National Guideline Clearinghouse
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Brief Summary

GUIDELINE TITLE

Depression. The treatment and management of depression in adults.

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Mental Health. Depression. The treatment and management of depression in adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Oct. 64 p. (Clinical guideline; no. 90).

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates previous versions: National Collaborating Centre for Mental Health. Depression: management of depression in primary and secondary care. London (UK): National Institute for Clinical Excellence (NICE); 2004. 67 p. [634 references]

National Collaborating Centre for Mental Health. Depression: management of depression in primary and secondary care. London (UK): National Institute for Clinical Excellence (NICE); 2007 Apr. 67 p. (Clinical guideline; no. 23).

BRIEF SUMMARY CONTENT

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Mental Health (NCCMH) on behalf of the National Institute for Health and Clinical Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance.

Box 1: Depression Definitions (taken from the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Revision [DSM-IV])

Subthreshold depressive symptoms: Fewer than 5 symptoms of depression.

Mild depression: Few, if any, symptoms in excess of the 5 required to make the diagnosis, and symptoms result in only minor functional impairment.

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

Severe depression: Most symptoms, and the symptoms markedly interfere with functioning. Can occur with or without psychotic symptoms.

Note that a comprehensive assessment of depression should not rely simply on a symptom count, but should take into account the degree of functional impairment and/or disability (see "Principles for Assessment, Coordination of Care, and Choosing Treatments" below).

This guideline is published alongside NICE guideline 91 Depression in adults with a chronic physical health problem (see the NGC summary), which makes recommendations on the identification, treatment and management of depression in adults aged 18 years and older who also have a chronic health problem.

Care of All People with Depression

Providing Information and Support, and Obtaining Informed Consent

When working with people with depression and their families or carers:

- Build a trusting relationship and work in an open, engaging and non-judgmental manner
- Explore treatment options in an atmosphere of hope and optimism, explaining the different courses of depression and that recovery is possible
- Be aware that stigma and discrimination can be associated with a diagnosis of depression
- Ensure that discussions take place in settings in which confidentiality, privacy and dignity are respected

When working with people with depression and their families or carers:

- Provide information appropriate to their level of understanding about the nature of depression and the range of treatments available
- Avoid clinical language without adequate explanation
- Ensure that comprehensive written information is available in the appropriate language and in audio format if possible
- Provide and work proficiently with independent interpreters (that is, someone who is not known to the person with depression) if needed

Inform people with depression about self-help groups, support groups and other local and national resources.

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

Ensure that consent to treatment is based on the provision of clear information (which should also be available in written form) about the intervention, covering:

- What it comprises
- What is expected of the person while having it
- Likely outcomes (including any side effects)

Advance Decisions and Statements

For people with recurrent severe depression or depression with psychotic symptoms and for those who have been treated under the Mental Health Act, consider developing advance decisions and advance statements collaboratively with the person. Record the decisions and statements and include copies in the person's care plan in primary and secondary care. Give copies to the person and to their family or carer, if the person agrees.

Supporting Families and Carers

When families or carers are involved in supporting a person with severe or chronic depression, consider:

- Providing written and verbal information on depression and its management, including how families or carers can support the person
- Offering a carer's assessment of their caring, physical and mental health needs if necessary
- Providing information about local family or carer support groups and voluntary organisations, and helping families or carers to access these
- Negotiating between the person and their family or carer about confidentiality and the sharing of information

Note: Depression is described as 'chronic' if symptoms have been present more or less continuously for 2 years or more.

Principles for Assessment, Coordination of Care and Choosing Treatments

When assessing a person who may have depression, conduct a comprehensive assessment that does not rely simply on a symptom count. Take into account both the degree of functional impairment and/or disability associated

with the possible depression and the duration of the episode.

In addition to assessing symptoms and associated functional impairment, consider how the following factors may have affected the development, course and severity of a person's depression:

- Any history of depression and co-morbid mental health or physical disorders
- Any past history of mood elevation (to determine if the depression may be part of bipolar disorder) (Refer if necessary to the NGC summary of the NICE guideline Bipolar Disorder)
- Any past experience of, and response to, treatments
- The quality of interpersonal relationships
- Living conditions and social isolation

Be respectful of, and sensitive to, diverse cultural, ethnic and religious backgrounds when working with people with depression, and be aware of the possible variations in the presentation of depression. Ensure competence in:

- Culturally sensitive assessment
- Using different explanatory models of depression
- Addressing cultural and ethnic differences when developing and implementing treatment plans
- Working with families from diverse ethnic and cultural backgrounds

When assessing a person with suspected depression, be aware of any learning disabilities or acquired cognitive impairments, and if necessary consider consulting with a relevant specialist when developing treatment plans and strategies.

When providing interventions for people with a learning disability or acquired cognitive impairment who have a diagnosis of depression:

- Where possible, provide the same interventions as for other people with depression.
- If necessary, adjust the method of delivery or duration of the intervention to take account of the disability or impairment.

Always ask people with depression directly about suicidal ideation and intent. If there is a risk of self-harm or suicide:

- Assess whether the person has adequate social support and is aware of sources of help.
- Arrange help appropriate to the level of risk (see "Risk Assessment and Monitoring" below).
- Advise the person to seek further help if the situation deteriorates.

