Primary Care Pathway: Difficult to Treat Depression

Quick links: Pathway primer | Expanded details | Provider resources | Patient resources

1. Diagnosis of major depressive disorder (MDD)

DSM–5–TR

2. Risk stratify using PHQ-9

PHQ–9

Evaluate suicide risk at every visit

Mild (5-9)
- Psychotherapy preferred +/- pharmacotherapy with first line agent
- Reassess in 4-6 weeks, if improved, proceed with routine follow up

Moderate (10-19)
- Psychotherapy and/or pharmacotherapy with first line agent
- Assess 20% improvement in PHQ-9 in 2-3 weeks

Severe (20-27)
- Psychotherapy with first line agent unless psychotic features. Psychotherapy after stabilization
- Assess 20% improvement in PHQ-9 in 2-3 weeks

Severe depression w/psychotic features

3. Pharmacotherapy

Suggested First Line Antidepressants:
- Bupropion XL 150 mg od initial dose/300 mg optimized dose
- Escitalopram 10 mg od initial dose/20 mg optimized dose
- Vortioxetine 5-10 mg initial dose/20 mg optimized dose

4. Other management supports

- Psychotherapy (eg. CBT, IPT, BA)
- Regular physical activity
- Sleep hygiene
- Limit/abstain from cannabis and alcohol use
- Light therapy
- Psychoeducation
- Complementary and alternative medicine

< 20% improvement in PHQ-9?

5. Increase dose/switch medication

- If psychotherapy alone - initiate first line medication
- If initial pharmacotherapy tolerated, increase to usual effective dose
- If initial pharmacotherapy not tolerated, switch to other first line medication

Switch

Assess 20% improvement in PHQ-9 in 2-3 weeks

No

≥ 20% improvement in PHQ-9?

Yes

6. Continue to optimize dose and reassess for response every 6-8 weeks. If remission, continue current dose for minimum 9-12 months

Incomplete remission

Consider augmentation or switch

Augment

Switch

8a. Suggested first line augmentation medications:

- Aripiprazole 1-2 mg initial dose/5 mg optimized dose
- Brexpiprazole 0.25-0.5 mg initial dose/2 mg optimized dose

7. Assess factors that can interfere with treatment success

If on first medication

If optimized first therapy, switch to other first line medication. Reassess 2-3 weeks for 20% improvement in PHQ-9

Switch

Yes

Continue to optimize dose and reassess for response in 6-8 weeks. If remission, continue current dose for 9-12 months

If on second medication

No

8. Augmentation:

If second therapy not tolerated or ineffective at optimized dose, combine best tolerated first line medication with one of the first line adjunctive medications.

Reassess 2-3 weeks for response

Not improved

Consider:
- Calling Specialist Link Psychiatry
- Optimizing adjunctive dose
- Switching adjunctive medications
- Ensure factors that can interfere with treatment success are revised
- RTMS
- Consider ECT through psychiatry referral

If you require non-urgent clinical advice, please call Specialist Link

9. FAQs

PATHWAY PRIMER

- Clinical depression is a common psychiatric disorder that significantly impacts quality of life and increases the risk of developing other health problems. Around 14% of Canadians have experienced a major depressive episode in their lifetime.[1] One third of patients who receive treatment for major depressive disorder will not achieve sustained remission.[2]
- Difficult-to-treat depression (DTD) is defined as persistent depression that continues to cause significant burden despite numerous treatment efforts (including pharmacological and non-pharmacological treatments).[3]
- This pathway was created to help guide treatment of patients with depression who are not responding to treatment and reduce the frustration from a provider and patient perspective. The pathway provides both non-pharmacologic and pharmacologic management strategies for DTD in the medical home.
- The pathway is designed for adult patients with difficult-to-treat depression. It is not indicated for pediatric/youth, geriatric or pregnant/breastfeeding populations as these subpopulations may have unique considerations — consider a Specialist Link call to psychiatry for advice on this population.
- Treatment recommendations were obtained from the Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 update on clinical guidelines for management of major depressive disorder in adults[4] with input from local experts.
- This content was thoroughly reviewed and approved by both psychiatrists and family physicians within the Difficult to Treat Depression Pathway Working Group of the Calgary Zone.

