



Complete Summary

GUIDELINE TITLE

Depression.

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Depression. Singapore: Singapore Ministry of Health; 2004 Mar. 54 p. [102 references]

GUIDELINE STATUS

This is the current release of the guideline.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [May 2, 2007, Antidepressant drugs](#): Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.
- [October 25, 2006, Effexor \(venlafaxine HCl\)](#): Published retrospective studies report that venlafaxine overdose may be associated with an increased risk of fatal outcome.
- [May 12, 2006, Paxil \(paroxetine\) and Paxil CR](#): Changes to the Clinical Worsening and Suicide Risk subsection of the WARNINGS section in the prescribing Information related to adult patients, particularly those who are younger adults.
- [December 8, 2005, Paxil \(paroxetine\)](#): Pregnancy category changed from C to D and new data and recommendations added to the WARNINGS section of prescribing information.
- [September 27, 2005, Paxil \(paroxetine\) and Paxil CR](#): Changes to the Pregnancy/PRECAUTIONS section of the Prescribing Information to describe the results of a retrospective epidemiologic study of major congenital malformations in infants born to women taking antidepressants during the first trimester of pregnancy.

COMPLETE SUMMARY CONTENT

**** REGULATORY ALERT ****

SCOPE

METHODOLOGY - including Rating Scheme and Cost Analysis

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

CATEGORIES

IDENTIFYING INFORMATION AND AVAILABILITY

DISCLAIMER

SCOPE

DISEASE/CONDITION(S)

Depression

Note: Treatment of major depression in bipolar disorder, psychotic depression, and cases with high suicide risk are not included in these guidelines.

GUIDELINE CATEGORY

Diagnosis

Evaluation

Management

Treatment

CLINICAL SPECIALTY

Family Practice

Internal Medicine

Psychiatry

Psychology

INTENDED USERS

Allied Health Personnel

Nurses

Physician Assistants

Physicians

Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

To raise awareness and assist in the detection of depression and to ensure that treatment is adequate and effective

TARGET POPULATION

Children, adults, and elderly patients at risk of depression

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Assessment of depression
 - Patient history
 - Mental state examination
 - Physical examination
 - Laboratory testing

Treatment

1. Psychoeducation
 - Educating the patient
 - Adequate follow-up
 - Lifestyle changes
2. Referral to a psychiatrist
3. Pharmacotherapy
 - Antidepressants: tricyclic antidepressants, selective serotonin reuptake inhibitors, venlafaxine, mirtazapine, and bupropion
 - Increasing dose
 - Switching antidepressants
 - Addition of a second antidepressant
4. Psychotherapy
 - Cognitive behaviour therapy
 - Interpersonal therapy
 - Psychodynamic psychotherapy
 - Problem-solving therapy
 - Couple/marital therapy
5. Concurrent combined psychotherapy and pharmacotherapy
6. Electroconvulsive therapy
7. Suicide prevention
 - Maintain contact, ensure close supervision, and engage support systems
 - Hospitalization
 - Self-administered rating scales

MAJOR OUTCOMES CONSIDERED

- Morbidity and mortality
- Recurrence and increased severity

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level Ia Evidence obtained from meta-analysis of randomised controlled trials

Level Ib Evidence obtained from at least one randomised controlled trial

Level IIa Evidence obtained from at least one well-designed controlled study without randomisation

Level IIb Evidence obtained from at least one other type of well-designed quasi-experimental study

Level III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies

Level IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

Grade A (evidence levels Ia, Ib) Requires at least one randomised controlled trial, as part of the body of literature of overall good quality and consistency addressing the specific recommendation

Grade B (evidence levels IIa, IIb, III) Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation

Grade C (evidence level IV) Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

Good Practice Points Recommended best practice based on the clinical experience of the guideline development group

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The recommendations that follow are those from the guideline's executive summary; detailed recommendations can be found in the original guideline document. Each recommendation is rated based on the level of the evidence and the grades of recommendation. Definitions of the grades of the recommendations (A, B, C, Good Practice Points) and level of the evidence (Level I-Level IV) are presented at the end of the "Major Recommendations" field.

C - 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 coexisting 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 page 32 in the original guideline document.)

