice nurse	Recognition	Assessment

**Figure 2 The stepped care model**

The guidance follows these five steps:

- recognition of depression in primary care and general hospital settings
- managing recognised depression in primary care – mild depression
- managing recognised depression in primary care – moderate to severe depression
- involvement of specialist mental health services including crisis teams – treatment-resistant, recurrent, atypical and psychotic depression, and those at significant risk
- depression needing inpatient care.

Each step introduces additional interventions; the higher steps assume interventions in the previous step.

### **1.3 Step 1: recognition of depression in primary care and general hospital settings**

Around half of all people with depression in the community do not present to their GP. In addition, at least two-thirds of depressed people who see their GP present with physical or somatic symptoms rather than psychological symptoms, making recognition harder. Moreover, many patients with established physical diseases become depressed during the course of their illness, and recognition of depression for this population is important and can lead to improved outcomes. The following recommendations are for healthcare professionals working in primary care and general hospital settings.

- 1.3.1.1 Screening should be undertaken in primary care and general hospital settings for depression in high-risk groups – for example, those with a past history of depression, significant physical illnesses causing disability, or other mental health problems, such as dementia. **C**
- 1.3.1.2 Healthcare professionals should bear in mind the potential physical causes of depression and the possibility that depression may be caused by medication, and consider screening if appropriate. **C**
- 1.3.1.3 Screening for depression should include the use of at least two questions concerning mood and interest, such as: “During the last month, have you often been bothered by feeling down, depressed or hopeless?” and “During the last month, have you often been bothered by having little interest or pleasure in doing things?” **B**

### **1.4 Step 2: recognised depression in primary care – mild depression**

The large majority of patients with depression (more than 80%) are cared for solely in primary care. Of those who use secondary care services most, if not all, continue to receive much of their care from the primary care team.

For a significant number of people with mild to moderate depression, brief interventions delivered by the primary care team are effective; for others – particularly if they have not responded to the initial brief intervention – more complex interventions, which could be provided in primary or secondary care, are required.

Many patients with milder depression respond to interventions such as exercise or guided self-help, although many improve while being monitored without additional help. More structured therapies, such as problem-solving, brief CBT or counselling can be helpful. Antidepressant drugs and psychological therapies, such as longer-term CBT or interpersonal psychotherapy (IPT), are not recommended as an initial treatment; these may be offered when simpler methods (for example, guided self-help or exercise) have failed to produce an adequate response.

### **1.4.1 General measures**

#### **Sleep and anxiety management**

1.4.1.1 Patients with mild depression may benefit from advice on sleep hygiene and anxiety management. **C**

#### **Watchful waiting**

1.4.1.2 For patients with mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, a further assessment should be arranged, normally within 2 weeks ('watchful waiting'). **C**

1.4.1.3 Healthcare professionals should make contact with patients with depression who do not attend follow-up appointments. **C**

#### **Exercise**

1.4.1.4 Patients of all ages with mild depression should be advised of the benefits of following a structured and supervised exercise

programme of typically up to 3 sessions per week of moderate duration (45 minutes to 1 hour) for between 10 and 12 weeks. **C**

### **Guided self-help**

- 1.4.1.5 For patients with mild depression, healthcare professionals should consider recommending a guided self-help programme based on cognitive behavioural therapy (CBT). **B**
- 1.4.1.6 Guided self-help should consist of the provision of appropriate written materials and limited support from a healthcare professional, who typically introduces the self-help programme and reviews progress and outcome. This intervention should normally take place over 6 to 9 weeks, including follow up. **B**

### **1.4.2 Psychological interventions**

For mild depression, a number of brief psychological interventions are effective. The choice of treatment should reflect the patient's preference based on informed discussion, past experience of treatment and the fact that the patient may not have benefited from other brief interventions. For all treatments the strength of the therapeutic alliance is important in ensuring a good outcome. Problem-solving is a brief treatment that can readily be learned by practice nurses and by GPs themselves.

- 1.4.2.1 In both mild and moderate depression, psychological treatment specifically focused on depression (such as problem-solving therapy, brief CBT and counselling) of 6 to 8 sessions over 10 to 12 weeks should be considered. **B**
- 1.4.2.2 In patients with depression who have significant comorbidity, consideration should be given to extending the duration of treatment for depression, making use, where appropriate, of treatments that focus specifically on the comorbid problems. **C**

- 1.4.2.3 The full range of psychological interventions should be made available to older adults with depression, because they may have the same response to psychological interventions as younger people. **C**
- 1.4.2.4 Current research suggests that the delivery of cognitive behavioural therapy via a computer interface (CCBT) may be of value in the management of anxiety and depressive disorders. This evidence is, however, an insufficient basis on which to recommend the general introduction of this technology into the NHS. **NICE 2002**
- 1.4.2.5 Since the publication of NICE guidance on CCBT (NICE 2002), new evidence reporting positive results for CCBT with mild and moderate depression has emerged. Clinicians considering the use of CCBT should consider this evidence in making decisions about the use of CCBT, pending the publication of the updated NICE guidance, which is scheduled for June 2005. **GPP**
- 1.4.2.6 Healthcare professionals providing psychological treatment should be experienced in the treatment of the disorder and competent in the delivery of the treatment provided. **GPP**
- 1.4.2.7 In all psychological interventions, healthcare professionals should develop and maintain an appropriate therapeutic alliance, because this is associated with a positive outcome independent of the type of therapy provided. **C**

### **1.4.3 Antidepressant drugs**

Randomised controlled trial (RCT) evidence indicates that for many patients there is little clinically important difference between antidepressants and placebo, and the placebo response is greatest in mild depression. For guidance on the use of antidepressant drugs, see section 1.5.2.

- 1.4.3.1 Antidepressants are not recommended for the initial treatment of mild depression, because the risk–benefit ratio is poor. **C**

1.4.3.2 The use of antidepressants should be considered for patients with mild depression that is persisting after other interventions, and those whose depression is associated with psychosocial and medical problems. **C**

1.4.3.3 The use of antidepressants should be considered when patients with a past history of moderate or severe depression present with mild depression. **C**

### **1.5 Step 3: recognised depression in primary care – moderate or severe**

Moderate or severe depression can be treated in both primary and secondary care and, as with mild depression, the choice of treatment will reflect patient preference, past experience of treatment and the fact that the patient may not have benefited from other interventions. With more severe depression, the risk of suicide should always be considered. Referral to secondary services should be based on this assessment, the degree of functional impairment and the presence of significant comorbidities or specific symptoms. Where trained mental health professionals are working in primary care, specialised treatments may be available in this setting.

#### **1.5.1 Risk to self or others**

1.5.1.1 Where a patient presents considerable immediate risk to self or others, urgent referral to a specialist mental health service should be arranged. **GPP**

#### **1.5.2 Antidepressant drugs**

There is more evidence for the effectiveness of antidepressant medication in moderate to severe depression than in milder depression. Antidepressants are as effective as psychological interventions, widely available and cost less. Careful monitoring of symptoms, side effects and suicide risk (particularly in those aged under 30) should be routinely undertaken, especially when

initiating antidepressant medication. Patient preference and past experience of treatment, and particular patient characteristics should inform the choice of drug. It is also important to monitor patients for relapse and discontinuation/withdrawal symptoms when reducing or stopping medication. Patients should be warned about the risks of reducing or stopping medication.

