

## The management of depression in primary care

### SUMMARY

This *Briefing* provides an overview of the management of depression in adults in primary care. It is largely based on the National Institute for Health and Clinical Excellence (NICE) guideline for the management of depression,<sup>1,2</sup> which includes the following recommendations:

#### Management of risk

- Screen patients who are at high risk of depression (e.g. those with a past history of depression, significant physical illnesses causing disability, or other mental health problems, such as dementia).
- Always ask patients directly about suicidal ideas and intent. Consider urgent referral to a specialist if the patient presents considerable immediate risk to themselves or others.
- Advise patients and carers to be vigilant for changes in mood, negativity and hopelessness, and suicidal intent, especially during high-risk periods (e.g. initiation of treatment, changing medications, increased personal stress).
- Consider additional support from the primary care team (e.g. telephone contact) for those at high risk of suicide.
- Make contact with people with depression who do not attend a follow-up appointment.
- Monitor patients frequently when initiating antidepressants (initially two-weekly, but weekly if <30 years old or at increased suicide risk). Prescribe limited quantities of antidepressants for those at high risk of suicide. Tricyclic antidepressants (TCAs) (except lofepramine) are more toxic in overdose than selective serotonin reuptake inhibitors (SSRIs).

#### Treatments

When deciding treatment, consider: severity of depression; treatment effectiveness, cost and availability; side effects and drug interactions; and problems in social or interpersonal relationships. Take into account patient preference and previous experiences of treatment.

- For mild depression, general advice and watchful waiting may be all that is required. If an intervention is necessary, antidepressants are not recommended initially. Consider exercise, and guided self-help based on cognitive behavioural therapy (CBT) or brief (6–8 sessions over 10–12 weeks) psychological therapy (problem solving therapy, counselling or CBT).
- Antidepressants should be offered ahead of psychological therapy in moderate depression, and should be prescribed together with longer-term psychological therapy (typically 16–20 sessions over 6–9 months) in severe depression.
- Longer-term psychological therapy should also be considered for patients who do not respond to a range of other interventions (e.g. antidepressants, brief CBT); for those patients who do not take, or refuse to take, antidepressants; and for those patients with recurrent depression who have relapsed despite antidepressants.

#### Antidepressants

There is no evidence for any clinically important difference in the efficacy of antidepressants. However, side-effect profiles vary, and this influences choice.

- When initiating antidepressants, warn patients of the possible side effects, the likely delay in their onset of effect, and the possibility of discontinuation/withdrawal symptoms if they are stopped abruptly or doses are missed. When antidepressants are withdrawn, do so slowly (e.g. over four weeks).
- Allow at least four weeks (six weeks for older people) before judging the effectiveness of an antidepressant. Continue antidepressants for at least six months after remission in moderate and severe depression.
- Prescribe SSRIs (generic fluoxetine or generic citalopram are reasonable choices) routinely ahead of TCAs, as they are less likely to cause unacceptable side effects.
- Venlafaxine and dosulepin should only be prescribed by mental health specialists.
- Avoid TCAs and venlafaxine in patients with cardiovascular disease.
- St John's wort is not recommended because potency varies between preparations and drug interactions are potentially serious.



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**Effective management of depression requires identifying those at risk and providing the appropriate treatments and supportive measures**

**Introduction**

Each year, one woman in every 15 and one man in every 30 will be affected by depression, and every GP will see between 60 and 100 people with depression.<sup>3</sup> Most patients receive all or part of their care for depression in primary care, and less than 20% ever use secondary care services.<sup>2</sup> Effective management of depression requires identifying those at risk and providing treatments and supportive measures to minimise suffering and the risk of self-harm and suicide, while making best use of available NHS resources. Depression is costly to the NHS and society as a whole. In 2000, there were about 2.6 million cases of depression in England. This cost the NHS an estimated £370 million, of which drug costs were £310 million.<sup>4</sup>

This *Briefing* provides an overview of the management of depression in primary care, and is largely based on the National Institute for Health and Clinical Excellence (NICE) depression guideline.<sup>1,2</sup> NICE advises that this guideline should be followed for all patients with depressive symptoms, with or without accompanying anxiety symptoms. The anxiety guideline<sup>5</sup> should be followed if a patient has anxiety without depression.<sup>1</sup>

The following areas are not covered: treatment of children and young people; management of people with more severe or complex disorders for which specialist treatment is appropriate; depression in pregnancy; postnatal depression; bipolar disorder; or seasonal affective disorder. Additional resources, which may be useful in these areas are outlined in an **online Supplement 1**, which is available on the NPC website ([www.npc.co.uk/ebt/merec.htm](http://www.npc.co.uk/ebt/merec.htm)).