Effective Delivery of Interventions for Depression

All interventions for depression should be delivered by competent practitioners. Psychological and psychosocial interventions should be based on the relevant treatment manual(s), which should guide the structure and duration of the intervention. Practitioners should consider using competence frameworks developed from the relevant treatment manual(s) and for all interventions should:

- Receive regular high-quality supervision.
- Use routine outcome measures and ensure that the person with depression is involved in reviewing the efficacy of the treatment.
- Engage in monitoring and evaluation of treatment adherence and practitioner competence – for example, by using video and audio tapes, and external audit and scrutiny where appropriate.

Consider providing all interventions in the preferred language of the person with depression where possible.

Stepped Care

The stepped-care model provides a framework in which to organize the provision of services, and supports patients, carers and practitioners in identifying and accessing the most effective interventions (see figure 1 below). In stepped care the least intrusive, most effective intervention is provided first; if a person does not benefit from the intervention initially offered, or declines an intervention, they should be offered an appropriate intervention from the next step.

Figure 1: The Stepped-Care Model

Focus of the Intervention	Nature of the Intervention
STEP 4: Severe and complex[a] depression; risk to life; severe self-neglect	Medication, high-intensity psychological interventions, electroconvulsive therapy, crisis service, combined treatments, multiprofessional and inpatient care
STEP 3: Persistent subthreshold depressive symptoms or mild to moderate depression with inadequate response to initial interventions; moderate and severe depression	Medication, high-intensity psychological interventions, combined treatments, collaborative care[b] and referral for further assessment and interventions
STEP 2: Persistent subthreshold depressive symptoms; mild to moderate depression	Low-intensity psychosocial interventions, psychological interventions, medication and referral for further assessment and interventions
STEP 1: All known and suspected presentations of depression	Assessment, support, psychoeducation, active monitoring and referral for further assessment and interventions

[a] Complex depression includes depression that shows an inadequate response to multiple treatments, is complicated by psychotic symptoms, and/or is associated with significant psychiatric comorbidity or psychosocial factors.

[b] Only for depression where the person also has a chronic physical health problem and associated functional impairment (see the NGC summary Depression in adults with a chronic physical health problem: treatment and management [NICE clinical guideline 91]).

Step 1: Recognition, Assessment and Initial Management

Case Identification and Recognition

Be alert to possible depression (particularly in people with a past history of depression or a chronic physical health problem with associated functional impairment) and consider asking people who may have depression two questions, specifically:

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

If a person answers 'yes' to either of the depression identification questions but the practitioner is not competent to perform a mental health assessment, they should refer the person to an appropriate professional. If this professional is not the person's general practitioner (GP), inform the GP of the referral.

If a person answers 'yes' to either of the depression identification questions, a practitioner who is competent to perform a mental health assessment should review the person's mental state and associated functional, interpersonal and social difficulties.

When assessing a person with suspected depression, consider using a validated measure (for example, for symptoms, functions and/or disability) to inform and evaluate treatment.

For people with significant language or communication difficulties, for example people with sensory impairments or a learning disability, consider using the Distress Thermometer and/or asking a family member or carer about the person’s symptoms to identify possible depression. If a significant level of distress is identified, investigate further.

Note: The *Distress Thermometer* is a single-item question screen that will identify distress coming from any source. The person places a mark on the scale answering: 'How distressed have you been during the past week on a scale of 0 to 10?' Scores of 4 or more indicate a significant level of distress that should be investigated further. [Roth AJ, Kornblith AB, Batel-Copel L, et al. (1998) Rapid screening for psychologic distress in men with prostate carcinoma: a pilot study. Cancer 82: 1904-8.]

Risk Assessment and Monitoring

If a person with depression presents considerable immediate risk to themselves or others, refer them urgently to specialist mental health services.

Advise people with depression of the potential for increased agitation, anxiety and suicidal ideation in the initial stages of treatment; actively seek out these symptoms and:

- Ensure that the person knows how to seek help promptly.
- Review the person's treatment if they develop marked and/or prolonged agitation.

Advise a person with depression and their family or carer to be vigilant for mood changes, negativity and hopelessness, and suicidal ideation, and to contact their practitioner if concerned. This is particularly important during high-risk periods, such as starting or changing treatment and at times of increased personal stress.

If a person with depression is assessed to be at risk of suicide:

- Take into account toxicity in overdose if an antidepressant is prescribed or the person is taking other medication; if necessary, limit the amount of drug(s) available
- Consider increasing the level of support, such as more frequent direct or telephone contacts
- Consider referral to specialist mental health services.

Step 2: Recognized Depression – Persistent Subthreshold Depressive Symptoms or Mild to Moderate Depression

General Measures

Depression with Anxiety

When depression is accompanied by symptoms of anxiety, the first priority should usually be to treat the depression. When the person has an anxiety disorder and comorbid depression or depressive symptoms, consult the NICE guideline for the relevant anxiety disorder (see Section 6 of the original guideline document) and consider treating the anxiety disorder first (since effective treatment of the anxiety disorder will often improve the depression or the depressive symptoms).