### **Starting treatment**

- 1.5.2.1 In moderate depression, antidepressant medication should be routinely offered to all patients before psychological interventions. **B**
- 1.5.2.2 Common concerns about taking medication should be addressed. For example, patients should be advised that craving and tolerance do not occur, and that taking medication should not be seen as a sign of weakness. **GPP**
- 1.5.2.3 All patients who are prescribed antidepressants should be informed, at the time that treatment is initiated, of potential side effects and of the risk of discontinuation/withdrawal symptoms. **C**
- 1.5.2.4 Patients started on antidepressants should be informed about the delay in onset of effect, the time course of treatment, the need to take medication as prescribed, and the possible discontinuation/withdrawal symptoms. Written information appropriate to the patient's needs should be made available. **GPP**

### **Monitoring risk**

- 1.5.2.5 Patients started on antidepressants who are considered to present an increased suicide risk or are younger than 30 years (because of the potential increased risk of suicidal thoughts associated with 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 significant. **C**

- 1.5.2.6 For patients at high risk of suicide, a limited quantity of antidepressants should be prescribed. **C**
- 1.5.2.7 When a patient with depression is assessed to be at a high risk of suicide, the use of additional support such as more frequent direct contacts with primary care staff or telephone contacts should be considered. **C**
- 1.5.2.8 Particularly in the initial stages of SSRI treatment, healthcare professionals should actively seek out signs of akathisia, suicidal ideation, and increased anxiety and agitation. They should also advise patients of the risk of these symptoms in the early stages of treatment and advise them to seek help promptly if these are at all distressing. **C**
- 1.5.2.9 In the event that a patient develops marked and/or prolonged akathisia or agitation while taking an antidepressant, the use of the drug should be reviewed. **C**

### **Continuing treatment**

- 1.5.2.10 Patients 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 2–4 weeks in the first 3 months and at longer intervals thereafter, if response is good. **C**
- 1.5.2.11 Antidepressants should be continued for at least 6 months after remission of an episode of depression, because this greatly reduces the risk of relapse. **A**
- 1.5.2.12 When a patient has taken antidepressants for 6 months after remission, healthcare professionals should review with the patient the need for continued antidepressant treatment. This review should include consideration of the number of previous

episodes, presence of residual symptoms, and concurrent psychosocial difficulties. **C**

### **The choice of antidepressants**

- 1.5.2.13 When an antidepressant is to be prescribed in routine care, it should be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are as effective as tricyclic antidepressants and are less likely to be discontinued because of side effects. **A**
- 1.5.2.14 When prescribing an SSRI, consideration should be given to using a product in a generic form. Fluoxetine and citalopram, for example, would be reasonable choices because they are generally associated with fewer discontinuation/withdrawal symptoms. **C**
- 1.5.2.15 Dosulepin, phenelzine, combined antidepressants, and lithium augmentation of antidepressants should only be routinely initiated by specialist mental health professionals, including General Practitioners with a Special Interest in Mental Health. **C**

*[The recommendations on venlafaxine (1.5.2.16 and 1.5.2.17 in the guideline published in 2004) have been deleted from this section]*

- 1.5.2.16 Toxicity in overdose should be considered when choosing an antidepressant for patients at significant risk of suicide. Healthcare professionals should be aware that the highest risk in overdose is with tricyclic antidepressants (with the exception of lofepramine) *but that venlafaxine is also more dangerous in overdose than other equally effective drugs recommended for routine use in primary care.* **C**
- 1.5.2.17 If a depressed patient being treated with an SSRI develops increased agitation early in treatment, the prescriber should provide appropriate information, and if the patient prefers the drug should be changed to a different antidepressant. Alternatively, a brief

period of concomitant treatment with a benzodiazepine should be considered, followed by a clinical review within 2 weeks. **C**

- 1.5.2.18 When a patient's depression fails to respond to the first antidepressant prescribed, the prescriber should check that the drug has been taken regularly and in the prescribed dose. **GPP**
- 1.5.2.19 If the response to a standard dose of an antidepressant is inadequate, and there are no significant side effects, a gradual increase in dose should be considered in line with the schedule suggested by the Summary of Product Characteristics. **C**
- 1.5.2.20 Prescribers should consider switching to another antidepressant if there has been no response at all after 1 month, but if there has been a partial response, a decision to switch can be postponed until 6 weeks. **C**
- 1.5.2.21 If an antidepressant has not been effective or is poorly tolerated and – after consideration of a range of other treatment options – the decision is made to offer a further course of antidepressants, then another single antidepressant should be prescribed. **C**
- 1.5.2.22 Reasonable choices for a second antidepressant include a different SSRI or mirtazapine, but consideration may also be given to other alternatives, including moclobemide, reboxetine *and lofepramine*. *Other tricyclic antidepressants (except dosulepin) and venlafaxine may be considered, especially for more severe depression.* **B**
- 1.5.2.23 When switching from one antidepressant to another, prescribers should be aware of the need for gradual and modest incremental increases of dose, of interactions between antidepressants and the risk of serotonin syndrome when combinations of serotonergic antidepressants are prescribed. Features include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus. **C**

- 1.5.2.24 Before prescribing mirtazapine, practitioners should take into account its propensity to cause sedation and weight gain. **A**
- 1.5.2.25 Before prescribing moclobemide, practitioners should take into account the need to wash out previously prescribed antidepressants. **A**
- 1.5.2.26 Before prescribing reboxetine, practitioners should take into account the relative lack of data on side effects. Patients taking reboxetine should be monitored carefully. **B**
- 1.5.2.27 Before prescribing tricyclic antidepressants, practitioners should take into account their poorer tolerability compared with other equally effective antidepressants, the increased risk of cardiotoxicity and their toxicity in overdose. **B**
- 1.5.2.28 Where a tricyclic is chosen as an antidepressant, lofepramine is a reasonable choice because of its relative lack of cardiotoxicity. **C**
- 1.5.2.29 Patients who start on low-dose tricyclic antidepressants and who have a clear clinical response may be maintained on that dose with careful monitoring. **C**
- 1.5.2.30 Patients started on low-dose tricyclic antidepressants should be carefully monitored for side effects and efficacy, and the dose gradually increased if there is lack of efficacy and no major side effects. **GPP**
- 1.5.2.31 *Before prescribing venlafaxine, practitioners should take into account the increased likelihood of patients stopping treatment because of side effects, and its higher cost, compared with equally effective SSRIs. **B***
- 1.5.2.32 *Before prescribing venlafaxine, practitioners should ensure pre-existing hypertension is controlled in line with the current NICE guideline on hypertension (see [www.nice.org.uk/CG034](http://www.nice.org.uk/CG034)).*

*Venlafaxine should not be prescribed for patients with uncontrolled hypertension.* **C**

