Guidelines for Managing Depression in Palliative Care

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Depression in Palliative Care

• High prevalence

• Affects compliance

• Symptom clusters

• Poorer prognosis
Existing standards

1. Screening for depression and anxiety should be part of every patient assessment. [Grade D]

2. All patients who are depressed should be questioned about suicidal thoughts and intent. [Grade D]

3. Treatment with antidepressants should be discussed with, and offered to, every patient where it is appropriate. [Grade D]

4. The aim of treatment and possible side effects should be explained to the patient and documented in the case notes. [Grade D]
5. Patients started on antidepressants who are not considered to be at increased risk of suicide, should be reviewed after 2 weeks and then regularly thereafter e.g. every 2 – 4 weeks to monitor clinical response. [Grade D]

6. If a patient is assessed to be at increased risk of suicide they should be seen after a week and subsequently frequently as appropriate until they are no longer considered to be at significant risk. If a patient is considered to be a risk to themselves or others it may be necessary to consider urgent referral to Mental Health Care Services. [Grade D]
Literature Review

1. Depression Screening Tools
2. Guidelines
   NICE, SIGN, EPCRC
3. Novel New Therapies?
## Commonly used depression-specific screening tools

<table>
<thead>
<tr>
<th>Screening Tool</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Single Item</strong></td>
<td>0.42-0.86</td>
<td>0.74-0.92</td>
</tr>
<tr>
<td>‘Are you depressed?</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Two item</strong></td>
<td>0.91-1.00</td>
<td>0.57-0.86</td>
</tr>
<tr>
<td>‘During the last month have you been bothered by</td>
<td></td>
<td></td>
</tr>
<tr>
<td>feeling down, depressed or hopeless</td>
<td></td>
<td></td>
</tr>
<tr>
<td>‘During the last month have you been bothered by</td>
<td></td>
<td></td>
</tr>
<tr>
<td>having little interest or pleasure in doing things</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hospital Anxiety and Depression Scale</strong></td>
<td>0.68-0.92</td>
<td>0.65-0.90</td>
</tr>
<tr>
<td>14 items 7 for anxiety, 7 for depression</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>The Brief Edinburgh Depression Scale</strong></td>
<td>0.72</td>
<td>0.83</td>
</tr>
<tr>
<td>6 items – guilt, fear, insomnia, sadness, coping</td>
<td></td>
<td></td>
</tr>
<tr>
<td>and self harm</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Summary- Screening Tools

- Mixed evidence improves outcomes
- No one scale superior
- Balance Validity v’s Brevity
- Heightened clinical suspicion
- Referral to mental health services if uncertainty
NICE Guidance

- **CG90** Depression in Adults (October 2009)
- **CG91** Depression with a chronic physical health problem (October 2009)
- **Quality Standards** (March 2011)
NICE Quality Standards

1 – Assessment

1. Assessment includes:
   – severity of symptoms,
   – the degree of associated functional impairment
   – the duration of the episode.
**NICE Quality Standards 2-3 – Clinicians**

Practitioners delivering pharmacological, psychological or psychosocial interventions

2. Should be competent.

3. Record health outcomes at each appointment and use the findings to adjust delivery of interventions.
NICE Quality Standards 4-5 - Severity

People with persistent subthreshold depressive symptoms or mild to moderate depression should:

4. Receive appropriate low-intensity psychosocial interventions.

5. Only be prescribed antidepressants on meeting specific clinical criteria in the NICE guidance.
6. People with moderate or severe depression (and no existing chronic physical health problem) should receive a combination of:

– antidepressant medication and either

– high-intensity cognitive behavioural therapy or interpersonal therapy.
NICE Quality Standards 6-9 – Severity

7. People with **moderate** depression and a chronic physical health problem should receive
   - an appropriate high-intensity psychological intervention.

8. People with **severe** depression and a chronic physical health problem should receive
   - a combination of antidepressant medication and individual cognitive behavioural therapy.
NICE Quality Standards 6-9 – Severity

9. People with:

i. moderate to severe depression

ii. and a chronic physical health problem

iii. with associated functional impairment,

whose symptoms are not responding to initial interventions should receive collaborative care.
**NICE Quality Standards**

10-13 – Timescales

10. People with depression who benefit from treatment with antidepressants are advised to
   – continue with treatment for **at least 6 months** after remission,
   – extending to at least 2 years for people at risk of relapse.

