

# The Management of Depression in Palliative Care

## DRAFT EUROPEAN CLINICAL GUIDELINES

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## Guideline Development Process

### Scope and Purpose

#### Overall objective

- To produce an evidence-based clinical guideline for the management of depression in palliative care, on behalf of the European Palliative Care Research Collaborative (EPCRC <http://www.epcrc.org>). The EPCRC is a project funded by the European Commission's Sixth Framework Programme, with the overall aim of improving the management of pain, depression and cachexia through translational research.

#### The patient group covered

- Adults who present with depression or depressive symptoms in the context of palliative care.

#### Target audience

- All health professionals involved in the provision of palliative care.

#### Rigour of development

- A Guideline Development Group was constituted, comprising clinicians and researchers based at King's College London. This group was responsible for coordinating guideline development, preparing written materials and conducting the literature review.
- An Expert Group was constituted to help identify clinical priorities and offer opinion on uncertain or contentious areas of clinical practice. The Expert Group was multi-national and multi-disciplinary, including patient representatives and professionals from palliative care, clinical psychology, psychiatry, general practice, psychiatric pharmacy, social work, oncology and chaplaincy.
- Key clinical questions considered important to patients and clinicians were identified by the Expert Group to define the scope of the guideline.
- The Delphi Method was used to ascertain and refine expert opinion on contentious recommendations.
- Evidence for these guidelines was provided by review of Cochrane Library, Medline, PubMed, Embase and other guidelines.
- A Cochrane review of antidepressants for depression in physical illness was conducted by the Guideline Development Group.
- The Oxford Centre of Evidence-based Medicine (CEBM) system will be used to grade the evidence and guidance recommendations.

#### Expert panel

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## Competing interests

Matthew Hotopf is an independent expert witness (instructed by the claimants' solicitor) in a group litigation on the potential for paroxetine to cause adverse events on withdrawal of treatment. Lauren Rayner, Annabel Price and Irene Higginson do not have any competing interests. No competing interests were declared by the members of the expert group.

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# 1 Prevention

*Good palliative care is of itself a key strategy for preventing depression at the end of life. Communication is crucial - between services, between health professionals, between patients and health professionals, and between patients and their families. Actively listening, empathizing and asking open-ended questions encourages patients to express their problems and preferences, in turn enabling health professionals to provide appropriate information and support. Palliative care aims to diminish distress by addressing symptoms, and control of pain and other troublesome physical symptoms are likely to be effective preventive strategies. Identifying patients 'at risk' facilitates increased support and sensitivity to the symptoms and signs of depression.*

## 1.1 Listening and communication

- Listen to the patient's problems, preferences, questions and concerns.
- Communicate in an open, engaging and non-judgmental manner.
- Determine the patient's desired level of information and involvement in treatment decisions.
- In accordance with the patient's wishes, discuss the disease and care plan, and involve them in treatment decisions.
- Avoid using clinical language without explanation.
- Facilitate communication between family members. Assess the quality of relationships with significant others, family roles, conflicts, and how these have changed as a result of the illness.
- Ask the patient about their needs at key stages, including upon diagnosis and at the beginning and end of treatment.
- Discuss, and where possible support, patients preferences about their place of care and death.
- Ensure discussions take place in settings in which the confidentiality, privacy and dignity of the patient are respected.

## 1.2 Information

- Ensure patients and carers have easy access to appropriate information on the nature, course and treatment of their illness, and the use and side effects of medication.
- Provide information in the appropriate language and audio format if possible.
- Discuss this information with patients in light of their individual circumstances.
- Inform patients about the range of local support available to them – which may include counselling, telephone helplines, self-help organizations and complementary therapies.

### 1.3 Optimal palliative care and support

- Ensure that patients' physical symptoms (e.g. pain, fatigue, breathlessness) are being assessed and managed effectively.
- Take account of psychosocial needs as well as physical ones.
- Consider referral to palliative care for symptom control, physical, emotional, social and spiritual support.
- Address potential deficits in social support which might happen in patients whose disabilities could impair opportunities to socialize (e.g. dysphasic, deaf, poor mobility).
- Assess patients' coping strategies. Where necessary, facilitate the development of new effective strategies to help patients regain a sense of control (e.g. staying active, taking a walk, engaging in social relationships, finding meaning in events).
- Advise patients and their families where to seek financial and practical support (e.g. advice on housing and employment issues, state benefits, mobility (e.g. disabled parking), help with personal care, cleaning and shopping).
- Self-help and support groups can be a source of valuable advice and peer support. Inform patients of the services available to them and advise them to attend.
- Health professionals should be aware that some patients may have spiritual needs, and arrange support from appropriate spiritual advisers (e.g. chaplains) when necessary.

