



MINISTRY OF HEALTH
SINGAPORE

Depression

MOH Clinical Practice Guidelines 1/2012



College of Family
Physicians, Singapore



Chapter of Psychiatrists
Academy of Medicine,
Singapore



College of Physicians,
Academy of Medicine,
Singapore



Singapore Medical
Association

Jan 2012

Levels of evidence and grades of recommendation

Levels of evidence

Level	Type of Evidence
1 ⁺⁺	High quality meta-analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1 ⁺	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1 ⁻	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2 ⁺⁺	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2 ⁺	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2 ⁻	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Grades of recommendation

Grade	Recommendation
A	At least one meta-analysis, systematic review of RCTs, or RCT rated as 1 ⁺⁺ and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1 ⁺ , directly applicable to the target population, and demonstrating overall consistency of results
B	A body of evidence including studies rated as 2 ⁺⁺ , directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1 ⁺⁺ or 1 ⁺
C	A body of evidence including studies rated as 2 ⁺ , directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2 ⁺⁺
D	Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2 ⁺
GPP (good practice points)	Recommended best practice based on the clinical experience of the guideline development group.

CLINICAL PRACTICE GUIDELINES

Depression

MOH Clinical Practice Guidelines 1/2012

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Statement of Intent

These guidelines are not intended to serve as a standard of medical care. Such standards are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.

The contents of this publication are guidelines for clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case. These guidelines should neither be construed as including all proper methods of care, nor exclude other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient, in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

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Foreword

Depression is a major health problem which impairs psychosocial and occupational functioning, and is associated with significant morbidity and mortality. In the 2004 Global Burden of Disease Study, depression was found to be the third leading cause of burden of disease worldwide and the top leading cause of burden of disease in middle and high income countries.* Likewise, depression is a major health problem in Singapore, with the 2010 Singapore National Mental Health Survey reporting a 6.3% lifetime prevalence of depression in the Singapore adult population.

The first edition of the MOH clinical practice guidelines on depression was published in 2004 to provide evidence-based guidance for the management of patients with depression. This second edition of the guidelines updates and expands the first edition with new evidence. Screening and diagnostic instruments are discussed in greater detail, and a new section providing guidance on the management of depression in pregnant patients has been added.

I hope that this set of guidelines will be able to assist people with depression and all healthcare professionals that care for them.

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DIRECTOR OF MEDICAL SERVICES**

*World Health Organization. The global burden of disease: 2004 update. 2008 [cited 2011 Oct 20]. Available from: http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/

Executive summary of recommendations

Details of recommendations can be found in the main text at the pages indicated.

Clinical evaluation

D The basic assessment of depression includes the history, the mental state examination and physical examination.

- Take a detailed history of the presenting symptoms and determine the severity and duration of the depressive episode. Establish history of prior episodes, prior manic or hypomanic episodes, substance abuse and other psychiatric illnesses. Look out for co-existing medical conditions. Check for family history of mental illness, depression and suicide. Establish the personal history and the available supports and resources. Evaluate functional impairment and determine life events and stressors.
- Do a mental state examination. This includes an evaluation of the severity of symptoms and assessment for psychotic symptoms. All assessments of depression will include an assessment of the risk of suicide, self-harm and risk of harm to others.
(See Annex II on pg 58).
- Do a physical examination to exclude a medical or surgical condition.
- Laboratory testing may be indicated if there is a need to rule out medical conditions that may cause similar symptoms.
(pg 20)

Grade D, Level 4

D Screening for depression may be beneficial when it is done in high-risk populations (such as individuals with significant physical illnesses causing disability) where the benefits outweigh the risks (pg 21).

Grade D, Level 4

C The PHQ-9 (patient health questionnaire 9) may be used to screen for depression in primary care (pg 21).

Grade C, Level 2+

D Referrals to a specialist are warranted when:

- there are co-morbid medical conditions for which expertise is required regarding drug-drug interactions,
 - there is diagnostic difficulty,
 - one or two trials of medication have failed,
 - augmentation or combination therapy is needed,
 - there are co-morbid substance abuse or severe psychosocial problems,
 - psychotic symptoms are present, or
 - specialised treatment like electroconvulsive therapy is indicated.
- (pg 22)

Grade D, Level 4

Principles of treatment

GPP Consider using the Clinical Global Impression scales (both severity and improvement component scales) to measure illness severity and treatment progress during consultations (pg 25).

GPP

Pharmacotherapy

A Antidepressants should be recommended as a first-line treatment in patients with moderate to severe depression, or sub-threshold depression that has persisted for 2 years or more (pg 26).

Grade A, Level 1+

D Antidepressants are a treatment option in short duration mild depression in adults and should be considered if there is a history of moderate to severe recurrent depression or if the depression persists for more than 2–3 months (pg 26).

Grade D, Level 4

D If the patient has previously responded well to and has had minimal side-effects with a drug, that drug is preferred. Alternatively, if the patient has previously failed to respond to an adequate trial of one antidepressant or found the side-effects of an antidepressant intolerable, that medication should generally be avoided (pg 27).

Grade D, Level 4

A Once an antidepressant has been selected, start with a low dose and titrate gradually to the full therapeutic dose, while assessing patients' mental state and watching for side-effects. The frequency of monitoring depends on the severity of the depression, suicide risk, the patient's cooperation and the availability of social support (pg 27).

Grade A, Level 1+

A A selective serotonin reuptake inhibitor (SSRI) antidepressant should be used as a first-line medication for treating depression, due to its favourable risk-benefit ratio, greater tolerability and safety in overdose (pg 28).

Grade A, Level 1++

A Selective serotonin reuptake inhibitor (SSRI) antidepressants should be prescribed as a first line medication for depression in patients with concomitant cardiovascular diseases due to their favourable risk-benefit ratio (pg 28).

Grade A, Level 1++

A The “newer” antidepressants can also be considered as other first-line options for treating depression. They include:

- Serotonin and Norepinephrine Reuptake Inhibitors (SNRI) (e.g. venlafaxine)
- Noradrenergic and Specific Serotonergic Antidepressants (NaSSA) (e.g. mirtazapine)
- Norepinephrine and Dopamine Reuptake Inhibitors (NDRI) (e.g. bupropion) (pg 28)

Grade A, Level 1+

D Where there are interactions with other drugs, use of escitalopram or sertraline should be considered as they have fewer propensities for interactions, appear to be safe and possibly protective of further cardiac events (pg 28).

Grade D, Level 4

A Due to their cardiotoxic adverse effect risks, tricyclic antidepressants (TCA) should be avoided in patients at high risk of cardiovascular disease, arrhythmias and cardiac failure (pg 29).

Grade A, Level 1++

A Older tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) should be reserved for situations when first-line medication treatment has failed (pg 29).

Grade A, Level 1+

B A new class of antidepressants, known as melatonin agonists, e.g. Agomelatine, may also be considered as an alternative treatment option for depression, if first-line medication is unsuitable or has failed (pg 29).

Grade B, Level 1+

D When an antidepressant is to be prescribed, tailor it to the patient with depression and a chronic physical health problem, and take into account the following:

- the presence of additional physical health disorders.
- the side effects of antidepressants, which may impact on the underlying physical disease (in particular, selective serotonin reuptake inhibitors may result in or exacerbate hyponatraemia, especially in older people.
- interactions with other medications.

(pg 29)

Grade D, Level 3

C The emergence of suicidal thinking and behaviour, or unusual changes in behaviour should be monitored during the early phases (generally the first 1-2 months) of antidepressant treatment, especially in children, adolescents and young adults between 18 to 24 years old (pg 29).

Grade C, Level 2+

A Initial and short-term (2-4 week) usage of a benzodiazepine together with an antidepressant may be considered where anxiety, agitation and/or insomnia becomes problematic to patients with depression (pg 30).

Grade A, Level 1++

C All antidepressants, once started, should be continued for at least 4 to 6 weeks (pg 30).

Grade C, Level 2+

A Patients with first episode of depression without psychotic symptoms should be treated with antidepressants at full treatment dose for 6-9 months after remission of symptoms (pg 30).

Grade A, Level 1++

B Patients who have a second episode of depression should be maintained on treatment for 1-2 years - the duration may depend on the risk factors for recurrence and the patient preference (pg 31).

Grade B, Level 1+

C Patients with more than two episodes of depression should be maintained on treatment for 2 years or longer, or even lifelong - the duration may depend on the risk factors for recurrence and the patient preference (pg 31).

Grade C, Level 2+

GPP Maintenance antidepressant treatment should be carried on for as long as necessary (pg 31).

GPP

B Using higher antidepressant doses may be helpful for patients who have shown a partial response and when only low or modest doses have been tried. The patient should be closely monitored for side-effects with the increase in dose (pg 32).

Grade B, Level 2++

B Switching is preferred to augmentation as an initial strategy in accordance with general principles that combinations should preferably not be used when monotherapy will suffice (pg 32).

Grade B, Level 2++

A Both switching within the class (i.e. from a selective serotonin reuptake inhibitor to another), as well as switching from a selective serotonin reuptake inhibitor to a different class of antidepressants, may be done as both have been found beneficial (pg 32).

Grade A, Level 1++

GPP When switching medications, clinicians should be vigilant for the onset of drug-drug interactions (e.g. Serotonin syndrome) and drug discontinuation reaction (pg 32).

GPP

A Lithium augmentation and thyroid hormone augmentation (using levothyroxine or triiodothyromine) are two traditional augmentation strategies that may be used for patients who have had previous antidepressant trials and have not responded to adequate trials of other individually prescribed antidepressants (pg 33).

Grade A, Level 1++

A When discontinuing antidepressants, antidepressants should be gradually tapered off instead of suddenly stopped, to reduce side effects of discontinuation (pg 33).

Grade A, Level 1++

Psychotherapy

A Psychotherapy alone is as efficacious as antidepressant medication in patients with mild to moderate major depression and may be used as first-line treatment (pg 34).

Grade A, Level 1++

A Cognitive-behavioural therapy is recommended when the depressed patient has distorted negative thoughts (pg 35).

Grade A, Level 1++

B Cognitive-behavioural therapy is also an effective maintenance treatment and is recommended for patients with recurrent depression who are no longer on medication (pg 35).

Grade B, Level 1+

Interpersonal therapy

B Interpersonal therapy is recommended for depressed patients with interpersonal difficulties (pg 35).

Grade B, Level 1+

A Psychodynamic-interpersonal therapy is a viable alternative treatment for depressed patients with interpersonal difficulties (pg 36).

Grade A, Level 1+

A Long-term psychodynamic psychotherapy is recommended for depressed patients with co-morbid personality disorder (pg 36).

Grade A, Level 1++

A Problem-solving therapy is recommended for primary care patients with mild depression (pg 36).