**Recognition and diagnosis of depression**

Depression is a broad and heterogeneous diagnostic grouping, central to which is depressed mood or loss of pleasure in most activities.<sup>1</sup> The NICE guideline recommends treatment according to the severity of depression, defined according to the 10th edition of the *International Classification of Diseases and Related Health Problems: Mental and Behavioural Disorders (ICD-10)* (see **Panel 1**).<sup>1,6</sup> An alternative, commonly-used American classification of depression is provided by the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)*.<sup>6</sup>

In practice, it is doubtful whether the severity of a depressive illness can realistically be captured in a single symptom count. Clinicians will wish to consider family and previous history, and the degree of associated disability, in making the assessment of severity.<sup>1</sup> The use of specific severity levels in this *Briefing* should be considered in this context. It is clearly important to distinguish mood changes that occur 'normally' in everyday life, which may require no more than reassurance or support, from symptoms that are sufficiently prolonged or pervasive to require more active management (e.g. with psychological therapy and/or antidepressants). Most patients seen and treated in primary care have mild depression, or have symptoms that do not meet criteria for a diagnosis of clinical depression.<sup>7</sup>

Only about half of the people with depression in the community consult their GP.<sup>1</sup> Of those who do consult their GP, only approximately half are recognised as having depression on first consultation.<sup>7</sup> It is, therefore, important that all health care professionals involved in diagnosis and management should have good consultation skills, so that a structured approach can be taken to the diagnosis and subsequent management of depression where appropriate.<sup>1</sup>

The NICE guideline recommends screening for depression in high-risk groups (e.g. patients with a past history of depression, significant physical illnesses causing disability, or other mental health problems, such as dementia).<sup>1</sup> Physical problems and medicines should be borne in mind as potential causes of depression. For initial screening, use of at least two questions concerning mood and interest are suggested before more detailed assessment:<sup>1</sup>

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

Answering "no" to both questions effectively eliminates the likelihood of depression

**Panel 1: Assessing the severity of depression (ICD-10)<sup>1,6</sup>**

The following is a guide for assessing the severity of an episode of depression. Symptoms should usually be present for at least two weeks for a diagnosis of depression (all severities).

- **Not clinically depressed** <4 symptoms.
- **Mild depression** 4 symptoms (including at least two key symptoms\*). Some difficulty in continuing with ordinary work and social activities.
- **Moderate depression** 5–6 symptoms (including at least two key symptoms\*). Considerable difficulty in continuing with social, work or domestic activities.
- **Severe depression** ≥7 symptoms with or without psychotic features (including all three key symptoms\*). Considerable distress or agitation, and unlikely to continue with social, work or domestic activities, except to a very limited extent.

**Symptoms**

\*Key symptoms

- Persistent sadness or low mood
- Loss of interest or pleasure
- Fatigue or low energy

Other 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

(negative predictive value 99%). However, answering "yes" to either question falsely identifies many who do not have depression (positive predictive value 18–22%).<sup>8</sup> Several more detailed practical questionnaires, with reasonable performance characteristics, are available to help further with the diagnosis of depression (see **online Supplement 1**).