### 1.4 Identification of "at risk groups"

- Risk factors for depression in palliative care.

Personal or family history of depression
Concurrent life stresses
Absence of social support
Younger age
Patients with advanced disease at diagnosis
Poorly controlled symptoms
Poor performance status or physical disabilities
Recent bereavement

- If identified as high risk, intensify support given (e.g. palliative care), monitor closely and consider psychological interventions.

## 2 Detection, diagnosis & assessment

*Given the prevalence of depression in palliative care, it is advisable to attempt to identify cases in all patients. Some health professionals use a depression screening tool to do this; others ask the patient one or two questions about mood as part of a general symptom assessment. There is mixed evidence on the ability of screening tools to improve patient outcomes. However, it is unlikely that screening for depression will cause patients harm, and due to the frequency of depression in this population, many palliative care services do screen patients. In introducing screening, it is important to ensure clinicians are able to perform competent clinical assessment, treatment and referral as appropriate. Validity of assessment must be balanced against brevity, so as not to burden frail patients with prolonged questioning. Diagnosing depression in palliative care is challenging. Depression is particularly difficult to differentiate from normal distress in this population, as advanced disease invariably invokes some fear and sadness. Health professionals must balance the risk of medicalising normal distress with the risk of under-detecting and under-treating depression. A further challenge is that the somatic symptoms of depression (e.g. fatigue, insomnia, poor appetite) mimic those of advanced disease, making it difficult to determine whether such symptoms are due to depression or physical illness. In addition, there are a number of differential diagnoses which can be confused with depression. Misdiagnosis may cause the underlying problem to be overlooked and prevent the patient receiving adequate treatment. If there is any doubt about the diagnosis, assessment should be undertaken by an experienced psychiatrist.*

### 2.1 Signs, symptoms & screening

- Typical presentations which should lead to an assessment of depression:

Low mood, tearfulness, irritability and distress
Withdrawal, loss of interest or pleasure in daily activities
Intractable physical symptoms or symptoms disproportionate to the degree of disease
Feelings of hopelessness, helplessness, worthlessness or guilt
Suicidal behaviour, requests for physician assisted suicide/ euthanasia, a wish to end it all, refusal of care

- Physical symptoms commonly associated with depression (e.g. appetite/ weight change, changes in sleep pattern, loss of energy, fatigue, psychomotor slowing, loss of libido, diminished concentration) may be due to physical illness or treatment, and therefore are less useful in making a diagnosis.
- Be aware of non-verbal cues (e.g. dejected demeanour, lack of movement, flat affect and reduced emotional reactivity).
- Clinicians should be comfortable asking about mood as part of a routine assessment. Patients may be more relaxed and open if depression is considered in the context of a general conversation about symptoms and coping.
- Depression is strongly associated with anxiety, so assessment of depression should include an assessment of anxiety. This should take into account affective symptoms (e.g. fear, dread), physical symptoms (e.g. breathlessness) and behavioural consequences (e.g. avoidance).

- Consider screening for depression among people with advanced cancer and patients receiving palliative care. Screening tools may be helpful in detecting possible cases of depression, but they are not diagnostic in confirming caseness and should not be used as a substitute for the clinical interview.
- Commonly used depression specific screening tools:

Screening tool	Sensitivity	Specificity
Single-item "Are you depressed?"	0.72-1.00	0.55-1.00
Two-item "During the last month, have you been bothered by feeling down, depressed or hopeless?" "During the last month, have you been bothered by having little interest or pleasure in doing things?"	0.91-0.97	0.56-0.86
Hospital Anxiety and Depression Scale 14 items, 7 for anxiety, 7 for depression. Excludes somatic symptoms.	0.68-0.75	0.67-0.74
The Brief Edinburgh Depression Scale  6 items covering guilt, insomnia, fear, sadness, inability to cope and thoughts of self-harm.	0.72	0.83

- To avoid burdening patients, consider using a generic symptom assessment scale that includes one or more questions on mood (e.g. the Palliative care Outcome Scale (POS), the Edmonton Symptom Assessment Scale (ESAS)), or an overall quality of life scale (e.g. EORTC QLQ). If the patient's response indicates depression, consider also using a depression specific screening tool or assessment scale.
- Some screening tools, such as the HADS, can be used to assess the severity of depression and monitor change over time (see 2.3). This can be beneficial as it avoids the need to use two different tools for screening and assessment.