Sleep Hygiene

Offer people with depression advice on sleep hygiene if needed, including:

- Establishing regular sleep and wake times
- Avoiding excess eating, smoking or drinking alcohol before sleep
- Creating a proper environment for sleep
- Taking regular physical exercise

Active Monitoring

For people who, in the judgment of the practitioner, may recover with no formal intervention, or people with mild depression who do not want an intervention, or people with subthreshold depressive symptoms who request an intervention:

- Discuss the presenting problem(s) and any concerns that the person may have about them
- Provide information about the nature and course of depression
- Arrange a further assessment, normally within 2 weeks
- Make contact if the person does not attend follow-up appointments

Low-Intensity Psychosocial Interventions

For people with persistent subthreshold depressive symptoms or mild to moderate depression, consider offering one or more of the following interventions, guided by the person's preference:

- Individual guided self-help based on the principles of cognitive behavioural therapy (CBT)
- Computerized cognitive behavioural therapy (CCBT)
- A structured group physical activity programme

Delivery of Low-Intensity Psychosocial Interventions

Individual guided self-help programmes based on the principles of CBT (and including behavioral activation and problem-solving techniques) for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- Include the provision of written materials of an appropriate reading age (or alternative media to support

access)
- Be supported by a trained practitioner, who typically facilitates the self-help programme and reviews progress and outcome
- Consist of up to six to eight sessions (face-to-face and via telephone) normally taking place over 9 to 12 weeks, including follow-up

CCBT for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- Be provided via a stand-alone computer-based or web-based programme
- Include an explanation of the CBT model, encourage tasks between sessions, and use thought-challenging and active monitoring of behavior, thought patterns and outcomes
- Be supported by a trained practitioner, who typically provides limited facilitation of the programme and reviews progress and outcome
- Typically take place over 9 to 12 weeks, including follow-up

Physical activity programmes for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- Be delivered in groups with support from a competent practitioner
- Consist typically of three sessions per week of moderate duration (45 minutes to 1 hour) over 10 to 14 weeks (average 12 weeks)

Group Cognitive Behavioral Therapy

Consider group-based CBT for people with persistent subthreshold depressive symptoms or mild to moderate depression who decline low-intensity psychosocial interventions.

Group-based CBT for people with persistent subthreshold depressive symptoms or mild to moderate depression should:

- Be based on a structured model such as 'Coping with Depression'
- Be delivered by two trained and competent practitioners
- Consist of 10 to 12 meetings of eight to ten participants
- Normally take place over 12 to 16 weeks, including follow-up

Drug Treatment

Do not use antidepressants routinely to treat persistent subthreshold depressive symptoms or mild depression because the risk–benefit ratio is poor, but consider them for people with:

- A past history of moderate or severe depression
- Initial presentation of subthreshold depressive symptoms that have been present for a long period (typically at least 2 years
- Subthreshold depressive symptoms or mild depression that persist(s) after other interventions

Although there is evidence that St John's wort may be of benefit in mild or moderate depression, practitioners should:

- Not prescribe or advise its use by people with depression because of uncertainty about appropriate doses, persistence of effect, variation in the nature of preparations and potential serious interactions with other drugs (including oral contraceptives, anticoagulants and anticonvulsants)
- Advise people with depression of the different potencies of the preparations available and of the potential serious interactions of St John's wort with other drugs.

Step 3: Persistent Subthreshold Depressive Symptoms or Mild to Moderate Depression with Inadequate Response to Initial Interventions, and Moderate and Severe Depression

Treatment Options

For people with persistent subthreshold depressive symptoms or mild to moderate depression who have not benefited from a low-intensity psychosocial intervention, discuss the relative merits of different interventions with the person and provide:

- An antidepressant (normally a selective serotonin reuptake inhibitor [SSRI])
- A high-intensity psychological intervention, normally one of the following options:
    - CBT
    - Interpersonal therapy (IPT)
    - Behavioural activation (but note that the evidence is less robust than for CBT or IPT)
    - Behavioural couples therapy for people who have a regular partner and where the relationship may contribute to the development or maintenance of depression, or where involving the partner is considered to be of potential therapeutic benefit.

For people with moderate or severe depression, provide a combination of antidepressant medication and a high-intensity psychological intervention (CBT or IPT).

The choice of intervention should be influenced by the:

- Duration of the episode of depression and the trajectory of symptoms
- Previous course of depression and response to treatment
- Likelihood of adherence to treatment and any potential adverse effects
- Person's treatment preference and priorities

For people with depression who decline an antidepressant, CBT, IPT, behavioral activation and behavioral couples therapy, consider:

- Counseling for people with persistent subthreshold depressive symptoms or mild to moderate depression
- Short-term psychodynamic psychotherapy for people with mild to moderate depression

Discuss with the person the uncertainty of the effectiveness of counseling and psychodynamic psychotherapy in treating depression.

Antidepressant Drugs

*Choice of Antidepressant**

Discuss antidepressant treatment options with the person with depression, covering:

- The choice of antidepressant, including any anticipated adverse events, for example side effects and discontinuation symptoms (see "Stopping or Reducing Antidepressants" below), and potential interactions with concomitant medication or physical health problems**
- Their perception of the efficacy and tolerability of any antidepressants they have previously taken

*For additional considerations on the use of antidepressants and other medications (including the assessment of the relative risks and benefits) for women who may become pregnant, please refer to the British National Formulary (BNF) and individual drug Summary of Product Characteristics (SPCs). For women in the antenatal and postnatal periods, see also the NICE clinical guideline 45 'Antenatal and postnatal mental health'.

**Consult appendix 1 of the BNF for information on drug interactions and the NGC summary Depression in adults with a chronic physical health problem: treatment and management (NICE clinical guideline 91).