Grade A, Level 1++

A Cognitive-behavioural therapy or psychodynamic interpersonal therapy should be delivered for a longer period (i.e. 16 weeks or longer) when the depression is severe (pg 37).

Grade A, Level 1+

D If a moderate improvement, at least, is not observed after 4-8 weeks of psychotherapy, a thorough review of the diagnosis, complicating conditions and issues, and treatment plan should be conducted. If there is no response, consider adding or changing to medication. If there is partial response, consider changing the intensity of psychotherapy, changing the type of psychotherapy, or adding or changing to medication (pg 37).

Grade D, Level 4

Psychoeducation and family intervention

A The following should be done:

- a. Educating the patient about the illness helps clarify uncertainty and misconceptions. Depression should be explained as a medical illness that is associated with changes in neurochemicals and brain functioning.
- b. Adequate follow-up improves treatment adherence, allows closer monitoring and earlier detection of changes in condition.
- c. Discuss the type and duration of treatment. If antidepressants are used it is advisable to explain that they are not addictive. Provide information on the different types of antidepressants available and about the possible side-effects.
- d. Advise on lifestyle changes such as exercise and reducing stress. (pg 38)

Grade A, Level 1++

GPP Where indicated and with patients' agreement, involve family members or friends in the care of people with depression so that there is adequate support (pg 38).

GPP

A Marital or couple therapy is effective and should be considered for patients with significant marital distress (pg 38).

Grade A, Level 1+

Electroconvulsive therapy

A Electroconvulsive therapy is an effective **short-term treatment** for major depressive disorder and should be considered in patients who have not responded to antidepressant therapy (pg 41).

Grade A, Level 1++

A Patients should be maintained on antidepressants following a successful response to electroconvulsive therapy (pg 41).

Grade A, Level 1+

D Electroconvulsive therapy may be considered as a **first-line treatment** for severely depressed patients with severe psychomotor retardation (associated with food refusal leading to nutritional compromise and dehydration), active suicidality and psychotic features (pg 41).

Grade D, Level 3

D Electroconvulsive therapy may also be considered in situations when a particularly rapid antidepressant response is required, such as in pregnancy and in those with comorbid medical conditions that preclude the use of antidepressant medications (pg 42).

Grade D, Level 3

Depression in children and adolescents

D Self-administered rating scales (or questionnaires) should not be used for diagnosis, but may be used for screening of symptoms, assessing severity and monitoring improvement in older children and adolescents (pg 43).

Grade D, Level 4

D When faced with a suicidal adolescent, doctors should maintain contact, ensure close supervision and engage support systems such as family and school, and consider a “no harm” contract if the adolescent is willing (pg 44).

Grade D, Level 4

D Hospitalization is indicated if suicide risk is high, support is unavailable and there are severe symptoms of depression (pg 44).

Grade D, Level 4

A Psychosocial interventions are recommended in initial treatment of depression in children and adolescents based on the literature and local clinical experience (pg 44).

Grade A, Level 1++

D Medication should not be the only treatment given to children and adolescents with depression but care should be given to increasing self esteem, coping skills to handle stress, adapting to the changes in life and improving relationships between family members and peers. Use of medications should be cautious and not necessarily first-line treatment for major depressive disorder (pg 45).

Grade D, Level 3

D Medications are usually indicated for children and adolescents with severe depression, who have psychotic symptoms or who have failed psychotherapy (pg 45).

Grade D, Level 4

C Selective Serotonin Reuptake Inhibitors (SSRIs) should be used with caution in children and adolescents (pg 45).

Grade C, Level 2+

A Combination of psychosocial interventions and SSRIs may be considered for moderate to severe depression in children and adolescents (pg 45).

Grade A, Level 1++

A Other antidepressants such as venlafaxine may be considered as second line treatment of depression in children and adolescents (pg 46).

Grade A, Level 1++

GPP Referral of a child or adolescent with depression to a psychiatrist could be considered in any of the following situations:

- failure to improve with psychosocial interventions or requiring specialised psychological interventions.
 - failure to improve after at least 4 weeks of medication treatment at maximum tolerated dose.
 - severe symptoms such as clear suicidal intention, disruptive psychotic symptoms.
- (pg 46)

GPP

Depression in pregnancy

C Consider using these two questions to effectively identify possible depression in pregnant and postpartum women:

1. “During the past month, have you often been bothered by feeling down, depressed or hopeless?”
2. “During the past month, have you often been bothered by having little interest or pleasure in doing things?”

If the woman answers “yes” to either question, consider asking this: “Is this something you feel you need or want help with?”
(pg 47, 48)

Grade C, Level 2+

D It is strongly recommended that specialist psychiatric care be arranged for pregnant or postpartum women with:

- past or present severe mental illness including schizophrenia, bipolar disorder, psychosis in the postnatal period and severe depression.
 - previous treatment by a psychiatrist/specialist mental health team including inpatient care.
 - a family history of maternal perinatal mental illness.
- (pg 48)

Grade D, Level 4

D Psychological therapies (including non-directive counselling and support) should be maximised as the first-line treatment strategy for peripartum depression and medication should be considered only in severe depression (pg 48).

Grade D, Level 4

D Early referral to a specialist with expertise in perinatal mental health is recommended for women with new-onset peripartum depression, unless it is mild (pg 49).

Grade D, Level 4

D Abrupt cessation of antidepressant medication for women with pre-existing depression can precipitate withdrawal symptoms that can be distressing. It is preferable to advise patients to reduce antidepressant dose to half first whilst arranging for referral (pg 49).

Grade D, Level 4

D Early referral to a psychiatrist with expertise in perinatal mental health is recommended for women with peripartum depression and pre-existing depressive illness (pg 49).

Grade D, Level 4

Depression in the elderly

D Referrals of elderly patients to specialists should be considered:

- when the diagnosis is in doubt,
 - when the depression is severe (as evidenced by psychotic depression, severe risk to health because of failure to eat or drink and suicidal risk),
 - when complex therapy is indicated as in cases with medical comorbidity, and
 - when the patient does not respond to an adequate antidepressant trial.
- (pg 50)

Grade D, Level 4

A Antidepressants are recommended in dysthymia as well as for mild to severe depression in the elderly. There is no difference in efficacy between the classes of antidepressants in the treatment of the elderly (pg 50).

Grade A, Level 1++

A Selective serotonin reuptake inhibitors (SSRIs) are recommended over tricyclic antidepressants (TCAs) as the first-line treatment choice for late-life depression (pg 51).

Grade A, Level 1++

B In frail elderly patients it is advisable to “start low, go slow”. In the acute phase at least six weeks of treatment may be needed to achieve optimal therapeutic effect (pg 51).

Grade B, Level 1+

B For frail elderly patients, a continuation period on the same dosage that improved them for 12 months is recommended for a first onset of major depression, longer for a recurrent episode. The duration of treatment is similar to the adult age group in the continuation and maintenance phases (pg 51).

Grade B, Level 1+

B Psychological interventions should be provided for the elderly with mild to moderate major depression (pg 51).

Grade B, Level 1+

B In severe major depression in the elderly, combination antidepressant and psychotherapy treatment is recommended (pg 51).

Grade B, Level 1+

B Supportive care should be offered to elderly patients and where relevant, their caregivers (pg 52).

Grade B, Level 1+

B Electroconvulsive therapy is indicated in the elderly:

- when the patient is actively suicidal,
 - when there is an urgent need to prevent deterioration in health (including food/fluid refusal),
 - in psychotic depression,
 - when there is inadequate response to two trials of medication,
 - when there is intolerance to medication, or
 - when there is good prior response.
- (pg 52)

Grade B, Level 1+

1 Introduction

Depression is a major health problem. It impairs psychosocial and occupational functioning and is associated with significant morbidity and mortality. In the 1990 Global Burden of Disease Study, depression was the fourth leading cause of disability in terms of physical, social and mental impact of disease. It is predicted that depression will become the second most important cause of disability worldwide by the year 2020.¹⁻²

Epidemiological studies have revealed a high prevalence of depression in many communities in the world; international surveys report that 9-20% of the population may be affected during their lifetime.^{3,4} In Singapore, the prevalence of depression was estimated (in 1998) to be 8.6% in adults and 5.7% in the elderly.^{5,6} Nation-wide epidemiological surveys done in 2003/4 revealed that the prevalence of depression was 4.9% in adults and 3.1% in elderly populations.^{7,8} The 2010 Singapore National Mental Health Survey reported that the lifetime prevalence of depression in Singapore adults was 6.3%.

Depression is a recurrent disorder. Each additional depressive episode increases the probability of subsequent episodes with a more rapid onset.⁹ The estimated risk of recurrence is 50%, 80-90% and greater than 90% after one, two and three episodes respectively.¹⁰

In addition, co-morbidity is an important clinical finding in depression and is associated with increased disease severity and a poorer prognosis.¹¹ Depression can co-exist with many medical conditions such as cancers (25-38%), diabetes (24%), coronary artery disease (16-19%), other psychiatric disorders, and may even be associated with medication use (See Annex I on pg 56). A local study of depression in diabetes revealed that 31% of diabetes sufferers in a specialist outpatient clinic also had depression.¹²

The most serious complication of depression is suicide. The lifetime risk of suicide in mood disorders has been estimated to be 10-15% and the risk of attempted suicide was increased 41-fold in depressed patients compared with those with other diagnoses.^{13,14} A recent review of suicides in Asia suggested that improving the accessibility and delivery of mental health services, and promoting responsible

media reporting of suicide are key initiatives in the efforts to reduce suicides in all communities.¹⁵

Unfortunately, under-recognition and under-treatment of depression are serious clinical issues requiring our attention. The 2003/4 epidemiological surveys in Singapore showed that only about 50% of individuals found to have depression were receiving any kind of treatment for their problem.¹⁶ It has also been estimated that 30-50% of cases of depression in primary care and medical settings are not detected.¹⁷ This is because a depressed mood may not necessarily be the presenting symptom. Instead multiple somatic complaints, co-existing medical or psychiatric illness, stressors and life-events may obscure the depression. A high index of suspicion and alertness is therefore crucial for recognition and diagnosis.

1.1 Aim

These guidelines are developed to raise awareness and assist in the detection of depression, and to ensure that treatment of depression is appropriate and effective.

1.2 Scope

These guidelines will cover the management of depression in children, adults, the elderly, and depression in pregnancy. Management of depression in bipolar disorder, psychotic depression and cases with high suicide risk are not included in these guidelines.

1.3 Target group

The content of the guidelines will be useful for all doctors treating patients with depression and will be a resource for allied health and nursing staff who assist in the care of depressed people. Efforts have been made to ensure that the guidelines are particularly useful for primary care physicians (family practitioners) who have an important role in the management of mild to moderate and stable mental health disorders in the community. The doctor treating the patient is ultimately responsible for the treatment decisions which should be made after reviewing the patient's history, clinical presentation and treatment options available.