## 2.2 Diagnosis

- If depression is suspected, undertake a clinical interview.
- This should involve assessment of the severity of symptoms, the duration of the episode and the degree of impairment.
- Take a thorough psychiatric history. It should not be assumed that this is the first episode of depression, precipitated by being terminally ill. Patients with a history of depression are much more likely to have a further episode. Information about previous episodes of depression and previous treatments should be sought.
- Consider **alternative diagnoses** for the clinical presentation. These may require a different response.

Examples of differential diagnoses are:

Delirium (may cause affective changes, agitation or withdrawal. Differentiating features include clouded consciousness, incoherent speech and involuntary movements).
Dementia (often associated with changes in mood and motivation. Distinguishing features include dysphasia, poor orientation and memory deficits).
Ongoing physical symptoms (may cause intense distress that may be mistaken for depression, which is ameliorated when symptoms are addressed)
Adverse drug reactions (depressed mood is a recognised side effect of many drugs, including steroids, and may be associated with opioid toxicity. Depressed mood may also result from harmful alcohol/ substance use or drug withdrawal (e.g. steroids and alcohol). A thorough alcohol and drug history is essential.
Space occupying lesion (e.g. cerebral metastases).
Other psychiatric disorders (e.g. psychotic disorders, anxiety disorder).
Other physical illnesses can present with depression-like symptoms (e.g. hypothyroidism).

Identification of an alternative explanation for the presentation may lead to the diagnosis of depression being rejected. For example, if the apparent depressive presentation is caused by hypoactive delirium, then antidepressants are best avoided. In other cases (e.g. in patients with cerebral metastases) it may be less clear that disease completely explains the depressive symptoms and treatment of depression might still go ahead. If there is uncertainty about the diagnosis, refer the patient to a mental health specialist.

- Consider **contributory factors**, which, if addressed, may alleviate or improve depressive symptoms.

Examples of contributory factors are:

<b>Biological contributory factors</b>
Uncontrolled physical symptoms (e.g. pain)
Drugs causing or contributing to depression (e.g. steroids)
Metabolic factors contributing to or causing depression (e.g. hypercalcaemia)
<b>Psychological contributory factors</b>
Lack of information related to diagnosis, prognosis etc.
Anger or blame related to diagnosis, diagnostic delay etc.
Fears and preoccupation related to prognosis, fears of dying and fear of symptoms leading up to death
Concerns for the welfare of relatives after death
Recent bereavement
<b>Social contributory factors</b>
Family conflict
Social isolation
Poor living conditions

Financial difficulties
Loss of function, roles, relationships
Concerns about place of care/ death

These are common difficulties which contribute to depression in many patients with advanced disease. Addressing these is a core component of palliative care and central to the management of depression in this context.

- In palliative care, it is particularly difficult to distinguish depression from normal sadness or adjustment disorder relating to declining health and fear of death. Take into account the patient's personality, family circumstances and the history of their illness and coping. If there is uncertainty about the diagnosis, refer the patient to a mental health specialist.
- Be mindful of recent life events/ losses which may have contributed to the patient's low mood.
- Diagnose depression according to recognised diagnostic criteria (e.g. DSM-IV or ICD-10).
- DSM-IV criteria:

### **Major Depressive Episode**

A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.

**Note:** Do not include symptoms that are clearly due to a general [medical condition](#), or mood-incongruent delusions or hallucinations.

(1) Depressed mood most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appears tearful).

**Note:** In children and adolescents, can be irritable mood.

(2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as indicated by either subjective account or observation made by others)

(3) Significant [weight loss](#) when not [dieting](#) or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.

**Note:** In children, consider failure to make expected weight gains.

(4) Insomnia or hypersomnia nearly every day

(5) Psychomotor agitation or retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down)

(6) Fatigue or loss of energy nearly every day

(7) Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick)

(8) Diminished ability to think or concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others)

(9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

B. The symptoms do not meet criteria for a Mixed Episode.

C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

E. The symptoms are not better accounted for by Bereavement, i.e., after the loss of a loved one, the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or motor retardation.

- For ICD-10 criteria see Appendix.
- Patients who have psychological distress but do not meet criteria for depressive disorder may well benefit from support, information, palliative care referral and psychological interventions (as for Prevention 1.1-1.4 and 4.1).