EXPANDED DETAILS

1. DSM-5-TR Diagnostic Criteria for Major Depressive Disorder (MDD)[5]

Specific DSM-5-TR criteria for MDD include:

a. At least 5 of the following symptoms are experienced nearly every day within the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) diminished interest or pleasure:
   1. Depressed mood (i.e. sad, empty, hopeless, tearful) most of the day
   2. Diminished interest or pleasure in most or all activities most of the day
   3. Significant weight loss or weight gain (>5% of body weight in one month), change in appetite
   4. Insomnia or hypersomnia
   5. Physical and mental restlessness or slowing that is apparent to others
   6. Fatigue or loss of energy
   7. Feelings of worthlessness or excessive/inappropriate guilt
   8. Diminished ability to think or concentrate, indecisiveness
   9. Recurrent thoughts of death or suicidal ideation

b. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

c. The episode is not attributable to the physiological effects of a substance or another medical condition.
   Note: criteria A–C represent a major depressive episode. Bereavement may resemble a depressive episode; the presence of MDD in addition to the normal response to a significant loss should be carefully considered.

d. At least one major depressive episode is not better explained by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or other schizophrenia spectrum/psychotic disorders.
e. There has never been a manic episode or a hypomanic episode. Note: this exclusion does not apply if all of the manic-like or hypomanic-like episodes are attributable to substance use or another medical condition.

2. Risk stratify using PHQ-9

The Patient Health Questionnaire-9 (PHQ-9) assesses the degree of depression severity via questionnaire.

- Online PHQ-9 form with severity scale: https://tools.camh.ca/phq9/
- Print version of PHQ-9 form: https://www.camh.ca/-/media/files/form-phq-9-pdf.pdf

Evaluate Suicide risk at every visit

- ASQ suicidal risk evaluation form
- If you are uncomfortable or have questions, consider calling Specialist Link.
- Urgent resources:
  - Distress Centre (403-266-4357 (HELP))
  - AHS Mental Health Help Line (1-777-303-2642)
  - Community Resource Team - Wood's Homes (403-299-9699 or text 587-315-5000)
  - Canada Suicide Prevention Services (833-456-4566)
  - Emergency or Urgent Care

3. Pharmacotherapy

- Recommendations are based primarily on severity of depression, but also consider past treatment response, patient preference, and treatment availability. CANMAT guidelines on treatment selection
- Combining psychological treatment with pharmacotherapy is more effective than either alone for acute treatment and may reduce risk of reoccurrence.
- For severe major depressive disorder with psychotic symptoms, the combination of a first-line antidepressant and an atypical antipsychotic (serotonin-dopamine activity modulator) is recommended; structured psychotherapy should not be considered until psychotic symptoms subside. If you are uncomfortable or have questions, consider calling Specialist Link.

Line of treatment	Class	Medication	Initial Dose[1]	Daily Dose range[1]	Optimized dose*	Common side-effects	Considerations
Medications that are highlighted are the top recommended first-line treatments due to the combination of best evidence for efficacy and tolerability identified in the 2023 CANMAT network meta-analysis.							
First line	SSRI	Citalopram	20 mg od	20-40 mg	40 mg	↑sexual dysfunction	Max 20mg/day in pts >60yo
		Escitalopram	10 mg od	10-20 mg	20 mg	↑sexual dysfunction	Consider dosage adjustments in geriatric patients, hepatic or severe renal impairment. Patients with anxiety features may benefit from starting on 5 mg.

		Fluoxetine	20 mg od qAM	20-60 mg	40 mg	↑drug interactions ↑sexual dysfunction	High concentration in breast milk
		Fluvoxamine	50 mg od qhs and increased to 100 mg od qhs after a few days	100-300 mg	200 mg	↑drug interactions ↑sexual dysfunction	
		Paroxetine	20 mg od	20-50 mg	40 mg	↑wt gain ↑drug interactions ↑sexual dysfunction higher withdrawal effects	not 1st line in pregnancy In elderly, no proven additional benefit beyond dose > 20mg/day Caution must be maintained when combining with other drugs that impact CYT 2D6 (such as codeine, tamoxifen)
		Sertraline	50 mg od	50-200 mg	150 mg	Most male sexual s/e	
	SNRI	Desvenlafaxine	25 to 50 mg od	50-100 mg	150 mg		
		Duloxetine	30 mg od, increase to 60 mg od in 1 to 2 weeks	60-120 mg	120 mg	↑sexual dysfunction	Not recommended with severe renal impairment, ESRD, or in hepatic impairment
		Levomilnacipran	initiated at 20 mg od for 2 days and then increased to 40 mg od	40-120 mg	80 mg		
		Venlafaxine-XR	37.5 to 75 mg od with food, qAM or qPM	75-225 mg	225 mg	higher withdrawal effects ↑nausea ↑sexual dysfunction	high concentration in breastmilk
	NDRI	Bupropion XL	150 mg od qAM	150-450 mg[2]	300 mg		
	α_2 antagonist, 5-HT2 antagonist	Mirtazapine	15 mg od qhs	15 mg	30 mg	↑wt gain sedating	Consider lower dose in elderly
	SRI; 5-HTIA agonist	Vilazodone	10 mg od with food for 7 days, followed by 20 mg od	20-40 mg	40 mg		
	SRI; 5-HTIA, 5-HTIB agonist, 5-HTID, 5-HT3A, 5HT7 agonist	Vortioxetine	5 to 10 mg od	10-20 mg	20 mg	Common side effect: nausea. Recommend taking with food. If nausea persists, recommend taking at bedtime.	
Second line	TCA	Amitriptyline	25 mg	75-300 mg	**		Start 10-25mg po qhs and increase by 10-25mg/d q2-3 days in elderly patients, may give divided doses