- 1.5.2.33 *For patients prescribed venlafaxine, blood pressure should be checked on initiation and regularly during treatment, particularly during dosage titration. For patients who experience a sustained increase in blood pressure, the dose should be reduced or discontinuation considered.* **C**
- 1.5.2.34 *Practitioners should monitor patients prescribed venlafaxine for the signs and symptoms of cardiac dysfunction, particularly in those with known cardiovascular disease, and take appropriate action as necessary.* **C**
- 1.5.2.35 *When prescribing antidepressants (particularly fluoxetine, fluvoxamine, paroxetine, tricyclic antidepressants, or venlafaxine), practitioners should be aware of clinically significant interactions with concomitant drugs. They should consider consulting appendix 1 of the 'British National Formulary'.* **C**
- 1.5.2.36 *Venlafaxine should only be prescribed at high dose (300 mg/day or more) under the supervision or advice of a specialist mental health medical practitioner.* **C**
- 1.5.2.37 *Although there is evidence that St John's wort may be of benefit in mild or moderate depression, healthcare professionals should not prescribe or advise its use by patients because of uncertainty about appropriate doses, variation in the nature of preparations and potential serious interactions with other drugs (including oral contraceptives, anticoagulants and anticonvulsants).* **C**
- 1.5.2.38 *Patients who are taking St John's wort should be informed of the different potencies of the preparations available and the uncertainty that arises from this. They should also be informed of the potential serious interactions of St John's wort with other drugs (including oral contraceptives, anticoagulants and anticonvulsants).* **C**

## Patient characteristics

### *Gender*

- 1.5.2.39 When considering which antidepressants to prescribe for female patients, the fact that they have poorer tolerance of imipramine should be taken into account. **B**

### *Age*

- 1.5.2.40 For older adults with depression, antidepressant treatment should be given at an age-appropriate dose for a minimum of 6 weeks before treatment is considered to be ineffective. If there has been a partial response within this period, treatment should be continued for a further 6 weeks. **C**
- 1.5.2.41 When prescribing antidepressants – in particular tricyclics – for older adults with depression, careful monitoring for side effects should be undertaken. **C**
- 1.5.2.42 Healthcare professionals should be aware of the increased frequency of drug interactions when prescribing an antidepressant to older adults who are taking other medications. **GPP**

### *Patients with dementia*

- 1.5.2.43 Depression in patients with dementia should be treated in the same way as depression in other older adults. **C**
- 1.5.2.44 Healthcare professionals should be aware that depression responds to antidepressants even in the presence of dementia. **C**

### *Patients with cardiovascular disease*

- 1.5.2.45 When initiating treatment in a patient with a recent myocardial infarction or unstable angina, sertraline is the treatment of choice as it has the most evidence for safe use in this situation. **B**

1.5.2.46 An ECG should be carried out *and blood pressure measurement taken* before prescribing a tricyclic antidepressant for a depressed patient at significant risk of cardiovascular disease. **GPP**

1.5.2.47 *Venlafaxine and tricyclic antidepressants (with the exception of lofepramine)* should not be prescribed for patients with a:

- *high risk of serious cardiac arrhythmias*
- *recent myocardial infarction.* **C**

### **Stopping or reducing antidepressants**

Although antidepressants are not associated with tolerance and craving, as experienced when withdrawing from addictive substances such as opiates or alcohol, some patients experience symptoms when stopping antidepressants or reducing the dose. These can include dizziness, nausea, paraesthesia, anxiety and headaches and, in this guideline, are referred to as discontinuation/withdrawal symptoms.

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

1.5.2.49 Patients should be advised to take the drugs as prescribed. This may be particularly important for drugs with a shorter half-life, such as paroxetine *and venlafaxine*, in order to avoid discontinuation/withdrawal symptoms. **C**

1.5.2.50 Healthcare professionals should normally gradually reduce the doses of the drug over a 4-week period, although some people may require longer periods. Fluoxetine can usually be stopped over a shorter period. **C**

- 1.5.2.51 If discontinuation/withdrawal symptoms are mild, practitioners should reassure the patient and monitor symptoms. If symptoms are severe, the practitioner should 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. **C**
- 1.5.2.52 Healthcare professionals should inform patients that they should seek advice from their medical practitioner if they experience significant discontinuation/withdrawal symptoms. **GPP**

### **1.5.3 Psychological treatments**

For moderate to severe depression, a number of structured psychological interventions of longer duration (usually of 16 to 20 sessions) from an appropriately trained member of the mental health team are effective. In addition to the evidence for their effectiveness, the choice of treatment will reflect patient preference and past experience of treatment. Most patients receiving these interventions will not have benefited from other interventions. The same principles underpinning the use of psychological therapies outlined for the treatment of mild depression (Step 2) also apply here.

Where depression is comorbid with another significant disorder, such as personality disorder, then treatment may need to be extended or varied.

#### **Cognitive behavioural therapies and interpersonal therapy**

The following recommendations focus on the provision of CBT. However, IPT can also be an effective treatment for depression. Where patient preference or clinician opinion favours the use of IPT, it may be appropriate to draw the patient's attention to the more limited evidence base for this therapy.

- 1.5.3.1 When considering individual psychological treatments for moderate, severe and treatment-resistant depression, the treatment of choice is CBT. IPT should be considered if the patient expresses a

preference for it or if, in the view of the healthcare professional, the patient may benefit from it. **B**

- 1.5.3.2 For moderate and severe depression, the duration of all psychological treatments should typically be in the range of 16 to 20 sessions over 6 to 9 months. **B**
- 1.5.3.3 CBT should be offered to patients with moderate or severe depression who do not take or who refuse antidepressant treatment. **B**
- 1.5.3.4 CBT should be considered for patients who have not had an adequate response to a range of other treatments for depression (for example, antidepressants and brief psychological interventions). **C**
- 1.5.3.5 CBT should be considered for patients with severe depression in whom the avoidance of side effects often associated with antidepressants is a clinical priority or personal preference. **B**
- 1.5.3.6 For patients with severe depression who are starting a course of CBT, consideration should be given to providing 2 sessions per week for the first month of treatment. **C**
- 1.5.3.7 Where patients have responded to a course of individual CBT, consideration should be given to follow-up sessions, which typically consist of 2 to 4 sessions over 12 months. **C**

#### **Initial presentation of severe depression**

- 1.5.3.8 When patients present initially with severe depression, a combination of antidepressants and individual CBT should be considered as the combination is more cost-effective than either treatment on its own. **B**

## **Couple-focused therapy**

- 1.5.3.9 Couple-focused therapy should be considered for patients with depression who have a regular partner and who have not benefited from a brief individual intervention. An adequate course of couple-focused therapy should be 15 to 20 sessions over 5 to 6 months. **B**

## **Psychodynamic psychotherapy**

- 1.5.3.10 Psychodynamic psychotherapy may be considered for the treatment of the complex comorbidities that may be present along with depression. **C**

## **1.5.4 Atypical depression**

Depression can present with atypical features, commonly over-eating and over-sleeping. The syndrome is also associated with mood reactivity and a longstanding pattern of interpersonal rejection and over-sensitivity. In comparison with major depressive disorder without atypical features, patients with atypical features are more often female, have a younger age of onset and a more severe degree of psychomotor slowing. Coexisting diagnoses of panic disorder, substance abuse and somatisation disorder are also common.