When an antidepressant is to be prescribed, it should normally be an SSRI in a generic form because SSRIs are equally effective as other antidepressants and have a favourable risk–benefit ratio. Also take the following into account:

- SSRIs are associated with an increased risk of bleeding, especially in older people or in people taking other drugs that have the potential to damage the gastrointestinal mucosa or interfere with clotting. In particular, consider prescribing a gastroprotective drug in older people who are taking non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin.
- Fluoxetine, fluvoxamine and paroxetine are associated with a higher propensity for drug interactions than other SSRIs**
- Paroxetine is associated with a higher incidence of discontinuation symptoms than other SSRIs.

Take into account toxicity in overdose when choosing an antidepressant for people at significant risk of suicide. Be aware that:

- Compared with other equally effective antidepressants recommended for routine use in primary care, venlafaxine is associated with a greater risk of death from overdose
- Tricyclic antidepressants (TCAs), except for lofepramine, are associated with the greatest risk in overdose

When prescribing drugs other than SSRIs, take the following into account:

- The increased likelihood of the person stopping treatment because of side effects (and the consequent need to increase the dose gradually) with venlafaxine, duloxetine and TCAs.
- The specific cautions, contraindications and monitoring requirements for some drugs. For example:
    - The potential for higher doses of venlafaxine to exacerbate cardiac arrhythmias and the need to monitor the person's blood pressure
    - The possible exacerbation of hypertension with venlafaxine and duloxetine
    - The potential for postural hypotension and arrhythmias with TCAs
    - The need for hematological monitoring with mianserin in elderly people**
- Non-reversible monoamine oxidase inhibitors (MAOIs), such as phenelzine, should normally be prescribed only by specialist mental health professionals.
- Dosulepin should not be prescribed.

Starting and Initial Phase of Treatment

When prescribing antidepressants, explore any concerns the person with depression has about taking medication, explain fully the reasons for prescribing, and provide information about taking antidepressants, including:

- The gradual development of the full antidepressant effect
- The importance of taking medication as prescribed and the need to continue treatment after remission
- Potential side effects
- The potential for interactions with other medications
- The risk and nature of discontinuation symptoms with all antidepressants, particularly with drugs with a shorter half-life (such as paroxetine and venlafaxine), and how these symptoms can be minimized
- The fact that addiction does not occur with antidepressants.

Offer written information appropriate to the person's needs.

For people started on antidepressants who are not considered to be at increased risk of suicide, normally see them after 2 weeks. See them regularly thereafter, for example at intervals of 2 to 4 weeks in the first 3 months, and then at longer intervals if response is good.

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

If a person with depression develops side effects early in antidepressant treatment, provide appropriate information and consider one of the following strategies:

- Monitor symptoms closely where side effects are mild and acceptable to the person
- Stop the antidepressant or change to a different antidepressant if the person prefers
- In discussion with the person, consider short-term concomitant treatment with a benzodiazepine if anxiety, agitation and/or insomnia are problematic (except in people with chronic symptoms of anxiety); this should usually be for no longer than 2 weeks in order to prevent the development of dependence

People who start on low-dose TCAs and who have a clear clinical response can be maintained on that dose with careful monitoring.

If the person's depression shows no improvement after 2 to 4 weeks with the first antidepressant, check that the drug has been taken regularly and in the prescribed dose.

If response is absent or minimal after 3 to 4 weeks of treatment with a therapeutic dose of an antidepressant, increase the level of support (for example, by weekly face-to-face or telephone contact) and consider:

- Increasing the dose in line with the SPC if there are no significant side effects or
- Switching to another antidepressant as described in the section "Switching Antidepressants" below if there are side effects or if the person prefers.

If the person's depression shows some improvement by 4 weeks, continue treatment for another 2 to 4 weeks. Consider switching to another antidepressant if:

- Response is still not adequate
- There are side effects
- The person prefers to change treatment

Psychological Interventions

Delivering High-Intensity Psychological Interventions

For all high-intensity psychological interventions, the duration of treatment should normally be within the limits indicated in this guideline. As the aim of treatment is to obtain significant improvement or remission the duration of treatment may be:

- Reduced if remission has been achieved
- Increased if progress is being made, and there is agreement between the practitioner and the person with depression that further sessions would be beneficial (for example, if there is a comorbid personality disorder or significant psychosocial factors that impact on the person's ability to benefit from treatment).

For all people with depression having individual CBT, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. Also consider providing:

- Two sessions per week for the first 2 to 3 weeks of treatment for people with moderate or severe depression
- Follow-up sessions typically consisting of three to four sessions over the following 3 to 6 months for all people with depression.

For all people with depression having IPT, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. For people with severe depression, consider providing two sessions per week for the first 2 to 3 weeks of treatment.

For all people with depression having behavioural activation, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. Also consider providing:

- Two sessions per week for the first 3 to 4 weeks of treatment for people with moderate or severe depression
- Follow-up sessions typically consisting of three to four sessions over the following 3 to 6 months for all people with depression.

Behavioral couples therapy for depression should normally be based on behavioral principles, and an adequate course of therapy should be 15 to 20 sessions over 5 to 6 months.

Delivering Counseling

For all people with persistent sub-threshold depressive symptoms or mild to moderate depression having counseling, the duration of treatment should typically be in the range of six to ten sessions over 8 to 12 weeks.

Delivering Short-Term Psychodynamic Psychotherapy

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

Treatment Choice Based on Depression Subtypes and Personal Characteristics

There is little evidence to guide prescribing in relation to depression subtypes or personal characteristics. The main issue concerns the impact of other physical disorders on the treatment of depression. Refer to the NGC summary Depression in adults with a chronic physical health problem: treatment and management (NICE clinical guideline 91) for further information.