11. People with depression whose treatment consists solely of antidepressants are regularly **reassessed** at **intervals of at least 2 to 4 weeks** for at least the first 3 months of treatment.
NICE Quality Standards
10-13 – Timescales

12. People with depression that has not responded adequately to initial treatment within 6 to 8 weeks have their treatment plan reviewed.

13. People who have been treated for depression who have residual symptoms or are considered to be at significant risk of relapse receive appropriate psychological interventions.
SIGN Guideline 114 - Non pharmaceutical management of depression (Jan 2010)

- Behavioural Activation (Grade A)
- Individual CBT (Grade A)
- Interpersonal Therapy (Grade A)
- Guided self help based on CBT (Grade A)
- Computerised CBT (Grade A)
- Structured Exercise (Grade B)
EPCRC Guidelines (December 2010)

Three themes:

1. Prevention
2. Detection, diagnosis and assessment
3. Treatment
Prevention

1. Listening and Communication
2. Information
3. Optimal palliative support
4. Psycho-social support for families and caregivers
5. Identification of at risk groups
6. Early referral to SPC
Detection

• Discuss mood as part of the patient’s routine symptom assessment.

• Validity v’s brevity

• Screening tools (e.g. the HADS) are helpful in detecting depression.

• However, screening is not diagnostic. If depression is suspected undertake a clinical interview
Diagnosis

• Diagnose depression according to standardised, validated diagnostic criteria (e.g. DSM-IV).

• Consider alternative diagnoses
  – (e.g. delirium, dementia, drug reactions, hypothyroidism, uncontrolled pain, cerebral metastases).

• Consider contributory factors
  – (e.g. spiritual distress, financial difficulties, family conflict, social isolation).
Distinguishing Depression?

Appropriate sadness at the end of life

Depression
### Characteristics of depression versus appropriate sadness

<table>
<thead>
<tr>
<th>DEPRESSION</th>
<th>SADNESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feels outcast and alone</td>
<td>Able to feel connected with others</td>
</tr>
<tr>
<td>Feeling of permanence</td>
<td>Feeling that some day will end</td>
</tr>
<tr>
<td>Regretful, rumination on mistakes</td>
<td>Able to enjoy happy memories</td>
</tr>
<tr>
<td>Extreme self-deprecation</td>
<td>Sense of self worth</td>
</tr>
<tr>
<td>Constant and remitting</td>
<td>Comes in waves</td>
</tr>
<tr>
<td>No hope/interest in future</td>
<td>Looks forward to things</td>
</tr>
<tr>
<td>Enjoys few activities</td>
<td>Retains capacity for pleasure</td>
</tr>
<tr>
<td>Suicidal thoughts/behaviour</td>
<td>Will to live</td>
</tr>
</tbody>
</table>

Assessment

• Assess:
  – The number, severity, context and duration of symptoms,
  – the degree of functional impairment
  – suicidal thoughts, plans and access to means.

• Use a validated assessment scale to measure severity of depression and response to treatment.

• If severe depression or uncertain diagnosis, refer to a mental health specialist.
Treatment

• Depends on severity and:
  – Should be individualised
  – Should consider life expectancy
• Should be pharmacological and non-pharmacological in nature
• There is no preferred anti-depressant but
  – mirtazapine, sertraline and citalopram are among the most effective and well tolerated antidepressants
Novel therapies – Ketamine for depression?

- Need for more rapid onset of antidepressant effects
- Pre-clinical studies
- Antidepressant effect within few hours
- Case reports single dose oral ketamine
- Rapid and sustained reduction in validated scales
- More research needed

Irwin SA, Iglewicz A. Journal of Palliative Medicine 13(7): 903-907
Proposed revised guidelines and standards
Guidelines - General principles (1)

- Depression is a common problem in patients with advanced cancer.
- Depression often is undetected, undertreated, or treated at a stage when there is insufficient time for medication to be effective.
- In patients with advanced cancer it may be very difficult to distinguish depression from physical symptoms of their illness and/or adjustment to significant life changes.
- Hopelessness, feelings of guilt and worthlessness, lack of self esteem, loss of energy, insomnia and appetite disturbance are characteristic symptoms of depression.
General principles (2)

- Anhedonia is the marked loss of pleasure, interest and enjoyment in normally pleasurable activities. If present it is helpful in differentiating major depression from the `normal` reaction to major physical illness and may help to identify those patients who may respond to antidepressants.