1.4 Development of guidelines

These guidelines have been produced by a committee of psychiatrists, clinical psychologists, pharmacists, medical social worker, patient representative and a family practitioner appointed by the Ministry of Health. They were developed by the adaptation of existing guidelines, by the review of relevant literature and by expert clinical consensus with consideration of local practice.

The following principles underlie the development of these guidelines:

- Treatment recommendations are supported by scientific evidence whenever possible (randomised controlled clinical trials represent the highest level of evidence) and expert clinical consensus is used when such data are lacking.
- Treatment should maximise therapeutic benefits and minimise side effects.

1.5 What's new in the revised guidelines

This edition of the guidelines contains updated recommendations based on latest evidence, as well as detailed discussions and recommendations on the management of depression in the following populations:

- children and adolescents
- pregnant women
- the elderly

1.6 Review of guidelines

Evidence-based clinical practice guidelines are only as current as the evidence that supports them. Users must keep in mind that new evidence could supersede recommendations in these guidelines. The workgroup advises that these guidelines be scheduled for review five years after publication, or when new evidence appears that requires substantive changes to the recommendations.

2 Clinical evaluation

2.1 Diagnosis and types of depression

The term “depression” is used to describe a normal emotional experience as well as a disorder. Normal sadness or unhappiness is, however, different from the nature, experience and severity of depressive symptoms in a disorder. The depressed mood in a depressive disorder is more pervasive, yielding affective, cognitive and somatic symptoms. They cause clinically significant distress and/or impairment in social, occupational and other areas of functioning.

2.1.1 Diagnostic criteria

The symptoms of depression are:

- Sleep increase/decrease
- Interest in formerly compelling or pleasurable activities diminished
- Guilt, low self esteem
- Energy poor
- Concentration poor
- Appetite increase/decrease
- Psychomotor agitation or retardation
- Suicidal ideation

The mnemonic **SIGECAPS** is a convenient way to remember them.

Both the DSM-IV and the ICD-10 require the presence of either a depressed mood or a loss of interest or pleasure together with other symptoms for 2 or more weeks for a diagnosis of depression.

DSM-IV¹⁸ Criteria for 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).

DSM-IV¹⁸ Criteria for major depressive episode (continuation)

(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 psychomotor retardation.

Major depressive disorder is a condition characterized by one or more major depressive episodes without a history of manic, mixed, or hypomanic episodes. These major depressive episodes are not due to a medical condition, medication, abused substance, or psychosis.

When depressed mood or loss of interest is present with 2 (or more) of the above symptoms most days for 2 or more years, then a diagnosis of **dysthymia** is made. In **dysthymia**, the depressive symptoms are chronic and longer-term but symptoms are less severe than in major depressive disorder.

Sometimes there are distinct stressors that cause distress and give rise to mild symptoms. When the symptoms of depression develop within 3 months of an identifiable stressor(s) a diagnosis of **adjustment disorder** (with depressed mood) is made.

Some depressive disorders are unique to women. These include **depression with postpartum onset** and **premenstrual dysphoric disorder**. In the latter, depressive and anxiety symptoms together with affective lability and decreased interest in activities usually occur in the last week of the luteal phase and remit within a few days of the onset of menses.

In some depressed patients the presenting features may be quite the opposite and the term **atypical depression** is used. The features are grouped into two, the vegetative features (overeating, oversleeping, weight gain, a mood that still responds to events, extreme sensitivity to interpersonal rejection, a feeling of heaviness in the limbs) and the anxious features (marked anxiety, difficulty falling asleep, phobic symptoms, symptoms of sympathetic arousal).

When diagnosing a major depressive disorder, also known as unipolar depression, it is important to exclude:

1. **Bipolar disorder**, characterised by episode/s of pathologically elevated mood (hypomania, mania);
2. **Secondary mood disorder**: depressive symptoms caused by substance use, medical conditions or medications.
3. **Grief reaction**: Depressed mood following a bereavement. This lacks the pervasiveness of a major depressive disorder, and is related to the loss. The depressive cognitive symptoms (self-blame, low self esteem etc) are typically mild or absent.

2.1.2 Severity

The depressive episode can be classified as mild, moderate or severe according to the number and types of symptoms present during the episode as well as the degree of impairment in social/occupational functioning consequent to the depression. Severe episodes are defined by the presence of most of the depressive symptoms and definite disability (e.g., inability to work). Mild episodes retain the ability to work but with great effort and normally have only five or six depressive symptoms. Moderate episodes have a severity that is intermediate between mild and severe. The presence of psychotic

symptoms qualifies an episode as severe. It is classified as a severe episode with psychotic features.

Validated depression scales are useful in determining the severity of the depression.

2.2 Assessment of depression and mental state examination

D The basic assessment of depression includes the history, the mental state examination and physical examination.¹⁹

- Take a detailed history of the presenting symptoms and determine the severity and duration of the depressive episode. Establish history of prior episodes, prior manic or hypomanic episodes, substance abuse and other psychiatric illnesses. Look out for co-existing medical conditions. Check for family history of mental illness, depression and suicide. Establish the personal history and the available supports and resources. Evaluate functional impairment and determine life events and stressors.
- Do a mental state examination. This includes an evaluation of the severity of symptoms and assessment for psychotic symptoms. All assessments of depression will include an assessment of the risk of suicide, self-harm and risk of harm to others. (See Annex II on pg 58).
- Do a physical examination to exclude a medical or surgical condition.
- Laboratory testing may be indicated if there is a need to rule out medical conditions that may cause similar symptoms.

Grade D, Level 4

2.3 Screening and diagnostic instruments

A range of self-rated and observer-rated questionnaires are available for the evaluation of depression (see Annex III on pg 59). They are useful for screening and/or gauging the severity of the illness and for monitoring symptom change.¹⁹

D Screening for depression may be beneficial when it is done in high-risk populations (such as individuals with significant physical illnesses causing disability) where the benefits outweigh the risks.²⁰

Grade D, Level 4

There is evidence to suggest that screening high risk populations for depression in primary care is beneficial, when coupled with care management programs and appropriate follow-up.^{21,22,23} However, there are concerns that those who are incorrectly identified as being at risk of depression (false positives) are subjected to unnecessary management or treatment.²⁴

C The PHQ-9 (patient health questionnaire 9) may be used to screen for depression in primary care.²⁵ Refer to Annex III for details.

Grade C, Level 2+

It is based on the diagnostic criteria for major depressive disorder in DSM IV. The questionnaire has been validated for use in primary care in Western populations and can also be used to monitor treatment.^{26,27} In recent years, some studies have also shown the questionnaire to be useful in assessing Chinese populations.^{28,29,30} The instrument however has not been validated in local populations.

2.4 Referral to a specialist

A referral to a specialist is indicated when the depression is associated with high suicide risk, in severe postnatal depression, when there are psychotic symptoms present and if the patient has symptoms suggestive of bipolar disorder. The treatment is more urgent and requires a different level of care.³¹⁻³²

D Referrals to a specialist are warranted when:

- there are co-morbid medical conditions for which expertise is required regarding drug-drug interactions,
- there is diagnostic difficulty,
- one or two trials of medication have failed,
- augmentation or combination therapy is needed,
- there are co-morbid substance abuse or severe psychosocial problems,
- psychotic symptoms are present, or
- specialised treatment like electroconvulsive therapy is indicated.

Grade D, Level 4

3 Principles of treatment

Depression is a highly treatable condition. The goals in the treatment of depression are to eliminate the symptoms of depression and to return the patient to his/her previous level of (socio-occupational) functioning.

3.1 Principles of treatment

Treatments for depression can be grouped into several broad categories: pharmacotherapy, psychotherapy, psychoeducation and family intervention, electroconvulsive therapy, and combination treatments. Each treatment has its own benefits and risks. Options from one or more of these categories could be used. Treatment must be appropriate, effective, optimal, associated with minimal adverse effects and acceptable to the patient.

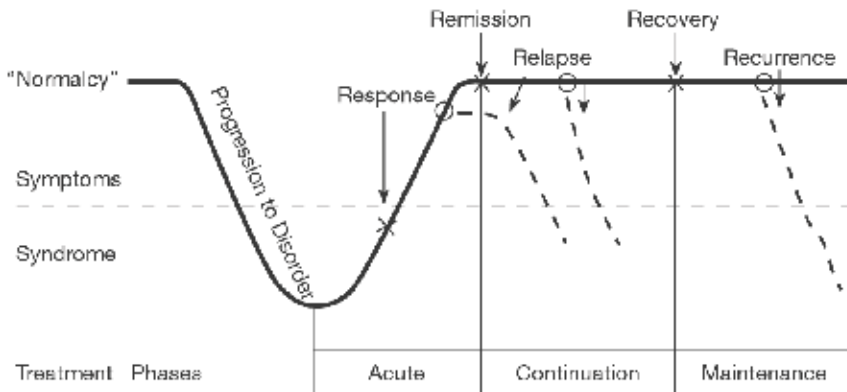
The key initial objectives of treatment are:

- 1) symptomatic remission of all the signs and symptoms of depression,
- 2) restore occupational and psychosocial function and
- 3) reduce the likelihood of relapse and recurrence.

3.2 Phases of treatment

The treatment of depression generally progresses in three phases: acute treatment, continuation treatment and maintenance treatment. The following chart presents the phases of treatment for major depression as well as the progression and risks of relapse and recurrence¹⁰ (see Figure 1 on pg 24).

Figure 1 Phases of treatment of major depression



Source: Kupfer DJ: Long-term treatment of depression. J Clin Psychiatry 1991; 52 (Suppl): 28-34. Copyright 1991. Physicians Postgraduate Press. Adapted and reprinted with permission.

Acute treatment aims to remove all signs and symptoms of the current episode of depression and to restore psychosocial and occupational functioning (a remission). A **remission** (absence of symptoms) may occur either spontaneously or with treatment. If the patient improves significantly, but does not fully remit with treatment, a **response** is declared. If the symptoms return and are severe enough to meet syndromal criteria within 6 months following remission, then a **relapse** (return of symptoms of the current episode) has occurred.

Continuation treatment is intended to prevent this relapse. Once the patient has been asymptomatic for at least 6 months following the acute phase (12 weeks) of an episode, **recovery** from the episode is declared. At recovery, continuation treatment may be stopped. For those with recurrent depressions, however, a new episode (**recurrence**) may occur months or years later.

Maintenance treatment is aimed at preventing a new episode of depression and may be prescribed for 1 year to a lifetime, depending on the likelihood of recurrences.