- 1.5.4.1 Patients whose depression has atypical features should be treated with an SSRI. **C**
- 1.5.4.2 Referral to mental health specialists should be considered for patients with atypical depression and significant functional impairment who have not responded to an SSRI. **GPP**

## **1.5.5 Chronic depression**

Chronic depression is diagnosed when a person meets the diagnostic criteria for depression for at least 2 years. Such patients may require combination treatments and attention to social and support factors that may maintain or ameliorate their difficulties. Patients who have had chronic depression may require rehabilitation to help them regain confidence to return to more

independent living. People who have had severe or chronic depression may require special help in returning to work. Work provides a number of protective factors for depression including structure to a day, social contacts and self-esteem.

1.5.5.1 Patients with chronic depression should be offered a combination of CBT and antidepressant medication. **A**

1.5.5.2 For male patients with chronic depression who have not responded to an SSRI, consideration should be given to a tricyclic antidepressant because men tolerate the side effects of tricyclic antidepressants reasonably well. **C**

1.5.5.3 For people with chronic depression who would benefit from additional social support, befriending should be considered 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. **C**

1.5.5.4 Where a patient's depression has resulted in loss of work or disengagement from other social activities over a longer term, a rehabilitation programme addressing these difficulties should be considered. **C**

## **1.5.6 Enhanced care in primary care**

In primary care, the following strategies can improve the effectiveness of treatments offered.

1.5.6.1 The provision of telephone support by appropriately trained members of the primary care team, informed by clear treatment protocols, should be considered for all patients, in particular for the monitoring of antidepressant medication regimes. **B**

1.5.6.2 Primary care organisations should consider establishing multifaceted care programmes that integrate – through clearly specified protocols – the delivery and monitoring of appropriate

psychological and pharmacological interventions for the care of people with depression. **C**

### **1.6 Step 4: specialist mental health services – treatment-resistant, recurrent, atypical and psychotic depression, and those at significant risk**

Specialist mental health professionals, including GPs with a Special Interest in mental health, provide assessment, treatment and consultancy services for this group of patients. They may do this in secondary care services or through attachment to primary care mental health teams. Patients may enter care directly at this step if they are assessed as requiring specialist services.

- 1.6.1.1 The assessment of patients 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. Assessment of psychosocial stressors, personality factors and significant relationship difficulties should also be undertaken, particularly where the depression is chronic or recurrent. **GPP**
- 1.6.1.2 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. **GPP**
- 1.6.1.3 Crisis resolution and home treatment teams should be used as a means of managing crises for patients 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. **C**

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

## **1.6.2 Treatment-resistant depression**

Some people with depression do not respond well to initial treatment. This guideline defines treatment-resistant depression as that which fails to respond to two or more antidepressants given sequentially at an adequate dose for an adequate time. Patients whose depression is treatment-resistant may benefit from psychological interventions. For chronically depressed patients, the combination of pharmacological and psychological treatment may be particularly effective. Patient preference, the level of risk, social and personal circumstances, and the drawbacks of all interventions will influence the choice of treatment.

### **Combined psychological and drug treatment**

- 1.6.2.1 For patients whose depression is treatment-resistant, the combination of antidepressant medication with CBT should be considered. **B**
- 1.6.2.2 For patients with treatment-resistant moderate depression who have relapsed while taking, or after finishing, a course of antidepressants, the combination of antidepressant medication with CBT should be considered. **B**

### **Drug treatments**

- 1.6.2.3 A trial of lithium augmentation should be considered for patients whose depression has failed to respond to several antidepressants and who are prepared to tolerate the burdens associated with its use. **B**
- 1.6.2.4 Before initiating lithium augmentation, an ECG should be carried out. **C**

1.6.2.5 *If venlafaxine has not been used before, it should be considered for patients whose depression has failed to respond to two adequate trials of other antidepressants. Consideration should be given to increasing the dose up to 'British National Formulary' limits if required, provided patients can tolerate the side effects. **C** See pages 23–28 for prescribing advice.*

*[The recommendations on venlafaxine (1.6.2.6 to 1.6.2.9 in the guideline published in 2004) have been deleted from this section]*

1.6.2.6 Augmenting an antidepressant with another antidepressant should be considered for patients whose depression is treatment resistant and who are prepared to tolerate the side effects. There is evidence for benefits from the addition of mianserin or mirtazapine to SSRIs. **C**

1.6.2.7 Where patients are treated with one antidepressant augmented by another, careful monitoring of progress and side effects is advised and the importance of this should be explained to the patient. Particular care should be taken to monitor for serotonin syndrome. **GPP**

1.6.2.8 When used to augment another antidepressant, mianserin should be used with caution, particularly in older adults, because of the risk of agranulocytosis. **C**

1.6.2.9 Where combinations of antidepressants other than mianserin with SSRIs and mirtazapine with SSRIs are considered, healthcare professionals should re-evaluate the adequacy of previous treatments carefully before proceeding, and consider seeking a second opinion. Any discussion should be documented in the notes. **C**

1.6.2.10 Phenelzine should be considered for patients whose depression has failed to respond to alternative antidepressants and who are prepared to tolerate the side effects and dietary restrictions

associated with its use. However, its toxicity in overdose should be considered when prescribing for patients at high risk of suicide. **C**

1.6.2.11 Augmentation of an antidepressant with carbamazepine, lamotrigine, buspirone, pindolol, valproate or thyroid supplementation is not recommended in the routine management of treatment-resistant depression. **B**

1.6.2.12 Dosulepin should not be initiated routinely because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose. **C**

1.6.2.13 There is insufficient evidence to recommend the use of benzodiazepine augmentation of antidepressants. **C**

### **Referral**

1.6.2.14 When a patient's depression has failed to respond to various strategies for augmentation and combination treatments, referral to a clinician with a specialist interest in treating depression should be considered. **GPP**

### **1.6.3 Recurrent depression and relapse prevention**

Antidepressants can contribute significantly to reducing the frequency of recurrence when prescribed as maintenance medication. Structured psychological treatments can also make a significant contribution.

#### **Drug advice**

1.6.3.1 Patients who have had two or more depressive episodes in the recent past, and who have experienced significant functional impairment during the episodes, should be advised to continue antidepressants for 2 years. **B**

- 1.6.3.2 Patients on maintenance treatment should be re-evaluated, taking into account age, comorbid conditions and other risk factors in the decision to continue maintenance treatment beyond 2 years. **GPP**
- 1.6.3.3 The antidepressant dose used for the prevention of recurrence should be maintained at the level at which acute treatment was effective. **C**
- 1.6.3.4 Patients who have had multiple episodes of depression, and who have had a good response to treatment with an antidepressant and lithium augmentation, should remain on this combination for at least 6 months. **B**
- 1.6.3.5 When one drug is to be discontinued in a patient taking an antidepressant with lithium augmentation, this should be lithium in preference to the antidepressant. **C**
- 1.6.3.6 The use of lithium as a sole agent to prevent recurrence of depression in patients with previous recurrences is not recommended. **C**

### **Psychological treatments**

- 1.6.3.7 CBT should be considered for patients with recurrent depression who have relapsed despite antidepressant treatment, or who express a preference for psychological interventions. **C**
- 1.6.3.8 Where a patient with depression has a previous history of relapse and poor or limited response to other interventions, consideration should be given to CBT. **B**
- 1.6.3.9 When patients with moderate or severe depression have responded to another intervention but are unable or unwilling to continue with that intervention, and are assessed as being at significant risk of relapse, a maintenance course of CBT should be considered. **B**

