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# Clinical practice guidelines for depression

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## ABSTRACT

**The Ministry of Health Clinical Practice Guidelines for Depression were prepared and distributed to all doctors in Singapore in early 2004. This article highlights salient points and discusses pharmacotherapy, psychotherapy and psychoeducation in managing cases of depression. Assessment of suicide risk is elaborated upon, although this was not discussed in the guidelines. The learning points will be enhanced if this article is reviewed together with the Ministry of Health Clinical Practice Guidelines.**


**Keywords: clinical practice guidelines, depression, pharmacotherapy, psychotherapy**

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## INTRODUCTION

Clinical Practice Guidelines (CGP) provide clinicians with treatment options that have been carefully evaluated. They support and guide treatment decisions while allowing flexibility[1], particularly where extensive options are available. The CGP for Depression were developed for these very same reasons[2]. Depression is a major mental illness with far-reaching implications. The prevalence of major depression in primary care practice is 4.8% to 9.2%, and the prevalence of all depressive disorders in primary care is 9% to 20%, making them the most common psychiatric problems in primary care[3]. As clinicians, the impetus is for timely recognition and treatment at an adequate dose and duration for response and prevention of complications. Depression is now recognised as having episodes of long duration, high rates of chronicity, relapse and recurrence, and significant psychosocial impairment and disability.

The World Health Organisation Global Burden of Disease Survey estimates that by the year 2020, major depression will be second only to ischaemic heart disease in the amount of disability experienced by the sufferers[4]. When the far-reaching emotional impact on families and carers, and the economic consequences of the illness are added, the burden reaches significant proportions[5]. Research and clinical data indicate that numerous risk factors are implicated in the genesis, the vulnerability to and recurrence of depression. It is important to note that these are wide-ranging factors from genetic, developmental, family, social and environmental factors to significant life events. Although family, twin and adoption studies indicate a genetic predisposition, the actual mode of transmission is unclear. Depression is one and a half to three times more common in first-degree biological relatives compared to the general population[6]. Another consistent finding is the gender difference; females are at higher risk with a lifetime prevalence almost twice that of males[7]. Certain personality traits may also increase vulnerability, in particular amongst those individuals who are unduly anxious, impulsive and obsessional[8]. Psychosocial stressors such as separation, loss and early sexual and/or physical abuse are other risk factors associated with an increased rate of depression.

Despite the availability of effective pharmacotherapy and psychological treatments, depressed patients are often under-diagnosed and under-treated[9]. This is why awareness, knowledge and recognition of the symptoms of the illness are crucial. While there are pathognomonic, biological, cognitive and physical symptoms, there is variability in the clinical presentation. Hence, a high index of suspicion and systematic inquiry are essential in eliciting information relevant to the diagnostic criteria. Most people will have mild to moderate depression and will consult family physicians and polyclinic doctors. Those with severe and complicated depression will need more specialised care, sometimes in a mental healthcare facility.

## CLINICAL PRESENTATION OF DEPRESSION

Depression may occur as a primary uncomplicated disorder in a single episode, or it may be recurrent, chronic or dysthymic. Depression could occur as a comorbid condition, either occurring after the onset of an established psychiatric disorder, such as panic

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**Table I. SIGECAPS.**

| | |
|---|---|
| **S** | **S**leep increase/decrease |
| **I** | **I**nterest in formerly compelling or pleasurable activities diminished |
| **G** | **G**uilt, low self esteem |
| **E** | **E**nergy poor |
| **C** | **C**oncentration poor |
| **A** | **A**ppetite increase/decrease |
| **P** | **P**sychomotor agitation or retardation |
| **S** | **S**uicidal ideation |