		Clomipramine	25 mg daily with meals, titrated up by 25 mg increments to a total daily dose of 150 mg by the end of 2 weeks	150-300 mg	**		
		Desipramine	25 mg	100-300 mg	**		
		Doxepin	25 mg	75-300 mg	**		
		Imipramine	25 mg	75-300 mg	**		Max 100mg/day in elderly
		Nortriptyline	25 mg	75-150 mg	**		Start 10-25mg po qhs and increase by 10-25mg/d q2-3 days in elderly patients
		Protriptyline	10 mg	10 to 40 mg	**		
		Trimipramine	25 mg	75-300 mg	**		
	RIMA	Moclobemide	300 mg daily dose (in two divided doses)	150-450 mg[3]	300 mg		
	SRI; 5-HT2 antagonist	Trazodone	150-200 mg a day, in two or three divided doses	150-400 mg	150 mg		
	DA, 5-HT, α_1 & α_2 antagonist; NRI	Quetiapine	50 mg	150-300 mg	150 mg		D/C if ANC <1000 or if unexplained ↓ in WBC
Third line	MAO inhibitor	Phenelzine	15 mg	45-90 mg	**		
		Tranylcypromine	10 mg	30-60 mg	**		

*Optimized dose is based on expert opinion. Higher doses beyond the optimized dose may increase the risk of side effects with limited increases in efficacy.
**No optimized dose recommended, individualization and close follow-up recommended
[1]Initial dose and dose ranges are taken from product monographs and UpToDate[6]
[2]Daily doses above 300 mg should be given in divided doses.
[3]Daily doses of 600 mg are commonly used, but at these higher doses, the MAOI drug and dietary restrictions should be followed.

CANMAT Table 3.4: Frequency of Adverse Effects of First-Line Antidepressants

	Nausea	Vomiting	Constipation	Diarrhea	Dry mouth	Headaches	Dizziness	Somnolence	Nervousness	Anxiety	Agitation	Insomnia	Fatigue	Sweating	Asthenia	Tremor	Anorexia	Incr. appetite
SSRIs																		
Citalopram	21	4		8	19			17	4	3	2		5	11		8	4	
Escitalopram	15		4	8	7	2	6	4	2	2		8	5	3		2	2	2
Fluoxetine	21				10			13	14	12		16		8	9	10	11	
Fluvoxamine			18	6	26	22	15	26	2	2	16	14		11	5	11	15	
Paroxetine	26	2	14	12	18	18	13	23	5	5	2	13		11	15	8	6	1
Sertraline	26	4	8	18	16	20	12	13	3	3	6	16	11	8		11	3	1
SNRIs																		
Desvenlafaxine[1]	22	3	9	11	11	20	13	4	<1	3	0	9	7	10		2	5	2
Duloxetine	20	5	11	8	15		9	7		3		11	8	6		3	8	
Levomilnacipran	17	5	9		10	17	8			2		6		9			3	
Milnacipran[2]	37	7	16		5	18	10			4		12		9		2	2	
Venlafaxine-IR		6	15	8	22	25	19	23	13	6	2	18		12	12	5	11	
Venlafaxine-XR	31	4	8	8	12	26	20	17	10	2	3	17		14	8	5	8	
Others																		
Agomelatine	≤9	≤9	≤9	≤9		≥10	≤9	≤9		≤9	<1	≤9	≤9	<1			<1	≤9
Bupropion SR[3]	11		≥10	4	≥10	≥10	7	3	5	5		≥10		2	2	3		
Bupropion XL	15	2	10		19		8			5		10		2		4	5	
Mirtazapine			13		25		7								8	2		17
Vilazodone[4]	24	5		29	7	14	8	5				6	3					3
Vortioxetine[5]	23	4	4	5	6		5	3				3	3	2			1	

	0-9%
	10-29%
	30% and higher

Note. When data from multiple doses were reported separately, the data from the minimum therapeutic dose was used (indicated by footnotes). Percentage rates taken from product monographs (based on clinical trial data and not placebo adjusted). Blank squares indicate no data reported. Not included are the side effects shown in Table 3.5 (sedation, weight gain, and sexual dysfunction).
[1]Data from 50 mg dose; [2]data from 50 mg dose; [3]data from 100–150 mg dose; [4]data from 40 mg dose; [5]data from 10 mg dose.