Do not routinely vary the treatment strategies for depression described in this guideline either by depression

subtype (for example, atypical depression or seasonal depression) or by personal characteristics (for example, sex or ethnicity) as there is no convincing evidence to support such action.

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

When prescribing antidepressants for older people:

- Prescribe at an age-appropriate dose taking into account the effect of general physical health and concomitant medication on pharmacokinetics and pharmacodynamics
- Carefully monitor for side effects.

For people with long-standing moderate or severe depression who would benefit from additional social or vocational support, consider:

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

Enhanced Care for Depression

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

For people with severe depression and those with moderate depression and complex problems, consider:

- Referring to specialist mental health services for a programme of coordinated multiprofessional care
- Providing collaborative care if the depression is in the context of a chronic physical health problem with associated functional impairment (Refer to the NGC summary Depression in adults with a chronic physical health problem: treatment and management [NICE clinical guideline 91] for the evidence base.)

Sequencing Treatments after Initial Inadequate Response

Some people have depression that does not respond well to initial treatment. This section describes strategies to adopt if this occurs.

Drug Treatments

When reviewing drug treatment for a person with depression whose symptoms have not adequately responded to initial pharmacological interventions:

- Check adherence to, and side effects from, initial treatment.
- Increase the frequency of appointments using outcome monitoring with a validated outcome measure.
- Be aware that using a single antidepressant rather than combination medication or augmentation (see "Combining and Augmenting Medications" below) is usually associated with a lower side-effect burden.
- Consider reintroducing previous treatments that have been inadequately delivered or adhered to, including increasing the dose.
- Consider switching to an alternative antidepressant.

Switching Antidepressants

When switching to another antidepressant, be aware that the evidence for the relative advantage of switching either within or between classes is weak. Consider switching to:

- Initially a different SSRI or a better tolerated newer-generation antidepressant
- Subsequently an antidepressant of a different pharmacological class that may be less well tolerated, for example venlafaxine, a TCA or an MAOI.

Do not switch to, or start, dosulepin because evidence supporting its tolerability relative to other antidepressants is outweighed by the increased cardiac risk and toxicity in overdose.

When switching to another antidepressant, which can normally be achieved within 1 week when switching from drugs with a short half-life, consider the potential for interactions in determining the choice of a new drug and the

nature and duration of the transition. Exercise particular caution when switching:

- From fluoxetine to other antidepressants, because fluoxetine has a long half-life (approximately 1 week)
- From fluoxetine or paroxetine to a TCA, because both of these drugs inhibit the metabolism of TCAs; a lower starting dose of the TCA will be required, particularly if switching from fluoxetine because of its long half-life
- To a new serotonergic antidepressant or MAOI, because of the risk of serotonin syndrome (features of serotonin syndrome include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus)
- From a non-reversible MAOI: a 2-week washout period is required (other antidepressants should not be prescribed routinely during this period).

Combining and Augmenting Medications

'Augmentation' is when an antidepressant is used with a non-antidepressant drug and 'combination' is when two antidepressants are used together.

When using combinations of medications (which should only normally be started in primary care in consultation with a consultant psychiatrist):

- Select medications that are known to be safe when used together
- Be aware of the increased side-effect burden this usually causes
- Discuss the rationale for any combination with the person with depression, follow General Medical Council (GMC) guidance if off-label medication is prescribed, and monitor carefully for adverse effects
- Be familiar with primary evidence and consider obtaining a second opinion when using unusual combinations, the evidence for the efficacy of a chosen strategy is limited or the risk–benefit ratio is unclear
- Document the rationale for the chosen combination.

If a person with depression is informed about, and prepared to tolerate, the increased side-effect burden, consider combining or augmenting an antidepressant with:

- Lithium **or**
- An antipsychotic such as aripiprazole*, olanzapine*, quetiapine* or risperidone* **or**
- Another antidepressant such as mirtazapine or mianserin.

When prescribing lithium:

- Monitor renal and thyroid function before treatment and every 6 months during treatment (more often if there is evidence of renal impairment)
- Consider electrocardiogram (ECG) monitoring in people with depression who are at high risk of cardiovascular disease
- Monitor serum lithium levels 1 week after initiation and each dose change until stable, and every 3 months thereafter.

When prescribing an antipsychotic, monitor weight, lipid and glucose levels, and side effects (for example, extrapyramidal side effects and prolactin-related side effects with risperidone).

The following strategies should not be used routinely:

- Augmentation of an antidepressant with a benzodiazepine for more than 2 weeks as there is a risk of dependence
- Augmentation of an antidepressant with buspirone,# carbamazepine,# lamotrigine# or valproate# as there is insufficient evidence for their use
- Augmentation of an antidepressant with pindolol# or thyroid hormones# as there is inconsistent evidence of effectiveness.

Note: In this guideline, drug names are marked with a # if they do not have UK marketing authorisation for the indication in question at the time of publication (October 2009). Informed consent should be obtained and documented.

Combined Psychological and Drug Treatment

For a person whose depression has not responded to either pharmacological or psychological interventions, consider combining antidepressant medication with CBT.

Referral

For a person whose depression has failed to respond to various strategies for augmentation and combination treatments, consider referral to a practitioner with a specialist interest in treating depression, or to a specialist service.