- Many of the antidepressants available currently have acceptable side effect profiles and are usually well tolerated. Depressed patients may benefit from treatment with antidepressant medication even within the last weeks of life.
Guidelines - Diagnosing depression

• Brief screening measures may be useful for identifying depression. Commonly used tools include the Hospital Anxiety and Depression Scale (HADS), the Brief Edinburgh Depression Scale (BEDS), a two item screening tool assessing low mood and loss of interest and the single item `Are you depressed?` The Distress thermometer is used for detecting psychological distress.

• It is important to consider risk factors for depression in palliative care, such as history of depression, absence of social support, concurrent life stresses, chronic pain, poor performance status and advanced disease at diagnosis [Level 4].

• Depression should be diagnosed using validated diagnostic criteria (e.g ICD-10 or DSM-IV). Table 1 gives the ICD-10 criteria for depression.
<table>
<thead>
<tr>
<th>Clinical significance</th>
<th>Mild depression</th>
<th>Moderate depression</th>
<th>Severe depression</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical significance</strong></td>
<td>Some difficulties in continuing with ordinary work and social activities but will probably not cease to function completely.</td>
<td>Considerable difficulty in continuing with social, work or domestic activities.</td>
<td>Considerable distress or agitation. Unlikely to continue with social, work or domestic activities.</td>
</tr>
<tr>
<td><strong>Duration of symptoms</strong></td>
<td>Duration of at least 2 weeks.</td>
<td>Duration of at least 2 weeks.</td>
<td>Duration of at least 2 weeks.</td>
</tr>
<tr>
<td><strong>Severity (see Table 15.2 below)</strong></td>
<td>Two of most typical symptoms plus two of the other symptoms.</td>
<td>Two or three of most typical symptoms plus three of the other symptoms. If four or more of the somatic symptoms are present the episode is diagnosed.</td>
<td>All three of typical symptoms plus at least four other symptoms of severe intensity.</td>
</tr>
</tbody>
</table>
Guidelines - Diagnosing depression

- If depression is suspected a clinical assessment should be undertaken including a thorough psychiatric history and an assessment of the intensity of depressive symptoms, the duration of the episode and the degree of functional impairment [Level 4].

- The severity of depression may be determined by considering the actual symptoms experienced by patients. Further details can be seen in Table 2. [Level 4]

- Clinical assessment can be supported by use of a standardised validated assessment scale such as the Hospital Anxiety and Depression Scale (HADS) to measure severity of depression and response to treatment. [Level 4]
### Table 2 Symptoms of depression [Level 4]

<table>
<thead>
<tr>
<th>Typical symptoms</th>
<th>Other symptoms</th>
<th>Somatic symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressed mood.</td>
<td>Reduced concentration and attention.</td>
<td>Loss of interest or pleasure in activities that are normally enjoyable.</td>
</tr>
<tr>
<td>Loss of interest.</td>
<td>Reduced self esteem and self-confidence.</td>
<td>Lack of emotional reactivity to normally pleasurable surroundings and events.</td>
</tr>
<tr>
<td>Reduced energy levels leading to increased fatigue and</td>
<td>Bleak and pessimistic views of the future.</td>
<td>Waking 2 hours or more before usual waking time.</td>
</tr>
<tr>
<td>reduced activity</td>
<td>Ideas or acts of self harm or suicide.</td>
<td>Objective evidence of psychomotor retardation or agitation.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Marked loss of libido.</td>
</tr>
</tbody>
</table>
Guidelines – Assessment of Suicide risk

- Patients who are depressed should be questioned about suicidal thoughts or intent. [Level 4]
- If a patient expresses thoughts or intent of suicide, the issues and meaning behind these should be fully assessed. Optimising physical symptom control and psychological support in such patients is particularly important. [Level 4]
- Antidepressant use has been associated with thoughts and intent of self harm particularly in patients <30 years old. Assessment of suicidal risk is particularly important when treatment is commenced or the dose adjusted. [Level 4]
Guidelines – Management of Suicide risk

• If there is a high risk of suicide, a limited quantity of antidepressants should be prescribed, preferably ones which are relatively safe in overdose (e.g SSRIs). [Level 4]

• It is important to consider increased support from the primary health care team, including direct contact. [Level 4]

• If a patient is assessed to be at considerable immediate risk of harm to themselves or others, urgent referral to Mental Health Services should be arranged. [Level 4].
Guidelines – treatment of depression

• Both pharmacological and psychological interventions should be considered. [Level 2+].