3.3 Monitoring of outcomes

The Clinical Global Impression (CGI) rating scales are commonly used measures of symptom severity, treatment response and treatment efficacy in studies of patients with mental disorders. The scales are quick to administer and helps clinicians to monitor patient progress in a consistent, systematic manner.

The scales have two components: the Clinical Global Impression - Severity scale (CGI-S) and the Clinical Global Impression - Improvement scale (CGI-I).

The Clinical Global Impression - Severity scale (CGI-S) is a 7-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment, relative to the clinician's past experience with patients who have the same diagnosis.

The Clinical Global Impression - Improvement scale (CGI-I) is a 7-point scale that requires the clinician to assess how much the patient's illness has improved or worsened relative to a baseline state (i.e. at initiation of treatment).

GPP Consider using the Clinical Global Impression scales (both severity and improvement sub-scales; refer to Annex VII) to measure illness severity and treatment progress during consultations.

GPP

4 Pharmacotherapy

The effective pharmacotherapeutic agents in the treatment of depression are the antidepressants and they have been shown to be effective in the treatment of all forms of depression.³³ The antidepressants that are available work through various pharmacologic mechanisms.³⁴

All classes of antidepressants have been consistently shown to be effective in treating depression. All placebo-controlled trials have consistently shown clinically significant treatment efficacy responses in depression rating scales.^{20,35,36}

The effectiveness of antidepressant medications is generally comparable both between and within the classes. The current evidence has not shown any one class or any antidepressant to be clearly superior in effectiveness to another.

In general, there are no clinically significant differences in efficacy and effectiveness between tricyclic antidepressants and Selective Serotonin Reuptake Inhibitors (SSRIs).³⁶⁻⁴⁰

A Antidepressants should be recommended as a first-line treatment in patients with moderate to severe depression, or sub-threshold depression that has persisted for 2 years or more.⁴¹

Grade A, Level 1+

Antidepressants are normally recommended as first-line treatment in patients whose depression is of at least moderate severity. Of this patient group, approximately 20% will respond with no treatment at all, 30% will respond to placebo and 50% will respond to antidepressant drug treatment.⁴² This gives a number needed to treat (NNT) of 3 for antidepressant compared to wait list control and 5 for antidepressant compared to placebo.⁴³

D Antidepressants are a treatment option in short duration mild depression in adults and should be considered if there is a history of moderate to severe recurrent depression or if the depression persists for more than 2–3 months.⁴⁴

Grade D, Level 4

Patients with mild depression may also improve spontaneously over time or respond to non-specific measures such as support, monitoring and low-intensity psychosocial interventions.⁴²

4.1 Choice of antidepressant medication

There are many classes of antidepressants available with different mechanisms of actions. Each class of antidepressants has its unique characteristics and precautions of usage. The prescriber needs to consider these factors and precautions when selecting antidepressants to be prescribed.^{19,31,32}

These factors include:

- Side-effect profile
- Safety and Tolerability
- Presence of co-morbid conditions
- Concurrent medications
- Patients with history of prior response
- Risk of lethality in overdose

More detailed sources of pharmacological information should be referred to ensure the safe and efficacious use of the antidepressant.

D If the patient has previously responded well to and has had minimal side-effects with a drug, that drug is preferred. Alternatively, if the patient has previously failed to respond to an adequate trial of one antidepressant or found the side-effects of an antidepressant intolerable, that medication should generally be avoided.^{19,31,32,45,46}

Grade D, Level 4

A Once an antidepressant has been selected, start with a low dose and titrate gradually to the full therapeutic dose, while assessing patients' mental state and watching for side-effects. The frequency of monitoring depends on the severity of the depression, suicide risk, the patient's cooperation and the availability of social support.⁴⁷⁻⁴⁹

Grade A, Level 1+

A A selective serotonin reuptake inhibitor (SSRI) antidepressant should be used as a first-line medication for treating depression, due to its favourable risk-benefit ratio, greater tolerability and safety in overdose.^{38, 50-53}

Grade A, Level 1++

SSRIs are safer and have higher tolerability profiles than tricyclic and tetracyclic antidepressants, causing fewer anticholinergic side effects and cardiovascular toxicities.⁵⁰⁻⁵³ They also show lower rates of treatment discontinuation.⁵⁰

A Selective serotonin reuptake inhibitor (SSRI) antidepressants should be prescribed as a first line medication for depression in patients with concomitant cardiovascular diseases due to their favourable risk-benefit ratio.⁵³⁻⁵⁵

Grade A, Level 1++

SSRIs are safer and have higher tolerability profiles than tricyclic and tetracyclic antidepressants, causing fewer anticholinergic side effects and cardiovascular toxicities.⁵³⁻⁵⁵

A The “newer” antidepressants can also be considered as other first-line options for treating depression.⁵⁶⁻⁵⁸ They include:

- Serotonin and Norepinephrine Reuptake Inhibitors (SNRI) (e.g. venlafaxine)
- Noradrenergic and Specific Serotonergic Antidepressants (NaSSA) (e.g. mirtazapine)
- Norepinephrine and Dopamine Reuptake Inhibitors (NDRI) (e.g. bupropion)

Grade A, Level 1+

Recent meta-analyses have suggested that the Serotonin and Norepinephrine Reuptake Inhibitor (SNRI), venlafaxine is more effective than SSRIs.⁵⁹

D Where there are interactions with other drugs, use of escitalopram or sertraline should be considered as they have fewer propensities for interactions, appear to be safe and possibly protective of further cardiac events.⁶⁰⁻⁶¹

Grade D, Level 4

A Due to their cardiotoxic adverse effect risks, tricyclic antidepressants (TCA) should be avoided in patients at high risk of cardiovascular disease, arrhythmias and cardiac failure.⁵⁴

Grade A, Level 1++

Among the tricyclics, the secondary amines (e.g. desipramine, nortriptyline) have fewer side effects and greater tolerability than the tertiary amines (e.g. amitriptyline, imipramine).³⁹

A Older tricyclic antidepressants and monoamine oxidase inhibitors (MAOIs) should be reserved for situations when first-line medication treatment has failed.⁶²

Grade A, Level 1+

B A new class of antidepressants, known as melatonin agonists, e.g. agomelatine, may also be considered as an alternative treatment option for depression, if first-line medication is unsuitable or has failed.⁶³⁻⁶⁴

Grade B, Level 1+

D When an antidepressant is to be prescribed, tailor it to the patient with depression and a chronic physical health problem, and take into account the following.⁶⁵⁻⁶⁶

- the presence of additional physical health disorders.
- the side effects of antidepressants, which may impact on the underlying physical disease (in particular, selective serotonin reuptake inhibitors may result in or exacerbate hyponatraemia, especially in older people.
- interactions with other medications.

Grade D, Level 3

C The emergence of suicidal thinking and behaviour, or unusual changes in behaviour should be monitored during the early phases (generally the first 1-2 months) of antidepressant treatment, especially in children, adolescents and young adults between 18 to 24 years old.⁹¹

Grade C, Level 2+

A Initial and short-term (2-4 week) usage of a benzodiazepine together with an antidepressant may be considered where anxiety, agitation and/or insomnia becomes problematic to patients with depression.⁶⁷

Grade A, Level 1++

A systematic review found that patients with combination treatment of antidepressants and anxiolytics (benzodiazepines) were more likely to show response at 1 and 4 weeks than patients with antidepressant treatment only (although the difference was no longer significant at 6-8 weeks).⁶⁷

The benefits of using benzodiazepines have to be balanced against the risk of developing dependence, tolerance and increased accident probabilities. The review concluded that early time-limited use of benzodiazepines in combination with an antidepressant drug may accelerate treatment response.⁶⁷

4.2 Duration of treatment

4.2.1 Acute phase

C All antidepressants, once started, should be continued for at least 4 to 6 weeks.⁶⁸⁻⁶⁹

Grade C, Level 2+

All antidepressants require 4 to 6 weeks to achieve their maximum therapeutic effects.⁷⁰ Some patients may begin to show improvement by the end of the first week and some by the second to third week.⁷¹ Generally if treatment is going to be effective, at least a partial symptomatic response will be seen by 4 to 6 weeks of medication.⁷²

4.2.2 Continuation phase

A Patients with first episode of depression without psychotic symptoms should be treated with antidepressants at full treatment dose for 6-9 months after remission of symptoms.⁷³⁻⁷⁴

Grade A, Level 1++

4.2.3 Maintenance phase

The maintenance antidepressant given is generally the same type and dosage found effective in the acute phase of treatment.

Indications for maintenance treatment

The following features are indications for maintenance treatment:^{19, 40}

1. Three or more episodes of major depression
Or
2. Two episodes of major depressive disorder and one or more of the following:
 - a) family history of bipolar disorder.
 - b) history of recurrence within one year after previously effective medication was discontinued.
 - c) a family history of recurrent major depression.
 - d) early onset (before age 20) of the first depressive episode.
 - e) depressive episodes were severe, sudden or life-threatening within the past 3 years.

B Patients who have a second episode of depression should be maintained on treatment for 1-2 years - the duration may depend on the risk factors for recurrence and the patient preference.^{75,76}

Grade B, Level 1+

C Patients with more than two episodes of depression should be maintained on treatment for 2 years or longer, or even lifelong - the duration may depend on the risk factors for recurrence and the patient preference.⁷⁷⁻⁷⁸

Grade C, Level 2+

GPP Maintenance antidepressant treatment should be carried on for as long as necessary.

GPP

4.3 Treatment options for partial and non-responders

Increased dose

B Using higher antidepressant doses may be helpful for patients who have shown a partial response and when only low or modest doses have been tried. The patient should be closely monitored for side-effects with the increase in dose.⁷⁹⁻⁸¹

Grade B, Level 2++

Switching strategy

B Switching is preferred to augmentation as an initial strategy in accordance with general principles that combinations should preferably not be used when monotherapy will suffice.⁸²⁻⁸³

Grade B, Level 2++

A Both switching within the class (i.e. from a selective serotonin reuptake inhibitor to another), as well as switching from a selective serotonin reuptake inhibitor to a different class of antidepressants, may be done as both have been found beneficial.^{84,85}

Grade A, Level 1++

However a modest advantage (NNT=22) has been found in a meta-analysis¹⁴ when switching is done to a different class of antidepressant in a SSRI resistant depression.^{84,85}

The process of switching (gradual tapering, washout and starting new, cross-tapering and abrupt switch) depends on the type and the pharmaco-dynamic and pharmaco-kinetic properties of antidepressants getting switched from and to.^{75, 86}

GPP When switching medications, clinicians should be vigilant for the onset of drug-drug interactions (e.g. Serotonin syndrome) and drug discontinuation reaction.

GPP

Choosing the right process will minimise such complications.