Continuation and Relapse Prevention

Support and encourage a person who has benefited from taking an antidepressant to continue medication for at least 6 months after remission of an episode of depression. Discuss with the person that:

- This greatly reduces the risk of relapse
- Antidepressants are not associated with addiction.

Review with the person with depression the need for continued antidepressant treatment beyond 6 months after remission, taking into account:

- The number of previous episodes of depression
- The presence of residual symptoms
- Concurrent physical health problems and psychosocial difficulties

For people with depression who are at significant risk of relapse or have a history of recurrent depression, discuss with the person treatments to reduce the risk of recurrence, including continuing medication, augmentation of medication or psychological treatment (CBT). Treatment choice should be influenced by:

- Previous treatment history, including the consequences of a relapse, residual symptoms, response to previous treatment and any discontinuation symptoms
- The person's preference

Using Medication for Relapse Prevention

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

- They have had two or more episodes of depression in the recent past, during which they experienced significant functional impairment
- They have other risk factors for relapse such as residual symptoms, multiple previous episodes, or a history of severe or prolonged episodes or of inadequate response
- The consequences of relapse are likely to be severe (for example, suicide attempts, loss of functioning, severe life disruption, and inability to work).

When deciding whether to continue maintenance treatment beyond 2 years, re-evaluate with the person with depression, taking into account age, comorbid conditions and other risk factors.

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

- Comorbid conditions
- Risk factors for relapse
- Severity and frequency of episodes of depression

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

Psychological Interventions for Relapse Prevention

People with depression who are considered to be at significant risk of relapse (including those who have relapsed despite antidepressant treatment or who are unable or choose not to continue antidepressant treatment) or who have residual symptoms, should be offered one of the following psychological interventions:

- Individual CBT for people who have relapsed despite antidepressant medication and for people with a significant history of depression and residual symptoms despite treatment
- Mindfulness-based cognitive therapy for people who are currently well but have experienced three or more previous episodes of depression

Delivering Psychological Interventions for Relapse Prevention

For all people with depression who are having individual CBT for relapse prevention, the duration of treatment should typically be in the range of 16 to 20 sessions over 3 to 4 months. If the duration of treatment needs to be extended to achieve remission it should:

- Consist of two sessions per week for the first 2 to 3 weeks of treatment
- Include additional follow-up sessions, typically consisting of four to six sessions over the following 6 months.

Mindfulness-based cognitive therapy should normally be delivered in groups of 8 to 15 participants and consist of weekly 2-hour meetings over 8 weeks and four follow-up sessions in the 12 months after the end of treatment.

Stopping or Reducing Antidepressants

Advise people with depression who are taking antidepressants that discontinuation symptoms may occur on stopping, missing doses or, occasionally, on reducing the dose of the drug. Explain that symptoms are usually mild and self-limiting over about 1 week, but can be severe, particularly if the drug is stopped abruptly. (Discontinuation symptoms include increased mood change, restlessness, difficulty sleeping, unsteadiness, sweating, abdominal symptoms and altered sensations.)

When stopping an antidepressant, gradually reduce the dose, normally over a 4-week period, although some people may require longer periods, particularly with drugs with a shorter half-life (such as paroxetine and venlafaxine). This is not required with fluoxetine because of its long half-life.

Inform the person that they should seek advice from their practitioner if they experience significant discontinuation symptoms. If discontinuation symptoms occur:

- Monitor symptoms and reassure the person if symptoms are mild
- Consider reintroducing the original antidepressant at the dose that was effective (or another antidepressant with a longer half-life from the same class) if symptoms are severe, and reduce the dose gradually while monitoring symptoms.

Step 4: Complex and Severe Depression

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

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

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

In specialist mental health services, after thoroughly reviewing previous treatments for depression, consider reintroducing previous treatments that have been inadequately delivered or adhered to.

Use crisis resolution and home treatment teams to manage crises for people with severe depression who present significant risk, and to deliver high-quality acute care. The teams should monitor risk as a high-priority routine activity in a way that allows people to continue their lives without disruption.

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

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

care plan should:

- Identify clearly the roles and responsibilities of all health and social care professionals involved
- Develop a crisis plan that identifies potential triggers that could lead to a crisis and strategies to manage such triggers
- Be shared with the GP and the person with depression and other relevant people involved in the person's care.

Inpatient Care, and Crisis Resolution and Home Treatment Teams

Consider inpatient treatment for people with depression who are at significant risk of suicide, self-harm or self-neglect.

The full range of high-intensity psychological interventions should normally be offered in inpatient settings. However, consider increasing the intensity and duration of the interventions and ensure that they can be provided effectively and efficiently on discharge.

Consider crisis resolution and home treatment teams for people with depression who might benefit from early discharge from hospital after a period of inpatient care.

Pharmacological Management of Depression with Psychotic Symptoms

For people who have depression with psychotic symptoms, consider augmenting the current treatment plan with antipsychotic medication (although the optimum dose and duration of treatment are unknown).

Electroconvulsive Therapy (ECT)

The recommendations in this section update the depression aspects only of 'Guidance on the use of electroconvulsive therapy' (NICE technology appraisal guidance 59).

Consider ECT for acute treatment of severe depression that is life-threatening and when a rapid response is required, or when other treatments have failed.

Do not use ECT routinely for people with moderate depression but consider it if their depression has not responded to multiple drug treatments and psychological treatment.

