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Major Depressive Disorder in Adults: Diagnosis & Management

Effective Date: December 15, 2013

Scope

This guideline provides recommendations on how to diagnose and manage major depressive disorder (MDD) in the primary care setting for non-pregnant patients aged 19 – 65 years. It does not include recommendations for MDD subtypes (e.g., postpartum depression, seasonal affective disorder, psychotic depression, atypical depression and melancholic depression), other depressive disorders (e.g., disruptive mood dysregulation disorder, persistent depressive disorder (dysthmymia), premenstrual dysphoric disorder, treatment resistant/induced depression), psychosis, bipolar disorder, anxiety disorders, or substance abuse disorders.

Key Recommendations

- Screen for MDD with 'two quick question' method.
- Use the Patient Health Questionnaire-9 (PHQ-9) to aid in diagnosing and monitoring patients.
- Assess suicide risk in all depressed patients.
- Several non-pharmacological and pharmacological interventions are available in the short, medium and long term.
- Antidepressants are continued for at least 6 months after remission.
- Treat to recover occupational and social functioning.

Epidemiology

Approximately 11% of Canadians meet criteria for MDD at some point in their lives and approximately 4% of Canadians suffer from MDD within any given year.[1] About 2% of people with depression commit suicide, and 50% of these individuals will have been in contact with their general practitioner in the month preceding the suicide.[2]

Diagnosis

Screening

Screen patients who present with symptoms for MDD.[3] Note that some patients present with somatic symptoms. Use the 'two quick question' screening method.[4]

In the past month:

1. Have you lost interest or pleasure in things you usually like to do?
2. Have you felt sad, low, down, depressed or hopeless?

An answer of yes to **either** question requires a more detailed assessment.

Assessment

The detailed assessment includes:

- Clinical interview to determine if the patient meets the Diagnostic and Statistical Manual of Mental Disorders (5th edition)[5] criteria to diagnose MDD by using S^2IGECAPS and focusing on functional status.

S	Sadness (depressed mood)
S	Sleep disturbance (insomnia, hypersomnia)
I	Interest reduced (anhedonia)
G	Guilt and self-blame
E	Energy loss and fatigue
C	Concentration problems
A	Appetite changes (low/increased appetite or weight loss/gain)
P	Psychomotor changes (retardation, agitation)
S	Suicidal thoughts

- Review PHQ-9 score and responses.* The PHQ-9 is a patient administered questionnaire that aids in the diagnosis and assesses the severity (e.g., mild, moderate, severe) of depression.[6-9]
- Consider:
  - Differential diagnosis, particularly screening for Bipolar I and II;
  - Past history of depression and its treatment;
  - Family history of a mood disorder;
  - Psychosocial stressors;
  - Any medical conditions associated with depression (e.g., chronic obstructive pulmonary disease, migraine, multiple sclerosis, back problems, cancer, epilepsy, asthma, stroke, thyroid disease, diabetes and heart disease);[10] and
  - Collateral information from family or friends.[10]

Differential Diagnosis

When arriving at the differential diagnosis, consider the following:

- Ruling out medical conditions that require laboratory tests (e.g., thyroid stimulating hormone, Vitamin B_{12});[11]
- Other psychiatric syndrome (e.g., adjustment disorder, anxiety disorder,† bipolar disorder I or II, psychosis, alcohol and/or substance abuse);[12] and
- Medications that mimic mood disorders (see *Appendix A: Medications that Mimic Mood Disorders*).

Suicide Risk Assessment ‡

Once patient has met MDD criteria, conduct a suicide risk assessment.[12-14]

- Ask the patient if they have thoughts of death or suicide, feel life is not worth living, have made a previous suicide attempt and if there is a family history of suicide.
- If the answer is yes to any of the above, ask about their plans for suicide (e.g., have they considered a method, do they have access to material required for suicide and if they have written a note).
- Consider emergency psychiatric consultation and in-patient treatment if the patient has: persistent suicidal thoughts; a previous suicide attempt; or a current plan.
- If the patient is considered low risk, discuss and/or create a safety plan with the patient, detailing steps the patient will take if their situation deteriorates[15] (see *Associated Document: Example of a Safety Plan*).

* *Depression should not be diagnosed or excluded solely on the basis of a PHQ-9 score. See Associated Document: Patient Health Questionnaire – 9 for more information.*

† *Generalized anxiety or worry can accompany depression symptoms. This should not be diagnosed separately if the excessive worry presents only during the major depressive event.*[5]

‡ *For more information on conducting a suicide risk assessment see the Associated Document: Resource Guide: Information Sources for Physicians.*

Management

Treatment[10]

The goal of acute treatment is remission of symptoms (e.g., PHQ-9 score < 5) and to restore psychosocial functioning. The goal of maintenance treatment is to return to full social and occupational function and to prevent recurrence.

- Establish treatment decisions on the severity of the depression, patient preference and availability of resources.
- Use the clinical interview and PHQ-9 score help to assess severity of depression and to evaluate treatment response.
- Assess suicide risk at each visit, especially in the acute phase.[16]
- Treatment of depression can also be impacted by stressors in interpersonal relationships, living conditions and social isolation. These stressors should also be assessed and managed.
- Initially follow up with patients weekly or biweekly, depending on severity, until acute treatment goals are met. Schedule periodic visits to ensure maintenance treatment goals are met.

Best results for treatment adherence occur when a therapeutic alliance has been formed between the physician and patient.[17,18] Involve patients in the management of their own illness by engaging them in discussion about the diagnosis and treatment options, developing a goal-oriented treatment plan[§], and monitoring for response and signs of relapse/recurrence (see *Associated Document: Resource Guide: Information Sources for Patients*).