### 2.3 Assessment scales

- For patients in whom depression is suspected, use a validated assessment scale to measure the severity of depression, and response to treatment.

Commonly used assessment scales:

Assessment tool	Sensitivity	Specificity
Beck Depression Inventory (BDI) 21 items	0.79-0.90	0.65-0.79
Hospital Anxiety and Depression Scale (HADS) 14 items, 7 for anxiety, 7 for depression.	0.74-0.78	0.75-0.85

### 2.4 Suicide risk

- Ask patients with psychological distress directly about suicidal ideas and intent.
- Be particularly vigilant during high risk periods such as during initiation of and changes to medication and increased personal stress.
- Assess whether patients with suicidal thoughts have adequate social support and appropriate sources of help.
- Ensure that the patient has limited access to potentially harmful medication (e.g. opiates) or sharp objects.
- Where a patient presents immediate risk to themselves, arrange urgent referral to a specialist mental health service.

- Ensure patient is aware of locally available services and has access to out of hours support (e.g. a 24 hour helpline/ palliative care on call).
- Consider hospitalisation.

## 2.5 Refer to mental health specialist if:

- If there is uncertainty about the diagnosis of depression.
- There is a past history of complex psychiatric disorder.
- The patient has severe or psychotic depression.
- The patient shows signs of suicidal ideation or intent (which might trigger emergency referral).
- Depression is interfering with the patient's decisional capacity.
- The patient presents a risk to others.
- The patient does not respond to treatment.

### 3 Patient management

*In palliative care, time is usually short. Management of depression must take into account the patient's prognosis. Patients usually take 2 to 4 weeks to begin to respond to antidepressants. For patients with a short life expectancy, psychological therapy needs to be brief and address the patient's immediate concerns. Health professionals should discuss all treatment options with the patient and ensure that they are well informed. Patients should have equal access to appropriate assessment and management of depression whether they are homecare, day care or inpatients. All treatments for depression should be delivered by health professionals who are competent to deliver the intervention. Response to treatment and side effects must be monitored regularly.*

#### 3.1 Coordinating care:

- There should be close collaboration between primary and secondary physical health services, palliative care and mental health services, where appropriate.

#### 3.2 Before deciding on treatment:

- Give patients and carers appropriate information on the nature of depression and the different treatment options. Keep use of technical language to a minimum (see 1.1, 1.2).
- Listen to patients' and carers' preferences and consider the experience and outcome of previous treatment/s.
- Consider likely prognosis and time required for treatment to be effective.
- Where symptoms of depression are mild and the patient has not reached the threshold for diagnosis of Major Depressive Disorder, it is reasonable to provide general palliative care, without starting specific treatments for depression (see 1.3 & 4.1). Patients with mild symptoms of depression should be monitored and reassessed regularly.

#### 3.3 Before starting treatment with an antidepressant:

- Consider possible contraindications (see 4.7.2).
- Consider possible side effects (negative & positive) and discuss with the patient (see 4.7.1). Explain to the patient that they may experience side effects before there is any therapeutic benefit.
- Explain that craving and tolerance do not occur.
- Discuss the risk of discontinuation symptoms (see 3.8).
- Inform patients about the delay in onset of effect, the duration of treatment and the need to take medication as prescribed, and continue after remission.
- Give the patient appropriate written information.
- If there is a high risk of suicide, prescribe a limited quantity of antidepressants, preferably ones which are relatively safe in overdose (e.g. SSRIs).

### 3.4 Formulating the treatment plan

- Conduct a baseline assessment using an appropriate validated measure of depression (see 2.3).
- Establish a clear agreement between all professionals on the responsibility for monitoring and treatment; this should be shared with the patient and their family (see 1.1).

### 3.5 Delivering treatment

- Treatments for depression should be delivered by health professionals who are competent to deliver the intervention.
- Psychological interventions should be based on the relevant treatment manual.
- Health professionals less confident in delivering treatment should receive regular supervision.

### 3.6 Reviewing treatment

- Review the patient for side effects in the first week of treatment. If adverse effects occur with antidepressant treatment, consider discontinuing treatment or changing to a different antidepressant.
- Patients started on antidepressants who are considered to be at risk of suicide should be reviewed after 1 week.
- Repeat assessment of mood every 2 weeks.
- Use a validated assessment scale to monitor outcome and measure change over time (see 2.3).
- Ensure that the patient is involved in reviewing the efficacy of the treatment.
- Monitor for signs of restlessness (akathisia), suicidal ideas, and increased anxiety and agitation, particularly in the early stages of treatment with an SSRI. If the patient becomes agitated following treatment with an SSRI consider changing antidepressant or a brief period of concomitant treatment with a benzodiazepine, followed by review.