Note: Agomelatine, Milnacipran not available in Canada.

CANMAT Table 3.5: Summary of comparative favourability ratings for first-line antidepressants

	Efficacy and drug-specific issues[1]					Tolerability issues			
Antidepressant	Efficacy	Acceptability[2]	Drug interactions	Discontin-uation		Sedation	Weight gain	Sexual dysfunction	Other Tolerability[2]
SSRIs									
Citalopram			QTc[3]						
Escitalopram									
Fluoxetine									
Fluvoxamine									
Paroxetine									
Sertraline									
SNRIs									
Desvenlafaxine									
Duloxetine									
Levomilnacipran									
Venlafaxine-XR									
Others									
Bupropion									
Mirtazapine									
Vilazodone									
Vortioxetine									
Not available in Canada									
Agomelatine			LFTs[4]						
Mianserin									
Milnacipran									

More favourable
Less favourable
Neutral[5]

Note. These comparative favourability ratings are based on a variety of data sources, including meta-analyses and RCTs, supplemented with expert consensus. Note that while ratings show those agents that have more favourable profiles (in green squares) and those with less favourable profiles (in red hatched squares), these are not absolute ratings; an agent can be selected for other clinical reasons despite having a rating as less favourable in a particular characteristic. Clear squares indicate neutral ratings and do not imply intermediate favourability.
[1] *Efficacy* refers to response rates in meta-analyses; *Acceptability* refers to all-cause discontinuation rates in meta-analyses; *Drug Interactions* include clinically significant interactions (see Q.3.j); *Discontinuation* refers to potential for discontinuation effects (see Q.6.d). [2] *Other Tolerability* refers to side effects other than sedation, weight gain, and sexual dysfunction; [3] QTc, indicates recommended monitoring for prolongation of QTc interval; [4] LFTs, indicates recommended monitoring of liver function tests (see Q.3.j). [5] Clear squares indicate neutral ratings and do not imply intermediate favourability ratings.

4. Non-Pharmacological Management

Lifestyle Interventions

- Regular physical activity (prescription to get active).
- Ensure quality sleep. Refer to the patient resource section for tools to support sleep hygiene.
- Limit/abstain from cannabis and alcohol use.
- Light therapy (10,000 lux fluorescent white light for 30 min daily in the morning, shortly after waking). Refer to the patient resource section light therapy options.
- Psychoeducation (CHOICE-D Patient and Family Guide to Depression Treatment).
- App and web-based psychotherapies: guided apps (e.g. BounceBack) are more effective than non-guided, but evidence favors psychotherapy/pharmacotherapy over digital health However, non-guided apps are free and easy for patients to try. Refer to the patient resource section for mindfulness tools. CANMAT guidelines on digital health interventions

Psychotherapy

- An optimal dose for a first-line psychotherapy is 12 to 16 sessions, twice-weekly.
- Refer to the provider and patient resources section for local psychotherapy resources.

First Line Psychological Treatments	Premise	Activities
Cognitive Behavioural Therapy (CBT)	Distorted beliefs about the self, the world, and the future maintain depressive affect	▪ Recognize negative cognitions ▪ Respond to negative thoughts and behaviours ▪ Problem solve and test assumptions
Interpersonal Therapy (IPT)	Current interpersonal issues maintain depressive affect	▪ Identify issue (role transition, role dispute, grief, interpersonal deficits) ▪ Focus on social context
Behavioural Activation (BA)	Depression is a consequence of compromised environmental sources of positive reinforcement	▪ Increase activity and access to rewarding experiences ▪ Address inertia, avoidance, social withdrawal
Second Line Psychological Treatments		
• Cognitive behavioural analysis system of psychotherapy (CBASP) • Mindfulness-based cognitive therapy (MBCT) • Problem-solving therapy (PST) • Short-term psychodynamic psychotherapy (STPP) • Transdiagnostic psychological treatment of emotional disorders		
Third Line Psychological Treatments		
• Acceptance & commitment therapy (ACT) • Long-term psychodynamic psychotherapy (PDT) • Metacognitive therapy (MCT) • Motivational interviewing (MI)		

Complementary and Alternative Medicine

The complementary and alternative treatments listed below have evidence for efficacy in treating major depressive episodes of mild severity but have not shown sufficient evidence for comparison to 1st-line psychotherapy or pharmacotherapy for moderate/severe depression. Consider complementary treatments alone only for mild severity depression or as adjuncts to standard treatment in moderate severity illness. Note that therapeutic dose ranges are inconsistent for most complementary and alternative treatments, therefore they should be recommended with caution.