**Table II. DSM IV Criteria for Depression.**

| Symptoms of Depression |
|---|
| 1. Depressed mood most of the day, nearly every day. |
| 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day. |
| 3. Loss of energy or fatigue nearly every day. |
| 4. Loss of confidence or self-esteem. |
| 5. Recurrent thoughts of death or suicide, or any suicidal behaviour. |
| 6. Diminished ability to think or concentrate, or indecisiveness, nearly every day. |
| 7. Unreasonable feelings of self-reproach or excessive or inappropriate guilt, nearly every day. |
| 8. Psychomotor agitation or retardation nearly every day. |
| 9. Insomnia or hypersomnia nearly every day. |
| 10. Change in appetite (decrease or increase with corresponding weight change). |

NB: Symptoms 1 and/or 2 and any 4 others must be present for at least two weeks.

disorder, obsessive-compulsive disorder or substance abuse, or complicating the psychiatric disorder. Between 30% and 70% of depressed patients receive a concurrent diagnosis of a personality disorder[10]. Furthermore, depression is common in patients with concurrent physical illnesses and can complicate the treatment of both disorders[11]. This is where it is often missed. Chronic physical illnesses, such as cancers, strokes, arthritis, chronic lung and heart diseases and endocrine disorders, to name a few, are associated with an increased risk of psychiatric disorders. Another failing is to view the depression as a natural consequence of the serious medical condition and not initiate treatment. Depression co-existing with chronic medical illness can be treated.

At the outset, it would be important to determine whether it is depression that a physician is seeing or whether the patient is presenting with a reaction to stress. Crying and tearing are common presentations in many conditions, even at times of happiness. Patients who complain of feeling depressed must be carefully assessed for the presence of depressive disorders. Depression can refer to a mood state or to a psychiatric disorder. One should not assume that dysphoria or sadness is synonymous with depression. For a diagnosis of depression, keep the nemonic SIGECAPS or the list of DSM IV symptoms in mind[12] (Tables I and II). The diagnosis of depression should only be made if all the requisite symptoms are present.

Sometimes, patients might present with atypical features such as mood reactivity (i.e. mood brightens in response to actual or potential positive events), increased appetite and weight gain and hypersomnia; this is called atypical depression. Yet, at other times, the diagnosis might be missed because the presentation is mainly with somatic complaints, such as fatigue, physical aches and pains, and the illness is masked. When there is significant stress, sadness and anxiety are common responses. But these reactions to stress are usually short-lived. Depression is not a normal response to stress.

Depression in the elderly may present with prominent hypochondriacal and somatic complaints, and less prominent complaints of sadness. Other common presenting symptoms include anxiety, apathy and poor concentration. Sometimes, the patient may complain of poor memory and present with a dementia-like picture. Organic causes of depression are more frequent in the elderly and need to be excluded through careful history-taking, physical examination and appropriate laboratory investigations.

The presentation of depression in children and adolescents may vary across the developmental stages. Children may show more anxiety symptoms, somatic complaints and auditory hallucinations. They may also present with behavioural problems because they are unable to verbalise their feelings. Adolescents present with more sleep and appetite disturbances, delusions, suicidal ideation and suicide attempts, compared to children but less than in adults.

For the evaluation of depression, subjective and objective questionnaires are available. They are useful when a depressive disorder is suspected and for monitoring symptom changes (refer to CPG for Depression Annex III for details).

## ASSESSING THE RISK OF SUICIDE

All depressed patients must be assessed for suicide risk. The illness is associated with despair, agitation and negative cognitions[13]. The patient is at risk of suicide not only in the acute phase of the illness but also as the depression lifts and the patient becomes energised sufficiently to act on the thoughts and plans of self-harm. It is important to always ask about suicide thoughts and plans.

**List I. Factors suggesting increased suicide risk.***

1. **Demographical factors**
   Male
   Single
   Older age group
   Recent loss
2. **Symptoms**
   Severe depression
   Anxiety
   Hopelessness
   Bipolar disorder
   Psychosis, especially with command hallucinations
   Substance use
3. **History**
   Past history of suicide attempts
   Family history of suicide
4. **Suicidal thoughts**
   Presence of a specific plan
   Means available to carry out the plan
   Absence of factors that would keep patient from completing the plan
   Rehearsal of the plan

* Adapted from SL Dubovsky, AN Dubovsky. Concise Guide to Mood Disorders: Introduction xxi-xxviii. 1st ed. Washington DC: American Psychiatry Publishing Inc, 2002.