### 3.7 Lack of response to antidepressant treatment

- If the patient has taken the antidepressant as prescribed, but has not responded to treatment after 4 weeks consider gradually increasing the dose (if there are no significant side effects), or switching to another antidepressant. Take into account the patient's preference.

### 3.8 Discontinuing treatment

- Some patients experience symptoms when stopping antidepressants. These may include dizziness, nausea, paraesthesia, anxiety, headaches.
- The propensity to cause discontinuation symptoms depends on the pharmacokinetic properties of the antidepressant, particularly their half life. Discontinuation symptoms therefore vary between antidepressants, and some antidepressants are arguably best avoided. Discontinuation

symptoms are more likely to occur when antidepressants are stopped abruptly, but can also occur if doses are missed in shorter half life antidepressants. Patients should be advised not to miss doses if at all possible, and to seek medical advice before stopping their antidepressant.

- The likelihood of developing discontinuation symptoms is probably reduced if the antidepressant dose is reduced slowly before stopping. If discontinuation symptoms occur despite this, increase the dose and reduce more slowly, or consider swapping to a longer half life antidepressant (e.g. fluoxetine) and then stopping.
- It may be inappropriate to continue antidepressant treatment in patients with very short life expectancy (hours, days). Consideration should be given to tapering the dose, or changing to a liquid preparation if this is feasible.

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## 4 Treatments

*In patients with depression without physical disease, psychotherapy and antidepressants are the mainstay of treatment. In palliative care, evidence is scarce, but there is little ground to suggest a radically different approach is necessary. Patients with severe or treatment resistant depression should be referred to a mental health specialist, and additional interventions should be considered (see 4.4). Health professionals planning a course of antidepressant treatment should consider contraindications and discuss possible side effects with the patient (including those that may be beneficial).*

### 4.1 Mild depression or adjustment disorder

<b>First-line treatment:</b>
Provide good palliative care
Assess quality of relationships with significant others. Facilitate communication between family members
Consider a guided self-help programme that consists of provision of appropriate written materials and support
Consider a brief psychological intervention (brief CBT, problem-solving therapy, counselling)
<b>If symptoms persist</b> (or the patient has a history of moderate/ severe depression):
Where mild depression persists after other intervention, consider use of an antidepressant
Reassess the patient, possibly revise the diagnosis

### 4.2 Moderate depression

<b>First-line treatment:</b>
Do all recommended as first-line treatment in 4.1
Antidepressant medication and/ or CBT
Given the lack of evidence on a clearly superior approach for moderate depression, treatment decisions should be based on patient and clinician preference
<b>If symptoms persist:</b>
Assess compliance to treatment
Consider switching to a different antidepressant of the same or different class
Consider combining antidepressant treatment and CBT
Reassess psychosocial environment, e.g. family/marital relationships

### 4.3 Severe depression (characterised either by psychotic symptoms, food or fluid refusal or severe and persistent suicidal ideation)

<b>First-line treatment:</b>
Refer to mental health specialist
Manage suicide risk
Antidepressant medication and psychological therapy
Consider using a hypnotic or sedative in sleep disturbed or very distressed patients
For patients with severe agitation or anxiety, treatment with benzodiazepines may be appropriate. Long-term use of benzodiazepines is discouraged due to risk of cognitive impairment and addiction. Consider using medication with a long half-life (e.g. diazepam)
<b>If symptoms persist :</b>
Assess compliance to treatment
Consider switching to a different antidepressant of the same or different class
For patients with psychotic depression, consider treating with anti-psychotics as well as antidepressants
Under the supervision of a mental health specialist, lithium augmentation or electroconvulsive therapy may be considered

#### 4.4 Treatment resistant depression (characterised by depression which has not responded to at least one course of antidepressant given at full dose for at least 6 weeks)

Assess compliance to treatment
Refer to a mental health specialist who can consider a wider range of treatment options
Consider switching antidepressant or adding another antidepressant e.g. mirtazapine and venlafaxine.
Though there is no robust evidence from randomised controlled trials (RCTs) that psychostimulants improve depression in palliative care, some clinicians do use them and report benefits. Psychostimulants should be viewed as an experimental treatment in this context. Patients should be monitored closely and treatment withdrawn early if there is no benefit
Under the supervision of a mental health specialist, lithium augmentation or electroconvulsive therapy may be considered