- St John's Wort (note: risk of serotonin syndrome when used in combination with serotonergic medications, risk for drug interactions)
- Acupuncture
- L-methyl folate
- SAM-e
- DHEA
- Omega-3
- Saffron, lavender, or roseroot

5. Increase dose / switch medication

- SwitchRX (https://www.switchrx.com/) is an online tool that helps guide practitioners when adjusting their patient's psychotropic treatment regimens. It includes up-to-date information on recommended doses, tapering and titration schedules, and clinical tips when switching antidepressants (requires registration and login, sign-up is free). When available, a PCN pharmacist can also be a resource in providing council on how to switch antidepressant medications based on the patient's treatment regimen.
- BCGuidelines.ca link to switching antidepressants: BCGuidelines.ca - switching antidepressants
- For difficult-to-treat depression, most antidepressants are increased by one dose before switching to an alternative treatment strategy.
- Increase to optimized doses only.
- Switch between first line therapies – regardless of class, only one switch is recommended before moving to augmentation strategies.
- For difficult-to-treat depression, augmenting is more successful than switch or dose optimization.

6. Follow-up and maintenance

The goals of the maintenance phase are to:

- maintain symptomatic remission
- restore functioning and quality of life to premorbid levels
- prevent recurrence of symptoms
- promote resilience

Patients with difficult-to-treat depression may not achieve operational definitions for remission (e.g., PHQ-9 ≤4); for these patients the therapeutic focus should be shifted from symptom remission toward prioritizing the highest possible improvement in functioning and quality of life. CANMAT guidelines for inadequate response to treatment

During the maintenance phase:

- Psychoeducation and self-management are integral to depression management.
- Use validated rating scales (e.g., PHQ-9) for monitoring treatment. CANMAT guidelines on monitoring treatment
- Maintenance psychotherapy (e.g., 4 "booster sessions" over 12 months) is recommended to retain and encourage behavioural strategies.

Strategies for discontinuation/deprescribing

- Patients may experience discontinuation symptoms when stopping antidepressants, especially if stopping abruptly.
- Taper gradually over several weeks or months, extending the time between dose reductions towards end of taper (unless there are clinical reasons requiring rapid discontinuation). If antidepressant use was <4 weeks, taper and discontinuation can be quick (i.e., ≤2 weeks).
- If severe discontinuation symptoms occur, return to previous higher dose with a subsequent slower tapering schedule.
- Psychological treatments during or preceding antidepressant discontinuation can reduce discontinuation effects. CANMAT guidelines for discontinuation

When to consider long-term therapy

Some patients have risk factors for recurrence and chronicity; for these patients antidepressant treatment should be continued for 2 years or more.

Risk Factors for Recurrence of Depressive Episodes
• Persistent residual symptoms (e.g., anhedonia, sleep problems, cognitive dysfunction) • History of childhood maltreatment (see provider resources for ACE questionnaire) • Greater severity of depressive episodes • Chronic depressive episodes • Presence of medical comorbidities (psychiatric or nonpsychiatric) • Greater number of previous episodes • Poor social support • Persistent stressful life events

7. Factors that can interfere with treatment success

Patient factors:

- Incorrect diagnosis (ADHD, bipolar disorder, BPD)
- Illness characteristics
- Comorbidities (psychiatric and/or non-psychiatric).
- Substance use
- Acute or chronic stressors (e.g., high ACE score)
- Sleep disorders

Medication factors:

- Inadequate dose
- Inadequate duration
- Poor adherence
- Side effects masking as symptoms
- Pharmacogenetic variability

8. Augmentation

After trialing two first line medications at optimized doses, consider augmentation with a first line medication. Consider earlier if there is a partial response to the initial antidepressant and it is well tolerated.