• There is a lack of research about the efficacy of psychological therapies in the management of depression in palliative care patients. Cognitive behavioural therapy (CBT) is the psychological therapy which has been most widely used and evaluated to relieve depressive symptoms but there is a lack of studies in palliative care patients. Problem-solving therapy is increasingly used in palliative care but data on its efficacy is limited. Other psychological interventions that may be useful in the management of depression in palliative care patients include interpersonal therapy, couple therapy, group therapy, guided imagery and mindfulness-based therapy [Level 3].
Guidelines – treatment of depression

- Patients who are prescribed antidepressants should be informed about:
  - Potential side-effects.
  - Possible delay in onset of action.
  - Likely duration of treatment.
  - Importance of compliance.
  - Possible symptoms that may be experienced on stopping or withdrawal from the antidepressant medication. [Level 4]

- Information leaflets appropriate to the needs of the patient should be provided. [Level 4]

- Patients should be advised about the likely delay in onset of any beneficial effect from antidepressant medication although the length of delay is difficult to estimate. Previous guidance has suggested a delay in onset of 4-6 weeks but new evidence suggests that benefit may be seen within a shorter timescale [Level 3]
Guidelines – treatment of depression

• It is important to monitor side effects and clinical response and to consider factors that may influence the response. This may include the physical condition of the patient, or treatment with drugs which may predispose to depression, such as corticosteroids. [Level 4]

• Prescribers should consider clinically significant interactions when prescribing antidepressants and should consult the British National Formulary, Appendix 1 for further guidance. [Level 4]

• If there is an inadequate response to the standard dose and no side-effects, the dose may be increased in accordance with the Summary of the Product Characteristics, but it may be advisable to increase the dose more slowly than in physically well patients. If there has been no response within 4-8 weeks, consider changing to an antidepressant from a different therapeutic group. [Level 4]
Guidelines – treatment of depression

• If appropriate, antidepressants should be continued for at least 6 months after remission of a first episode of depression, to ensure adequate treatment and reduce the risk of relapse. If there are recurrent episodes, treatment should be continued for longer. [Level 1+]

• In exceptional cases in patients with reduced life expectancy the use of psychostimulants, such as methylphenidate, may be considered in view of the very rapid the onset of action. [Level 4] (see Guidelines on the Use of Psychostimulants). However they are not generally recommended due to strong evidence of adverse effects and inadequate evidence of benefit. [Level 4].

• The Committee on Safety of Medicines (UK) advises that hyponatraemia has been associated with all classes of antidepressant drugs. [Level 3] It is more common in the elderly and may be due to inappropriate anti-diuretic hormone secretion. Hyponatraemia should be considered as a possible aetiology in all patients who develop drowsiness, confusion or fits whilst taking antidepressant medication. [Level 4]
Guidelines - antidepressants

General Points

• Antidepressants generally reduce the seizure threshold. Caution is required with other pro-convulsive drugs such as antipsychotics or with conditions that predispose to seizures e.g. cerebral tumours. Tricyclics are often more problematic compared to SSRIs. Citalopram is usually considered the drug of choice in patients vulnerable to seizures. [Level 4]

• When choosing an antidepressant it is also useful to consider the available formulations other than tablets/capsules. Fluoxetine is available as a liquid. Paroxetine comes as an oral suspension. Citalopram and escitalopram come as oral drops and mirtazapine is available as a melt. [Level 4]