Augmentation strategy

When an augmentation strategy is used, a pharmacologic agent is used to enhance the effect of an antidepressant. This is preferred for patients who have had previous antidepressant trials and have not responded to adequate trials of other individually prescribed antidepressants.

A Lithium augmentation and thyroid hormone augmentation (using levothyroxine or triiodothyronine) are two traditional augmentation strategies that may be used for patients who have had previous antidepressant trials and have not responded to adequate trials of other individually prescribed antidepressants.^{87,88}

Grade A, Level 1++

4.4 Discontinuation of antidepressants

A When discontinuing antidepressants, antidepressants should be gradually tapered off instead of suddenly stopped, to reduce side effects of discontinuation.⁸⁹⁻⁹⁰

Grade A, Level 1++

Discontinuation symptoms may occur after missed doses if the antidepressant prescribed has a short half life.⁷⁵

5 Psychotherapy

Psychotherapy is the psychological treatment of psychiatric disorders through the establishment of a relationship between the therapist and patient for the purpose of alleviating psychological symptoms and preventing or correcting maladaptive patterns of behaviour.

Individuals suffering depression typically prefer psychological treatment to medication and value improvements in quality of life; hence a range of psychological interventions may be offered.⁹²⁻⁹³

A Psychotherapy alone is as efficacious as antidepressant medication in patients with mild to moderate major depression and may be used as first-line treatment.⁹²⁻⁹³

Grade A, Level 1++

The decision to use psychotherapy depends on patient preference, patient suitability (able to be self-aware and able to communicate thoughts and feelings), therapist availability and severity of the illness.⁹²

Clinical features that may suggest the use of psychotherapeutic interventions include the presence of significant psychosocial stressors, intrapsychic conflict, interpersonal difficulties, or a co-morbid personality disorder.⁴⁰

Marked vegetative symptoms such as psychomotor retardation, severe early morning awakening or weight loss would favour the use of pharmacotherapy as first-line treatment.

The frequency of psychotherapy sessions may range from once a week to several times per week in the acute phase.

Although a range of psychotherapeutic interventions are available they all have common therapeutic factors, such as:⁹⁴

- 1) A trained therapist.
- 2) Establishment of a treatment alliance between therapist and patient.
- 3) A theory that offers a plausible explanation for the patient's symptoms.

- 4) Expectations of patient change and renewal of a sense of hope.
- 5) A structured series of contacts between the therapist and patient designed to bring about change.

There is only limited evidence that the various forms of psychotherapy have differential effects.^{95,96}

Cognitive-behavioural therapy

Among the specific psychotherapeutic interventions, cognitive-behavioural therapy (CBT) has the best documented efficacy for the treatment of depression.⁹⁷ It focuses on identifying and modifying distorted, negatively biased thoughts.

A Cognitive-behavioural therapy is recommended when the depressed patient has distorted negative thoughts.⁹⁷

Grade A, Level 1++

B Cognitive-behavioural therapy is also an effective maintenance treatment and is recommended for patients with recurrent depression who are no longer on medication.⁹⁸

Grade B, Level 1+

Interpersonal therapy

This therapy focuses on clarification and resolution of difficulties in current interpersonal relationships and has good evidence of efficacy. The basic assumption is that dealing with these relationship issues whether they contributed to or were the consequences of depression, would lead to relief and resolution of the depressive symptoms.

B Interpersonal therapy is recommended for depressed patients with interpersonal difficulties.⁹⁹

Grade B, Level 1+

Psychodynamic psychotherapy

Short-term psychodynamic psychotherapy especially psychodynamic-interpersonal therapy is comparable to cognitive-behavioural therapy. It focuses on the therapist-client relationship as a vehicle for revealing and resolving interpersonal difficulties.¹⁰⁰

A Psychodynamic-interpersonal therapy is a viable alternative treatment for depressed patients with interpersonal difficulties.

Grade A, Level 1+

A Long-term psychodynamic psychotherapy is recommended for depressed patients with co-morbid personality disorder.¹⁰¹

Grade A, Level 1++

When longer forms of psychodynamic psychotherapy are employed, they are frequently associated with broader long-term goals such as personality change.¹⁰¹

Problem-solving therapy

Problem-solving therapy is as effective as antidepressants for primary care patients with mild depression.¹⁰² Therapist and patient work together to identify and prioritise key problem areas, break problems down into specific manageable tasks, problem solve, and develop appropriate coping behaviours for problems.

A Problem-solving therapy is recommended for primary care patients with mild depression.

Grade A, Level 1++

Group therapy

There is less evidence for the efficacy of group therapy, compared to individual forms of psychotherapy especially for severe depression.¹⁰²

Duration of treatment

There is little data on optimal duration of psychotherapy. Cognitive-behavioural therapy has been given in 12 sessions at weekly intervals and interpersonal therapy in 16-20 sessions at weekly intervals.

A Cognitive-behavioural therapy or psychodynamic interpersonal therapy should be delivered for a longer period (i.e. 16 weeks or longer) when the depression is severe.

Grade A, Level 1+

D If a moderate improvement, at least, is not observed after 4-8 weeks of psychotherapy, a thorough review of the diagnosis, complicating conditions and issues, and treatment plan should be conducted. If there is no response, consider adding or changing to medication. If there is partial response, consider changing the intensity of psychotherapy, changing the type of psychotherapy, or adding or changing to medication.⁴⁰

Grade D, Level 4

6 Psychoeducation and family intervention

Psychoeducation includes the illness concept of depression, the expectation for response (that is, instillation of hope) and the need to adhere to the treatment regime.³¹

Strategies such as providing information and advice are useful in relieving anxiety, enhancing compliance and assisting recovery.^{103,104}

A The following should be done:

- a. Educating the patient about the illness helps clarify uncertainty and misconceptions. Depression should be explained as a medical illness that is associated with changes in neurochemicals and brain functioning.
- b. Adequate follow-up improves treatment adherence, allows closer monitoring and earlier detection of changes in condition.
- c. Discuss the type and duration of treatment. If antidepressants are used it is advisable to explain that they are not addictive. Provide information on the different types of antidepressants available and about the possible side-effects.
- d. Advise on lifestyle changes such as exercise and reducing stress.¹⁰⁵

Grade A, Level 1++

GPP Where indicated and with patients agreement, involve family members or friends in the care of people with depression so that there is adequate support.

GPP

This involvement is particularly important when there is a risk of suicide.

Couple/marital therapy

A Marital or couple therapy is effective and should be considered for patients with significant marital distress.¹⁰⁶

Grade A, Level 1+

Kung (2000)¹⁰⁷ reviewed various models of marital therapy as an approach to treatment with married depressed patients. These models have also been developed and empirically tested in the past two decades. Empirical evidence for the efficacy of these models, suggested that elements of marital therapy that are conducive to effective treatment outcome.

The studies under review have some differences in patient characteristics (including gender, initial marital distress, diagnosis: depression, dysthymia, or both, and severity of disorder) and research design (with or without control group, different comparison groups, number of therapy sessions, and the administration of follow-up evaluations). However, the general conclusions that can be drawn on the efficacy of marital therapy in treating depressed patients indicate that:

- (1) marital therapy is effective in reducing patients' depressive symptomatology compared to their pretreatment conditions.
- (2) most treatment models are related to greater symptom reduction for maritally distressed patients when compared to a control group.

7 Electroconvulsive therapy

Electroconvulsive therapy (ECT) has been in use for more than 50 years in the treatment of psychiatric disorders. It is an exceptionally effective treatment for depression. It has been shown in controlled clinical trials to have efficacy that is superior to placebo, simulated electroconvulsive therapy and antidepressant medication therapy.¹⁰⁸⁻¹⁰⁹ 80-90% of patients with major depressive disorder showed improvement with electroconvulsive therapy.¹¹⁰

Most studies assessed the efficacy of electroconvulsive therapy at the end of the course of electroconvulsive therapy. Most patients were rarely followed up beyond the course of electroconvulsive therapy. Hence it is not known how long the short term benefits of the electroconvulsive therapy are maintained.¹¹¹ It is recommended that patients be maintained on antidepressants following a successful response to electroconvulsive therapy.¹¹²⁻¹¹⁴

Procedure

Electroconvulsive therapy is performed only after informed written consent is given by the patient. The procedure of electroconvulsive therapy involves the induction of a grand mal seizure by means of an electrical pulse through the brain.

Electroconvulsive therapy is administered under general anaesthesia and each induction of a seizure is considered one treatment. A course of electroconvulsive therapy consists of several such treatments and should be such that maximal remission of symptoms is achieved. This typically involves six to 12 treatments. Electroconvulsive therapy is typically administered every other day. There is no significant difference in outcomes between twice weekly and three times weekly treatment.⁸²

The electroconvulsive therapy electrodes can be placed on both sides of the head (bilateral placement) or one side of the head (unilateral placement). Bilateral electroconvulsive therapy is found to be more effective than unilateral electroconvulsive therapy but may cause more cognitive impairment. The dose stimulus varies from patient to patient but should be titrated to induce an adequate seizure that is typically at least 15-25 seconds in duration. Higher dose stimulus is more

effective than lower dose but also cause more cognitive impairment. Thus the choice of electrode placement and stimulus parameters should balance efficacy against the risk of cognitive impairment.⁸²⁻⁸⁷

Adverse events

Electroconvulsive therapy is generally a very safe treatment. The common side effects of electroconvulsive therapy are transient headaches, muscle soreness, nausea and memory impairment.

Following each electroconvulsive therapy treatment is a transient postictal confusional state and a longer period of anterograde and retrograde amnesia. The anterograde memory impairment typically resolves in a few weeks after cessation of electroconvulsive therapy. Some degree of retrograde amnesia, particularly for recent memories, may continue for patients receiving bilateral electroconvulsive therapy. This retrograde amnesia manifests as difficulty remembering information learned prior to the course of electroconvulsive therapy.¹¹⁵⁻¹¹⁸

The risk of death with electroconvulsive therapy is very low, around 1 per 10,000 patients.¹¹⁹ This rate is comparable to that which would be expected from a series of brief anaesthetic procedures alone. Most deaths occur in high-risk cases, and are usually due to cardiac causes.