#### 4.5 Short prognosis

For patients with short prognosis, the threshold for treatment resistant depression should be lowered to 4 weeks.
Choice of antidepressant may be different for patients with short prognosis. Consider the use of tricyclic antidepressants (TCAs) or mirtazapine, which may have earlier onset of action than SSRIs.
Agitation and distress may be due to organic disorder (e.g. delirium, adverse drug reaction). Treat agitation symptomatically – consider use of benzodiazepines or neuroleptics.
Some clinicians report benefit from using psychostimulants in patients with a short life expectancy. However, they should be viewed as experimental in this context. Patients should be monitored closely and treatment withdrawn early if there is no benefit

## 4.6 Choice of psychological therapy

- Psychological therapy is usually patients' preferred strategy for treating depression.
- There is some evidence from RCTs that psychotherapy is useful for treating depressive states in advanced cancer patients.
- Brief interventions may be preferable due to the poor physical health status of palliative care patients.
- RCT evidence suggests that non-mental health specialists can be trained to deliver psychological therapy (1-4) Ensure that healthcare professionals providing psychological treatment are competent in the delivery of the treatment provided.

### 4.6.1 Cognitive Behavioural Therapy (CBT)

- Cognitive Behavioural Therapy (CBT) is the most widely used and widely evaluated psychological therapy for depression. Though there is a scarcity of studies in palliative care, numerous RCTs have demonstrated the effectiveness of CBT in patients without physical illness.
- CBT focuses on identifying and restructuring dysfunctional thought patterns. It helps patients identify those thought patterns that trigger emotional distress, and then change these to be more realistic and constructive.
- There is evidence that CBT in palliative care can improve some outcomes.

### 4.6.2 Problem-solving therapy

- Problem-solving therapy is a short, focused intervention that helps patients cope with problems they are facing in the lives.
- Together patient and clinician identify a specific problem occurring in the patient's life, discuss possible solutions, choose a strategy and work out the steps to resolution of the problem.
- There has been little evidence on the effectiveness of problem-solving therapy, but its simplicity and brevity make it a popular choice for palliative care patients.

### 4.6.3 Other therapies with psychological benefits

Guided imagery	Use of the imagination to invoke senses and feelings that bring a sense of calmness and empowerment
Expressive group therapy	Some evidence of efficacy in metastatic breast cancer patients. Therapy is prolonged, therefore may not be suitable for end-stage patients
Couple therapy	Some evidence of efficacy in reducing depressive symptoms in cancer patients. May be first-line treatment in patients with obvious relationship difficulties
Dignity therapy	An experimental intervention to help bolster patients' sense of meaning and purpose at the end of life. Contraindicated in patients with severe depression.

Interpersonal therapy	Brief therapy focusing on the patient's personal relationships and interactions with others
Creative therapies (e.g. music, art therapy)	May benefit palliative care patients by supporting emotional and spiritual expression, and promoting relaxation, pain control and a sense of well-being

#### 4.7 Choice of antidepressant

- There is no direct evidence from palliative care populations (or indeed the wider population of people with physical illness) to suggest one antidepressant is preferable over others. A recent review indicated that some second generation antidepressants are marginally better tolerated and more effective than others (5). We recommend therefore that clinicians become familiar with two or three of the better performing antidepressants and we suggest that Mirtazapine, Sertraline and Citalopram are a reasonable selection for use in palliative care patients. Apart from the 15mg and 45mg preparations of mirtazapine, these drugs are all similarly inexpensive (at least in UK). Amitriptyline and other tricyclic antidepressants are potential second-line medicines, which may be useful in patients with neuropathic pain, and there is some evidence that these drugs may have a marginally quicker onset of action in patients with physical illness.