1. Lifestyle – Self-Care[19]

Recommend lifestyle management for all patients with depression. Discuss the importance of a healthy lifestyle such as:

- Regular exercise
- Healthy regular meals
- Sleep hygiene
- Avoiding substance use
- Adequate housing
- Stress management strategies
- Engaging in at least one pleasurable activity a day
- Keeping a daily mood chart

2. Self-Management[20]

Recommend self-management for all patients with depression. When appropriate, use education and self-management resources (see *Associated Document: Resource Guide: Information Sources for Physicians*), including available community resources and self-help agencies. Self-management programs may be helpful to prevent relapses.

3. Psychotherapy

Recommend psychotherapy in the acute phase of mild to moderate depression and/or maintenance phase of depression treatment to prevent relapse. First-line psychotherapies are cognitive behavioral therapy and interpersonal psychotherapy (see *Appendix B: First-Line Psychotherapies for Treatment of Depression*).

Psychotherapies are as effective as antidepressant medications, and for some patients, combined treatment with pharmacotherapy and psychotherapy is more effective than psychotherapy alone.[21] Combined treatment should be considered for patients with chronic or severe episodes, psychiatric co-morbidity, or poor response to pharmacotherapy.

Patients referred for psychotherapy or engaging in self-management programs should also be monitored for treatment response at monthly or bimonthly intervals. Inter-professional communication is extremely important when treating shared patients.

§ *GPSC incentive fee may be available for mental health planning.*

4. Pharmacological Management

Recommend antidepressant medications for patients with moderate to severe depression.

Many first-line antidepressants are available with different neurochemical actions and side effect profiles (see *Appendix C: First-Line Antidepressants*). Most systematic reviews have not shown any clinically significant differences in efficacy among first-line antidepressants;[22] however, consider the following clinical factors when choosing a medication for patients.[23]

- Symptom profile
- Medical co-morbidity
- Psychiatric co-morbidity
- Risk of pregnancy
- Patient preference
- Previous therapeutic response
- Tolerability profile
- Drug discontinuation symptoms
- Drug-drug interactions
- Cost

Initially, patients are typically prescribed a first-line antidepressant (see *Appendix C: First-Line Antidepressants* for more information). If there is no response to an adequate trial (e.g., 2-4 weeks at the maximum dosage) of the first-line antidepressant or its side effects are intolerable, switch to another first line agent, which could include another agent in the same class (see *Appendix D: Switching Antidepressants*).

Antidepressant partial or poor response may be augmented with another agent; at this point psychiatric consultation is recommended. Consider reviewing drug and alcohol use again.

Engage the patient in an open dialogue about side effects when prescribing antidepressants. Specifically discuss the potential increase in suicidal ideation and potential for sexual dysfunction. Agitation and suicide risk may increase early in pharmacological treatment. Patients should be carefully monitored at least every 1-2 weeks when starting drug therapy.[24] Ask the patient to review the safety plan (see *Associated Document: Example of a Safety Plan*) and seek out emergency help if symptoms become more prominent and suicidal thoughts become more persistent. Treatment-related sexual dysfunction usually persists, and if intolerable, changing therapy may be warranted.[24]

Promote antidepressant adherence, by addressing any medication concerns of the patient and by providing them with the following information.[24]

- Antidepressants are not addictive.
- Do not stop antidepressants without medical consultation, even if feeling better, to avoid withdrawal symptoms.
- Take antidepressants as directed.
- Some improvement may be observed as early as the first 1-2 weeks, but full benefit may not be observed until 4-8 weeks.
- Mild side effects (e.g., gastrointestinal, headaches) are common but transient; however, persistent symptoms should be reported.

Maintenance Treatment

Continue patients on antidepressants for at least 6 months after full remission of symptoms or achievement of treatment goals.[25] Use the same dosage as in the acute phase. Monitor for medication side effects and medical co-morbidity.

When ending pharmacological treatment, the following are recommended.

- Be aware of the discontinuation syndrome (see *Appendix E: Discontinuation Syndrome of Antidepressant Medication*).
- Educate patients about early signs of relapse of MDD symptoms.
- Schedule a patient visit 2-4 weeks after discontinuation and patient follow-up every 2-3 months for the first 6 months after stopping therapy.

Other Management

Consultation with a psychiatrist is recommended for:

- Bipolar disorder, psychotic symptoms and/or a substance use disorder;
- Risk of suicide or harm to others;
- Severe co-morbid psychiatric or medical illness;
- History of treatment resistance;
- Failed to respond to standard treatment (at adequate dosage and time-period);
- An unclear diagnosis that needs a more comprehensive evaluation; and
- Therapeutic relationship has broken down.

Resources

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▸ Diagnostic Code: 311

▸ Appendices

- Appendix A: Medications that Mimic Mood Disorders
- Appendix B: First-Line Psychotherapies for Treatment of Depression
- Appendix C: First-Line Antidepressants
- Appendix D: Switching Antidepressants
- Appendix E: Discontinuation Syndrome of Antidepressant Medications

▸ Associated Documents

The following document accompanies this guideline:

- Patient Health Questionnaire-9 (PHQ-9)
- Example of a Safety Plan
- Resource Guide: Information Sources for Physicians
- Resource Guide: Information Sources for Patients

This guideline is based on scientific evidence current as of the Effective Date.