Indications

A Electroconvulsive therapy is an effective **short-term treatment** for major depressive disorder and should be considered in patients who have not responded to antidepressant therapy.^{108, 120}

Grade A, Level 1++

A Patients should be maintained on antidepressants following a successful response to electroconvulsive therapy.¹¹²⁻¹¹⁴

Grade A, Level 1+

D Electroconvulsive therapy may be considered as a **first-line treatment** for severely depressed patients with severe psychomotor retardation (associated with food refusal leading to nutritional compromise and dehydration), active suicidality and psychotic features.^{115, 121-123}

Grade D, Level 3

D Electroconvulsive therapy may also be considered in situations when a particularly rapid antidepressant response is required, such as in pregnancy and in those with comorbid medical conditions that preclude the use of antidepressant medications.¹²⁴⁻¹²⁵

Grade D, Level 3

Prior histories of positive response to electroconvulsive therapy and patient preference are important considerations that may influence the decision to select electroconvulsive therapy as a treatment modality.¹¹⁵

Contraindications

Although there is no absolute contraindication to electroconvulsive therapy, certain conditions are associated with greater risk of adverse events. These include recent myocardial infarction, congestive heart failure, cardiac arrhythmia, recent stroke, bleeding or unstable cerebral vascular aneurysm or malformation, pheochromocytoma, retinal detachment, space occupying lesions in the brain and other conditions leading to raise intracranial pressure.

In such situations, the relative risks and benefits of electroconvulsive therapy treatment should be carefully weighed in collaboration with a physician, cardiologist, anesthesiologist, neurologist or neurosurgeon, as the case requires.¹¹⁵

8 Depression in children and adolescents

Depression is common in children and adolescents, and has a propensity for persisting into adulthood if not adequately treated. Depression affects between 2 to 8% of youths. Studies in Singapore suggest it may vary between 2.5 to 18%.¹²⁶⁻¹²⁷

Recognition of symptoms

The symptoms of depression in children and adolescents may vary across different developmental stages and diverse ethnic groups.¹²⁸ Children may show more anxiety, somatic complaints and auditory hallucinations. Children verbalise feelings less but develop behavioural problems, e.g. temper tantrums.¹²⁹

Adolescents manifest more sleep and appetite disturbances, delusions, suicidal ideation and attempts compared to children but less than adults.¹³⁰ Children and adolescents are also more likely to have concomitant physical illness.¹³¹

Diagnosis and screening

The DSM-IV-TR criteria for depression in children and adolescents are the same as those for adults, with the exception that the condition of “irritable mood” is also an acceptable criterion for children and adolescents, in addition to the criterion of “depressed mood”.

D Self-administered rating scales (or questionnaires) should not be used for diagnosis, but may be used for screening of symptoms, assessing severity and monitoring improvement in older children and adolescents.¹³¹

Grade D, Level 4

A general scale that is widely used and validated and is available on the Internet (www.youthinmind.com) is the Strengths and Difficulties Questionnaire (SDQ).¹³²

The Patient Health Questionnaire-2 (PHQ-2)¹³³ is a useful two-item screener for depression with scores of 3 or more as having high sensitivity and specificity in adolescents¹³⁴. A local 20-item Asian Depression Scale for Children (ACDS-20); has also been developed and validated.¹³⁵ (See Annex III on pg 59-60).

Suicide

Suicide risk assessment is important for children and adolescents with depression.

D When faced with a suicidal adolescent, doctors should maintain contact, ensure close supervision and engage support systems such as family and school, and consider a “no harm” contract if the adolescent is willing.¹³⁶

Grade D, Level 4

D Hospitalization is indicated if suicide risk is high, support is unavailable and there are severe symptoms of depression.¹³⁶

Grade D, Level 4

Treatment

A Psychosocial interventions are recommended in initial treatment of depression in children and adolescents based on the literature and local clinical experience.

Grade A, Level 1++

However, both psychosocial interventions and medications have been shown to be useful.

Psychosocial interventions include close supervision and monitoring by the treating physician, engaging support networks in the family and schools as well as psychological treatments.

Psychological treatments include cognitive-behavioural therapy and interpersonal therapy, which have been shown to be efficacious in the treatment of depression in youths.¹³⁷⁻¹³⁹

Other psychological interventions include psychodynamic psychotherapy, interpersonal therapy, family therapy, supportive psychotherapy and group psychotherapy.

D Medication should not be the only treatment given to children and adolescents with depression but care should be given to increasing self esteem, coping skills to handle stress, adapting to the changes in life and improving relationships between family members and peers. Use of medications should be cautious and not necessarily first-line treatment for major depressive disorder.¹⁴⁰

Grade D, Level 3

D Medications are usually indicated for children and adolescents with severe depression, who have psychotic symptoms or who have failed psychotherapy.¹³⁹

Grade D, Level 4

C Selective Serotonin Reuptake Inhibitors (SSRIs) should be used with caution in children and adolescents.¹⁴¹

Grade C, Level 2+

Although many studies show that SSRIs are efficacious and safe, only fluoxetine has been approved for use in children and adolescents by the US and UK drug regulatory bodies. There are reports of possible increased risk of suicidal thinking in using an SSRI such as paroxetine.¹⁴²

Children and adolescents often have many psychosocial factors that contribute to their depression and these should be explored before medication is used. Cognitive-behavioural therapy showed modest effect size in recent meta-analytic studies.¹³⁷ There are reports of possible increased risk of suicidal thinking in using an SSRI such as paroxetine.

A Combination of psychosocial interventions and SSRIs may be considered for moderate to severe depression in children and adolescents.

Grade A, Level 1++

The Treatment for Adolescents with Depression Study (TADS), a 12-week randomised controlled trial, compared cognitive behavioural therapy alone, fluoxetine alone, combined cognitive behavioural therapy and fluoxetine, and placebo in 439 youths aged 12–17 years with a diagnosis of major depressive disorder.

Combined treatment was more effective in reducing symptoms of depression (71.0% improved) than fluoxetine alone (60.6% improved), cognitive behavior therapy alone (43.2% improved), or placebo (34.8% improved).¹⁴³ However, this was contradicted in another large trial in the UK.¹⁴⁴

A Other antidepressants such as venlafaxine may be considered as second line treatment of depression in children and adolescents.

Grade A, Level 1++

The Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) trial, a 12 week randomised controlled trial of 334 adolescents aged 12-18 years, showed that for adolescents with depression not responding to an adequate initial treatment with an SSRI, the combination of cognitive behavioral therapy and a switch to another antidepressant resulted in a higher rate of clinical response than did a medication switch alone.

However, a switch to another SSRI was just as efficacious as a switch to venlafaxine and resulted in fewer adverse effects.¹⁴⁵

GPP Referral of a child or adolescent with depression to a psychiatrist could be considered in any of the following situations:

- failure to improve with psychosocial interventions or requiring specialised psychological interventions.
- failure to improve after at least 4 weeks of medication treatment at maximum tolerated dose.
- severe symptoms such as clear suicidal intention, disruptive psychotic symptoms.

GPP

Use of electroconvulsive therapy is rarely indicated but has been shown to be safe in adolescents.¹⁴⁶

9 Depression in pregnancy

Depression in pregnant and postpartum women is a major public health issue given its prevalence and impact on mothers, foetuses and infants.

Locally up to 12% of pregnant women and 7% of postpartum women suffer from depression reflecting worldwide trends.¹⁴⁷⁻¹⁴⁸ Antenatal depression is well known to be associated with a whole range of adverse maternal outcomes, e.g. substance abuse, poor antenatal compliance or nutrition, and possibly an increased risk of premature labour.¹⁴⁹

Untreated antenatal depression continues into the postpartum period in up to 50% of the cases,¹⁵⁰⁻¹⁵¹ and postpartum depression too has significant adverse outcomes. These include unfavourable parenting practices¹⁵² and impaired mother-infant bonding, which in turn is known to affect the intellectual and emotional development of the infant.¹⁵³ The gravest outcome, of course, is maternal suicide and infanticide.¹⁵⁴

The guideline draws on the best available evidence. However, there are significant limitations to the evidence base, including limited data on the risks of psychotropic medication during pregnancy and breastfeeding, particularly with more recently introduced drugs. No psychotropic drug has marketing authorisation specifically for pregnant or breastfeeding women.

9.1 Screening and early recognition

C Consider using these two questions to effectively identify possible depression in pregnant and postpartum women.¹⁵⁵⁻¹⁵⁶

1. “During the past month, have you often been bothered by feeling down, depressed or hopeless?”

2. “During the past month, have you often been bothered by having little interest or pleasure in doing things?”

If the woman answers “yes” to either question, consider asking this: “Is this something you feel you need or want help with?”^{155,156}

Grade C, Level 2+

Screening also includes identifying those at greater risk of adverse outcomes.

D It is strongly recommended that specialist psychiatric care be arranged for pregnant or postpartum women with:

- past or present severe mental illness including schizophrenia, bipolar disorder, psychosis in the postnatal period and severe depression
- previous treatment by a psychiatrist/specialist mental health team including inpatient care
- a family history of maternal perinatal mental illness.¹⁵⁵

Grade D, Level 4

9.2 Treatment of peripartum depression

For new onset depressive illness:

Treatment considerations should aim to minimise risk of harm to developing foetus or nursing infant, balancing this against the benefits of treatment (viz ameliorating adverse effects of illness on mother and child).

D Psychological therapies (including non-directive counselling and support) should be maximised as the first-line treatment strategy for peripartum depression and medication should be considered only in severe depression.^{155, 157}

Grade D, Level 4

D Early referral to a specialist with expertise in perinatal mental health is recommended for women with new-onset peripartum depression, unless it is mild.^{155, 157}

Grade D, Level 4

For women with pre-existing depressive illness:

Consider risk of relapse as high as 70% if antidepressants stopped.¹⁵⁸

D Abrupt cessation of antidepressant medication for women with pre-existing depression can precipitate withdrawal symptoms that can be distressing. It is preferable to advise patients to reduce antidepressant dose to half first whilst arranging for referral.^{155, 158}

Grade D, Level 4

D Early referral to a psychiatrist with expertise in perinatal mental health is recommended for women with peripartum depression and pre-existing depressive illness.¹⁵⁵

Grade D, Level 4

10 Depression in elderly

Several factors modify the presentation of depression in the elderly.¹⁵⁹ While there may be reduced complaints of sadness, hypochondriasis and somatic concerns may be more prominent. Marked anxiety, apathy and poor concentration are other frequent presenting symptoms. Sometimes the presentation is with subjective complaints of poor memory or a dementia-like picture.

D Referrals of elderly patients to specialists should be considered:

- when the diagnosis is in doubt,
- when the depression is severe (as evidenced by psychotic depression, severe risk to health because of failure to eat or drink and suicidal risk),
- when complex therapy is indicated as in cases with medical co-morbidity, and,
- when the patient does not respond to an adequate antidepressant trial.¹⁶⁰

Grade D, Level 4

Organic causes of depression are more frequent in the elderly¹⁶¹ so careful history, physical examination and laboratory tests as indicated are needed.