- Reassess current medications and discontinue those with unclear benefits to minimize polypharmacy.
- Side effect intolerance of first-line adjunctives may lead to opting for second-line treatments.
- CANMAT recommendations for adjunctive treatments

Line of Treatment	Adjunctive Agent	Initial Dose*	Dose Range[1]	Optimized dose*	Considerations
First Line	Aripiprazole	1-2 mg	2-10 mg	5 mg	qAM
	Brexpiprazole	0.25-0.5 mg	0.5-2 mg	2 mg	
Second line	Bupropion	150 mg	150-450 mg	300 mg	
	Cariprazine	1.5 mg	1.5-3 mg	3 mg	
	Intranasal esketamine	**	56-84 mg intranasally	**	ketamine treatment may not be financially accessible for some patients

	IV racemic ketamine	**	0.5-1.0 mg/kg IV	**	ketamine treatment may not be financially accessible for some patients
	Lithium	150 mg	600-1200 mg (therapeutic serum level: 0.5-0.8 mmol/L)	300 mg	Monitoring drug levels
	Mirtazapine	7.5-15 mg	30-60 mg	30 mg	sedating
	Modafinil	**	100-400 mg	**	
	Olanzapine	2.5 mg	2.5-10 mg	5 mg	
	Quetiapine-XR	50 mg	150-300 mg	150 mg	
	Risperidone	0.5 mg	1-3 mg	2 mg	
	Triiodothyronine	25 mcg	25-50 mcg	50 mcg	
Investigational	Psychedelic-assisted therapy	n/a	n/a	n/a	Insufficient research on efficacy
Not recommended	Cannabis	n/a	n/a	n/a	Evidence that cannabis worsens depression outcomes

*Initial dose and optimized dose are based on expert opinion. Higher doses beyond the optimized dose may increase the risk of side effects with limited increases in efficacy.
**No optimized dose recommended, individualization and close follow-up recommended.
[1]Dose ranges are taken from product monographs.

Neuromodulation Treatments

Neuromodulation treatments alter CNS activity through electrical or magnetic stimulation of the brain. They are usually used when first-line psychotherapy and medications have not been successful. Consider patient preference and feasibility issues (availability, patient burden) when considering neuromodulation treatments.

Repetitive transcranial magnetic stimulation (rTMS)

- Stimulation or inhibition of cortical neurons using focused magnetic field pulses. Externally applied over the scalp using a magnetic coil.
- 20 to 40 minutes per session, 5 days per week for 4 to 6 weeks (depending on type of rTMS and protocol)
- Recommended for treatment-resistant depression (persistent symptoms despite adequate trials of at least 2 different antidepressants).
- rTMS can be recommended as a first-choice treatment if there are tolerability concerns with medication or if it was effective in a previous depressive episode.
- Advantages: no cognitive side effects, procedure is non-surgical and does not require anesthesia.
- RTMS can be referred through Access Mental Health. RTMS application
- More rTMS resources: https://www.specialistlink.ca/rtms-resources

Electroconvulsive therapy (ECT)

- Electrical stimulus adjusted to individualized parameters transmitted to the brain via electrodes placed on scalp to induce a brief seizure (~30 seconds). Procedure is non-surgical and delivered under general anaesthesia.
- Acute course is 6 to 12 sessions.
- More efficacious for difficult-to-treat depression than other neuromodulation treatments. Also efficacious for severe depression, treatment resistant depression, psychotic or catatonic features, older patients.
- ECT can be used as a first-line treatment in severe illness (e.g., a major depressive episode with psychotic or catatonic features, severe suicidal ideation, and deteriorating physical condition)
- Advantages: high response rate, generally safe and well tolerated, antidepressants can usually be continued (excepting benzodiazepines, anticonvulsants, lithium, and cannabis, which should be held or discontinued before ECT)

- Limitations: stigma, concerns about cognitive adverse effects, high relapse rates after cessation. Generally, rTMS should be considered before ECT due to its less invasive nature and ability of the patient to continue to work or go to school during treatment.
- ECT requires psychiatry referral.

9. FAQs

- Identification and approach to akathisia: akathisia is a syndrome of motor restlessness characterized by mental unease and the urge to move.[7] SSRIs and SNRIs are associated with an increased risk of akathisia, agitation, and aggression in individuals under 25. Akathisia is also a common side effect with aripiprazole and brexpiprazole. Medication-induced akathisia can be managed by lowering the dose or switching to a different medication. Barnes Akathisia Rating Scale: BARS Scale
- Considerations with 'anxious depression': there is no evidence for better responses with any specific medication, therefore all first-line medications are recommended for anxious distress. Start low dose, expect side effect sensitivity, severity.
- Comorbidity management: consider scales – ASRS (ADHD screen), AUDIT (alcohol use disorder screen), MDQ (bipolar screen) with emphasis on treating the diagnosis that is most disabling. The choice of pharmacotherapy should consider potential drug interactions and side effect profiles that do not worsen comorbid conditions while minimizing polypharmacy.
- Utility of pharmacogenetics: the routine use of pharmacogenetic testing is not recommended because the clinical benefits are too modest and inconsistent to justify the delay in treatment associated with obtaining testing results.