For people whose depression has not responded well to a previous course of ECT, consider a repeat trial of ECT only after:

- Reviewing the adequacy of the previous treatment course
- Considering all other options
- Discussing the risks and benefits with the person and/or, where appropriate, their advocate or carer.

When considering ECT as a treatment choice, ensure that the person with depression is fully informed of the risks associated with ECT, and with the risks and benefits specific to them. Document the assessment and consider:

- The risks associated with a general anaesthetic.
- Current medical comorbidities
- Potential adverse events, notably cognitive impairment
- The risks associated with not receiving ECT.

The risks associated with ECT may be greater in older people; exercise particular caution when considering ECT treatment in this group.

A decision to use ECT should be made jointly with the person with depression as far as possible, taking into account, where applicable, the requirements of the Mental Health Act 2007. Also be aware that:

- Valid informed consent should be obtained (if the person has the capacity to grant or refuse consent) without the pressure or coercion that might occur as a result of the circumstances and clinical setting.
- The person should be reminded of their right to withdraw consent at any time.
- There should be strict adherence to recognized guidelines about consent, and advocates or carers should be involved to facilitate informed discussions.
- If informed consent is not possible, ECT should only be given if it does not conflict with a valid advance

decision, and the person's advocate or carer should be consulted.

The choice of electrode placement and stimulus dose related to seizure threshold should balance efficacy against the risk of cognitive impairment. Take into account that:

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

Assess clinical status after each ECT treatment using a formal valid outcome measure, and stop treatment when remission has been achieved, or sooner if side effects outweigh the potential benefits.

Assess cognitive function before the first ECT treatment and monitor at least every three to four treatments, and at the end of a course of treatment.

Assessment of cognitive function should include:

- Orientation and time to reorientation after each treatment
- Measures of new learning, retrograde amnesia and subjective memory impairment carried out at least 24 hours after a treatment.

If there is evidence of significant cognitive impairment at any stage consider, in discussion with the person with depression, changing from bilateral to unilateral electrode placement, reducing the stimulus dose or stopping treatment depending on the balance of risks and benefits.

If a person's depression has responded to a course of ECT, antidepressant medication should be started or continued to prevent relapse. Consider lithium augmentation of antidepressants.

Transcranial Magnetic Stimulation

Current evidence suggests that there are no major safety concerns associated with transcranial magnetic stimulation (TMS) for severe depression. There is uncertainty about the procedure's clinical efficacy, which may depend on higher intensity, greater frequency, bilateral application and/or longer treatment durations than have appeared in the evidence to date. TMS should therefore be performed only in research studies designed to investigate these factors. (This recommendation is taken from 'Transcranial magnetic stimulation for severe depression' [NICE interventional procedure guidance 242]).

CLINICAL ALGORITHM(S)

None provided

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EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Recommendations are based on clinical and cost effectiveness evidence, and where this is insufficient, the Guideline Development Group (GDG) used all available information sources and experience to make consensus recommendations.

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IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

National Collaborating Centre for Mental Health. Depression. The treatment and management of depression in adults. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Oct. 64 p. (Clinical guideline; no. 90).

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 (revised 2009 Oct)

GUIDELINE DEVELOPER(S)

National Collaborating Centre for Mental Health - National Government Agency [Non-U.S.]

SOURCE(S) OF FUNDING

National Institute for Health and Clinical Excellence (NICE)

GUIDELINE COMMITTEE

Guideline Development Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

The Guideline Development Group: Professor Ian Anderson (Chair, Guideline Development Group), Professor of Psychiatry, University of Manchester; Professor Stephen Pilling, Joint Director, National Collaborating Centre for Mental Health; Director, Centre for Outcomes Research and Effectiveness, University College London; Ms Alison Barnes, Service user member; Ms Linda Bayliss, Research Assistant (May 2008 to August 2008), National Collaborating Centre for Mental Health; Ms Victoria Bird, Research Assistant, National Collaborating Centre for Mental Health; Ms Rachel Burbeck, Lead Systematic Reviewer, National Collaborating Centre for Mental Health; Dr Carolyn Chew-Graham, General Practitioner, Senior Lecturer in Primary Care, University of Manchester; Mr Jeremy Clarke, Psychological therapist, Lambeth Primary care Trust; Mr Matthew Dyer, Health Economist, National Collaborating Centre for Mental Health; Ms Esther Flanagan, Project Manager (2009), National Collaborating Centre for Mental Health; Ms Catherine Harris, Carer member and Local Councillor; Ms Sarah Hopkins, Project Manager (until 2008), National Collaborating Centre for Mental Health; Dr Mark Kenwright, Consultant Cognitive Behavioural Psychotherapist; Ealing Cognitive Behavioural Therapy Service; Professor Willem Kuyken, Professor of Clinical Psychology and Co-Director Mood Disorders Centre, University of Exeter Psychology; Ms Angela Lewis, Research Assistant, National Collaborating Centre for Mental Health; Professor Glyn Lewis, Professor of Psychiatric Epidemiology, University of Bristol; Mr Ryan Li, Project Manager (2008), National Collaborating Centre for Mental Health; Mr Brendan Masterson, Clinical Nurse Leader, Affective Disorders Unit, Bethlem Royal Hospital; Dr Nick Meader, Systematic Reviewer, National Collaborating Centre for Mental Health; Mr Alan Meudell, Service user member, Healthy Minds at Work; Dr Alex Mitchell, Consultant Psychiatrist and Honorary lecturer in liaison psychiatry, University of Leicester; Dr Richard Moore, Clinical Psychologist, Cambridge; Dr Suffiya Omarjee, Health Economist, National Collaborating Centre for Mental Health; Ms Carol Paton, Chief Pharmacist, Oxleas NHS Foundation Trust; Dr Alejandra Perez, Systematic Reviewer, National Collaborating Centre for Mental Health; Ms Maria Rizzo, Research Assistant, National Collaborating Centre for Mental Health; Ms Peny Retsa, Health Economist (until 2008), National Collaborating Centre for Mental Health; Ms Jennie Robertson, Research Assistant (from September 2008), National Collaborating Centre for Mental Health; Mr Rob Saunders, Research Assistant, National Collaborating Centre for Mental Health (2008); Ms Christine Sealey, Centre Manager, National Collaborating Centre for Mental Health; Ms Beth Shackleton, Project Manager, National Collaborating Centre for Mental Health (until 2008); Dr Thomas Shackleton, General Practitioner, Suffolk; Ms Sarah Stockton, Senior Information Scientist, National Collaborating Centre for Mental Health; Dr Clare Taylor Editor, National Collaborating Centre for Mental Health; Ms Jane Wood, Nurse, Strategic Development Manager, Mental Health, Leeds Primary Care Trust