• Table 3 illustrates some antidepressants in common use.
<table>
<thead>
<tr>
<th>Class of Antidepressant</th>
<th>Drug Name</th>
<th>Dose (oral)</th>
<th>Additional Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>Fluoxetine</td>
<td>Usual dose is 20mg-60mg daily. Reduce dose in elderly.</td>
<td>Increased risk of extrapyramidal reactions with haloperidol. Interacts with phenytoin and carbamazepine. More complicated than others to change from if response poor (see Table 15.4). Will reduce analgesic benefit of codeine/tramadol.</td>
</tr>
<tr>
<td></td>
<td>Paroxetine</td>
<td>Usual dose is 20mg-40mg daily. High doses with specialist advice. Reduce dose in elderly.</td>
<td>Licensed for panic disorder and anxiety. These symptoms may get worse when first starting the drug. Need to give in the morning as acts as a stimulant. Withdrawal syndrome reported more often than with any other SSRI. Interacts with phenytoin and carbamazepine. Will reduce analgesic benefit of codeine/tramadol.</td>
</tr>
<tr>
<td></td>
<td>Sertraline</td>
<td>Usual dose is 50mg-100mg daily. Maximum dose is 200mg.</td>
<td>Useful in anxious patients, renal failure or patients with a cardiac history. Does not interfere with the metabolism of anti-epileptic drugs or haloperidol.</td>
</tr>
<tr>
<td></td>
<td>Citalopram</td>
<td>Usual dose is 10mg-20mg daily. Maximum dose is 60mg daily. Reduce dose in the elderly.</td>
<td>Also available as oral drops. Does not interfere with metabolism of other drugs. Licensed for panic disorder. NB: 10mg tablet = 8mg (4 drops) oral drops</td>
</tr>
<tr>
<td>Tricyclics</td>
<td>Amitriptyline</td>
<td>10mg-150mg daily.</td>
<td>Contraindicated in patients with cardiac disease. Useful choice if pre-existing neuropathic pain. Recent studies have shown that lower doses may have antidepressant effect. High incidence of adverse effects</td>
</tr>
<tr>
<td></td>
<td>Lofepramine</td>
<td>Usual dose is 140mg - 210mg daily (divided doses). May need lower.</td>
<td>Has fewer sedative and antimuscarinic effects compared to amitriptyline.</td>
</tr>
<tr>
<td>Noradrenergic selective serotonin antagonist (NaSSA)</td>
<td>Mirtazapine</td>
<td>Usual dose is 15mg-45mg at night. Similar dose for elderly patients.</td>
<td>Good anti-emetic receptor profile. Fast onset of action. Sedative effect at low dose and may be associated with weight gain and blood dyscrasias. Patients should be advised to report fevers, sore throats, stomatitis or other signs of infection during treatment and in the event of any of these symptoms the full blood count should be checked and the drug stopped if blood dyscrasias suspected. Best avoided in immunocompromised patients eg those having chemotherapy. Change antidepressant if no effect within 4 weeks.</td>
</tr>
</tbody>
</table>
Guidelines-Selective serotonin re-uptake inhibitors

- Selective serotonin re-uptake inhibitors (SSRIs) are not superior in efficacy to tricyclic antidepressants but there is evidence that they are better tolerated. They should be considered as first-line treatment for depression. [Level 1-]
- SSRIs have the potential to increase the risk of bleeding from the upper gastrointestinal tract in all patients. The risk is increased for patients with other risk factors such as receiving non steroidal anti-inflammatory agents (including aspirin), liver failure, peptic ulcer disease or oesophageal varices. [Level 4]
- If SSRIs are co-administered with tramadlo there is a theoretical risk of serotonin syndrome and therefore this combination must be used cautiously. Characteristics of the serotonin syndrome include restlessness, tremor, shivering, myoclonus, confusion, convulsions and extreme cases may result in death. Other antidepressants may also trigger serotonin syndrome. Serotonin syndrome rarely occurs after taking only 1 drug with serotonergic activity and is more likely to occur when 2 or more drugs with serotonergic activity are taken together. [Level 4]
Guidelines - Tricyclic antidepressants

- Tricyclic antidepressants (TCA) such as amitriptyline, are an alternative option but are more likely to be associated with side effects e.g. the increased risk of cardiotoxicity; greater toxicity in overdose than agents of similar potency. [Level 3]. Tricyclics other than lofepramine should not be prescribed for patients at high risk of serious cardiac arrhythmias or patients who have recently suffered a myocardial infarction. [Level 4]. Lofepramine has a relative lack of cardiotoxicity compared to other tricyclics but should still be used with caution in such patients. [Level 4]