A Antidepressants are recommended in dysthymia as well as for mild to severe depression in the elderly. There is no difference in efficacy between the classes of antidepressants in the treatment of the elderly.¹⁶²

Grade A, Level 1++

However, the elderly are more sensitive to the unwanted actions of some antidepressants. Particularly troublesome are peripheral and central anticholinergic effects such as constipation, urinary retention, delirium and cognitive dysfunction, antihistaminergic effects such as sedation and anti-adrenergic effects such as postural hypotension.¹⁶³ Newer antidepressants may be better tolerated and safer especially in overdose.¹⁶⁴⁻¹⁶⁵

A Selective serotonin reuptake inhibitors (SSRIs) are recommended over tricyclic antidepressants (TCAs) as the first-line treatment choice for late-life depression.¹⁶⁶

Grade A, Level 1++

However, whenever prescribing SSRIs, hyponatremia may be caused by syndrome of inappropriate secretion of antidiuretic hormone among older patients taking SSRIs.

The elderly generally take longer to recover from depression.

B In frail elderly patients it is advisable to “start low, go slow”.¹⁶¹ In the acute phase at least six weeks of treatment may be needed to achieve optimal therapeutic effect.¹⁵⁹

Grade B, Level 1+

B For frail elderly patients, a continuation period on the same dosage that improved them for 12 months is recommended for a first onset of major depression, longer for a recurrent episode. The duration of treatment is similar to the adult age group in the continuation and maintenance phases.¹⁶⁷⁻¹⁶⁹

Grade B, Level 1+

B Psychological interventions should be provided for the elderly with mild to moderate major depression.

Grade B, Level 1+

There is strong evidence that psychotherapy is efficacious, particularly cognitive behavioural therapy and interpersonal therapy.^{164, 166-167} There is some evidence of efficacy for brief dynamic psychotherapy, problem solving therapy and life review.^{164, 170}

B In severe major depression in the elderly, combination antidepressant and psychotherapy treatment is recommended.^{169, 171}

Grade B, Level 1+

Even simple support to patient and caregiver is associated with fairly high rates of symptom resolution in mild depression.¹⁷²

B Supportive care should be offered to elderly patients with depression and where relevant, their caregivers.

Grade B, Level 1+

Electroconvulsive therapy is effective in treating the elderly depressed.¹⁷³ It is generally safe and does not cause serious long-term cognitive side-effects.¹⁷⁴

B Electroconvulsive therapy is indicated in the elderly:

- when the patient is actively suicidal,
- when there is an urgent need to prevent deterioration in health (including food/fluid refusal),
- in psychotic depression,
- when there is inadequate response to two trials of medication,
- when there is intolerance to medication, or
- when there is good prior response.

Grade B, Level 1+

11 Cost-effectiveness issues

Major depression is expected to become the second leading contributor to disease burden worldwide by 2020.¹⁻² Because of its chronic nature, the economic burden posed by depression on the health-care system is profound. A review of cost-of-illness studies in depression indicated that a total cost of dealing with depression accounted for US\$65 billion at 1998 prices in the US, including both direct and indirect costs, and accounted for US\$962.5 million at 1998 prices in the UK with inclusion of direct costs only.

Many cost-effectiveness analyses comparing SSRIs and TCAs have been conducted. A systematic review of health economic evidence of depression by National Institute for Clinical Excellence (NICE) suggested that SSRIs were more cost-effective than TCAs for the first-line treatment of major depression. The review also highlighted that the published pharmaco-economic evidence is not sufficient to inform on the single most cost-effective antidepressant for the first-line treatment of major depression in the UK.

NICE further conducted a comparative cost-effectiveness of antidepressant therapy alone and the combination of antidepressant therapy with cognitive-behavioural therapy for the routine treatment of patients with moderate/severe depression. The findings indicated that combination therapy was both more effective and more costly than antidepressant therapy alone, with the incremental cost effectiveness ratio (ICER) estimates ranging from £5,777 to £4,887 per Quality Adjusted Life Year (QALY) gained for severe depression; and from £14,540 to £12,299 per QALY gained for moderate depression. The NICE recommended that combination therapy was a cost-effectiveness treatment for patient with severe depression, but not a cost-effectiveness treatment for patient with moderate depression in the UK.

A similar study of comparison of antidepressant therapy alone and the combination of antidepressant therapy with cognitive-behavioural therapy for treatment of patients with moderate/severe depression was conducted in Japan. The study found that combination therapy was both more effective and more costly than antidepressant therapy alone from the health care system perspective, and was more effective with less costly from the societal perspective. The authors recommended

that combination therapy should be a preferred therapy for management of patients with depression from the societal perspective in Japan.

In sum, depression places a major direct economic burden on patients, carers and the healthcare system. Efficient service provision could greatly reduce this burden and ensure that best care is delivered within the budget constraint.

12 Clinical quality improvement

The following clinical quality improvement parameters, based on recommendations made in these guidelines, are proposed:

1. Percent of patients with depression who are assessed using the clinical global impression scales (both severity and improvement component scales) during consultations.
2. Percent of newly-diagnosed patients with depression on antidepressant medication, who receive at least 4 weeks of pharmacotherapy.

Annex I Factors associated with depression

Medical conditions associated with depression

- Hypothyroidism
- Malignancy
- Parkinson's disease
- Myocardial Infarction
- Stroke
- Endocrinopathies (Cushing's syndrome, adrenal insufficiency, carcinoid, hyperparathyroidism)
- Infections (hepatitis, mononucleosis, influenza or other viral illnesses)
- Chronic disease (congestive heart failure, diabetes, systemic lupus erythematosus, rheumatoid arthritis)
- Alcoholism or other substance abuse/dependence
- Fibromyalgia/chronic fatigue syndrome
- B12 or folate deficiency
- Sleep disorders

Medications associated with depression

- Drugs of abuse (alcohol, amphetamines, cocaine, marijuana)
- Anti-hypertensives (reserpine, methyldopa, beta blockers)
- Psychoactive drugs (analgesics, sedative-hypnotics, anxiolytics)
- Steroid hormones (prednisone, oral contraceptives)
- Chemotherapy agents (vincristine, vinblastine, procarbazine, L-asparaginase)
- Levodopa
- Cholesterol lowering agents

Psychiatric disorders associated with depression

- Bipolar disorder
- Dysthymia
- Grief, bereavement
- Anxiety disorder
- Post-traumatic stress disorder
- Somatoform disorders
- Eating disorders
- Sleep disorders
- Substance abuse
- Anxiety disorders

Life situations associated with depression

- Coping with illness
- Marital discord
- Child rearing difficulties
- Work stress
- Abuse (domestic violence, physical or sexual abuse)

Adapted from the following sources:

- Depression: A Guide to Diagnosis and Treatment, Brigham and Women's Hospital.
- University of Michigan Health System Depression Guidelines, June 1998.

Annex II Assessment of suicide risk

Demographic factors

Social isolation (living alone, single) and lack of family support
Older male
Recent loss

Check the history

History of prior suicide attempts especially if multiple/severe attempts
Family history of suicide
Substance abuse/dependency
Presence of physical illness

Assess for

Severe depression
Anxiety
Hopelessness
Psychosis especially with command hallucinations

Ask about suicidal thinking

Presence of a specific plan.
Means available to carry out the suicide plan.
Absence of factors that would keep the patient from completing the plan.
Rehearsal of the plan including preparations such as letters, will.

Asking about suicidal thoughts and plans will not prompt a suicide attempt. It may be appropriate to ask a series of questions about how the individual views the future and whether there are feeling of hopelessness and helpless and thoughts about death before going on to directly asking about actual thoughts and plans.

Annex III Screening tools for depressive disorders

1. **Hamilton Depression Rating Scale (HAM-D)**

This is used on patients already diagnosed with depression and has its strength in evaluating and charting the severity of the illness. Its length makes it less practical in clinical settings. The commonly used version has 17 items and includes many somatic symptoms such as decreased appetite, weight loss, fatigue, anxiety symptoms and insomnia.

The HAM-D is free and can be found and downloaded from the Internet for use.

2. **Hospital Anxiety and Depression Scale (HADS)**

This fairly short self-rated scale covers depression (7 questions) and anxiety (7 questions). It was developed for use in general medical patients and does not focus on somatic symptoms which are common among medical patients.

The HADS can be purchased from the suppliers' website at:
www.gl-assessment.co.uk/

3. **Montgomery-Asberg Depression Rating Scale (MADRS)**

This is a 10-item clinician-rated scale that includes somatic symptoms. It is used to measure the severity of depressive episodes.

The MADRS is available from the Internet and may be reproduced by individual researchers or clinicians for their own use without seeking permission; however the scale must be copied in full and all copies must acknowledge the following source: Montgomery, S.A., Åsberg, M. A new depression scale designed to be sensitive to change. *British Journal of Psychiatry*. 1979;134:382-389.

4. Beck Depression Inventory (BDI)

This is a subjective scale to be completed by the patient. It has items that focus on the depressive cognition of the patient.

The BDI can be purchased from the supplier's website at www.pearsonassessments.com

5. Patient Health Questionnaire-9 (PHQ-9)

The PHQ-9 is a brief and useful instrument for use in primary care. It can be self-administered and is used for screening, monitoring, as well as assessing the diagnosis and severity of depression. PHQ-9 scores of ≥ 10 had a sensitivity of 88% and specificity of 88% for major depression.

The PHQ-9 is free and can be found and downloaded from the Internet for use.

Scales relevant to children and adolescents:

1. Center for Epidemiologic Studies Depression Scale (CESD)

This is a 20-item self-report initially designed for an American epidemiological survey by the National Institute of Mental Health.

The CESD is free and can be found and downloaded from the Internet for use.

2. Child Depression Inventory (CDI)

This is a 27-item self-report scale for identifying depressive symptoms in children which has been well validated in large populations both in the West and in Asia.

The CDI can be purchased from the supplier's website at www.mhs.com

3. Asian Children Depression Scale (ACDS)

This is a 20-item self-administered scale that was developed for Singapore children for the purpose of an epidemiological survey. It has been validated and shows good psychometric properties.