**List II: Classes of antidepressants (based upon mechanism of action).**

1. Classical mechanism
   Tricyclic antidepressants
2. Enzyme inhibition

a) Irreversible and nonselective classical MAO inhibitor

b) Reversible inhibitor of MAO-A (also known as RIMA)

3. Serotonin selective reuptake inhibitors (SSRIs).
   - Fluvoxamine, Paroxetine, Sertraline, Citalopram, Fluoxetine,
4. Dual serotonin and norepinephrine reuptake inhibitor (SNRI).
   - Venlafaxine
5. Serotonin – 2 antagonist and reuptake inhibitor (SARI).
   - Nefazodone
6. Noradrenergic and specific serotonergic antidepressants (NaSSAs).
   - Mirtazapine
7. Norepinephrine and dopamine reuptake inhibitor (NDRI).
   - Bupropion

There are known factors that increase the risk of suicide and these are listed in List I. It is not known how these risk factors interact, or whether one is more important that the other, but they should alert one to the increased risk. When a patient reports active plans and thoughts of suicide, and assessment indicates there is little to prevent the person from making an attempt, immediate steps must be taken to protect the patient. This can be done by hospitalisation, or in some cases, be under close observation in the care of family or friends. There are some patients who report chronic suicidal thoughts for years. However the acute risk of suicide usually lasts a few hours or days. When the patient is hospitalised and under observation, steps can be taken to resolve the crisis and start treatment for depression.

## COMMUNICATING

Communication with depressed patients and their families/carers plays an important part in the therapeutic relationship, particularly when patients resist the diagnosis. There is a need to recognise and deal with their resistance. Engagement, rapport and trust are crucial to keep the patient in therapy. The family physician can enhance the therapeutic relationship by listening to the patient, attend to their agenda, give them the time they need, and addressing their emotions explicitly. Offers of comfort, such as offering some tissues if they are crying, can be helpful. Reflecting emotions and validating how they feel are also useful. These simple techniques will convey to the patient that the doctor is empathic and concerned about his/her welfare.

## EDUCATION

Educating the patient about the diagnosis, and explaining the management, are important in dealing with the doubts, fears and myths of depression. Emphasis should be placed on the medical nature of the depression and that it is treatable. There is also a need to advise on lifestyle changes, exercise, reducing alcohol and smoking, and stress management.

## TREATMENT OF DEPRESSION

It will be clear from the guidelines that there are many treatment choices. The guidelines recommend three modalities of treatment for depression; namely: pharmacotherapy, psychotherapy and electroconvulsive therapy (ECT). In choosing an antidepressant, always consider the simplicity or complexity of the presenting illness, the patient's prior treatment history and the risk factors present. The goals of treatment are simple: achieve symptomatic remission of all signs and symptoms of depression, restore occupational and psychosocial functioning, and reduce the likelihood of relapse and recurrence. This entails different phases of treatment: the acute phase, which aims for remission; the continuation phase, which aims to prevent relapse; and for some patients, a maintenance phase, which aims to prevent a new episode of depression.