### Treatment of depression

The NICE guideline recommends a 'stepped-care' approach to the treatment of depression (see **Table 1**).<sup>1</sup> For many people with mild or moderate depression, brief non-drug interventions delivered by the primary care team are effective, but drug therapy and/or more extensive psychological therapy may be necessary for those who do not respond or have more severe depression.<sup>1</sup> Non-drug therapies are recommended initially for people with mild depression, whereas antidepressants are preferred for initial treatment of moderate depression.<sup>1</sup>

Referral to specialist mental health services, including GPs with a Special Interest in Mental Health, should be based on the assessment of severity, taking into account the degree of functional impairment and the presence of significant co-morbidities or specific symptoms.<sup>1</sup> Urgent referral should be made for those who present considerable immediate risk to themselves or others.<sup>1</sup> Other reasons for considering referral include: a request by the patient or their relatives to do so; self-neglect; atypical, treatment-resistant, chronic, recurrent, or psychotic depression; and severe agitation accompanying severe depression.<sup>1</sup> Inpatient and specialist secondary care treatments such as electroconvulsive therapy (ECT) may be required for patients who are assessed as being at high risk of self-harm or suicide.<sup>1</sup>

Many treatment approaches may be equally effective, especially for those patients with mild and moderate depression who are not considered to be at substantial risk of self-harm. Regardless of severity, choice of treatment should take into account evidence for efficacy, safety and cost of the intervention, patient preference, past or family history, experiences of previous interventions, and the presence of associated problems in social or interpersonal relationships. In older adults with depression, their physical state, living conditions, and social isolation should be assessed. The availability of psychological therapies may also influence choice.<sup>1</sup>

Where management is shared between primary and secondary care, a clear agreement should be established between all professionals on the responsibility for monitoring and treatment, and this should be shared with the patient and, where appropriate, with families and carers.<sup>1</sup>

**Table 1: The stepped-care model for the management of depression<sup>1</sup>**

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

### Non-drug therapies

Some people with mild depression may prefer to avoid an intervention, and others may improve in any case without them. For these people, general advice and watchful waiting should be considered.<sup>1</sup> Watchful waiting involves arranging a further appointment, normally within two weeks. If the patient does not attend the follow-up appointment, a member of the health care team should contact them. Patients of all ages with mild depression should be advised of the benefits of a structured and supervised **exercise** program (typically up to three sessions per week of 45–60 minutes duration for 10–12 weeks). Advice on sleep hygiene and anxiety management may also help (see supplement to *MeReC Briefing* No. 17, [www.npc.co.uk/ebt/merec.htm](http://www.npc.co.uk/ebt/merec.htm)).<sup>1</sup>

If an intervention is necessary, consider **guided self-help** using books or a self-help manual that is based on **cognitive behavioural therapy** (CBT) and designed specifically for the purpose.<sup>1</sup> This typically takes place over 6–9 weeks including follow-up. Some examples are provided in the **online Supplement 1**. As an alternative, computerised CBT may be considered. *Beating the Blues* is a computerised CBT package that is supported by evidence from randomised controlled trials (RCTs).<sup>9</sup> These self-help therapies have the advantage of requiring less input from health care professionals, who typically assist the patient to use the materials, monitor their outcome and provide support and encouragement.

A wide range of psychological therapies can also be considered. These so called 'talking-therapies' are provided by trained health care professionals within the NHS. However, access to these services is generally restricted by the high level of demand and the limited availability of therapists, especially in some geographical areas. **Brief psychological therapies** (typically 6–8 sessions over 10–12 weeks) that can be considered for people with

**Consider watchful waiting for patients who initially present with mild depression**



## Panel 2: Adverse effects of antidepressants

Refer to the Summaries of Product Characteristics ([www.medicines.org.uk](http://www.medicines.org.uk)) for details of possible adverse effects for individual antidepressants. Many adverse effects are transient and usually subside within the first few weeks of treatment, but in some cases they can be severe and persistent, and this may result in non-adherence or discontinuation.<sup>10</sup>

SSRIs are generally better tolerated than TCAs in primary care.<sup>11</sup> All TCAs cause, to varying degrees, antimuscarinic (anticholinergic) side effects (dry mouth, blurred vision, constipation, urinary retention, sweating), sedation and postural hypotension.<sup>2</sup> The tricyclic-related drugs (e.g. trazodone) have a lower incidence of antimuscarinic side effects than TCAs.<sup>12</sup> Some TCAs and related antidepressants (e.g. amitriptyline, clomipramine, doxepin, maprotiline, mianserin, dosulepin, trazodone, trimipramine) are more sedative than others (e.g. amoxapine, imipramine, lofepramine, nortriptyline).<sup>12</sup> SSRIs, as a class, are associated with less antimuscarinic side effects, postural hypotension or sedation than TCAs. However, they have other side effects that may be problematic. The most common are nausea, diarrhoea and headache.<sup>2</sup> Mirtazapine has few antimuscarinic effects but can cause weight gain and sedation.<sup>2,12</sup> Adverse effects of reboxetine include insomnia, sweating, dry mouth and constipation.<sup>2</sup> Moclobemide has a low potential for producing antimuscarinic side effects, weight gain and symptomatic postural hypotension.<sup>2</sup> Venlafaxine has a broad range of side effects similar to those of the TCAs and SSRIs.<sup>12</sup>