- 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 C, Level IV)

C - Referrals to a psychiatrist are warranted when

- there are comorbid medical conditions for which expertise is required regarding drug-drug interactions
- there is diagnostic difficulty
- one or two trials of medication have failed
- if augmentation or combination therapy is needed
- for those with comorbid substance abuse or severe psychosocial problems
- the patient is pregnant or plans to become pregnant
- for postnatal depression
- if specialized treatment like electroconvulsive therapy is indicated but unavailable in the primary care setting

(Grade C, Level IV)

C - Once an antidepressant has been selected, start with a low dose and titrate to the full therapeutic dose gradually, while assessing patients mental state and watching for the development of side-effects. The frequency of monitoring will depend on the severity of the depression, suicide risk, the patient's cooperation, and the availability of social supports. **(Grade C, Level IV)**

B - All antidepressants, once started should be continued for at least 4 to 6 weeks. **(Grade B, Level IIb)**

C - If there is little or no improvement after switching, it is recommended that a psychiatric referral is sought for the following:

1. Augment the first antidepressant with a second medication (Augmentation)
2. Add a second antidepressant to the first (Combination)

(Grade C, Level IV)

GPP - At the end of the Continuation phase the antidepressant medication should be gradually tapered to avoid discontinuation symptoms. Patients should be followed up during the next few months to ensure that a new depressive episode does not occur. If recurrence occurs, the patient is likely to respond to the same antidepressant at the same dosage that was effective previously, which should then be continued for 6 months. **(GPP)**

A - Psychotherapy alone is as efficacious as antidepressant medication in patients with mild to moderate major depression and can be used as first-line treatment. **(Grade A, Level Ia)**

A - Cognitive Behaviour Therapy is also an effective maintenance treatment and is recommended for patients with recurrent depression who are no longer on medication. (**Grade A, Level Ia**)

A -Concurrent combined psychotherapy and pharmacotherapy is recommended in severe depression and chronic depression as it is more effective than either alone in these conditions. (**Grade A, Level Ib**)

B - Electroconvulsive therapy may be considered as the first-line treatment for patients with severe depression, depression with psychotic features, marked functional impairment, catatonic stupor, high suicide risk, or food refusal leading to nutritional compromise. It is also considered in any other situation 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. (**Grade B, Level IIb**)

Definitions:

Grades of Recommendations

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Grade C (evidence level IV) Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

Good Practice Points Recommended best practice based on the clinical experience of the guideline development group

Levels of Evidence

Level Ia Evidence obtained from meta-analysis of randomised controlled trials

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Level IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

CLINICAL ALGORITHM(S)

A clinical algorithm is provided in the original guideline document for Pharmacotherapy of Major Depressive Disorder.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Overall Benefits

Increased awareness and appropriate diagnosis and treatment of depression

Specific Benefits

- Selective serotonin reuptake inhibitors are better tolerated. They are less associated with anticholinergic adverse effects, cardiotoxicity, sedation, or weight gain. They have been shown to be more effective than tricyclic antidepressants (TCAs) for patients with atypical depressive symptoms such as hypersomnia, hyperphagia, mood reactivity, and hypersensitivity to rejections.
- Among the specific psychotherapeutic interventions, Cognitive Behaviour Therapy (CBT) has the best documented efficacy for the treatment of depression. It focuses on identifying and modifying distorted, negatively biased thoughts.

POTENTIAL HARMS

- Caution is needed when switching from one antidepressant to another because of the possibility of drug interactions. The first antidepressant may either be stopped or tapered before starting the next antidepressant without any washout period; the exceptions are with fluoxetine, which has a long half-life, and with moclobemide, for which a three-day washout is recommended.
- A combination of desipramine or other tricyclic antidepressants (TCA) with a selective serotonin reuptake inhibitor (SSRI) may produce a more rapid onset of action.
- Caution is advised as both are substrates of the CYP2D6 isoenzyme, a common metabolic pathway for drug metabolism, and plasma concentrations of TCAs are likely to rise, increasing the risk of cardiotoxicity.
- There are reports of possible increased risk of suicidal thinking in using an SSRI such as paroxetine.
- Tricyclic antidepressants may cause a wide-range of side-effects due to widespread receptor blockade. These side-effects could lead to poor

compliance and use of suboptimal therapeutic doses and can be lethal in overdose.

