

Clinical guidelines for depressive disorders

Summary of recommendations relevant to family physicians

Sidney H. Kennedy, MD, FRCPC Raymond W. Lam, MD, FRCPC Brian Morris, MD, CCFP
for the CANMAT Depression Work Group

Major depressive disorder (MDD) is an illness of great importance in public health. In primary care practices, patients with major depression have greater levels of disability than those with other chronic conditions, such as diabetes, arthritis, chronic back pain, or hypertension.¹ According to the World Health Organization, by 2020 depression will cause more disability than infectious diseases, cancer, or accidents and will be second only to ischemic heart disease as a cause of disability.²

In the summer of 2001, a working group of the Canadian Network for Mood and Anxiety Treatments (CANMAT) partnered with the Canadian Psychiatric Association to publish *Clinical Guidelines for the Treatment of Depressive Disorders*.³ The full text of the guidelines, with references, is available on both websites: www.canmat.org and www.cpa-apc.org. Most of the recommendations were based on level I (meta-analysis or replicated randomized controlled trials) or level II evidence (at least one randomized controlled trial). Statements made in this summary are based on the guidelines and are not specifically referenced. We summarize the recommendations relevant to family physicians.

Definitions, diagnosis, and prevalence

The guidelines focus on management of MDDs. An episode of major depression, according to DSM-IV criteria, involves at least 2 weeks of depressed mood or loss of interest or pleasure, along with several other symptoms, all of which cause substantial distress or functional impairment. Other disorders with similar symptoms include dysthymic disorder (which is less severe), bipolar disorder (which includes episodes of mania or hypomania), bereavement, and adjustment disorder with depressed mood. Seasonal affective disorder and postpartum depression are considered as subtypes, or specifiers, of MDD.

The 1-year prevalence of MDD in Canada is 3.2% to 4.6%; women are affected twice as often as men. Mortality rates are higher among depressed patients, partly through suicide (2.2% of depressed patients will die by suicide), but also through effects on other causes of death. For instance, depressed patients are three times more likely to die in the year after an episode of unstable angina than nondepressed patients and four times more likely to die in the first 3 months after myocardial infarction.

Role of psychotherapy

Every family physician caring for patients with MDDs offers some form of psychotherapy, if only through the strength of the patient-physician relationship and through providing compassion, support, and information. The guidelines differentiate between this level of psychotherapy, which can be termed supportive psychotherapy or clinical management, and more formal psychotherapy.

Among the formal methods, several have been carefully studied in randomized controlled trials, in comparison with each other or in comparison with antidepressant medication. Cognitive behavioural therapy and interpersonal therapy are as effective as antidepressant medications in mild-to-moderate depression and can be recommended as first-line therapies (level I evidence). Family physicians can use one of these types of psychotherapy as treatment for MDDs under two conditions. They must have sufficient training (including supervision of therapy patients) and experience in the methods or must have, as a referral source, another local clinician with knowledge of these methods, and patients must express a preference for this type of therapy, usually because of personal belief favouring nonpharmacologic therapy or concerns about potential side effects of medication.

If a specific form of psychotherapy is to be recommended for an episode of major depression, based on patient preference and the availability of a trained clinician, the guidelines stress that it should be one of the empirically validated types of treatment: cognitive behavioural therapy or interpersonal therapy. Problem-solving therapy, developed specifically for primary care, is another empirically validated treatment.

Bibliotherapy, or directed reading, is an alternative for patients who are unable to access psychotherapy. Helping patients work through a book such as *The Feeling Good Handbook*⁴ or *Mind over Mood*⁵ can be a useful adjunct to treatment.

Pharmacotherapy

For most patients with MDD who present to family physicians, the cornerstone of treatment is antidepressant medication. Extensive studies through randomized clinical trials support evidence-based recommendations for use of various agents. A new recommendation concerns the goal

of treatment: clinicians are urged to aim for full remission or recovery, defined as the virtual absence of depressive symptoms. Patients who have residual or minimal symptoms continue to suffer psychosocial disability and are also at much higher risk of recurrence.

Three groups of antidepressant medication can be distinguished. The classic agents include tricyclic agents (TCAs), such as amitriptyline; heterocyclic agents, such as maprotiline; and monoamine oxidase inhibitors, such as phenelzine. The selective serotonin reuptake inhibitors (SSRIs) currently available are citalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. The third class, termed novel agents, includes bupropion, mirtazapine, moclobemide, nefazodone, trazodone, and venlafaxine.