- Tricyclic antidepressants may be useful in patients who have co-existing neuropathic pain. [Level 4]

- The side effect profiles of individual antidepressants may influence the choice of drug. Some side effects of tricyclic antidepressants, such as constipation, dry mouth, cognitive impairment and confusion, may be problematic in palliative care patients, but others, such as sedation and reduced secretions, may be helpful in certain situations. [Level 4]
**Guidelines – stopping antidepressants**

- If a patient has been taking antidepressants for 6 weeks or more the drug should not be stopped abruptly. Exceptions to this rule are:
  - If the drug has caused a serious adverse effect e.g. a cardiac arrhythmia in association with a tricyclic antidepressant, or
  - The patient is entering the terminal phase. [Level 4]

- Antidepressants should be withdrawn slowly, preferably over 4 weeks, by weekly reductions in dose. One exception to this rule is fluoxetine. At a dose of 20mg daily this may be stopped abruptly because of the long plasma half-life and active metabolite, but at higher doses gradual withdrawal is required. [Level 4]
Guidelines – stopping antidepressants

• Symptoms may occur as a direct result of stopping the drug. This usually takes place within 5 days of stopping treatment. The symptoms may vary in form and intensity. They may also occur during the process of reducing a dose or, in the case of drugs with a short half-life, (e.g. paroxetine, venlafaxine) after missed doses. For SSRIs the commonest symptoms include a flu-like illness, dizziness exacerbated by movement, insomnia, excessive (vivid) dreaming and irritability. If these symptoms occur the rate of drug withdrawal should be slowed and the patient reassured. Symptoms usually do not last longer than 1–2 weeks. The drug should only be restarted if the symptoms are severe or prolonged. [Level 4]

• Withdrawal of tricyclic antidepressants can cause cholinergic rebound with symptoms including headache, restlessness, diarrhoea, nausea and vomiting. [Level 4]
**Guidelines - Changing antidepressants**

- The dose of the original drug should be slowly reduced and the new drug slowly introduced.
- The speed of the “cross-tapering” may need to be adjusted according to how well the patient tolerates the process. [Level 4]
- Some drugs should never be co-administered and in these cases cross-tapering should be avoided. Potential risks of administering two antidepressants together include pharmacokinetic interaction (e.g. the increase in tricyclic antidepressant level caused by some SSRIs) and pharmacodynamic interactions, such as the serotonin syndrome. [Level 4]
Guidelines - Changing antidepressants

• If changing between two very similar anti-depressants e.g. different SSRIs, cross-tapering may not be required as administration of the second agent is likely to ameliorate the withdrawal effects of the first. [Level 4] An exception to this is fluoxetine. Any switch from fluoxetine to another antidepressant should be done slowly and cautiously (see Table 4). This is due to the long half-life and active metabolites. [Level 4]

• Table 4 has been adapted from the guidelines of the South Maudsley NHS Foundation Trust, UK Medicines Information and Bazire and gives further advice on how antidepressants should be switched or discontinued. This advice is derived from manufacturer’s information and is partly theoretical. Caution is advised in all cases. The evidence is not specific to palliative care patients. In the palliative care setting it is important to remember that there may be limited time to achieve an improvement in the mood of the patient and hence in their quality of life. A more rapid switch under close medical supervision may be indicated. [Level 4]
Guidelines - Changing antidepressants