## INITIAL TREATMENT

Counselling and supportive therapy alone will often benefit those with mild symptoms, with the occasional

**Table III. Some common side-effects of antidepressants*.**

| | Side-effects | | | | | |
|---|---|---|---|---|---|---|
| Name of antidepressant | Anticholinergic | Sedation | Orthostatic hypotension | Cardiac arrhythmias | Gastroinstestsinal distress | Weight gain |
| Amitriptyline | ++++ | ++++ | ++++ | +++ | + | ++++ |
| Clomipramine | ++++ | ++++ | ++ | +++ | + | ++++ |
| Imipramine | +++ | +++ | ++++ | +++ | + | ++++ |
| Fluxetine | O | O | O | O | +++ | O |
| Fluvoxamine | O | O | O | O | +++ | O |
| Paroxetine | + | + | O | O | +++ | + |
| Sertraline | O | O | O | O | +++ | O |
| Venlafaxine | + | + | O | O | +++ | O |
| Mirtazapine | + | +++ | O | O | O | +++ |

* Adapted from Institute for Clinical Systems Improvement (ICSI) Healthcare Guidelines: Major Depression, Panic Disorder and Generalized Anxiety Disorder in Adults in Primary Care. Bloomington, MN: Institute for Clinical Systems Improvement; 2002.

need for hypnotics, if sleep is a problem. In patients who are reluctant to start antidepressants, or patients with comorbid medical conditions who may be unable to tolerate the antidepressants, psychotherapy may be considered as a first-line treatment. Antidepressants should be instituted if there is a lack of improvement or worsening of symptoms while the patient is receiving psychotherapy.

## ANTIDEPRESSANTS AS FIRST-LINE TREATMENT

If antidepressants are used as the first line of treatment, it is important to remember that all the antidepressants are equally effective and no single antidepressant results in remission for all patients (List II). The specific medication choice will not only be determined by patient factors (such as comorbid medical conditions and concomittant medications, the side-effect profile and tolerability), but also by the availability and cost of the antidepressant. The Guidelines recommend either tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs) as first-line antidepressants. TCAs may be more effective in severely-depressed patients but if there is a suicide risk, TCAs must be avoided because of their lethality in overdose. In patients with atypical depressive symptoms (hypersomnia, hyperphagia, mood reactivity and hypersensitivity to rejection), SSRIs are more effective than TCAs. A reversible monoamine oxidase inhibitor (RIMA) can also be used.

Doctors need to familiarise themselves with the common side-effects of the various antidepressants. The patient should be cautioned that the therapeutic effects will not be immediately experienced, and advised on the possible one- to three-week time lag to initial improvement of symptoms. This will deal with their expectations and improve compliance. More frequent follow-ups may be needed in the initial stages and this depends on the severity of depression, suicide risk, patient's cooperation and availability of social supports. Subsequent visits will depend on the response to treatment. When initiating antidepressant therapy, it should be remembered that starting doses are generally lower for the elderly and those with concomitant medical or surgical illnesses. Monotherapy with a single antidepressant is recommended in the Guidelines. Generally, starting doses are low with gradual titration to the full therapeutic dose. At each visit, the mental state should be monitored, and assessment of the symptoms and suicide risk, and the development of side-effects made (Table III).

## ACUTE PHASE OF TREATMENT

The acute phase of treatment is accepted as lasting 12 weeks. Efficacy of the treatment is gauged by amelioration of symptoms. Some symptoms, such as sleep and appetite, may improve relatively quickly. All antidepressants require four to six weeks to achieve their maximum therapeutic effects. Generally, if treatment is going to be effective, at least a partial symptomatic response will be seen by four to six weeks. Therefore, it is advisable that antidepressants, once started, should be continued for this period of time, provided there are no adverse effects. The improvement in the mood would be seen by the end of twelve weeks. However, other symptoms such as low self-esteem, and social and occupational recovery

**Table IV. Summary of management of depression.**

| |
|---|
| **Aims of treatment** |
| Full remission of symptoms and return to full function. |
| Prevent relapses or recurrences. |
| **Primary care setting** |
| First episode depression – monotherapy with TCAs or SSRIs for 4 to 6 weeks. |
| If partial response or non-response, increase the dose or switch to an antidepressant of the same or different class. |
| If one or two trials of antidepressants have failed, the guidelines recommend referral to a psychiatrist. |
| **Tertiary care setting** |
| Consider augmentation with another medication, Lithium or Thyroxine or other agent. |
| Combination of two antidepressants from different classes. |
| Psychotherapy |
| ECT |

may take longer. If at four weeks after starting treatment there is no improvement, or after six to eight weeks there is only partial improvement, the treatment should be reviewed[14]. There are several options available. These include increasing the dose when there has been at least a partial response, to switching antidepressants as well as augmentation and combination therapy. Generally it would be best to seek specialist opinion for the latter two options. (Table IV)

