An approach to managing depression
Defining and measuring outcomes

Atul Khullar, MD    Roger S. McIntyre MD, FRCP(C)

ABSTRACT

OBJECTIVE To provide family physicians with a contemporary approach to formulating a treatment model for major depressive disorder that integrates definitions of new therapeutic end points, familiarizes them with tools for assessing these end points, and describes newer methods for enhancing outcome.

SOURCES OF INFORMATION Canadian Psychiatric Association Guidelines for the Treatment of Depressive Disorders, relevant articles from a MEDLINE search using the MeSH headings “full remission” and “depression,” and the authors’ clinical experience.

MAIN MESSAGE Major depressive disorder is an episodic, relapsing, and sometimes chronic illness. Depressive symptoms in primary care settings are often vague reports of anhedonia, anxiety, and nonspecific somatic complaints. Therapeutic objectives in depression are full remission of depressive symptoms, prevention of recurrence, and restoration of function. Depression rating scales can be useful for monitoring and treating depression.

CONCLUSION The proposed therapeutic model anticipates the chronic course of illness, defines treatment end points, encourages longer duration of treatment, and includes both pharmacologic and lifestyle therapies. The 7-item Hamilton Depression Rating Scale can assist clinicians in determining when full remission has occurred.

This article has been peer reviewed.
Cet article a fait l'objet d'une évaluation externe.

Major depressive disorder (MDD) is a prevalent, progressive, and often chronic disease. It is currently estimated to be the fourth leading cause of disability worldwide and is expected to rise to second behind ischemic heart disease by the year 2020 (level I evidence). Researchers estimate that up to 11% of global disability is attributable to depressive symptoms. Frequent users of family physicians’ services often manifest syndromal or subsyndromal symptoms of anxiety and depression (level I evidence). The most common ambulatory presentation of MDD is a confluence of anhedonia, nonspecific somatic symptoms, and psychich anxiety.

Clinicians are often uncertain when to initiate, augment, and continue treatment for these patients, particularly in the context of busy family practice. Modern treatment models for MDD promote delineation of precise and relevant end points, the concept of full remission, and a lengthening of maintenance treatment. Standardized rating instruments are useful to monitor end points and therapeutic progress. This article provides an overall approach to integrating these conceptual perspectives into the practical management of MDD.

Sources of information
The approach outlined in this paper is based on a combination of relevant papers from a MEDLINE search using the MeSH headings “full remission” and “depression,” the 2001 Canadian Psychiatric Association Clinical Guidelines for the Treatment of Depressive Disorders (level I to III evidence), the National Institute of Mental Health Sequenced Treatment Alternatives to Relieve Depression treatment protocol and algorithm, and the authors’ clinical experience when level I or II evidence is lacking.

Case
A 48-year-old divorced woman with no children, who has been employed as an elementary schoolteacher, has been a patient of yours for 6 years. The past 2 years are notable for frequent visits with a symptom pattern of menopausal difficulties, fatigue, and occasional muscle aches. She has no recorded history of syndromal depression, but she has intermittently reported diminished interest in activities and difficulties getting to sleep. Her signature presentation is physical tension, worry, superficial engagement, and requests for weekly office appointments. She is difficult to reassure, and her current mental status is inextricably linked to ongoing interpersonal difficulties at her school.

Over the past 2 months she has uncharacteristically missed work on several occasions due to fatigue and diminished interest in her job. Results of a focused physical examination and basic blood tests are normal. She is diagnosed with major depression and, in retrospect, likely with preceding subsyndromal depression of several years’ duration.

The severity of her depression is assessed with the 7-item Hamilton Depression Rating Scale (HAM-D7). Her score of 15 of a possible 26 is consistent with depression of moderate severity. She denies current suicidal thoughts, and there is no history of syndromal anxiety disorders or suicide attempts.

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Ruling out bipolar disorder

Researchers estimate that up to 25% of people with anxious depression in primary care have bipolar disorder (BD) (level II evidence). Depression is also often the index presentation of bipolar illness, and people with BD typically present to primary care physicians while experiencing depressive symptoms (level II evidence). Several variables that correlate to higher risk of subsequent bipolarity occur in depressive illness. Bipolarity can be assessed easily in family practice settings with rating instruments such as the Mood Disorders Questionnaire (MDQ) (Table 1). Further treatment and diagnostic issues in BD are beyond the scope of this paper. They have been reviewed extensively in this journal and elsewhere.