### Cardiac effects and cardiovascular disease (CVD)

Depression is a significant and independent risk factor for coronary heart disease.<sup>13,14</sup> Agents known to have cardiac side effects, such as TCAs and venlafaxine, should be avoided where possible in people at risk of CVD. Cardiac side effects are less of a concern with SSRIs, mianserin, trazodone, reboxetine, mirtazapine and moclobemide.<sup>2</sup> Before prescribing TCAs for people at significant risk of CVD, an electrocardiogram (ECG) should be carried out and blood pressure measured.<sup>1</sup> In high doses (e.g. >200mg daily) venlafaxine can produce hypertension in some people,<sup>2</sup> and cardiotoxicity has been reported at therapeutic doses. The Committee on Safety of Medicines (CSM) considers that venlafaxine should not be used in patients with heart disease (e.g. cardiac failure, coronary artery disease, ECG abnormalities including pre-existing QT prolongation), patients with electrolyte imbalance or in patients who are hypertensive.<sup>15</sup> Sertraline is the treatment of choice when initiating antidepressant treatment in a patient with a recent myocardial infarction or unstable angina.<sup>1</sup> This recommendation is based primarily on the SADHART study, a RCT that demonstrated improvements in depression over 24 weeks without any adverse effects on cardiac function.<sup>16</sup>

### Gastrointestinal bleeding

Observational studies suggest that SSRIs increase the risk of developing gastrointestinal (GI) bleeding.<sup>17,18</sup> Patients treated with antidepressants with the highest affinity for the serotonin transporter (fluoxetine, sertraline, clomipramine and paroxetine) appear at greatest risk.<sup>19</sup> Compared to patients receiving no treatment, the absolute risk increase is relatively small, resulting in around three extra cases of upper GI bleeds requiring hospitalisation per 1000-patient years of treatment.<sup>17</sup> The risk increase is similar to that of NSAIDs.<sup>17,19</sup> The risk appears to be enhanced if aspirin or NSAIDs are taken concomitantly (estimates of risks, relative to non-users, vary from 3-fold to 16-fold<sup>17,18</sup>). People with a history of GI disorders, or aged 80 years old or more, are also at greater risk.<sup>17</sup> SSRIs should be used cautiously in these people.

### Sexual dysfunction

Sexual dysfunction is a side effect of antidepressants<sup>20-23</sup> that is frequently overlooked in men and women,<sup>20</sup> and may result in dissatisfaction, non-adherence and relapse. It is often claimed that serotonergic agents are associated with a higher frequency of sexual dysfunction than other antidepressants.<sup>21,22</sup> However, evidence from clinical trials is not sufficiently robust to confirm this.<sup>20</sup> When prescribing any antidepressant it is important to be aware of sexual side effects, and to counsel and monitor patients accordingly. Treatments should be tailored to individual patient circumstances and needs.<sup>20</sup> Unfortunately, there are few good-quality investigations of the management of sexual side effects of antidepressants to guide treatment.<sup>23</sup>

### Hyponatraemia

Hyponatraemia is associated with all types of antidepressants, and should be considered in any person taking antidepressants who develops drowsiness, confusion, nausea, cramps or seizures.<sup>24</sup> It is particularly of concern in elderly patients who are taking SSRIs and diuretics.<sup>25</sup>

Refer to the Summaries of Product Characteristics for more details ([www.medicines.org.uk](http://www.medicines.org.uk)).