• When switching between antidepressants it is important to be aware of gradual and modest incremental increases of dose, interactions and the risk of serotonin syndrome. [Level 4]
<table>
<thead>
<tr>
<th>From</th>
<th>To</th>
<th>Citalopram</th>
<th>Fluoxetine</th>
<th>Mirtazapine</th>
<th>Paroxetine</th>
<th>Sertraline</th>
<th>Tricyclic antidepressants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td></td>
<td>Withdraw then start fluoxetine at 10mg daily.</td>
<td>Cross taper cautiously.</td>
<td>Withdraw and start paroxetine at 10mg daily.</td>
<td>Withdraw then start sertraline at 25mg daily.</td>
<td><strong>Either</strong> cross taper cautiously or reduce citalopram to minimum dose, stop, then introduce tricyclic.</td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Stop fluoxetine,* Wait 4-7 days. Start citalopram at 10mg daily and increase slowly.</td>
<td><strong>Either</strong> cross taper cautiously or stop fluoxetine,* start mirtazapine cautiously 4-7 days later</td>
<td>Stop fluoxetine,* Wait 4-7 days then start paroxetine at 10mg daily.</td>
<td>Stop fluoxetine,* Wait 4-7 days, then start sertraline at 25mg daily.</td>
<td>Stop fluoxetine,* Wait 4-7 days. Start tricyclic at very low dose and increase very slowly.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td><strong>Either</strong> cross taper cautiously or withdraw then start citalopram.</td>
<td><strong>Either</strong> cross taper cautiously or withdraw then start fluoxetine.</td>
<td><strong>Either</strong> cross taper cautiously or withdraw then start paroxetine.</td>
<td><strong>Either</strong> cross taper cautiously or withdraw then start sertraline.</td>
<td>Withdraw gradually then stop mirtazapine, start tricyclic the following day.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Withdraw and then start citalopram.</td>
<td>Withdraw and then start fluoxetine.</td>
<td>Cross taper cautiously.</td>
<td>Withdraw and start sertraline at 25mg daily.</td>
<td><strong>Either</strong> discontinue paroxetine gradually and stop, start TCA after gap of few days or taper paroxetine dose to 10mg/day &amp; introduce TCAD at very low dose. After several days discontinue paroxetine &amp; increase TCAD dose to therapeutic levels.</td>
<td>Cross taper cautiously with very low dose of tricyclic.</td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>Withdraw, then start citalopram</td>
<td>Withdraw, then start fluoxetine</td>
<td>Cross taper cautiously</td>
<td>Withdraw, then start paroxetine</td>
<td><strong>Either</strong> half dose and add sertraline then slow withdrawal. or reduce TCA dose to 25-50mg, start citalopram at usual starting dose, then discontinue TCA over next 5-7 days.</td>
<td>Cross taper cautiously.</td>
<td></td>
</tr>
<tr>
<td>Tricycles</td>
<td><strong>Either</strong> half dose and add citalopram, then slow withdrawal or reduce TCA dose to 25-50mg, start citalopram at usual starting dose, then discontinue TCA over next 5-7 days.</td>
<td><strong>Either</strong> half dose and add fluoxetine then slow withdrawal or reduce TCA dose to 25-50mg, start fluoxetine at usual starting dose, then discontinue TCA over next 5-7 days.</td>
<td><strong>Either</strong> half dose and add paroxetine then slow withdrawal or reduce TCA dose to 25-50mg, start paroxetine at usual starting dose, then discontinue TCA over next 5-7 days.</td>
<td><strong>Either</strong> half dose and add sertraline then slow withdrawal or reduce TCA dose to 25-50mg, start sertraline at usual starting dose, then discontinue TCA over next 5-7 days.</td>
<td>Cross taper cautiously.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stopping antidepressants</td>
<td>Reduce over 4 weeks</td>
<td>*At 20mg/day just stop.</td>
<td>Reduce over 4 weeks</td>
<td>Reduce over 4 weeks or longer if necessary.</td>
<td>Reduce over 4 weeks.</td>
<td>Reduce over 4 weeks.</td>
<td></td>
</tr>
</tbody>
</table>

* Asterisk indicates an important condition or action.
**Proposed revised standards**

1. Screening for depression and anxiety should be part of every patient assessment. [Grade D]

2. In all patients suspected of being depressed a clinical assessment should be undertaken including a thorough psychiatric history and an assessment of the intensity of depressive symptoms, the duration of the episode and the degree of functional impairment [Grade D]

3. All patients who are depressed should be questioned about suicidal thoughts and intent. [Grade D]

4. Treatment with antidepressants and psychological interventions should be discussed with and offered to every patient where it is appropriate. The aim of treatment and potential side-effects should be explained to the patient. [Grade D]
6. Documentation should include the information given to the patient about the treatment and the health outcomes.

7. Patients started on antidepressants who are not considered to be at increased risk of suicide, should be reviewed after 2 weeks and then regularly thereafter e.g. every 2 – 4 weeks to monitor clinical response. [Grade D]

8. If a patient is assessed to be at increased risk of suicide they should be seen after a week and subsequently frequently as appropriate until they are no longer considered to be at significant risk. [Grade D]