## SWITCHING AND AUGMENTATION STRATEGIES

Increasing the dose is useful only if there is a partial response or if sub-therapeutic doses were used. The switching strategy works for partial or non-responders. The switch may be to an antidepressant from the same class, for example from one SSRI to another (but this is useful if there was at least a partial response to the initial SSRI). Switching within TCAs is generally not useful. The switch could also be to an antidepressant of a different class, for example from a SSRI to a SNRI. Caution is needed in the switch because of possible drug interactions. A washout period is not needed, except with Fluoxetine which has a long half-life and Moclobemide (RIMA) which requires a three-day washout period. Antidepressants should be continued for at least six months after the acute phase and followed by maintenance treatment when indicated as listed in the Guidelines.

## ENDING TREATMENT WITH ANTIDEPRESSANTS

When the decision is made to stop treatment, the antidepressant dose should be gradually tapered to avoid discontinuation symptoms. Follow-up and assessments will still be needed to ensure that a new episode does not occur. This is why patient education on what to look out for, and advice to return earlier if symptoms recur, is crucial. If, unfortunately, the depression recurs, restart the antidepressant at the same dose that was effective earlier.

## RECENT PUBLIC HEALTH ADVISORY

Soon after these guidelines were prepared, the US Food and Drug Administration (FDA) introduced warnings on antidepressants as part of a public health advisory. This was after an initial report on studies with Paroxetine and subsequent reports on studies of other antidepressants, which appeared to suggest an increased risk of suicidal behaviour in children treated with antidepressants. It warned physicians that the patient's depression may become worse and that he may develop suicidal thinking or behaviour after the initiation of treatment or when the dose either increases or decreases, and as a result, implemented labelling changes[15]. However, although there are no studies showing a convincing link between drug therapy and suicide, the FDA is continuing to review available clinical data on this matter. The Health Science Authority in Singapore has a position statement on this issue in its website. **Author's afternote:** There is also a recent advisory on the use of Paroxetine in pregnant females, and prescribers should note the "Dear Health Professional Letter" and product insert on this antidepressant.

## PSYCHOTHERAPY

There is a wide range of therapies ranging from simple counselling and supportive therapy to more specialised cognitive-behaviour therapy, interpersonal therapy, psychodynamic psychotherapy, problem-solving therapy, and group and marital therapy. The latter therapies have been shown to be efficacious for the treatment of depression and will require referral to specialists with skills and training in these therapies. This can be done by referring the patient to any psychiatrist in a hospital or psychiatric specialist clinic. Psychotherapy is generally time-limited. The focus is on current problems and symptom resolution. Psychotherapy alone is insufficient for severe and/or psychotic major depressive disorders.

## COMBINATION THERAPY

Combined treatment with both medication and psychotherapy would be advantageous for patients who have at least shown some response to either

treatment alone. It is also of use for those with a history of chronic episodes or poor inter-episode recovery, long-term psychosocial problems and/or difficulties adhering to treatment.

## ELECTROCONVULSIVE THERAPY

Electroconvulsive therapy (ECT) is reserved for moderate or severe depressions, depressions with psychotic symptoms not responding to pharmacological treatment, and when a rapid response is needed, such as when a patient is actively suicidal and refusing to eat or drink. It involves a passage of a brief electrical current lasting about two milliseconds to induce a controlled seizure. Common side-effects include a transient confusional state after the procedure, and short-term memory loss which recovers by four to six weeks. The mortality risk associated with the procedure is very low at about one per 10,000 patients and there is no evidence that it causes brain damage[16,17].

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