1.6.3.10 Mindfulness-based CBT, usually delivered in a group format, should be considered for people who are currently well but have experienced three or more previous episodes of depression, because this may significantly reduce the likelihood of future relapse. **B**

#### **1.6.4 Atypical depression**

1.6.4.1 Phenelzine should be considered for women whose depression is atypical, and who have not responded to, or who cannot tolerate, an SSRI. However, its toxicity in overdose should be considered when prescribing for patients at high risk of suicide. **C**

1.6.4.2 All patients receiving phenelzine require careful monitoring (including taking blood pressure) and advice on interactions with other medicines and foodstuffs, and should have their attention drawn to the product information leaflet. **C**

#### **1.6.5 Recommendations for the pharmacological management of psychotic depression**

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

### ***1.7 Step 5: depression needing inpatient care***

Certain specialist services – inpatient services and specialist treatments such as electroconvulsive therapy – will be provided by secondary care services. These services are for patients who are severely depressed and who may be assessed as being at high risk of self-harm or suicide.

### 1.7.1 Inpatient care

Depressed people are admitted to inpatient care for a number of reasons related to severity of the disorder, concerns with self-care and neglect, and suicide risk. It is important that acute psychiatric wards make every effort to provide a place of sanctuary that is non-threatening and enables healthcare professionals to provide appropriate care. Activities conducive to recovery for depression should be provided. Boredom and rumination can affect recovery.

- 1.7.1.1 Inpatient treatment should be considered for people with depression who are at significant risk of suicide or self-harm. **C**
- 1.7.1.2 Crisis resolution and home treatment teams should be considered for patients with depression who might benefit from an early discharge from hospital after a period of inpatient care. **C**

### 1.7.2 Electroconvulsive therapy

- 1.7.2.1 It is recommended that electroconvulsive therapy (ECT) is used only to achieve rapid and short-term improvement of severe symptoms after an adequate trial of other treatment options has proven ineffective, and/or when the condition is considered to be potentially life-threatening, in individuals with a severe depressive illness. **NICE 2003**
- 1.7.2.2 The decision as to whether ECT is clinically indicated should be based on a documented assessment of the risks and potential benefits to the individual, including: the risks associated with the anaesthetic; current comorbidities; anticipated adverse events – particularly cognitive impairment – and the risks of not having treatment. **NICE 2003**
- 1.7.2.3 The risks associated with ECT may be enhanced during pregnancy, in older people, and in children and young people, and therefore clinicians should exercise particular caution when considering ECT treatment in these groups. **NICE 2003**

- 1.7.2.4 Valid consent should be obtained in all cases where the individual has the ability to grant or refuse consent. The decision to use ECT should be made jointly by the individual and the clinician(s) responsible for treatment, on the basis of an informed discussion. This discussion should be enabled by the provision of full and appropriate information about the general risks associated with ECT and about the risks and potential benefits specific to that individual. Consent should be obtained without pressure or coercion, which may occur as a result of the circumstances and clinical setting, and the individual should be reminded of his or her 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. **NICE 2003**
- 1.7.2.5 In all situations where informed discussion and consent is not possible, advance directives should be taken fully into account and the individual's advocate and/or carer should be consulted. **NICE 2003**
- 1.7.2.6 Clinical status should be assessed after each ECT session and treatment should be stopped when a response has been achieved, or sooner if there is evidence of adverse effects. Cognitive function should be monitored on an ongoing basis, and at a minimum at the end of each course of treatment. **NICE 2003**
- 1.7.2.7 It is recommended that a repeat course of ECT should be considered under the circumstances indicated in 1.7.2.1 only for individuals who have severe depressive illness, and who have previously responded well to ECT. In patients who are experiencing an acute episode but have not previously responded, a repeat trial of ECT should be undertaken 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. **NICE 2003**

1.7.2.8 Because the longer-term benefits and risks of ECT have not been clearly established, it is not recommended as a maintenance therapy in depressive illness. **NICE 2003**

## 2 Notes on the scope of the guidance

All NICE guidelines are developed in accordance with a scope document that defines what the guideline will and will not cover. The scope of this guideline was established at the start of the development of this guideline, following a period of consultation; it is available from [www.nice.org.uk/Docref.asp?d=23413](http://www.nice.org.uk/Docref.asp?d=23413)

This guideline is relevant to people aged 18 and older with depression, and to all healthcare professionals involved in the help, treatment and care of people with depression and their carers. These include the following.

- Professional groups (including general practitioners, psychiatrists, clinical psychologists, mental health nurses, community psychiatric nurses, social workers, practice nurses, secondary care medical, nursing and paramedical staff, occupational therapists, pharmacists and physicians) who share in the treatment and care of people with a diagnosis of depression.
- Professionals in other health and non-health sectors who may have direct contact with, or are involved in the provision of health and other public services for, those diagnosed with depression; this may include prison doctors, the police and professionals who work in the criminal justice and education sectors.
- Those with responsibility for planning services for people with depression and their carers – including directors of public health, NHS trust managers and managers in primary care trusts.

The guidance does not specifically address:

- the diagnosis or treatment of depression in young people younger than 18 years or in the context of a separate physical disorder
- dysthymia, seasonal affective disorder or postnatal depression.

## **3 Implementation in the NHS**

### ***3.1 Resource implications***

Local health communities should review their existing practice in the treatment and management of depression against this guideline. The review should consider the resources required to implement the recommendations set out in section 1, the people and processes involved and the timeline over which full implementation is envisaged. It is in the interests of patients that the implementation timeline is as rapid as possible.

Relevant local clinical guidelines, care pathways and protocols should be reviewed in the light of this guidance and revised accordingly.

Information on the cost impact of this guideline in England is available on the NICE website and includes a template that local communities can use ([www.nice.org.uk/CG023costtemplate](http://www.nice.org.uk/CG023costtemplate)).

### ***3.2 General***

The implementation of this guideline will build on the National Service Frameworks for Mental Health in England and Wales and should form part of the service development plans for each local health community in England and Wales. The National Service Frameworks are available for England from [www.dh.gov.uk/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_4009598](http://www.dh.gov.uk/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4009598), and for Wales from [www.wales.nhs.uk/sites/home.cfm?orgid=438](http://www.wales.nhs.uk/sites/home.cfm?orgid=438)

### **3.3 Audit**

Suggested audit criteria are listed in appendix D. These can be used as the basis for local clinical audit, at the discretion of those in practice.

## **4 Key research recommendations**

The Guideline Development Group identified the following key research recommendations to address gaps in the evidence base.