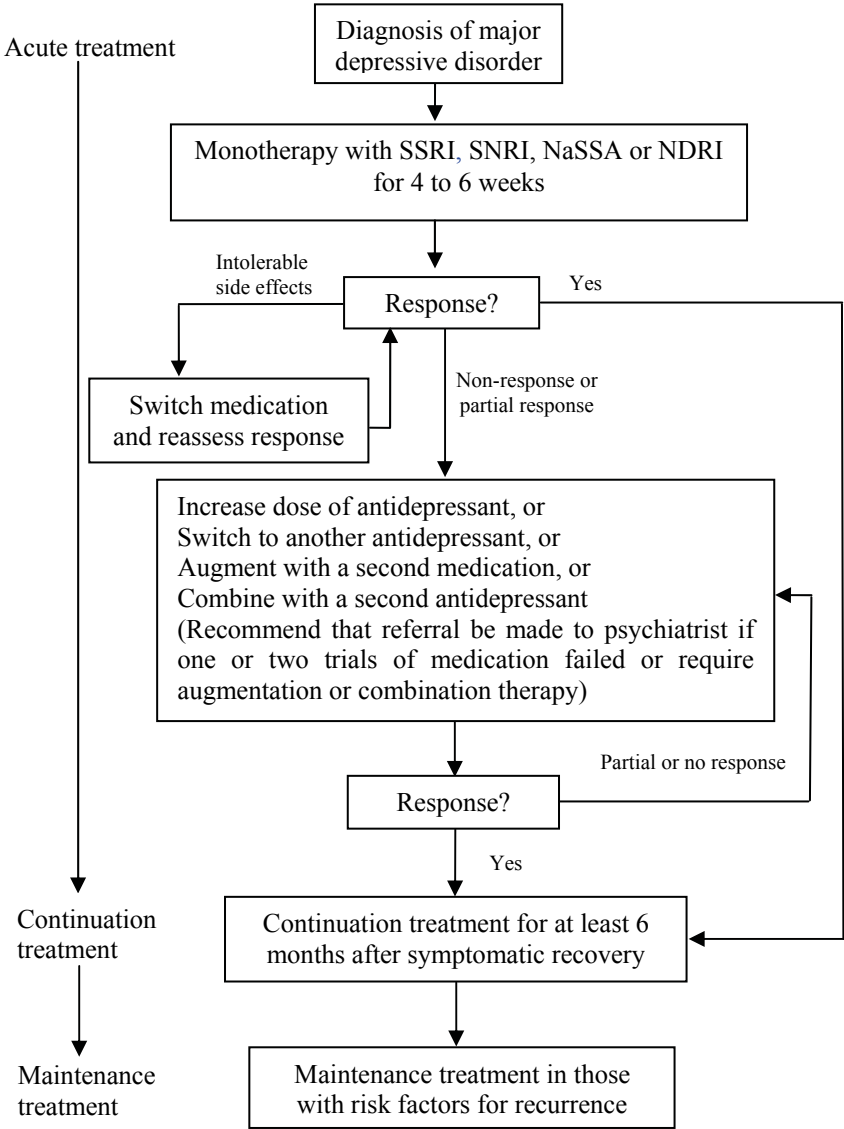
Permission to use the ACDS can be requested from the authors at: daniel_fung@imh.com.sg

4. Patient Health Questionnaire-2 (PHQ-2)

The PHQ-2 can be used to screen for depression in a "first step" approach. The PHQ-2 includes the first two items of the Patient Health Questionnaire (PHQ-9; see section above), based on DSM-IV criteria. Patients who screen positive with the PHQ-2 should be further evaluated with other screening or diagnostic instruments.

The PHQ-2 is free and can be found and downloaded from the Internet for use.

Annex IV Flow chart for pharmacotherapy of major depressive disorder



Annex V Pharmacologic classes of antidepressants

I. Selective Serotonin Reuptake Inhibitors (SSRIs)

- fluoxetine
- fluvoxamine
- sertraline
- paroxetine
- escitalopram
- citalopram

II. Tricyclic Antidepressants (TCAs)

- amitriptyline
- nortriptyline
- imipramine
- clomipramine
- dothiepin
- doxepin

III. Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)

- venlafexine
- duloxetine

IV. Noradrenergic and Specific Serotonergic Antidepressants (NaSSAs)

- mirtazapine

V. Norepinephrine and Dopamine Reuptake Inhibitors (NDRIs)

- bupropion

VI. Monoamine Oxidase Inhibitors

- moclobemide

VII. Melatonin Agonist

agomelatine acts as an agonist at melatonin receptors (MT-1 and MT-2) as well as antagonistic effects at the serotonin 5HT(2c) receptor.

Annex VI Recommendations to switching antidepressants

Table 1 Switching antidepressants

(Adapted from South London and Maudsley NHS Trust Prescribing Guidelines, 10th Edition⁷⁵)

From	To	Recommended Advice
MAO-I	Any other drug	Withdraw and wait for 2 weeks washout period
Moclobemide (RIMA)	Any other drug	Withdraw and wait for 24 hours
TCA / Reboxetine	MAO-I Moclobemide	Withdraw and wait for 1 week
	Other TCA / Reboxetine	Cross taper cautiously
	Trazadone and SSRI	Halve dose, add SSRI/Trazadone and withdraw TCA slowly
	Venlafaxine	Cross taper cautiously, start Venlafaxine low dose 37.5mg at night
	Mirtazepine	Withdraw and then start Mirtazepine cautiously
	Duloxetine	Cross taper cautiously, start Duloxetine at 60mg alternate day
SSRI (except Fluoxetine)	MAO-I Moclobemide	Withdraw and wait for 1-2 weeks washout

From	To	Recommended Advice
	TCA Reboxetine Venlafaxine Mirtazepine Duloxetine Other SSRI	Cross taper cautiously with low dose TCA Withdraw and start Venlafaxine 37.5mgs at night Withdraw and start Mirtazepine cautiously Abrupt switch possible, start Duloxetine at 60mg/day Withdraw and start new SSRI
Fluoxetine	MAO-I Moclobemide TCA Venlafaxine, Mirtazepine, Other SSRIs and Trazadone	Withdraw and wait for a longer washout 5-6 weeks Withdraw and wait for 4-7days, start TCA at very low dose and increase cautiously Withdraw and wait for 4-7days, start alternate drug cautiously / in low doses
Venlafaxine	MAO-I Moclobemide TCA, Reboxetine SSRI, Trazadone Mirtazepine Duloxetine	Withdraw and wait for 1 week Cross taper cautiously with very low doses Withdraw before starting Duloxetine cautiously

From	To	Recommended Advice
Mirtazepine	MAO-I, Moclobomide TCA, SSRI, Reboxetube Venlafaxine Duloxetine	Withdraw and wait for 1 week washout Withdraw and start TCA / SSRI / Reboxetine Cross taper cautiously Withdraw and start Duloxetine at 60mgs alternate days
Duloxetine	MAO-I Moclobemide TCA, Reboxetine SSRI, Mirtazepine, Trazadone, Venlafaxine	Withdraw and wait at least 5 days Cross taper cautiously with very low dose TCA Withdraw and start new drug
Stopping antidepressant		Reduce over 4 weeks or longer for Paroxetine and Venlafaxine. Fluoxetine dose of 20mgs can be abruptly stopped and doses of above 20mgs recommended to reduce over a period of 2 weeks

Annex VII Clinical Global Impression (CGI) scale

Considering your total clinical experience with this particular population, how would you rate this patient's mental condition at this time?

1) Severity of Illness

- 1 = Normal (not at all mentally ill)
- 2 = Borderline mentally ill
- 3 = Mildly mentally ill
- 4 = Moderately mentally ill
- 5 = Markedly mentally ill
- 6 = Severely mentally ill
- 7 = Extremely mentally ill

2) Global Improvement

- 0 = Not assessed
- 1 = Very much improved
- 2 = Much improved
- 3 = Minimally improved
- 4 = No change
- 5 = Minimally worse
- 6 = Much worse
- 7 = Very much worse

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Self-assessment (MCQs)

After reading the Clinical Practice Guidelines, you can claim one CME point under Category 3A (Self-Study) of the SMC Online CME System. Alternatively, you can claim one CME point under Category 3B (Distance Learning - Verifiable Self Assessment) if you answer at least 60% of the following MCQs correctly. You can submit your answers through the SMJ website at this link: <http://smj.sma.org.sg/cme/smj/index.html> (*the link will only be available once the February 2012 issue of the SMJ becomes available*). The answers will be published in the SMJ April 2012 issue and at the MOH webpage for these guidelines after the period for submitting the answers is over.

Instruction: *Indicate whether each statement is true or false.*

	True	False
1. For depression in the elderly,		
A) organic causes are more frequent.	<input type="checkbox"/>	<input type="checkbox"/>
B) subjective complaints of memory problem are less common.	<input type="checkbox"/>	<input type="checkbox"/>
C) selective serotonin reuptake inhibitors (SSRI) are recommended as first line treatment.	<input type="checkbox"/>	<input type="checkbox"/>
D) it generally takes longer to respond to antidepressant treatment.	<input type="checkbox"/>	<input type="checkbox"/>
2. Evaluate these statements on peripartum depression:		
A) psychological therapy is the mainstay of treatment.	<input type="checkbox"/>	<input type="checkbox"/>
B) medication is recommended for all patients.	<input type="checkbox"/>	<input type="checkbox"/>
C) withdrawal of antidepressants is recommended for depressed patients who get pregnant as the risk of relapse is low.	<input type="checkbox"/>	<input type="checkbox"/>
D) family history and personal history of depression are both important risk factors for postnatal depression.	<input type="checkbox"/>	<input type="checkbox"/>

	True	False
3. The following treatment can contribute to a reduction in depressive symptomatology for depressed patients who are married or have couple relational difficulties:		
A) couple crisis intervention.	<input type="checkbox"/>	<input type="checkbox"/>
B) couple/marital therapy.	<input type="checkbox"/>	<input type="checkbox"/>
C) group work for couples.	<input type="checkbox"/>	<input type="checkbox"/>
D) psychoeducation in couple lifestyle change.	<input type="checkbox"/>	<input type="checkbox"/>
4. The following are useful in relieving anxiety, enhancing compliance and assisting recovery:		
A) educating the patient about the illness helps clarify uncertainty and misconceptions.	<input type="checkbox"/>	<input type="checkbox"/>
B) adequate follow-up improves treatment adherence, allows closer monitoring and earlier detection of changes in condition.	<input type="checkbox"/>	<input type="checkbox"/>
C) discuss the type and duration of treatment. If antidepressants are used it is advisable to explain that they are not addictive. Provide information on the different types of antidepressants available and about the possible side-effects.	<input type="checkbox"/>	<input type="checkbox"/>
D) advise on lifestyle changes such as exercise and reducing stress.	<input type="checkbox"/>	<input type="checkbox"/>
5. Tricyclic Antidepressants (TCAs):		
A) are still the first-line treatment for major depressive disorder.	<input type="checkbox"/>	<input type="checkbox"/>
B) should be avoided in patients at increased risk of cardiovascular disease, arrhythmias and cardiac failure.	<input type="checkbox"/>	<input type="checkbox"/>
C) should be the antidepressant class of choice when there are presence of interactions with other medications.	<input type="checkbox"/>	<input type="checkbox"/>
D) usage is not favoured over the Selective Serotonin Reuptake Inhibitors (SSRIs) due to their unfavourable risk-to-benefit ratio.	<input type="checkbox"/>	<input type="checkbox"/>

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