Drug	Half Life	Forms	Usual Dose
Mirtazapine (Noradrenergic specific serotonergic antidepressant (NaSSAs))	20-40 hours	Tablets (30mg) Orodispersible tablets (15/30/45mg) Oral solution (15mg)	15-45mg/day (max 45mg/day)
Sertraline (SSRI)	24-36 hours	Tablets (50/100mg)	50mg/day (max 200mg/day)
Citalopram (SSRI)	26-40 hours	Tablets (10/20/40mg) Oral drops (40mg)	20-40mg/day (max 60mg/day)
Amitriptyline (TCA)	9-36 hours	Tablets (10/25/50mg) Solution (25/50mg)	75-200mg/day (max 200mg/day)

- Given the lack of evidence for a clearly superior antidepressant, treatment decisions should be based on:

Type of comorbid illness
Patient's symptom profile
Pharmacological properties (e.g. half-life, interactions etc)
Potential side effects (some of which may be beneficial)
Clinician familiarity and preference

#### 4.7.1 Special considerations

Mirtazapine	Benefits <ul style="list-style-type: none"> <li>• May increase appetite</li> <li>• May reduce nausea</li> <li>• Sedative effect may be beneficial for some patients</li> <li>• May have early onset of action, therefore a good choice for patients with a short prognosis</li> <li>• Available as oro-dispersible tablet</li> <li>• Suitable in heart failure and diabetes</li> </ul>
	Possible side effects <ul style="list-style-type: none"> <li>• Sedation, dizziness, constipation, hypertension, weight gain, oedema, orthostatic hypotension, dry mouth, fatigue, tremor, dizziness, confusion, anxiety, arthralgia, myalgia</li> </ul>
	Cautions <ul style="list-style-type: none"> <li>• Possible increased serotonergic effects when given with tramadol or venlafaxine</li> <li>• Enhances anticoagulant effect of warfarin</li> </ul>
Sertraline	Benefits <ul style="list-style-type: none"> <li>• Beneficial for renal impairment</li> <li>• First choice for recent cardiac event</li> </ul>
	Possible side effects <ul style="list-style-type: none"> <li>• Nausea, vomiting, drowsiness, dizziness, dry mouth, anorexia, dyspepsia, diarrhoea, insomnia, sweating, sexual dysfunction, agitation, hyponatraemia, pancreatitis, hepatitis, jaundice, liver failure, tachycardia, amnesia, paraesthesia, aggression, urinary incontinence, menstrual irregularities</li> </ul>
	Cautions <ul style="list-style-type: none"> <li>• Risk of ventricular arrhythmias if taken with droperidol</li> <li>• Increased risk of bleeding when given with aspirin</li> </ul>
Citalopram	Benefits <ul style="list-style-type: none"> <li>• Beneficial for agitated depression/anxiety, nausea</li> <li>• Relatively safe for patients at risk of seizures</li> <li>• Available as oral suspension</li> </ul>
	Possible side effects <ul style="list-style-type: none"> <li>• Nausea, vomiting, anorexia, dyspepsia, diarrhoea, dry mouth, dizziness, insomnia, sweating, sexual dysfunction, agitation, hyponatraemia, palpitation, tachycardia, postural hypotension, confusion, impaired concentration, amnesia, migraine, paraesthesia, taste disturbance, increased salivation, rhinitis, tinnitus, polyuria, micturition disorders, euphoria, abnormal dreams</li> </ul>
	Cautions <ul style="list-style-type: none"> <li>• Increased risk of bleeding when given with aspirin</li> </ul>
Amitriptyline	Benefits <ul style="list-style-type: none"> <li>• May have an earlier onset of action than SSRIs.</li> <li>• May be beneficial for patients with insomnia or neuropathic pain</li> <li>• If a patient is already on a low dose for neuropathic pain, it may be</li> </ul>

	<p>beneficial to increase this dose, rather than introduce another antidepressant</p> <ul style="list-style-type: none"> <li>• There is strong evidence that TCAs are equally, if not more effective than SSRIs. Recent research suggests that the greater risk adverse events associated with TCAs may have been exaggerated</li> </ul>
	<p>Possible side effects</p> <ul style="list-style-type: none"> <li>• Dry mouth, constipation, hypotension, tachycardia, urinary retention, confusion, dizziness, sleep disturbance, drowsiness, arrhythmia, abdominal pain, stomatitis, palpitation, oedema, restlessness, fatigue, mydraiasis, increased intra-ocular pressure, sexual dysfunction, nausea, sweating</li> </ul>
	<p>Cautions</p> <ul style="list-style-type: none"> <li>• Greater toxicity in overdose than SSRIs</li> </ul>

- For drug interactions refer to national prescribing guidelines (e.g. the British National Formulary <http://bnf.org/bnf/> in the UK, the Drug Commission of the German Medical Council <http://www.akdae.de/35/10/67-Depression-2006-2Auflage.pdf> in Germany, [www.medinteract.net](http://www.medinteract.net) in Spain).