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

THE GUIDELINES AND PROTOCOLS ADVISORY COMMITTEE

The principles of the Guidelines and Protocols Advisory Committee are to:

- encourage appropriate responses to common medical situations
- recommend actions that are sufficient and efficient, neither excessive nor deficient
- permit exceptions when justified by clinical circumstances

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Appendix A: Medications That Mimic Mood Disorders

Class	Selected Agents
Central nervous system (CNS) medications	• Anticonvulsants (e.g., barbiturates, vigabatrin, topiramate) • Antiparkinsonian drugs (e.g., levodopa, amantadine) • Anti-migraine agents (e.g., flunarizine)
Cardiovascular system (CVS) medications	• Beta-blockers* (especially propranolol, metoprolol) • Centrally-acting antihypertensives (e.g., clonidine, methyldopa) • Vasodilators (e.g., hydralazine) • Antiarrhythmics (e.g., amiodarone, digoxin)
Hormonal agents	• Corticosteroids • Gonadotropic-releasing hormone agonists (e.g., leuprolide, goserelin)
Anti-infectives	• Antiretrovirals (efavirenz) • Interferon-α • Antimalarial (mefloquine)
Miscellaneous	• Isotretinoin • Clomiphene citrate

* *Controversy in Care:*[1] *a connection between the use of beta-blockers and depression has long been hypothesized, especially propranolol and metoprolol. This association is supported by many case reports and small reviews. However, a meta-analysis and more recent reviews failed to demonstrate this association.*

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Appendix B: First-Line Psychotherapies for Treatment of Depression

Psychotherapy	General Principles	Typical Length of Therapy
Cognitive Behavioral Therapy (CBT)	• Identify automatic, maladaptive thoughts and distorted beliefs that lead to depressive moods. • Learn strategies to modify these beliefs and practice adaptive thinking patterns. • Use a systematic approach to reinforce positive coping behaviours.	8-12 sessions
Interpersonal Therapy (IPT)	• Identify significant interpersonal/relationship issues that led to, or arose from, depression (unresolved grief, role disputes, role transitions, social isolation). • Focus on 1 or 2 of these issues, using problem-solving, dispute resolution, and social skills training.	12-16 sessions

Resources for Psychological Treatment in BC

- Psychiatrists by referral.
- Private psychologists, particularly those with CBT training; the BC Psychological Association (604-730-0522; www.psychologists.bc.ca) operates a referral service.
- Ambulatory psychiatric clinics, day programs at hospitals, or community mental health centres.
- Changeways – a best-practice, group-based psychoeducational program for depression, offered in a number of hospitals and community health centres throughout the province. www.changeways.com

Note: Funding for psychotherapy services may be available through the patient's Employee Assistance Plan and/or Extended Health Care benefits.

Appendix C: First-Line Antidepressants

"First-line" antidepressant treatment represents a balance of efficacy, tolerability and expert consideration per the Canadian Network for Mood and Anxiety Treatments (CANMAT) recommendations. Other pharmacotherapies are reserved for situations where first-line antidepressants are not indicated or cannot be used, or when first-line treatments have not worked.

Generic Name (Trade Name), Dosage Forms and Strengths	Usual Adult Daily Dose*	Adverse Reactions	Cost per 30 Days †	Therapeutic Considerations	Elimination Half-Life (h)
Selective Serotonin Reuptake Inhibitors (SSRIs) Note: SSRIs can be associated with prolonged corrected QT interval. This can lead to Torsades de Pointes (a rare cardiac arrhythmia), especially at higher doses and if taking multiple QT interval prolonging medications. Risk factors for QT prolongation syndrome include: low ventricular ejections fraction (<40%), left ventricular hypertrophy, dilated cardiomyopathy; myocardial ischemia, myocarditis; congenital long QT syndrome; bradycardia, AV and SA blocks; electrolyte abnormalities (hypokalemia, hypomagnesemia, hypocalcemia); use of multiple QT interval prolonging medications, older age (> 65 years); and female sex. For those at significant risk, baseline and follow up ECGs may be warranted using clinical judgment, but routine ECG monitoring prior to starting an antidepressant in every patient is not necessary.					
citalopram (Celexa®, CTP 30®, G) Tabs: 10 mg, 20 mg, 30 mg, 40 mg	Usual: 10-40 mg Maximum: 40 mg	**CNS:** sleep disturbances (insomnia, sedation), tremor, headache **CVS:** orthostatic hypotension, ECG changes **Anticholinergic:** dry mouth, sweating, constipation **GI:** nausea, vomiting, diarrhea, constipation, ↑ risk of GI bleed **Sexual disturbances:** ↓ libido, impotence, ejaculatory disturbances, anorgasmia. (likely to persist during SSRI therapy) **Hyponatremia:** can occur. (may cause fatigue or delirium) **Serotonin Syndrome:** agitation, tachycardia, tremor hyperreflexia. (combination with other serotonergic dugs also increase risk of syndrome) **Bleeding risk[5,6]:** especially when combined with ASA, NSAID or anticoagulants.	$6-11 (Regular coverage)	• [§] SSRIs have "flat" dose-response curves. For depression, most patients respond to initial lower dose. Higher doses are used for treatment of OCD. Do not ↑ dose until steady state is reached (i.e., ~4 weeks for fluoxetine, and 1-2 weeks for others). • Therapeutic effect seen after 7-28 days. • Citalopram and escitalopram have fewest drug interactions among SSRIs. • Fluoxetine is most anorexic and stimulating, has active metabolite and has long half-life. • Fluvoxamine is most nauseating, constipating and sedating among SSRIs (can be given at bedtime). • Paroxetine has most anticholinergic adverse effects & anxiety, and can cause weight gain. • Sertraline has most diarrhea and male sexual dysfunction among SSRIs. It has few drug interactions.	23-45
escitalopram (Cipralex®, Cipralax MELTZ®) Tabs: 10 mg, 20 mg Orodispersible Tabs: 10 mg, 20 mg	Usual: 10-20 mg Maximum: 20 mg (or 10 mg in elderly, patients with liver problems, on omeprazole or cimetidine)		$56-60 (Tabs: Regular coverage)		27-32
fluoxetine (Prozac®, G) Caps: 10 mg, 20 mg Solution: 20 mg/5 mL	Usual: 10-40 mg Maximum:[§] 80 mg		$15-30 (Regular coverage)		24-144 (parent); 200-330 (metabolite)
fluvoxamine (Luvox®, G) Tabs: 50 mg, 100 mg	Usual: 50-200 mg Maximum:[§] 300 mg		$7-25 (Regular coverage)		9-28
paroxetine (Paxil®, Paxil® CR, G) Tabs: 10 mg 20 mg, 30 mg, 40 mg CR Tabs: 12.5 mg, 25 mg	Usual: 10-40 mg (or 12.5-50 mg for CR tablets) Maximum:[§] 60 mg		$7-30 (Regular coverage)		3-65
sertraline (Zoloft®, G) Caps: 25 mg, 50 mg, 100 mg	Usual: 50-150 mg Maximum:[§] 200mg		$13-27 (Regular coverage)		22-36 (parent); 62-104 (metabolite)
Norepinephrine Dopamine Reuptake Inhibitors (NDRIs)					
bupropion (Wellbutrin® SR, Wellbutrin® XL, G) SR Tabs: 100 mg, 150 mg XL Tabs: 150 mg, 300 mg	Usual: 150-300 mg Maximum: 300 mg	**CNS:** sleep disturbances (insomnia, nightmares), agitation, seizures (high dose, or abrupt dose ↑), headache **CVS:** orthostatic hypotension, dizziness **GI:** ↓ appetite, anorexia	$8-37 (Regular coverage)	• SR Tabs: Max.150 mg per dose. Doses >150 mg per day should be given BID, preferably with ≥8 hours between doses. • XL Tabs: once daily dosing (AM). • Therapeutic effect seen after 7-28 days. • May ↓ seizure threshold. Contraindicated in patients with current or history of seizure disorder, bulimia or anorexia nervosa, or undergoing alcohol or benzodiazepine withdrawal. • Rarely inhibits sexual functioning.	10-14 (parent); 20-27 (metabolite)