- 4.1 Research is needed into the cost effectiveness of routine screening of populations known to be at high risk of depression.
- 4.2 Adequately powered RCTs reporting all relevant outcomes, including relapse rates, comparing the efficacy of different models of CBT, IPT and behaviour therapy should be undertaken to identify differential individual response to treatment and how this relates to the severity of baseline depression symptoms.
- 4.3 Efficacy studies of the role of guided self-help in a stepped-care programme are needed. The focus of such studies should be on the role of guided self-help in both early intervention and maintenance.
- 4.4 Adequately powered RCTs reporting all relevant outcomes, including relapse rates and adverse events, comparing the effectiveness of different antidepressants should be undertaken in order to identify differential individual response to treatment, including how this relates to gender and ethnicity.
- 4.5 Suicidal ideas, self-harming behaviour and completed suicide should be carefully and prospectively measured in large, independent multicentre trials using a variety of methods. Particular attention should be paid to the first 4 weeks of treatment.
- 4.6 Trials should be undertaken of the efficacy of a range of social support interventions for socially isolated and vulnerable groups of people with depression.

- 4.7 Long-term trials of maintenance treatment with antidepressants are needed to determine the optimum dose and duration of treatment.
- 4.8 Further research is needed on all aspects of the pharmacological treatment of depression in the elderly, in particular in those older than 80 years. There is a special need for research evidence on optimum treatment and maintenance doses for elderly people.
- 4.9 An adequately powered RCT reporting all relevant outcomes should be undertaken to assess the efficacy of antipsychotics (both singly and in combination with antidepressants) in the treatment of psychotic depression.
- 4.10 The efficacy of organisational interventions, such as chronic disease management programmes or other programmes of enhanced care for depression should be tested in large-scale multicentre trials in the NHS.

## **5 Other versions of this guideline**

### ***Full guideline***

The National Institute for Clinical Excellence commissioned the development of this guidance from the National Collaborating Centre for Mental Health. The Centre established a Guideline Development Group, which reviewed the evidence and developed the recommendations. The full guideline 'Depression: management of depression in primary and secondary care' is published by the National Collaborating Centre for Mental Health; it is available from its website ([www.rcpsych.ac.uk/cru/nccmh.htm](http://www.rcpsych.ac.uk/cru/nccmh.htm)), the NICE website ([www.nice.org.uk](http://www.nice.org.uk)) and on the website of the National Electronic Library for Health ([www.nelh.nhs.uk](http://www.nelh.nhs.uk)).

The members of the Guideline Development Group are listed in appendix B. Information about the independent Guideline Review Panel is given in appendix C.

The booklet 'The guideline development process – an overview for stakeholders, the public and the NHS' has more information about the Institute's guideline development process. It is available from the Institute's website and copies can also be ordered by telephoning 0870 1555 455 (quote reference N1233).

*In 2006, NICE commissioned the National Collaborating Centre for Mental Health to revise the recommendations on the use of venlafaxine in the light of the revised prescribing advice on the drug issued by the Medicines and Healthcare products Regulatory Agency. The Centre set up an independent working group to develop the revised recommendations (see appendix B). Information about the independent Guideline Review Panel is given in appendix C.*

### **Information for the public**

A version of this guideline for people with depression, their advocates and carers, and for the public is available from the NICE website ([www.nice.org.uk/CG023publicinfo](http://www.nice.org.uk/CG023publicinfo)) or from the NHS Response Line (0870 1555 455; quote reference number N1238). This is a good starting point for explaining to patients the kind of care they can expect. A version in Welsh is available from the NICE website.

### **Quick reference guide**

A quick reference guide for healthcare professionals is also available from the NICE website ([www.nice.org.uk/CG023quickrefguide](http://www.nice.org.uk/CG023quickrefguide)) or from the NHS Response Line (0870 1555 455; quote reference number N1237).

## **6 Related NICE guidance**

*Antenatal and postnatal mental health. NICE clinical guideline 45 (2007). Available from: [www.nice.org.uk/CG045](http://www.nice.org.uk/CG045)*

*Hypertension: management of hypertension in adults in primary care. NICE clinical guideline 34 (2006). Available from: [www.nice.org.uk/CG034](http://www.nice.org.uk/CG034)*

*Depression in children and young people: identification and management in primary, secondary and community care. NICE clinical guideline 28 (2006). Available from: [www.nice.org.uk/CG028](http://www.nice.org.uk/CG028)*

Anxiety: management of generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults in primary, secondary and community care. NICE clinical guideline 22 (*amended 2007*). Available from: [www.nice.org.uk/CG022](http://www.nice.org.uk/CG022)

Guidance on the use of computerised cognitive behavioural therapy for anxiety and depression. NICE technology appraisal guidance 51 (2002). Available from: [www.nice.org.uk/TA051](http://www.nice.org.uk/TA051)

Guidance on the use of electroconvulsive therapy. NICE technology appraisal guidance 59 (2003). Available from: [www.nice.org.uk/TA059](http://www.nice.org.uk/TA059)

## **7 Review date**

*NICE expects to make a decision on a full update later in 2007. The updated guideline will be available within 2 years of the start of the review process.*

## Appendix A: Grading scheme

All evidence was classified according to an accepted hierarchy of evidence that was originally adapted from the US Agency for Healthcare Policy and Research Classification (see Box 1). Recommendations were then graded A to C on the basis of the level of associated evidence or noted as a GPP or NICE recommendation (see Box 1) – this grading scheme is based on a scheme formulated by the Clinical Outcomes Group of the NHS Executive (1996).

**Table 1** Hierarchy of evidence and recommendation grading scheme

Level	Type of evidence	Grade	Evidence
<b>I</b>	Evidence obtained from a single randomised controlled trial or a meta-analysis of randomised controlled trials	<b>A</b>	At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level I) without extrapolation.
<b>IIa</b>	Evidence obtained from at least one well-designed controlled study without randomisation	<b>B</b>	Well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels II or III); or extrapolated from level I evidence.
<b>IIb</b>	Evidence obtained from at least one other well-designed quasi-experimental study		
<b>III</b>	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies		
<b>IV</b>	Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities	<b>C</b>	Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level IV). This grading indicates that directly applicable clinical studies of good quality are absent or not readily available.
		<b>GPP</b>	Recommended good practice based on the clinical experience of the GDG.
<b>NICE</b>	Evidence from NICE clinical guideline or technology appraisal	<b>NICE</b>	
Adapted from Eccles M, Mason J (2001). How to develop cost-conscious guidelines. Health Technology Assessment 5 (16)			
NHS Executive. Clinical Guidelines: Using Clinical Guidelines to Improve Patient Care Within the NHS. London: 1996.			

## **Appendix B: The Guideline Development Group**

### **Guideline Development Group**

#### **Professor Sir David Goldberg**

Chair, Guideline Development Group

Emeritus Professor of Psychiatry, Institute of Psychiatry, King's College,  
London

#### **Mr Stephen Pilling**

Facilitator, Guideline Development Group

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Medical Director and Consultant Psychiatrist, Community Health Sheffield  
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#### **Mr Ted Foster**

Patient Representative

National Advisory Panel Member – Mind Link

#### **Mr John Gates**

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**National Collaborating Centre for Mental Health**

**Ms Rachel Burbeck**, Lead Systematic Reviewer

**Ms Michelle Clark**, Project Manager (to September 2003)

**Dr Cesar de Olivera**, Systematic Reviewer

**Dr Catherine Pettinari**, Senior Project Manager (from September 2003)

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**Dr Judit Simon**, Health Economist

**Dr Clare Taylor**, Editor

**Ms Lisa Underwood**, Research Assistant

**Dr Craig Whittington**, Senior Systematic Reviewer

**Ms Heather Wilder**, Information Scientist

***Working group to consider amendments to the recommendations concerning venlafaxine***

*The working group was set up by the National Collaborating Centre for Mental Health*

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**National Collaborating Centre for Mental Health**

**Ms Rachel Burbeck**, Lead Systematic Reviewer

NICE Guideline – depression (amended April 2007)

**Dr Catherine Pettinari, Senior Project Manager**

**Mr Stephen Pilling, Co-director**

## **Appendix C: The Guideline Review Panel**

The Guideline Review Panel is an independent panel that oversees the development of the guideline and takes responsibility for monitoring its quality. The Panel includes experts on guideline methodology, health professionals and people with experience of the issues affecting patients and carers. The members of the Guideline Review Panel were as follows.