If increased agitation develops early in treatment with an SSRI, consider a change to a different antidepressant or a brief period of concomitant treatment with a benzodiazepine, followed by a review within two weeks.<sup>1</sup>

Where a TCA is chosen, lofepramine is a reasonable choice because of its relative lack of cardiotoxicity.<sup>1</sup> Because of an increased cardiac risk and toxicity in overdose, dosulepin is restricted to specialist use and should not be prescribed routinely.<sup>1</sup>

There is no convincing evidence for any clinically significant efficacy benefit of the newer antidepressants, venlafaxine, mirtazapine, or reboxetine, over other antidepressants.<sup>1</sup> Because of concerns over cardiotoxicity and toxicity in overdose, venlafaxine should only be initiated and subsequently supervised by specialist mental health practitioners, including GPs with a Special Interest in Mental Health.<sup>1,15</sup>

**Duloxetine**<sup>▼</sup> (*Cymbalta*<sup>®</sup>) was not considered in the NICE review<sup>2</sup> as it was only licensed for the treatment of depression in December 2004. Although there is some evidence for a benefit of duloxetine over placebo, more clinical studies and experience are required to establish its safety profile, and whether it offers any advantage over other antidepressants.<sup>26,27</sup> Therefore, it would seem sensible only to consider duloxetine after SSRIs and other more established antidepressants.<sup>27</sup>

Moclobemide is a reversible inhibitor of monoamine oxidase (MAOI) type A. It has the advantage over traditional MAOIs, such as phenelzine, in not requiring strict dietary restrictions, and drug interactions are less problematic. It appears to be as equally accepted and tolerated by patients as SSRIs, but is not widely used in the UK.<sup>2</sup>

### Increasing dose or switching antidepressants

It is important to use doses of antidepressants that are sufficiently high for effective treatment but not so high as to cause toxic effects.<sup>12</sup> If

**Venlafaxine prescribing should only be initiated and subsequently supervised by a mental health specialist**

**Panel 3: Switching antidepressants<sup>1</sup>**

SSRIs are recommended as first-line antidepressants. If there is no response, or the SSRI is poorly tolerated, a range of other treatment options should be considered. If it is decided to offer an alternative antidepressant, then:

- Another single agent should be used e.g. a different SSRI or mirtazapine. Alternatives include moclobemide, reboxetine or a TCA (except dosulepin).
- Be aware of the need for gradual and modest increases of dose, of interactions between antidepressants, and the risk of serotonin syndrome\* when combinations of serotonergic antidepressants are prescribed.
- If switching to mirtazapine, be aware that it can cause sedation and weight gain.
- If switching to moclobemide, be aware of the need to 'wash out' previously prescribed antidepressants.
- If switching to reboxetine, be aware of the relative lack of data on its side effects, and monitor carefully.
- If switching to a TCA, consider their poorer tolerability compared with other equally effective antidepressants, and the increased risk of cardiotoxicity and toxicity in overdose.

\* Features of serotonin syndrome include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus.

there is only a limited response to an antidepressant, a gradual dose increase in line with the schedule suggested by the Summary of Product Characteristics ([www.medicines.org](http://www.medicines.org)) can be considered.<sup>1</sup> However, for the majority of SSRIs in the treatment of depression, clinical trial data do not show an additional benefit from increasing the dose above the recommended daily dose.<sup>15</sup> It should also be remembered that failure to respond to treatment with an antidepressant could also be a result of non-adherence to the prescribed dosing regimen.

Switching to another antidepressant can be considered after a month if there has been no response or the antidepressant has been poorly tolerated (this can be postponed to six weeks if there has been a partial response) (see **Panel 3**).<sup>1</sup>

**Low-dose TCAs**

Evidence for currently recommended dosing levels for TCAs is not well established.<sup>2,28</sup> A review of 'therapeutic' doses of TCAs (amitriptyline:  $\geq 100$  mg/day, mean 162 mg/day) versus lower doses of TCAs (amitriptyline: mean 61 mg/day) found no clinically significant differences between them on response, although patients on the lower doses were less likely to leave treatment early due to side effects.<sup>2</sup> The NICE guideline recognises that some patients may have a clear clinical response on low-dose TCAs and can be maintained on this dose with careful monitoring.<sup>1</sup>