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7 Barnes TRE (2003) The Barnes Akathisia Rating Scale–Revisited. Journal of Psychopharmacology. 17(4):365-370. doi:10.1177/0269881103174013

BACKGROUND

About this pathway

- The Difficult to Treat Depression pathway was originally developed in 2025 as part of the Calgary Zone's Specialist Link and clinical pathways initiative. They were co-developed by the Calgary Zone's specialty integration task group, which includes medical leadership and staff from Calgary and area Primary Care Networks, the Department of Family Medicine, the Department of Psychiatry, and Alberta Health Services.
- The creation of this pathway aims to support adults with depression requiring medication augmentation, enabling management within primary care while benefiting from specialty care support. This approach seeks to minimize referrals to psychiatry for patients whose care could be optimized in primary care. Additionally, the pathway intends to enhance clinicians' awareness of resources for managing difficult to treat depression and boost primary care providers' confidence in treating this patient population.

Authors and conflict of interest declaration

- This pathway was developed by a multistakeholder working group comprised of primary care and specialty providers. For more information, contact info@calgaryareapcns.ca.

Pathway review process, timelines

- Primary care pathways undergo scheduled review every three years, or earlier if there is a clinically significant change in knowledge or practice. The next scheduled review is June 2028. However, we welcome feedback at any time. Please email comments to info@calgaryareapcns.ca.

Copyright information

DISCLAIMER

This pathway represents evidence-based best practice but does not override the individual responsibility of health care professionals to make decisions appropriate to their patients using their own clinical judgment given their patients' specific clinical conditions, in consultation with patients/alternate decision makers. The pathway is not a substitute for clinical judgment or advice of a qualified health care professional. It is expected that all users will seek advice of other appropriately qualified and regulated health care providers with any issues transcending their specific knowledge, scope of regulated practice or professional competence.

PROVIDER RESOURCES

Advice options

- Non-urgent telephone advice via Specialist Link or other local specialist referral platforms connects family physicians, nurse practitioners and specialists in real time via a tele-advice line. Family physicians, nurse practitioners and specialists can request non-urgent advice from Adult Psychiatry via specialistlink.ca or by calling 403-910-2551. This service is available from 8 a.m. to 5 p.m. Monday to Friday (excluding statutory holidays). Calls are returned within two (2) hours.

Resource	Location
BCGuidelines.ca guide to switching antidepressants	https://www2.gov.bc.ca/assets/gov/health/practitioner-pro/bc-guidelines/depress_appd.pdf
Canadian Mental Health Association	https://cmha.calgary.ab.ca/
Centre for Clinical Intervention	https://www.cci.health.wa.gov.au/Resources/For-Clinicians/Depression
rTMS resources	https://www.specialistlink.ca/rtms-resources
rTMS clinic external request for consultation	https://www.specialistlink.ca/assets/rTMS_EXTERNAL_referral_request
SwitchRX: support for medication transitions	https://www.switchrx.com/
UpToDate antidepressant doses	https://www.uptodate.com/contents/image?imageKey=PC/53818
Screening Tools	
Adverse Childhood Experience (ACE) questionnaire	https://cfpcn.ca/wp-content/uploads/2024/01/RPMC-ACEs-questionnaire-and-patient-handoutApr2019.pdf
Ask suicide-screening questions (ASQ)	https://www.nimh.nih.gov/sites/default/files/documents/research/research-conducted-at-nimh/asq-toolkit-materials/asq-tool/screening_tool_asq_nimh_toolkit_0.pdf
Adult ADHD self-report (ASRS) scale	https://www.caddra.ca/wp-content/uploads/ASRS.pdf
Alcohol Use Disorders Identification Test (AUDIT)	https://nida.nih.gov/sites/default/files/files/AUDIT.pdf
Barnes Akathisia Rating Scale (BARS)	https://simpleandpractical.com/wp-content/uploads/2014/09/Barnes-Akathisia-Rating-Scale-BARS.pdf
General Anxiety Disorder (GAD-7) scale	https://www.camh.ca/-/media/files/formgad7-pdf.pdf
Patient Health Questionnaire (PHQ-9) print form	https://www.camh.ca/-/media/files/form-phq-9-pdf.pdf
Patient Health Questionnaire (PHQ-9) online questionnaire	https://tools.camh.ca/phq9/
Mood Disorder Questionnaire (MDQ)	https://www.ohsu.edu/sites/default/files/2019-06/cms-quality-bipolar_disorder_mdq_screener.pdf
Sheehan Disability Scale	https://cliniquedemedecinefamilialedecowansville.ca/wp-content/uploads/2023/03/sheehan-disability-scale.pdf
Publications	
CANMAT 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults	https://journals.sagepub.com/doi/10.1177/07067437241245384
CANMAT 2023 depression guidelines slide sets	https://www.canmat.org/2025/04/17/2023-depression-guidelines-slide-sets/
Non-urgent Advice	
Specialist Link	https://www.specialistlink.ca/
Urgent Services	