The 17-item Hamilton Depression Scale (HAM-D17) has been the criterion standard for objective measurement of depressive symptoms in mood disorders research (level I evidence). The clinical utility of the HAM-D17 is diminished somewhat by the length of time required to administer the interview and by the possible lack of inter-rater reliability. A truncated form of the HAM-D17 with cutoff scores for full remission is useful in family practice settings. On the basis of a sample of 292 patients with major depression who received standard clinical treatment at a university clinic, a 7-item rating scale was derived using the seven items with the greatest frequency and sensitivity to change with treatment (Table 2).

A score of 3 or less on the HAM-D7 was found to correlate with the HAM-D17 definition of full remission. Sensitivity (95%), specificity (84%), and positive (94%) and negative (86%) predictive values of this relation were all high. The HAM-D7 takes only a few minutes to complete and could be efficient and practical for enhancing care of people suffering from MDD. There is no prescribed pattern for use of the HAM-D7, but we suggest using it whenever clinical monitoring is required (ie, 5 to 6 weeks after therapy when dose optimization is being considered) (level III evidence).

Other shorter scales, based on the HAM-D17, have been developed and have demonstrated comparable or superior sensitivity and specificity to the HAM-D17 (level I and II evidence). Unlike the HAM-D7, their clinical utility has remained unclear. Self-administered scales, such as the Beck Depression Inventory (BDI), are popular with some clinics because of their ease of administration and efficiency. The BDI is, however, less sensitive than many conventional physician-rated scales at assessing antidepressant efficacy (level I evidence).

These rating scales are not diagnostic tools by any means; diagnosis of MDD remains a clinical decision. Using standardized objective instruments, however, has benefitted management of several medical disorders (eg, fasting blood glucose and hemoglobin A1c for diabetes). Unfortunately, standardized outcome instruments have been underused in psychiatry. As illustrated in our case, they can help in assessing the severity of psychiatric symptoms, establishing treatment efficacy, and comparing various interventions. They can also help to determine full remission, facilitate record keeping, and assist in evaluating patients’ core depressive symptoms.

Avenues of treatment, such as interpersonal therapy (IPT), cognitive behavioral therapy (CBT), and pharmacotherapy, are thoroughly discussed, and

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Table 1. Factors in depressed patients that increase suspicion of past or future bipolarity

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<thead>
<tr>
<th>Factor</th>
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<tr>
<td>Onset before age 25</td>
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<td>Family history of bipolar illness</td>
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<tr>
<td>History of attention hyperactivity deficit disorder</td>
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<tr>
<td>Pharmacologic- or substance-induced mania or hypomania</td>
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<td>Seasonal affective disorder</td>
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<tr>
<td>Postpartum depression or psychosis</td>
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<tr>
<td>Episodic comorbid anxiety disorder</td>
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<tr>
<td>Comorbid personality disorder (especially borderline)</td>
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<td>Hypersomnia</td>
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<td>Substance abuse</td>
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Adapted from Manning et al, and Lish et al.
### Table 2. The 7-item Hamilton Rating Scale for Depression (HAM-D7)

**Depressed mood** (sadness, hopeless, helpless, worthless)

*Have you been feeling down or depressed this past week? How often have you felt this way and for how long?*

- 0. Absent
- 1. Indicated only on questioning
- 2. Spontaneously reported verbally
- 3. Communicated nonverbally (facial expression, posture, voice, weeping tendency)
- 4. Patient reports *virtually only* these feeling states in spontaneous verbal and nonverbal communication

**Feelings of guilt (self-criticism, self-reproach)**

*In the past week, have you felt guilty about something you’ve done, or that you’ve let others down? Do you feel you’re being punished for being sick?*

- 0. Absent
- 1. Self-reproach (letting people down)
- 2. Ideas of guilt or ruminating about past errors or sinful deeds
- 3. Present illness is a punishment. Delusions of guilt
- 4. Hears accusatory or denunciatory voices or experiences threatening visual hallucinations

**Interest, pleasure, level of activities (work and activities)**

*Are you as productive at work and at home as usual? Have you felt interested in doing the things that usually interest you?*

- 0. No difficulty
- 1. Fatigue, weakness, or thoughts or feelings of incapacity (related to work, activities, hobbies)
- 2. Loss of interest (directly reported or indirectly through listlessness, indecision, and vacillation)
- 3. Decrease in actual time spent in activities or decrease in productivity. (In hospital, rate 3 if patient does not spend at least 3 hours daily in activities exclusive of ward chores.)
- 4. Stopped working due to current illness. (In hospital, rate 4 if patient only does ward chores or fails to perform ward chores unassisted.)