#### 4.7.2 Physical disease contraindications of antidepressants

<b>Cardiovascular disease</b>	
Recent myocardial infarction	Tricyclics contraindicated
Heart block	MAOIs contraindicated
Congestive heart failure	Tricyclic: risk postural hypotension Lithium excretion lowered by ACE inhibitors and diuretics
Aortic or cerebral aneurysm	ECT contraindicated
Hypertension	Lithium excretion reduced by diuretics MAOIs enhance hypertensives Avoid venlafaxine
<b>Eye disease</b>	
Glaucoma	Tricyclics, duloxetine, mirtazapine contraindicated
<b>Genito-urinary disease</b>	
Prostatic hypertrophy	Tricyclics worsen symptoms – risk of retention of urine due to anticholinergic action
Renal failure	Risk of toxicity from lithium
<b>Neurological disease</b>	
Epilepsy	All antidepressants lower seizure threshold Maprotiline contraindicated Interactions between SSRIs and anticonvulsants (raised levels of phenytoin, carbamazepine) Avoid carbamazepine with MAOIs

Intracranial space occupying lesion	ECT contraindicated
Raised intracranial pressure	ECT contraindicated
Cerebrovascular accident	ECT potentially dangerous MAOIs contraindicated
Parkinson's disease	Interaction between fluoxetine and selegiline (confusional state)
Migraine	Interaction between fluoxetine and selegiline (confusional state)
<b>Liver failure</b>	Decrease dose of all antidepressants If severe, tricyclics contraindicated
<b>Gastrointestinal disease</b>	
Upper GI tract disease	SSRIs may worsen nausea SSRIs may cause GI bleeding in at risk individuals
Lower GI tract disease	Tricyclic levels raised by cimetidine
Severe diarrhoea	Tricyclics may worsen constipation
<b>Endocrine disease</b>	
Phaeochromocytoma	MAOIs and moclobemide contraindicated
Hyperthyroidism	Tranlycypromine and moclobemide contraindicated Caution with venlafaxine
<b>Blood disorders</b>	
Agranulocytosis	Tricyclics and mianserin contraindicated
Sickle cell disease	Caution with ECT, anaesthetic risk
Warfarin treatment	Avoid mirtazapine
<b>Porphyria</b>	Avoid tricyclics

#### 4.8 Complementary therapies

- There is little evidence for complementary therapies, though they are frequently offered by palliative care providers.
- There is some RCT evidence that aromatherapy massage reduces depressive symptoms in cancer patients, although not specifically in patients with depressive disorder.

## Appendix

ICD-10 criteria for diagnosis of depression:

<b>Clinical significance</b>
Some difficulty in continuing with ordinary work and social activities, but will not cease to function completely in mild depressive episode; considerable difficulty in continuing with social, work or domestic activities in moderate depressive episode; considerable distress or agitation, and unlikely to continue with social, work, or domestic activities, except to a very limited extent in severe depressive episode
<b>Duration of symptoms</b>
A duration of at least 2 weeks is usually required for diagnosis for depressive episodes of all three grades of severity
<b>Severity</b>
Depressed mood, loss of interest and enjoyment, and reduced energy leading to increased fatigability and diminished activity in typical depressive episodes; other common symptoms are: (1) Reduced concentration and attention (2) Reduced self-esteem and self-confidence (3) ideas of guilt and unworthiness (even in mild type of episode) (4) Bleak and pessimistic views of the future (5) Ideas or acts of self-harm or suicide (6) Disturbed sleep (7) Diminished appetite  Typical examples of "somatic" symptoms are: loss of interest or pleasure in activities that are normally enjoyable; lack of emotional reactivity to normally pleasurable surroundings and events; waking in the morning 2 h or more before the usual time; depression worse in the morning; objective evidence of definite psychomotor retardation or agitation; marked loss of appetite; weight loss; marked loss of libido.  For mild depressive episode, two of most typical symptoms of depression and two of the other symptoms are required. If four or more of the somatic symptoms are present, the episode is diagnosed: With somatic symptoms.  For moderate depressive episode, two of three of most typical symptoms of depression and at least three of the other symptoms are required. If four or more of the somatic symptoms are present, the episode is diagnosed: With somatic symptoms. For severe depressive episode, all three of the typical symptoms noted for mild and moderate depressive episodes are present and at least four other symptoms of severe intensity are required.

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