Generic Name (Trade Name), Dosage Forms and Strengths	Usual Adult Daily Dose*	Adverse Reactions	Cost per 30 Days †	Therapeutic Considerations	Elimination Half-Life (h)
Selective Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)					
desvenlafaxine (Pristiq®) XR Tabs: 50 mg, 100 mg	Initial: 50 mg Usual: 50 mg Maximum: 100 mg	Generally dose-related. **CNS:** sleep disturbances, headache, agitation, hostility, suicidal urges **CVS:** modest, sustained ↑ in BP and HR, dizziness, orthostatic hypotension **Anticholinergic:** dry mouth, sweating, constipation **GI:** nausea **Sexual disturbances:** ↓ libido, delayed orgasm/ejaculation, anorgasmia. **Serotonin Syndrome:** agitation, tachycardia, tremor hyperreflexia. (combination with other serotornergic dugs also increase risk of syndrome)	$89 (No coverage)	• Therapeutic effect seen after 7-28 days. • Major active metabolite of venlafaxine. • Monitor BP for 2 months at each dose level. Do not use in patients with uncontrolled hypertension.	11
duloxetine (Cymbalta®) Caps: 30 mg, 60 mg	Initial: 30 mg Usual: 30-60 mg Maximum: 120 mg		$62-124 (No coverage)	• Therapeutic effect seen after 7-28 days. • Less effect on BP. Has been associated with hepatic injury. Do not use in patients with underlying liver disease, or substantial alcohol use, or severe renal insufficiency.	8-19
venlafaxine (Effexor® XR, G) XR Caps: 37.5 mg, 75 mg, 150 mg	Initial: 37.5-75 mg Usual: 75-225 mg Maximum: 375 mg		$11-32 (Regular coverage)	• Therapeutic effect seen after 7-28 days. • Monitor BP for 2 months at each dose level. Do not use in patients with uncontrolled hypertension.	9-21 (absorption half-life)
Noradrenergic/Specific Serotonergic Agents (NaSSAs)					
mirtazapine (Remeron®, Remeron®, G) Tabs: 15 mg, 30 mg, 45 mg Orally disintegrating tabs: 15 mg, 30 mg, 45 mg	Initial: 15 mg (or 7.5 mg in elderly) Usual: 15-30 mg Maximum: 60 mg	**CNS:** fatigue, sedation **Anticholingeric:** dry mouth constipation **Endocrine:** ↑ appetite, carbohydrate craving, weight gain, ↑ cholesterol **Sexual disturbance:** occasionally occurs (<2%)	$3-5 (Regular coverage)	• Therapeutic effects seen after 7-28 days. • ↓ sleep latency and ↑ sleep duration. May be of benefit in patients with marked anorexia, insomnia, or agitation. • Caution in patients with compromised liver or renal function.	20-40
Reversible Inhibitor of MAO-A (RIMA)					
moclobemide (Manerix®, G) Tabs: 100 mg, 150 mg, 300 mg	Initial: 300 mg (divided BID) Usual: 300-600 mg (some respond to 150 mg daily, but most require >450 mg) Maximum: 600 mg	**CNS:** insomnia (especially if given in the evening), headache, sedation, restlessness, anxiety, agitation **Anticholinergic:** dry mouth, blurred vision **CVS:** orthostatic hypotension, dizziness **GI:** nausea, abdominal pain, constipation	$10-20 (Regular coverage)	• Therapeutic effects seen after 7-28 days. • Take after meals to minimize tyramine-related responses (e.g., headache); avoid ingesting large quantities of tyramine-rich foods. • Hypertensive reactions may occur in patients with thyrotoxicosis or pheochromocytoma. • Enzyme inhibition is reversible (within 24 hours). • ↑ REM sleep.	1-3