**St John's wort is not recommended for the treatment of depression**

The dose should be gradually increased if there is lack of efficacy and no major side effects.<sup>1</sup>

**Withdrawal of antidepressants and discontinuation/withdrawal symptoms**

Antidepressants are not associated with tolerance and craving, as experienced with addictive substances such as opiates or alcohol. However, some patients experience discontinuation/withdrawal symptoms when stopping antidepressants or reducing the dose.<sup>1</sup> These symptoms can vary in form and intensity and occur in any combination (see **Table 2**). They may be new symptoms or symptoms that are hard to distinguish from the symptoms of the underlying illness. They may be mistaken for a relapse of illness or the emergence of a new physical illness leading to unnecessary investigations or re-introduction of the antidepressant.<sup>29</sup> Paroxetine and venlafaxine, in particular, seem to be associated with a higher frequency of discontinuation/withdrawal symptoms than other SSRIs.<sup>15</sup> Planned antidepressant withdrawal is expected at some point for most patients, and needs to be managed carefully (see **Panel 4**).

**St John's wort**

An extract of the plant *Hypericum perforatum* (St John's wort) is commonly used for a range of indications including depression. A recent Cochrane review found that several specific extracts of St John's wort might be effective for treating mild to moderate depression,<sup>30</sup> although the data were not convincing. More recent larger placebo-controlled studies appear to show smaller effects than older generally smaller studies.<sup>30,31</sup> While recognising that there is evidence that St John's wort may be of benefit in mild or moderate depression, the NICE guideline advises against its use because of uncertainty about appropriate doses, variation in the nature of preparations and potential serious interactions with other drugs (e.g. oral contraceptives, anticoagulants and anticonvulsants).<sup>1,32,33</sup> If patients are taking St John's wort they should be informed of the uncertainties regarding its potency in different preparations and the potential for serious interactions if taken with other drugs.<sup>1</sup>

**Older people**

The prevalence of depression in older people in primary care (i.e.  $\geq 65$  years) is similar to that of younger adults (ages 35–64)<sup>4</sup> Co-morbid medical conditions are common in older people and can have a significant negative effect on depression and vice versa.<sup>34</sup> There are few specific studies of treatments for depression in older people. Therefore, treatment with antidepressants or non-drug interventions must be guided by studies in younger adults. However, antidepressants may be effective in lower doses in older people compared with younger adults, and take longer to work.<sup>35</sup>

**Table 2: Discontinuation/withdrawal symptoms<sup>2</sup>**

TCAs	SSRIs and venlafaxine	MAOIs
'Flu-like' symptoms (chills, myalgia, excessive sweating, headache, nausea) Insomnia Excessive dreaming	'Flu-like' symptoms 'Shock-like' sensations Dizziness exacerbated by movement Insomnia Excessive dreaming Irritability Crying spells	Agitation Irritability Ataxia Movement disorders Insomnia Somnolence Vivid dreams Cognitive impairment Slowed speech Pressured speech

The full range of psychological therapies should be considered for older people with depression.<sup>1</sup> SSRIs are generally an appropriate first choice if an antidepressant is required, particularly in those at high-risk of CVD. TCAs can be particularly troublesome for some elderly patients because of antimuscarinic side effects.<sup>36</sup> Specific NICE guideline recommendations for use of antidepressants in older people are listed in **Panel 5**.<sup>1</sup>

### Suicide and depression

In England and Wales, the incidence of suicide in the general population is about nine per 100,000 per year, although the incidence of deliberate self-harm or attempted suicide is thought to be 30-times higher than this.<sup>37</sup> The presence and severity of depressive symptoms are strongly associated with attempted suicide.<sup>38</sup> Therefore, patients with depression should always be asked directly about suicidal ideas and intent.<sup>1</sup> Patients and carers should be advised to be vigilant for changes in mood, negativity and hopelessness, and suicidal ideas, particularly during high-risk periods, such as during initiation/changes to medication and increased personal stress. They should be asked to contact the appropriate health care professional if concerned. Patients with suicidal ideas should be assessed for adequate social support and be made aware of sources of help, and advised to seek help if the situation worsens. Where a patient presents considerable immediate risk to themselves or others, urgent referral to a specialist mental health service should be arranged. It is important that contact (e.g. by telephone) is made with patients who do not attend follow-up appointments.<sup>1</sup>