Guideline Review Panel: Mr Peter Robb (Chair), Consultant Ear, Nose and Throat Surgeon, Epsom and St Helier University Hospitals and The Royal Surrey County NHS Trusts; Mr John Seddon, Lay member; Dr Christine Hine, Consultant in Public Health (Acute Commissioning), Bristol and South Gloucestershire Primary Care Trusts (PCTs); Dr Greg Rogers, GP, Kent; Dr John Harley, Clinical Governance and Prescribing Lead and GP, North Tees PCT

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

With a range of practical experience relevant to depression in the Guideline Development Group (GDG), members were appointed because of their understanding and expertise in healthcare for people with depression and support for their families and carers, including: scientific issues; health research; the delivery and receipt of healthcare, along with the work of the healthcare industry; and the role of professional organisations and organisations for people with depression and their families and carers.

To minimise and manage any potential conflicts of interest, and to avoid any public concern that commercial or

other financial interests have affected the work of the GDG and influenced guidance, members of the GDG must declare as a matter of public record any interests held by themselves or their families which fall under specified categories. These categories include any relationships they have with the healthcare industries, professional organisations and organisations for people with depression and their families and carers.

Individuals invited to join the GDG were asked to declare their interests before being appointed. To allow the management of any potential conflicts of interest that might arise during the development of the guideline, GDG members were also asked to declare their interests at each GDG meeting throughout the guideline development process. The interests of all the members of the GDG are listed in Appendix 2 of the full version of the original guideline document (see "Availability of Companion Documents" field), including interests declared prior to appointment and during the guideline development process.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates previous versions: National Collaborating Centre for Mental Health. Depression: management of depression in primary and secondary care. London (UK): National Institute for Clinical Excellence (NICE); 2004. 67 p. [634 references]

National Collaborating Centre for Mental Health. Depression: management of depression in primary and secondary care. London (UK): National Institute for Clinical Excellence (NICE); 2007 Apr. 67 p. (Clinical guideline; no. 23).

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Depression: treatment and management of depression in adults, including adults with a chronic physical health problem. Quick reference guide. London (UK): National Institute for Health and Clinical Excellence; 2009 Oct. 27 p. (Clinical guideline; no. 90 and 91). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.

Print copies: Phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and ref: N2016.

The following are also available:

- Depression: the treatment and management of depression in adults. Full guideline. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009. 585 p. (Clinical guideline; no. 90). Electronic copies: Available in Portable Document Format (PDF) format from the National Institute for Health and Clinical Excellence (NICE) Web site.
- Depression in adults. Appendices to full version. London (UK): National Institute for Health and Clinical Excellence; 2009 Oct. Various p. (Clinical guideline; no. 90). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Depression in adults. Costing statement. London (UK): National Institute for Health and Clinical Excellence; 2009 Oct. Various p. (Clinical guideline; no. 90). Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.
- Depression in adults. Slide set. London (UK): National Institute for Health and Clinical Excellence; 2009. 21 p. (Clinical guideline; no. 90). Electronic copies: Available from the NICE Web site.
- Depression in adults. Audit support. London (UK): National Institute for Health and Clinical Excellence; 2009. 20 p. (Clinical guideline; no. 90). Electronic copies: Available from the NICE Web site.
- The guidelines manual 2009. London (UK): National Institute for Health and Clinical Excellence (NICE); 2009 Jan. Electronic copies: Available in Portable Document Format (PDF) from the NICE Web site.

PATIENT RESOURCES

The following is available:

- Treating depression in adults: understanding NICE guidance--information for people who use NHS services. National Institute for Clinical Excellence (NICE), 2009 Oct. 24 p. Available in English and Welsh from the

National Institute for Health and Clinical Excellence (NICE) Web site.

Print copies: phone NICE publications on 0845 003 7783 or email publications@nice.org.uk and refer to N2017.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on February 14, 2005. The information was verified by the guideline developer on September 5, 2006. This summary was updated by ECRI on November 22, 2006, following the FDA advisory on Effexor (venlafaxine HCl). This NGC summary was updated by ECRI Institute on April 16, 2010.

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