Abbreviations: AM morning; **ASA** acetylsalicylic acid; **AV** atrioventricular nodal; **BID** twice daily; **BP** blood pressure; **Caps** capsules; **CNS** central nervous system; **CR** controlled-release; **CVS** cardiovascular system; **ECG** electrocardiogram; **G** generic brands available; **GI** gastrointestinal; **HR** heart rate; **max** maximum; **mg** milligrams; **mL** millilitres; **NSAID** Nonsteroidal anti-inflammatory drugs; **OCD** obsessive-compulsive disorders; **REM** rapid eye movement; **SA** sinoatrial nodal; **SR** sustained-release; **SSRI** selective serotonin reuptake inhibitor; **Tabs** tablets; **XL** or **XR** extended-release.

Footnotes:

* Dose should be individualized. Dosage adjustment may be required in patients with hepatic or renal impairment. Refer to latest product monographs and regularly review current Health Canada advisories, warnings and recalls at www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/index_e.html.

† Pricing is approximate as per PharmaCare Formulary Search on May 23, 2013 (www.health.gov.bc.ca/pharmacare/benefitslookup/) and does not include dispensing fee or additional markups. They are calculated based on the "Usual adult daily doses" in this table. "Regular coverage", also known as "regular benefit", does not require Special Authority. Regular benefit drugs may be fully or partially covered. Coverage is subject to drug price limits set by PharmaCare and to the patient's PharmaCare plan rules and deductibles. See: www.health.gov.bc.ca/pharmacare/plans/index.html and www.health.gov.bc.ca/pharmacare/policy.html for further information.

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Appendix D: Switching Antidepressants

Switching antidepressants can be accomplished by the following strategies:

1. ***Direct switch:*** stop the first antidepressant abruptly and start new antidepressant the next day.
2. ***Taper & switch immediately:*** gradually taper the first antidepressant, then start the new antidepressant immediately after discontinuation.
3. ***Taper & switch after a washout:*** gradually withdraw the first antidepressant, then start the new antidepressant after a washout period.
4. ***Cross-tapering:*** taper the first antidepressant (usually over 1-2 week or longer), and build up the dose of the new antidepressant simultaneously.

The following table is intended for general guidance only. Whichever strategy is used, patients should be closely monitored for symptoms and adverse events. The duration of tapering should be determined individually for each patient. Physicians should balance the risk of discontinuation symptoms versus risk of delay in new treatment. The washout period is mostly dependent on the $t_{1/2}$ of the first drug.

Switching From	To →	SSRIs (except fluoxetine)	Fluoxetine	SNRIs	NDRI (bupropion)	NaSSA (mirtazapine)	RIMA (moclobemide)	TCA
SSRIs (except fluoxetine)	→	Taper & stop, then start new SSRI at a low dose[1,†]	Taper & stop, then start fluoxetine at low dose (10 mg)[1,†]	Taper & stop[5] (or to low dose),[1] then start low dose SNRI & ↑ very slowly.[1,3,5,†]	Taper & stop[5] (or to low dose),[2] then start bupropion.	Taper & stop[5] (or to low dose),[1] then start mirtazapine cautiously.[‡]	Taper & stop, wait 1 week, then start moclobemide.[1,5]	Cross-taper cautiously with very low dose TCA.[1,3,5,‡,§]
Fluoxetine*	→	Stop fluoxetine, wait 4-7 days. Start the new SSRI at low dose & ↑ slowly.[1,2,5]		Stop fluoxetine, wait 4-7 days. Start with low dose SNRI & ↑ very slowly.[3,5]	Stop fluoxetine, wait 4-7 days. Start bupropion.[5]	Stop fluoxetine, wait 4-7 days, then start mirtazapine cautiously.[5,‡]	Stop fluoxetine, wait 5 weeks, start moclobemide.[3,5]	Stop fluoxetine, wait 4-7 days. Start TCA at very low dose & ↑ very slowly.[1,5,‡,§]
SNRIs	→	Cross-taper cautiously with low dose of SSRI.[1,5]	Cross-taper cautiously with low dose of fluoxetine.[1,5]	Taper & stop, then start new SNRI.[1]	Taper & stop (or to low dose), then start bupropion cautiously.[5]	Cross-taper cautiously.[1]	Taper & stop, wait 1 week, then start moclobemide.[1,5]	Cross-taper cautiously with very low dose of TCA.[1,5,§]
NDRI (bupropion)	→	Taper & stop, then start SSRI (consider lower starting dose).[4,5]	Taper & stop, then start fluoxetine (consider lower starting dose).[4,5]	Taper & stop, then start SNRI at low dose & ↑ slowly.[4,5]		Taper & stop, then start mirtazapine cautiously (consider lower starting dose).[4,5]	Taper & stop, wait 1 week, then start moclobemide.[5]	Taper & stop, then start TCA at a low dose & ↑ slowly.[5]
NaSSA (mirtazapine)	→	Taper & stop[5] (or to low dose),[1] then start SSRI cautiously.	Taper & stop[5] (or to low dose),[1] then start fluoxetine cautiously.	Taper & stop[5] (or to low dose),[1] then start SNRI cautiously.	Taper & stop, then start fluoxetine cautiously.[5]		Taper & stop, wait 1 week, then start moclobemide.[1]	Taper & stop[5] (or to low dose),[1] then start cautiously with low dose of TCA.
RIMA (moclobemide)	→	Taper & stop, wait 24 hours, start SSRI.[1,5]	Taper & stop, wait 24 hours, start fluoxetine.[1,5]	Taper & stop, wait 24 hours, start SNRI.[1,5]	Taper & stop, wait 24 hours, start SNRI.[1,5]	Taper & stop, wait 24 hours, start SNRI.[1,5]		Taper & stop, wait 24 hours, start TCA.[1,5]
TCA	→	Gradually ↓ dose by up to 50% & start SSRI at normal starting dose, then slowly withdraw TCA over few weeks.[1,5,§]	Gradually ↓ dose by up to 50% & start fluoxetine at normal starting dose, then slowly withdraw TCA over few weeks.[1,5,§]	Cross-taper cautiously, start with low dose SNRI.[1,5]	Taper & stop[4] (or to low dose),[5] then start mirtazapine cautiously.	Taper & stop (or to low dose),[1,5] then start mirtazapine cautiously.	Taper & stop, wait 1 week, then start moclobemide.[1]	Cross-taper cautiously[1,5] (switching is of questionable benefit).[4]