**Tension, nervousness (psychic anxiety)**

*Have you been feeling more tense or nervous than usual? Have you been worrying a lot?*

- 0. No difficulty
- 1. Subjective tension and irritability
- 2. Worrying about minor matters
- 3. Apprehensive attitude apparent in face or speech
- 4. Fears expressed without being questioned

**Physical symptoms of anxiety (anxiety, somatic)**

*In this past week, have you had any of these symptoms? Gastrointestinal (dry mouth, wind, indigestion, diarrhea, cramps, belching); cardiovascular (palpitations, headaches); respiratory (hyperventilation, sighing); urinary frequency, sweating*

**NOTE:** DO NOT RATE IF CLEARLY DUE TO MEDICATION

- 0. Absent
- 1. Mild
- 2. Moderate
- 3. Severe
- 4. Incapacitating

**Energy level (somatic symptoms)**

*How has your energy been this past week? Have you felt tired? Have you had any aches or pains or felt any heaviness in your limbs, back, or head?*

- 0. None
- 1. Heaviness in limbs, back, or head (backache, headache, muscle aches; loss of energy and fatigue)
- 2. Any clear-cut symptoms rate 2 points

**Suicide (ideation, thoughts, plans, attempts)**

*Have you thought life is not worth living or you’d be better off dead? Have you thought of hurting or killing yourself? Have you done anything to hurt yourself?*

- 0. Absent
- 1. Feels life is not worth living
- 2. Wishes to be dead (or any thoughts of possible death to self)
- 3. Suicidal ideas or gestures
- 4. Attempts at suicide (any serious attempt rates 4 points)

**Total score (out of 26)**

*Depression severity*

- 20+ Severe
- 12-20 Moderate
- 4-12 Mild
- Score ≤3 Indicates full remission
- Score ≥4 Indicates no or partial response

Adapted from McIntyre et al.21
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the patient selects pharmacotherapy with an antidepressant. Treatment is then initiated with a first-line agent. The goal of treatment is full remission of symptoms (HAM-D7 score ≤3), restoration of function, and prevention of recurrence. Her chronic symptoms indicate she is vulnerable to recurrence, suggesting a need for longer-term therapy (ie, minimum of 1 to 2 years of maintenance treatment).

Recent evidence has led to a fundamental reclassification of MDD as a chronic illness that should have clear and relevant therapeutic end points (level II evidence). In diabetes, the goal is long-term glucose control with end points that can be easily and reliably monitored. Analogous to this, most patients with MDD require long-term symptom control with the acceptable end point being full remission (level I evidence). This, in turn, can be easily and reliably monitored with a depression rating scale, such as the HAM-D7.

Most research indicates that only 30% to 40% of MDD patients ever reach full remission (level I evidence), and about half of those considered to respond to treatment still have serious residual symptoms (level II evidence). Nonremission in depression should be thought of as active illness. It portends higher rates of chronicity, relapse, poor outcomes, and suicide (level I evidence). This is again comparable to the situation of diabetes where failure to reach end points has been related to poor outcomes. This evidence has led to clear guidelines for acceptable levels of glucose control similar to the current recommendations for full remission as an acceptable level of control of MDD.

Table 3. Psychotherapeutic treatment of an initial episode of major depression: Lines of treatment are derived from a combination of evidence and clinical experience. Evidence for combined, sequential, and crossover combinations of psychotherapy and pharmacotherapy are discussed in depth elsewhere.

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<th>FIRST LINE</th>
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<tr>
<td>Individual cognitive behavioural therapy or interpersonal therapy* (level I evidence)</td>
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<td>Group cognitive behavioural therapy or interpersonal therapy† (level II evidence)</td>
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<td>SECOND LINE</td>
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<tr>
<td>Individual behavioural therapy* (level II evidence)</td>
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<tr>
<td>THIRD LINE</td>
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<tr>
<td>Brief individual psychodynamic therapy* (level III evidence)</td>
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* Might be as efficacious as pharmacotherapy for mild-to-moderate depression, but likely less effective for more severe episodes.
† Less efficacious; more evidence for individual forms of therapy.

A comprehensive review of validated treatments for an initial episode of MDD has been discussed elsewhere (levels I to III evidence).

Over several visits, the patient is educated about depression and how it can affect functioning in work and relationships. The physician provides supportive therapy and mentions local support groups for people with depressive illness. Other resources, such as the Feeling Good Handbook and website addresses for the National Depressive and Manic-Depressive Association (www.nmmda.org) and the Canadian Network for Mood and Anxiety Treatments (www.canmat.org) are discussed.