Increased prescribing of antidepressants was statistically associated with a fall in suicide rates between 1993 and 2002. Better diagnosis and treatment of depression, including less use of TCAs, is a possible explanation, but this has not been conclusively demonstrated.<sup>39</sup> Self-poisoning accounts for about a quarter of suicides in England, and of these 20% result from antidepressant overdoses.<sup>37</sup> To reduce the risk of self-poisoning in patients at high risk of suicide, a limited quantity of antidepressants should be prescribed. The greater toxicity in overdose of TCAs (except lofepramine) compared with SSRIs should be borne in mind.<sup>1</sup> Additional support, more frequent direct contact with primary care staff, or telephone contact should also be considered.<sup>1</sup>

There is epidemiological evidence that the risk of self-harm in depressed patients is greatest around the time of presentation for medical care.<sup>37</sup> Suicidal thoughts have been shown to increase during the early stages of treatment with antidepressants, regardless of type.<sup>40</sup> However, there has been particular concern about SSRIs in this respect over recent years.<sup>37</sup>

#### Panel 4: Avoiding antidepressant discontinuation/withdrawal symptoms<sup>1</sup>

- Inform patients about the possibility of discontinuation/withdrawal symptoms on stopping antidepressants, missing doses or reducing the dose. These symptoms are usually mild and self-limiting but can occasionally be severe, particularly if the drug is stopped abruptly.
- Advise patients to take their drugs as prescribed, particularly drugs with a shorter half-life (such as paroxetine).
- Reduce doses gradually over a 4-week period; some people may require longer periods. Fluoxetine can usually be withdrawn over a shorter period, because of its longer half-life.
- For mild discontinuation/withdrawal symptoms, reassure the patient and monitor symptoms.
- For severe symptoms, consider reintroducing the original antidepressant at the effective dose (or another antidepressant with a longer half-life from the same class) and reduce gradually while monitoring symptoms.
- Ask patients to seek advice from their medical practitioner if they experience significant discontinuation/withdrawal symptoms.

Although SSRIs are associated with an increased risk of self-harm and suicidal thoughts in children and adolescents,<sup>41</sup> such an association has not been clearly demonstrated for adults. A systematic review of published RCTs (any clinical condition) found a two-fold increase in the odds of fatal and non-fatal suicidal attempts in users of SSRIs compared with users of placebo or other therapeutic interventions (excluding TCAs).<sup>42</sup> However, a review of published and unpublished trials (limited to adults with depression) comparing SSRIs with placebo, submitted to the Medicines and Healthcare products Regulatory Agency (MHRA) for safety review, identified no evidence for an increased risk of completed suicide, and only weak evidence of an increased risk of self-harm.<sup>43</sup>

The safety of SSRIs is being kept under close continual review by the MHRA, and any changes to their advice will be issued accordingly ([www.mhra.gov.uk](http://www.mhra.gov.uk)). Current advice, which is reflected in the NICE guideline,<sup>1</sup> is for careful and frequent patient monitoring by health care professionals and, where appropriate, carers, during the early stages of treatment. This is particularly important if a patient experiences worsening of symptoms or new symptoms after starting treatment.<sup>15</sup> Patients started on antidepressants, who are considered to present an increased suicide risk, or are younger than 30 years, should be closely monitored (i.e. normally seen after one week and frequently thereafter as appropriate) until the risk is no longer considered significant.<sup>1</sup>

*Patients should be monitored closely during the early stages of treatment with antidepressants*

#### Panel 5: Recommendations for antidepressants in older people<sup>1</sup>

- Give antidepressant treatments at an age-appropriate dose for a minimum of six 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 six weeks.
- When prescribing antidepressants (in particular TCAs) for older people with depression, carefully monitor for side effects.
- Health care professionals should be aware of the increased frequency of drug interactions when prescribing an antidepressant to older people who are taking other medications.
- Depression in patients with dementia should be treated in the same way as depression in other older people. Be aware that depression responds to antidepressants even in the presence of dementia.