Abbreviations: mg milligrams; **NaSSA** noradrenergic/specific serotonergic antidepressant; **NDRI** norepinephrine dopamine reuptake inhibitor; **RIMA** reversible inhibitor of monoamine oxidase A; **SNRI** selective serotonin norepinephrine reuptake inhibitor; **SSRI** selective serotonin reuptake inhibitor; **TCA** tricyclic antidepressants.

Footnotes:

* Exercise particular caution when switching from fluoxetine to other antidepressant. Significant concentrations of fluoxetine or its active metabolite may be present for 5 weeks after stopping.[1,3,5]

† Direct switching using may also be possible, but precise equivalent doses of SSRIs and SNRIs have not been established.[2,3,5]

‡ Fluvoxamine (CYP450 1A2 inhibitor), paroxetine and fluoxetine (CYP450 2D6 inhibitors) can cause ↑ TCA blood levels for several weeks.[3,5]

§ Do not co-administer clomipramine with SSRIs or SNRIs.[1,5]

References

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4. Virani A, Bezchlibnyk-Butler KZ, Jeffries JJ (Eds). Clinical handbook of psychotropic drugs. Cambridge, MA: Hogrefe & Huber Publishers, 2009.
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Appendix E: Discontinuation of Antidepressant Medications

- All classes of antidepressant have been linked to discontinuation syndrome. It is more frequently reported in patients discontinuing drugs with shorter half-lives, or who have been treated for longer periods.
- Antidepressant discontinuation symptoms typically appear shortly (hours to days) after stopping or reducing the doses of the drug, and last 1-2 weeks if untreated. A wide array of physiological and psychological signs and symptoms has been reported. To facilitate rapid recognition, the **FINISH** mnemonic can be used: [1]

F	Flu-like symptoms
I	Insomnia
N	Nausea
I	Imbalance
S	Sensory disturbances (headache, dizziness, "electric shock" sensations)
H	Hyperarousal

- The antidepressant withdrawal syndrome is different from the classical withdrawal syndrome associated with central nervous system depressant drugs (craving, drug-seeking behaviors, or other prominent symptoms such as diaphoresis, tachycardia, etc).[2]
- To prevent symptoms, discontinuation of antidepressants should be done gradually.
  - Patients should be forewarned of the possibility of discontinuation syndrome;[1,3]
  - Supervised dose reduction gradually over 3-4 weeks or longer may be required (gradual dose tapering for fluoxetine not usually required due to its long half-life).
- Physician should maintain a high index of suspicion for antidepressant withdrawal syndrome. Any symptoms reported by patients should prompt the physician to question for accidental/intentional missed doses, dose reductions, drug discontinuation.[1]
- To distinguish antidepressant discontinuation syndrome from relapse of depression, the physician can focus on symptoms such as dizziness, "electric shock" sensations, headache, and nausea (uncommon in relapse). Discontinuation syndrome typically resolves in 1-2 weeks, and can be rapidly reversed after restarting the antidepressant (also uncommon in relapse).[1]
- If antidepressant discontinuation syndrome occurs and other causes of symptoms have been ruled out, the physician should provide reassurance that the symptoms are reversible, transient, and not life-threatening. Available options are:
  1) restarting the antidepressant at the original dose and taper even more slowly;
  2) if slower tapering is poorly tolerated or not possible, switch to an agent with a longer half-life (e.g., fluoxetine).[1]

References

1. Warner CH, Bobo W, Warner C, et al. Antidepressant discontinuation syndrome. Am Fam Physician. 2006;74:449-56.
2. Robinson DS. Antidepressant discontinuation syndrome. Primary Psychiatry. 2006;13:23-4.
3. Schatzberg AF, Blier P, Delgado PL, et al. Antidepressant discontinuation syndrome: consensus panel recommendations for clinical management and additional research. J Clin Psychiatry. 2006; 67(Suppl 4):27-30.