**Dr Chaand Nagpaul**

GP, Stanmore

**Mr John Seddon**

Patient Representative

**Professor Kenneth Wilson**

Professor of Psychiatry of Old Age and Honorary Consultant Psychiatrist, Cheshire and Wirral Partnership NHS Trust

**Dr Paul Rowlands**

Consultant Psychiatrist, Derbyshire Mental Health Services Mental Health Care Trust

**Dr Roger Paxton**

R&D Director, Newcastle, North Tyneside and Northumberland Mental Health NHS Trust

***The members of the Guideline Review Panel for the amended recommendations were as follows.***

**Professor Mike Drummond (Chair)**

Professor of Health Economics, Centre for Health Economics, University of York

**Dr Graham Archard**

General Practitioner, Dorset

**Mr Barry Stables**  
Lay Representative

## **Appendix D: Audit criteria**

### ***Possible objectives for an audit***

One or more audits could be carried out in different care settings to ensure that:

- appropriate screening protocols are in place
- treatment options, including psychological interventions, are appropriately offered and provided for individuals with depression.

### ***People who could be included in an audit***

A single audit could include all individuals with depression. Alternatively, individual audits could be undertaken on specific groups of individuals such as:

- people with treatment-resistant depression
- a sample of patients with depression who are prescribed an antidepressant in primary care.

### ***Measures that could be used as a basis for an audit***

Please see tables overleaf.

Criterion	Measured by	Exception	Definition of terms
<p><b>1. Screening in primary and general hospital settings</b></p> <p>Screening in primary and general hospital settings should be undertaken for depression in high-risk groups, for example, those with a past history of depression, significant physical illnesses causing disability or other mental health problems, such as dementia.</p>	<p>100% of primary care and general hospital settings should have protocols in place that set out the procedures for screening high-risk groups.</p>	<p>None</p>	<p>Operational policies of relevant organisations should contain copies of relevant protocols and implementation and audit plans for screening high-risk groups.</p>
<p><b>2. Watchful waiting</b></p> <p>For patients with mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, a further assessment should be arranged, normally within 2 weeks ('watchful waiting').</p>	<p>100% of patients identified as depressed who are not offered or who decline an active intervention should have arranged a follow-up appointment within 2 weeks.</p>	<p>People who are offered the follow up but who, for personal or practical reasons, are not able to attend within 2 weeks.</p>	<p>The notes should indicate that the healthcare professional responsible has discussed the need for follow up and an arrangement has been made for an appointment.</p>

<p><b>3. Antidepressants in mild depression</b></p> <p>Antidepressants are not recommended for the initial treatment of mild depression, because the risk–benefit ratio is poor.</p>	<p>Antidepressants should not routinely be used in the treatment of mild depression.</p>	<p>Exceptions include:</p> <ul style="list-style-type: none"> <li>A patients who have previously had moderate or severe depression</li> <li>B patients who have not responded to other interventions</li> <li>C patients who have significant psychosocial or other stressors.</li> </ul>	<p>The notes should indicate for all patients receiving antidepressants that they are suffering from moderate or severe depression or that one or more of the exceptions set out in this audit apply.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>
<p><b>4. Guided self-help</b></p> <p>For patients with mild depression, healthcare professionals should consider recommending a guided self-help programme based on CBT.</p>	<p>100% of patients with mild depression who have expressed a preference for guided self-help or have declined other interventions should be considered for guided self-help.</p>	<p>Those who request or have taken up the offer of another intervention.</p>	<p>The notes should indicate that the patient was informed of the possibility of guided self-help.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>

<p><b>5. Short-term psychological treatment</b></p> <p>In both mild and moderate depression, psychological treatment specifically focused on depression (such as problem-solving therapy, brief CBT and counselling) of 6 to 8 sessions over 10 to 12 weeks should be considered.</p>	<p>100% of patients with mild and moderate depression who have not responded to an alternative, less complex intervention (for example, guided self-help) should be considered for short-term psychological treatment.</p>	<p>Those who request or have taken up the offer of another intervention.</p>	<p>The notes should indicate that the patient was informed of the possibility of short-term psychological treatment.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>
<p><b>6. Prescription of an SSRI</b></p> <p>When an antidepressant is to be prescribed in routine care, it should be an SSRI because they are as effective as tricyclic antidepressants and their use is less likely to be discontinued because of side effects.</p>	<p>100% of patients initiated on an antidepressant in routine care should be prescribed an SSRI.</p>	<p>Exceptions are patients who:</p> <ul style="list-style-type: none"> <li>A have had previous adverse reactions to SSRIs</li> <li>B are on other medication that may have interactions with an SSRI</li> <li>C have evidence of benefit from a non-SSRI when previously treated with an antidepressant.</li> </ul>	<p>For all patients initiated on non-SSRI antidepressants in primary care the reason for the exception should be recorded in the notes.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>

<p><b>7. Tolerance and craving, discontinuation/withdrawal symptoms</b></p> <p>All patients prescribed antidepressants should be informed that, although the drugs are not associated with tolerance and craving, discontinuation/withdrawal symptoms may occur on stopping, missing doses or, occasionally, on reducing the dose of the drug. These symptoms are usually mild and self-limiting but can occasionally be severe.</p>	<p>100% of patients prescribed antidepressants should be informed of the possibility of discontinuation/withdrawal symptoms.</p>	<p>None</p>	<p>The notes should indicate that the patient was informed of the possibility of the occurrence of discontinuation/withdrawal symptoms.</p>
<p><b>8. Combined treatment for severe depression</b></p> <p>When patients present initially with severe depression, a combination of antidepressants and individual CBT should be considered as the combination is more cost-effective than either treatment on its own.</p>	<p>100% of patients who meet the criterion are started on combined treatment and complete the course of CBT.</p>	<p>Patients who have declined such an offer of combination treatment or have been unable to tolerate the side effects of medication.</p>	<p>The notes should indicate for all patients with severe depression were considered for combined treatment. The notes should record whether the patient completes a full course of treatment.</p>