Meta-analyses comparing the efficacy of TCAs with that of SSRIs have found comparable rates of response among outpatients. Similarly, meta-analyses comparing novel agents to TCAs have shown novel agents to have efficacy comparable to that of older agents. In comparing one of the novel agents, venlafaxine, to SSRIs, two meta-analyses showed venlafaxine to give higher rates of response and remission than the SSRIs. Because the remission rate for SSRIs in these studies was lower than that reported in other trials, however, the issue remains controversial. **Table 1** summarizes the recommendations for treatment of MDDs, as presented in the guidelines.

Subtype of depressive disorder affects choice of therapy, according to published clinical trials. **Table 2** lists first-line therapy for each subtype described in the guidelines: note that comparative studies of all agents for all subtypes have not been conducted.

The recommended duration of treatment has changed in the last decade. Current guidelines suggest that patients who respond to antidepressant medication during a single episode of depression should continue to take the drug, at the same dose, for 9 months (8 to 12 weeks to attain remission, then 6 months for maintenance). Therapy

Table 1. Recommendations for treating major depressive disorder

First-line treatments
<ul style="list-style-type: none"> • SSRIs and novel agents (level I evidence) • Venlafaxine might have higher remission rates than SSRIs (level I evidence)
Second-line treatments
<ul style="list-style-type: none"> • Amitriptyline and clomipramine have greater efficacy than SSRIs among hospitalized patients (level II evidence) • Safety and tolerability issues need to be addressed • In the frail elderly, nortriptyline has fewer adverse effects than amitriptyline or clomipramine
Third-line treatments
<ul style="list-style-type: none"> • Other tricyclic agents and monoamine oxidase inhibitors, because of safety and tolerability issues (level II evidence)

SSRIs — selective serotonin reuptake inhibitors

should be continued for at least 2 years for older patients; those with psychotic features; and those whose episodes are recurrent, frequent, difficult to treat, or severe. When antidepressant medication is stopped, patients should be cautioned about discontinuation syndrome, which includes such symptoms as insomnia, nausea, paresthesia, and hyperarousal; these symptoms can be reduced by tapering the dose of antidepressant rather than stopping it abruptly.

Response to antidepressant medication should be evident, to some degree, by 4 weeks, with full response by 8 to 12 weeks. Patients who have shown no response by 4 weeks should be reevaluated. The diagnosis should be reconsidered, adherence to medication assessed, adjunctive psychotherapy considered, or early referral to a psychiatrist sought: some sort of further intervention is usually required. Pharmacologic strategies for patients not responding at 4 weeks include switching to a different antidepressant, adding a second antidepressant, or augmenting therapy with an agent such as lithium.

Table 2. Subtypes of depression and their first-line treatments: *These recommendations are evidence-based; however, it is likely that all selective serotonin reuptake inhibitors and novel antidepressants will have some benefit in all of these subtypes. When treating patients with these agents, physicians' familiarity with, comfort with, and knowledge of a specific agent should be considered along with the evidence-based recommendations.*

DEPRESSION SUBTYPE	FEATURES	FIRST-LINE TREATMENT (ALPHABETICAL ORDER)
Atypical features	Mood reactivity, weight gain, hypersomnia	Fluoxetine, moclobemide, sertraline (level II evidence)
Melancholic features	Loss of interest or pleasure	Paroxetine, venlafaxine (level I evidence)
Psychotic features	Delusions or hallucinations	Electroconvulsive or antidepressant-antipsychotic combination therapy (level I evidence)
Seasonal pattern	Onset and remission at characteristic times	Bright-light therapy (level I evidence)
"Anxious" depression	Serious anxiety symptoms	Mirtazapine, moclobemide, paroxetine, sertraline, venlafaxine (level I evidence)
Postpartum depression	Onset within 4 weeks after delivery	Fluoxetine, cognitive-behavioural therapy (level II evidence)



Adverse effects are a common concern with antidepressant medications. With TCAs, the most common side effects are anticholinergic and cardiovascular; with SSRIs and novel agents, one of the most troublesome side effects is sexual dysfunction, which can mean impaired desire, arousal, or orgasm. Low rates of sexual dysfunction (roughly 10% of patients) are seen with bupropion, mirtazapine, moclobemide, and nefazodone; intermediate rates (10% to 30% of patients) with venlafaxine; and higher rates (generally 30% to 50% of patients) with the SSRIs.

Conclusion

Depression is a common illness that family physicians see and treat daily. Among the evidence-based recommendations made in these guidelines, two of the most important changes are the goal of therapy (full remission, with no residual symptoms), and the duration of therapy (at least 9 months for a first episode). ❖

Dr Kennedy is Psychiatrist-in-Chief of the University Health Network and is a Professor of Psychiatry at the University of Toronto in Ontario. Dr Lam is Professor and Head of the Division of Clinical Neuroscience in the Department of Psychiatry at the University of British Columbia in Vancouver.

Dr Morris is Medical Director of Science and Medicine Canada in Toronto.

Competing interests

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