Patient Health Questionnaire (PHQ-9)

Name: _____ Date: _____

Over the last 2 weeks, how often have you been bothered by any of the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

For office coding: Total Score _____ = _____ + _____ + _____

Total Score _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

How to Score the PHQ-9

Major depressive disorder (MDD) is suggested if:

- Of the 9 items, 5 or more are checked as at least 'more than half the days'
- Either item 1 or 2 is checked as at least 'more than half the days'

Other depressive syndrome is suggested if:

- Of the 9 items, between 2 to 4 are checked as at least 'more than half the days'
- Either item 1 or 2 is checked as at least 'more than half the days'

PHQ-9 scores can be used to plan and monitor treatment. To score the instrument, tally the numbers of all the checked responses under each heading (not at all=0, several days=1, more than half the days=2, and nearly every day=3). Add the numbers together to total the score on the bottom of the questionnaire. Interpret the score by using the guide listed below.

Guide for Interpreting PHQ-9 Scores		
Score	Depression Severity	Action
0 - 4	None-minimal	Patient may not need depression treatment.
5 - 9	Mild	Use clinical judgment about treatment, based on patient's duration of symptoms and functional impairment.
10 - 14	Moderate	Use clinical judgment about treatment, based on patient's duration of symptoms and functional impairment.
15 - 19	Moderately severe	Treat using antidepressants, psychotherapy or a combination of treatment.
20 - 27	Severe	Treat using antidepressants with or without psychotherapy.

Functional Health Assessment

The instrument also includes a functional health assessment. This asks the patient how emotional difficulties or problems impact work, life at home, or relationships with other people. Patient response of 'very difficult' or 'extremely difficult' suggest that the patient's functionality is impaired. After treatment begins, functional status and number score can be measured to assess patient improvement.

Note: Depression should not be diagnosed or excluded solely on the basis of a PHQ-9 score. A PHQ-9 score ≥ 10 has a sensitivity of 88% and a specificity of 88% for major depression.[1] Since the questionnaire relies on patient self-report, the practitioner should verify all responses. A definitive diagnosis is made taking into account how well the patient understood the questionnaire, as well as other relevant information from the patient.

Reference: Kroenke K, Spitzer RL, Williams JB. The PHQ-9: Validity of a brief depression severity measure. J Gen Intern Med. 2001;16(9):606-613.

Safety Plan

If you have thoughts of hurting yourself, start at Step 1. Go through each step until you are safe. Remember: Suicidal thoughts can be very strong. It may seem they will last forever. With support and time, these thoughts will usually pass. When they pass, you can put energy into sorting out problems that have contributed to you feeling so badly. The hopelessness you may feel now will not last forever. It is important to reach out for help and support. You can get through this difficult time. Since it can be hard to focus and think clearly when you feel suicidal, please copy this and put in places where you can easily use it, such as your purse, wallet or by the phone.

1. Do the following activities to calm/comfort myself:

2. Remind myself of my reasons for living:

3. Call a friend or family member.

   Name and phone number:

4. Call a backup person if person above is not available.

   Name and phone number:

5. Call a care provider (psychologist, psychiatrist, therapist).

   Name and phone number:

6. Call my local crisis line - phone number:

7. Go somewhere I am safe:

8. Go to the Emergency Room at the nearest hospital.

9. If I feel that I can't get to the hospital safely, call 911 and request transportation to the hospital. They will send someone to transport me safely.

Source: Samra J, Bilsker D. Coping with Suicidal Thoughts [Internet]. Vancouver: Consortium for Organizational Mental Health; 2007 [cited 2013 Jun 21]. 7 p, available from: www.sfu.ca/carmha/publications/coping-with-suicidal-thoughts.html

Depression: Resource Guide for Physicians

Physician Resources

- **BC Guidelines**, www.BCGuidelines.ca - Anxiety and Depression in Children and Youth – Diagnosis and Treatment, Problem Drinking
- **BC Mental Health and Addiction Services**, www.bcmhas.ca/ – resources and information on services for reproductive mental health issues as well as other mood disorders related to children and women
- **Family Physician Guide for Depression, Anxiety Disorders, Early Psychosis and Substance Use Disorders** – information on how to detect, diagnose and manage Major Depressive Disorder (MDD) subtypes and other mood disorders (e.g., anxiety and bipolar disorders) in the primary care setting, as well as information on suicide risk assessments. Available at: www.health.gov.bc.ca/library/publications/year/2008/fpg_full.pdf
- **HealthLink BC** - information on MDD and MDD subtypes and other mood disorders, www.HealthLinkBC.ca or by telephone 8-1-1.
- **Mood Chart** – example of a mood chart you can provide your patients. Available from: www.blackdoginstitute.org.au/docs/moodchartfordepressionandhowtomonitoryourprogress.pdf
- **Motherisk** – information on antidepressant use during pregnancy, website: www.motherisk.org/women/index.jsp
- **PHQ-9 website** – downloads of the PHQ-9 in various languages and instructions for scoring, Website: www.phqscreeners.com/
- **Practice Support Program Adult Mental Health Learning** – detailed information, resources and tools on MDD subtypes and other mood disorders (e.g., anxiety and bipolar disorders) Website: www.gpscbc.ca/psp/learning
- **Rapid Access to Consultative Expertise (RACE)** – telephone access to specialists for guidance and advice on patients as well as assistance with care plans (where available). Check website regularly for updates on expansion of service throughout BC. Website: www.raceconnect.ca/