Other important longitudinal variables in treatment of MDD include a therapeutic alliance, social stressors, psychotherapy, and psychoeducation. Therapy can range from brief, informal, supportive therapy provided by the physician to more formal structured cognitive, dynamic, and interpersonal therapy provided by others. The type of psychotherapy selected is dependent on patient variables, but many therapies have proved helpful (Table 3).

Psychoeducation can be easily facilitated through books and websites. Support groups and socialization with peers might not be as available, but should be encouraged. Social stressors need to be dealt with as much as possible by patients themselves with some guided assistance from physicians. We have found that a focused problem-solving approach is often beneficial (level III evidence).
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Four weeks of adequate doses yields some reduction in symptoms, but a repeat HAM-D7 score of 10 indicates nonremission. Increasing the dose of antidepressant results in remission 2 weeks later (HAM-D7 score 2). The patient tolerates the antidepressant with only some transient nausea and is pleased with her progress. Regular follow up (eg, every 2 to 4 weeks) revealed re-emergence of her symptoms approximately 6 months later. The patient reports no identifiable acute stressors and has complied with therapy. She denies suicidal thoughts or other comorbidity. Her depressive symptoms are objectively reassessed with the HAM-D7 (total score 12).

Unfortunately, few depressed people (20% to 40%) experience sustained remission of symptoms (level I evidence). Strategies to reach full remission after failure of an initial antidepressant agent or psychotherapeutic approach remain controversial. Augmentation with various non-antidepressant agents, combining psychotherapy and pharmacotherapy, as well as switching antidepressants are suggested (level I to III evidence). Evidence favouring these approaches is still emerging, and studies demonstrating the superior efficacy of one strategy over another are largely unavailable. This is disconcerting considering that up to half of patients with MDD might require a major change in treatment at some time (level II evidence). Despite dose optimization, full remission is not achieved. The patient is still not interested in formal psychotherapy as adjunct treatment. Lithium is declined largely due to its side effect profile. An alternative class of antidepressant was added and the dose optimized. She tolerates this treatment and once again achieves remission within 2 weeks (HAM-D7 score 2). Ongoing maintenance treatment with these antidepressants is recommended for the foreseeable future. The role of exercise is also discussed as a possible strategy for improving results. The HAM-D7 is not routinely employed in regular follow up, but is readily available if she reports breakthrough symptoms. She begins to integrate regular exercise into her lifestyle.

A popular treatment combines antidepressant agents together. This approach is permitted in part because newer medications are safer and more easily tolerated. There is, however, little rigorous (ie, level I) evidence for combining antidepressants; common strategies have been extensively outlined in Canadian Family Physician and elsewhere (level I to III evidence). Polypharmacy can have both assets and liabilities; combination strategies are commonplace and potentially beneficial for other chronic illnesses, such as diabetes and congestive heart failure. Combination strategies have long been common in management of mental illness. It is estimated that 6% to 12% of family practice patients with mental illness are prescribed more than one psychotropic medication (level II evidence). Newer lifestyle treatments, such as exercise (level II to III evidence), are emerging as relevant adjunct treatments for depressed patients and should not be overlooked. Recommending exercise is particularly sage advice, considering the high rates of obesity among depressed patients. Unlike other chronic illnesses, MDD is a somewhat fluid and dynamic diagnosis that often is complicated by comorbidity. Ongoing reevaluation and integration of new symptoms and information into treatment will help clinicians successfully manage patients with MDD.
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The patient has been stable for 6 months. She reports improved performance at work and fewer somatic symptoms. She still has residual symptoms of anxiety and continued difficulties with the school principal, but she notes an improved ability to cope. She is currently content with the state of her treatment and seeks medical services much less frequently.

Conclusion

Recent research has promoted an important shift in the concept of MDD. It is now thought of as a chronic illness that often requires long-term multimodal treatment and monitoring of end points, analogous to diabetes. Full remission is a valid, objective, and achievable therapeutic end point. Several emerging strategies to reach this goal are under investigation. Using depression rating scales can help determine the severity of MDD, assess treatment efficacy, determine whether remission has occurred, and facilitate comprehensive treatment of this familiar illness in family practice.

Competing interests

Dr McIntyre is a consultant and speaker for AstraZeneca Canada Inc, Eli Lilly Canada Inc, Janssen-Ortho Inc, Organon Canada Ltd, Wyeth Canada, Lundbeck Canada Inc, GlaxoSmithKline, OxyPharmaceuticals Inc, Biovail Pharmaceuticals Canada, and Pfizer Canada Inc. He has received research funding from Wyeth Canada, GlaxoSmithKline, Merck Frost Canada Inc, and Servier Canada Inc.

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References