<p><b>9. Maintenance treatment with antidepressants</b></p> <p>Patients who have had two or more depressive episodes in the recent past, and who have experienced significant functional impairment during the episodes, should be advised to continue antidepressants for 2 years.</p>	<p>100% of patients who meet the criterion and are started on maintenance treatment stay on the treatment for at least 2 years.</p>	<p>Patients who have declined such an offer of treatment or have been unable to tolerate the side effects of medication.</p>	<p>The notes should indicate for all patients in receipt of maintenance antidepressants the reasons for being placed on a maintenance course.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>
<p><b>10. Combined treatment for treatment-resistant depression</b></p> <p>For patients whose depression is treatment resistant, the combination of antidepressant medication with CBT should be considered.</p>	<p>100% of patients whose depression is treatment resistant and who have not responded to other treatments, or who declined the offer of such treatments, should be considered for combined CBT and antidepressants.</p>	<p>Patients who have been offered alternative treatments for treatment-resistant depression.</p>	<p>The notes should indicate that the patient was informed of the possibility of combination treatment.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>

<p><b>11. CBT for recurrent depression</b></p> <p>CBT should be considered for patients with recurrent depression, who have relapsed despite antidepressant treatment, or who express a preference for psychological interventions.</p>	<p>100% of patients whose depression is recurrent and who have relapsed despite antidepressant treatment, or who express a preference for a psychological treatment, should be considered for CBT.</p>	<p>Patients with recurrent depression who have relapsed despite antidepressant treatment or who express a preference for psychological treatment.</p>	<p>The notes should indicate that the patient was informed of the possibility of CBT.</p> <p>The notes should record whether the patient completes a full course of treatment.</p>
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## **Appendix E: Assessing the severity of depression in primary care**

### **Key symptoms:**

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

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
- poor concentration or indecisiveness
- low self-confidence
- poor or increased appetite
- suicidal thoughts or acts
- agitation or slowing of movements
- guilt or self-blame.

### ***Then ask about past, family history, associated disability and availability of social support***

#### **1. Factors that favour *general advice and watchful waiting*:**

- four or fewer of the above symptoms
- no past or family history
- social support available
- symptoms intermittent, or less than 2 weeks duration
- not actively suicidal
- little associated disability.

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

- five or more symptoms
- past history or family history of depression
- low social support
- suicidal thoughts
- associated social disability.

**3. Factors that favour *referral to mental health professionals*:**

- poor or incomplete response to two interventions
- recurrent episode within 1 year of last one
- patient or relatives request referral
- self-neglect.

**4. Factors that favour *urgent referral to a psychiatrist*:**

- actively suicidal ideas or plans
- psychotic symptoms
- severe agitation accompanying severe (more than 10) symptoms
- severe self-neglect.

**ICD-10 definitions**

Mild depression: four symptoms

Moderate depression: five or six symptoms

Severe depression: seven or more symptoms, with or without psychotic features

## Appendix F: Glossary

**Advance directives:** Written instructions in which a patient specifies in advance of treatment his or her preferred treatments and identifies the treatments he or she does not wish to receive. These are used to guide clinicians in the event that the patient becomes unable to make decisions for him or herself. Advance directives allow people, for instance, to state their wishes with regard to electroconvulsive therapy, or drugs they know give them bad side effects. The patient should understand the nature of the condition for which treatment may be required, the need for treatment, the expected benefits of the proposed treatment, and the possible adverse consequences. Advance directives cannot be used to refuse treatment altogether when a person is subject to the Mental Health Act.

**Akathisia:** A condition of inner restlessness in which there is a difficulty in sitting still; a common extrapyramidal side effect of neuroleptic drugs, and, more rarely, of SSRIs.

**Atypical depression:** A subtype of major depressive disorder in which patients have reactive mood and at least two of the following four symptoms:

- hyperphagia
- hypersomnia
- leaden paralysis
- a lifetime history of interpersonal sensitivity to rejection, resulting in functional impairment.

**Befriending:** A community-based intervention in which a trained volunteer meets and talks with a patient with depression for a minimum of 1 hour each week and acts as a friend.

**Cognitive behavioural therapy (CBT):** A discrete, time-limited, structured psychological intervention, derived from the cognitive-behavioural model of affective disorders in which the patient:

- works collaboratively with a 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.

**Computerised cognitive behavioural therapy (CCBT):** A form of CBT that 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.

**Couple-focused therapy:** A time-limited, psychological intervention 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 they may develop relationships that are more supportive and with less conflict.

**Counselling:** A time-limited psychological intervention (regular planned meetings of usually 50 minutes or 1 hour in length). 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. In the guideline, an intervention was classified as counselling if it 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.

**Crisis resolution and home treatment teams:** Services that provide intensive home-based, crisis-orientated treatment of an acute psychiatric episode by staff with a special remit to deal with such situations during and beyond office hours. The objective is to manage acute episodes in the community rather than in inpatient care.

**Discontinuation/withdrawal symptoms:** Symptoms experienced by some patients when stopping or reducing antidepressants, including dizziness, nausea, paraesthesia, anxiety and headaches.

**Dysthymia:** A disorder characterised by chronic low mood of fluctuating intensity that does not currently fulfil the criteria for recurrent depressive disorder, mild or moderate severity, in terms of either severity or duration of individual episodes. There are variable phases of mild depression and comparative normality. Despite tiredness, feeling down and not enjoying much, people with dysthymia are usually able to cope with everyday life.

**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 is designed specifically for the purpose.

**Interpersonal psychotherapy (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.

**Mindfulness-based CBT:** a form of cognitive behavioural therapy (see above) that develops a person's ability to be attentive to and aware of their negative thoughts, but not to react to them. The idea is to change a person's relationship to their negative thoughts, rather than the content of their thoughts.

**Monoamine oxidase inhibitors (MAOIs):** A class of antidepressants that help brain neurotransmitters remain active longer, which may lead to a reduction in symptoms of depression.

**Multiple episodes of depression:** Three or more episodes of depression in the past 5 years, or more than five episodes altogether.

**Problem-solving therapy:** A discrete, time-limited, structured psychological intervention that focuses on learning to cope with specific problems areas and where the therapist and patient work collaboratively to identify and prioritise key problem areas, break problems down into specific manageable tasks, solve problems, and develop appropriate coping behaviours for problems.

**Psychodynamic psychotherapy:** psychological interventions, derived from a psychodynamic/psychoanalytic model in which:

- therapist and patient explore and gain insight into conflicts and how these are represented in current situations and relationships including the therapy relationship (such as transference and counter-transference)
- patients are given an opportunity to explore feelings, and conscious and unconscious conflicts, originating in the past, and the technical focus is on interpreting and working through conflicts
- therapy is non-directive and patients are not taught specific skills such as thought monitoring, re-evaluation or problem-solving.

**Screening:** Screening is defined by the guideline development group as a simple test performed on a large number of people to identify those who have depression.

**Selective serotonin reuptake inhibitors (SSRIs):** A class of antidepressant medications that increase the level of serotonin, a neurotransmitter believed to influence mood, in the brain.

**Sleep hygiene:** Behavioural practices that promote continuous and effective sleep.

**Stepped-care model:** A sequence of treatment options to offer simpler and less expensive interventions first and more complex and expensive interventions if the patient has not benefited, based on locally agreed protocols.

**Suicidal ideas:** Thoughts about committing suicide.

**Telephone support:** Augmentation of a therapeutic intervention designed to improve the effectiveness of the intervention; it usually consists of a limited number of telephone contacts, which have a facilitative and monitoring function.

**Tricyclic antidepressants (TCAs):** An older class of antidepressants used to treat depression by increasing levels of the neurotransmitters serotonin and noradrenaline.