- In pregnancy and nursing mothers, the relative risks and benefits of using antidepressants must be carefully weighed. There is no evidence of increased risk of teratogenesis or spontaneous abortions following exposure to antidepressants such as TCAs and SSRIs in early pregnancy. Antidepressants, however, are secreted in breast milk, and levels of antidepressants have been detected in infant serum samples. Paroxetine has the lowest milk/plasma ratio amongst the SSRIs.
- The common side effects of electroconvulsive therapy (ECT) are transient headaches, muscle soreness, nausea, and memory impairment. Following each ECT 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 ECT. Some degree of retrograde amnesia, particularly for recent memories, may continue for patients receiving bilateral ECT. This retrograde amnesia manifests as difficulty remembering information learned prior to the course of ECT.

CONTRAINDICATIONS

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Although there is no absolute contraindication to electroconvulsive therapy (ECT), 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 ECT treatment should be carefully weighed in collaboration with a physician, cardiologist, anesthesiologist, neurologist, or neurosurgeon, as the case requires.

QUALIFYING STATEMENTS

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- These guidelines are not intended to serve as a standard of medical care. Standards of medical care 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 to 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, nor should they be construed as including all proper methods of care or excluding 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.
- 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 if new evidence appears that requires substantive changes to the recommendations.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about [availability](#), see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health. Depression. Singapore: Singapore Ministry of Health; 2004 Mar. 54 p. [102 references]

ADAPTATION

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

DATE RELEASED

2004 Mar

GUIDELINE DEVELOPER(S)

Chapter of Psychiatrists Academy of Medicine Singapore - Professional Association
National Medical Research Council (Singapore Ministry of Health) - National

Government Agency [Non-U.S.]
Singapore Ministry of Health - National Government Agency [Non-U.S.]
Singapore Psychiatric Association - Professional Association

SOURCE(S) OF FUNDING

Singapore Ministry of Health (MOH)

GUIDELINE COMMITTEE

Workgroup on Depression

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Workgroup Members: A/Prof Mahendran Rathi, Chief & Senior Consultant, Department of General Psychiatry, Institute of Mental Health/Woodbridge Hospital (Chairman); Dr Low Bee Lee, Senior Consultant Psychiatrist & Head, Department of Psychological Medicine, Tan Tock Seng Hospital; Dr Khare Chandrashekhar B, Consultant Psychiatrist, Department of Psychological Medicine, National University Hospital; Dr Gwee Kok Peng, Consultant Psychiatrist, Department of General Psychiatry & Deputy Head, Psychotherapy Services, Institute of Mental Health/Woodbridge Hospital; Dr Chiam Peak Chiang, Chief & Senior Consultant Psychiatrist, Dept of Geriatric Psychiatry, Institute of Mental Health/Woodbridge Hospital; Dr Kok Lee Peng, Consultant Psychiatrist, Kok & Tsoi Psychiatric Clinic; Dr Wang Chee Cheng, Adrian, Deputy Chief & Consultant, Department of Psychiatric Rehabilitation, Institute of Mental Health/Woodbridge Hospital; Dr Yap Hwa Ling, Senior Consultant Psychiatrist, Division of Psychological Medicine, Changi General Hospital; Dr Fung Shuen Sheng, Daniel, Deputy Chief & Consultant, Department of Child & Adolescent Psychiatry, Institute of Mental Health/Woodbridge Hospital; Dr Ho Han Kwee, Family Physician & Doctor-in-charge, Choa Chua Kang Polyclinic; Dr Soon Shok Wen, Winnie, Senior Family Physician & Doctor-in-charge, Ang Mo Kio Polyclinic

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Singapore Ministry of Health Web site](#).

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Patient education brochure on depression. Singapore: Singapore Ministry of Health; 2004. 27 p.

Electronic copies: Available in Portable Document Format (PDF) from the [Singapore Ministry of Health Web site](#).

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

NGC STATUS

This NGC summary was completed by ECRI on July 6, 2004. This summary was updated by ECRI on August 15, 2005, following the U.S. Food and Drug Administration advisory on antidepressant medications. This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Paxil (paroxetine). This summary was updated by ECRI on December 12, 2005, following the U.S. Food and Drug Administration advisory on Paroxetine HCL - Paxil and generic paroxetine. This summary was updated by ECRI on May 31, 2006 following the U.S. Food and Drug Administration advisory on Paxil (paroxetine hydrochloride). This summary was updated by ECRI on November 22, 2006, following the FDA advisory on Effexor (venlafaxine HCl). This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs.

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