Self-Management Resources

- **Antidepressant Skills Workbook** – a self-help workbook developed at the Centre for Applied Research in Mental Health & Addiction at Simon Fraser University. Also available in Chinese and Punjabi. Free download available from: www.carmha.ca/selfcare/
- **The Feeling Good Handbook** by David D. Burns, Plume Books, 1999.
- **Mind Over Mood** by Dennis Greenberger and Christine A. Padesky, Zipper Books, 1995.
- **BC Partners for Mental Health and Addictions Information** - provides Mental Disorders, Depression and Anxiety Disorders Toolkits, website: www.mentalhealthaddictions.bc.ca
- **Chronic Disease Self-Help Management Program** - a patient education program offered in communities throughout British Columbia, which teaches practical skills on managing chronic health problems, website: www.coag.uvic.ca/cdsmp
- **Canadian Mental Health Association** - telephone 1-800-555-8222, website: www.cmha-bc.org

Self-Management Resources continued

- **Mood Disorders Association of BC** - telephone 604-873-0103.
- **MoodGYM** - a free Internet-based cognitive behavior therapy intervention (CBT), website: moodgym.anu.edu.au
- **Bounce Back** - a free evidence-based program to help adults experiencing symptoms of depression or anxiety resulting from stress or other life events. Requires practitioner referral.
  Website: www.cmha.bc.ca/how-we-can-help/adults/ bounceback

Note: some patients, especially those with more severe symptoms, may not be able to take advantage of self-management while acutely ill but is recommended as treatment in the maintenance phase.

Resources for Psychological Treatment in BC

- Psychiatrists by referral.
- Private psychologists, particularly those with CBT training; the BC Psychological Association (604-730-0522; www.psychologists.bc.ca) operates a referral service.
- Ambulatory psychiatric clinics, day programs at hospitals, or community mental health centres.
- Changeways – a best-practice, group-based psychoeducational program for depression, offered in a number of hospitals and community health centres throughout the province, website: www.changeways.com

Suicide Prevention and Crisis Support

- **The Crisis Intervention and Suicide Prevention Centre of British Columbia** – provides local crisis centre phone numbers.

  Distress Line Numbers: BC-wide: **1-800-SUICIDE (1-800-784-2433)**
  Greater Vancouver: **604-872-3311**
  Toll free: Lower Mainland & Sunshine Coast: **1-866-661-3311**
  TTY: **1-866-872-0113**
  Seniors' Distress Line: **604-872-1234**

  Online Distress Services: www.youthinbc.com
  www.crisiscentrechat.ca
  www.crisiscentre.bc.ca

- **Centre for Suicide Prevention (Canada)** – provides information on suicide and suicidal behavior.
  Website: www.suicideinfo.ca

Depression: Resource Guide for Patients

Your primary care provider thinks you may have depression. Here are the 10 things you need to know about depression:

1. You are not alone. Four percent of Canadians will have depression in any given year.
2. Anyone can have depression. Depression affects people of all ages and from all walks of life.
3. Depression is NOT caused by being weak or having a 'bad attitude'.
4. The cause of depression is not fully known but it can be treated.
5. You should follow the treatment given. Common treatments include antidepressant medications, psychotherapy and self-care.
6. Antidepressants work well with little side-effects for many people when taken properly.
7. Antidepressants are not addictive and you should not stop taking them without medical advice.
8. Psychotherapy can be as helpful as antidepressants.
9. There are other tools to help you take care of yourself (self-care), see resources below.
10. If at any point you feel like ending your own life, seek medical help immediately. You are not alone.

General Information and Support about Depression

- **Mental Health Information Line** - provides taped information on provincial mental health programs as well as symptoms, causes, treatment, support groups and publications relating to a number of mental illnesses.
  This is a 24 hour line. Toll free: **1-800-661-2121**, Vancouver: **604- 669-7600**
- **HealthLink BC** - provides free-of-charge medically approved information on depression and resources available to BC residents. Access registered nurses 24/7 and pharmacists seven days a week from 5pm to 9am. Toll free: **8-1-1**, Deaf and hearing impaired: **7-1-1**; Internet calling service providers: **604-215-8110**. Website: www.healthlinkbc.ca
- **Mood Disorders Association of BC** – provides support and education to patients and families on mood disorders and other mental illnesses. Toll-free: **1-855-282-7979**, Phone: **1-604-873-0103.** Website: www.mdabc.net
- **Canadian Mental Health Association, BC Division** – provides resources and support on various mental illnesses and local BC branch information. Toll-free (BC only): **1-800-555-8222**, Phone: **1-604-688-3234** Website: www.cmha.bc.ca

Depression Self-Care

- **Antidepressant Skills Workbook** – a self-help workbook developed at the Centre for Applied Research in Mental Health & Addiction at Simon Fraser University. Also available in Chinese and Punjabi.
  Free download available from: www.carmha.ca/selfcare/
- **The Feeling Good Handbook** by David D. Burns, Plume Books, 1999.
- **Mind Over Mood: Change How You Feel by Changing How You Think** by Dennis Greenberger and Christine A. Padesky, 1995.
- **Here to Help BC** – a website created by the BC Partners for Mental Health and Addictions Information to provide information and resources for depression, anxiety and other mental health disorders. Website: www.heretohelp.bc.ca/

Depression Self-Care continued

- **Chronic Disease Self-Management Program** – a patient education program offered in communities throughout BC, which teaches practical skills on managing chronic health conditions. Website: www.selfmanagementbc.ca/
- **MoodGYM** – a free Internet-based cognitive behavior therapy intervention. Website: moodgym.anu.edu.au
- **Bounce Back** – a free evidence-based program to help adults experiencing symptoms of depression or anxiety resulting from stress or other life events. Requires physician referral. Website: www.cmha.bc.ca/how-we-can-help/adults/bounceback

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