Urgent Single Session Counselling Services	
Eastside Community Mental Health Service	Phone number: 403-299-9699. https://www.woodshomes.ca/eastside-community-mental-health-services/
Sheldon Chumir	https://www.albertahealthservices.ca/findhealth/Service.aspx?id=1064160&serviceAtFacilityID=1099658
South Calgary Health Centre	Phone number: 403-943-9374; https://www.albertahealthservices.ca/findhealth/service.aspx?serviceAtFacilityId=1018206#contentStart
Crisis Intervention	
AHS Mental Health Help Line	Phone number: 1-877-303-2642; https://www.albertahealthservices.ca/findhealth/Service.aspx?id=6810&serviceAtFacilityID=1047134
Canada Suicide Prevention Services	Phone number: 833-456-4566; https://www.crisisservicescanada.ca/en/
Community Resource Team-Wood's Homes	Phone number: 403-299-9699 or text 587-315-5000; https://www.woodshomes.ca/
Distress Centre	Phone number: 403-266-4357 (HELP); https://www.distresscentre.com/
Emergency Room or Urgent Care	https://www.albertahealthservices.ca/findhealth/search.aspx?type=facili
Mobile Response Team (MRT)	activated via the Distress Centre phone number: 403-266-4357 (HELP)

PATIENT RESOURCES

General Information on Depression		
Resource Type	**Resource name**	**URL**
Handout	CHOICE-D Patient and Family Guide to Depression Treatment	https://www.canmat.org/wp-content/uploads/2019/07/Choice-D-Guide-Public.pdf
Handout	rTMS FAQ	For-Patients---rTMS-FAQ-March-2025.pdf
Website	Centre for Clinical Interventions: Looking after yourself	https://www.cci.health.wa.gov.au/Resources/Looking-After-Yourself/Depression
Website	ECT information	https://myhealth.alberta.ca/Health/aftercareinformation/pages/conditions.aspx?hwid=abq4733
Website	Helpguide.org	https://www.helpguide.org/mental-health/depression
Website	Light therapy options	https://sad.psychiatry.ubc.ca/resources/public-resources/how-to-get-a-light-device/
Website	My Health Alberta: Depression	https://myhealth.alberta.ca/health/Pages/conditions.aspx?hwid=hw30709
Workbook	Antidepressant Skills Workbook	https://www.sfu.ca/carmha/publications/antidepressant-skills-workbook.html
Youtube video	rTMS information	https://www.youtube.com/watch?v=oWDg-HGDAZU
Mindfulness Tools		
App	ACT Coach	https://apps.apple.com/ca/app/act-coach/id804247934
App	Calm	https://www.calm.com/
App	Deep Breathing	https://apps.apple.com/us/app/breathscape-deep-breathing
App	Headspace	https://www.headspace.com/
App	Insight Timer	https://insighttimer.com/
App	Smiling Mind	https://www.smilingmind.com.au/
Guided App	BounceBack	https://cmha.ca/bounce-back/
Text	Text 4 Hope	https://www.albertahealthservices.ca/amh/Page17019.aspx

Website	Deep breathing Exercises	https://www.psychologytools.com/resource/relaxed-breathing
Website	Mood Gym	https://www.moodgym.com.au/
Website	Palouse Mindfulness	https://palousemindfulness.com/
Website	Tara Brach (Meditation)	https://www.tarabrach.com/
Website	The Breath Project	https://thebreathproject.org/
Website	The Happiness Project	https://thehappinesstrap.com/free-resources/
Website	Together All	https://togetherall.com/en-ca/
Self Help Books		
Author		**Title**
Andrew Seubert		The Courage to Feel: A practical Guide to the Power and Freedom of Emotional Honesty
Bessel Van Der Kolk		The Body Keeps the Score: Brain, Mind, and Body in the Healing of Trauma
David D. Burns, MD		The Feeling Good Handbook
Dennis Greenberger and Christine A. Padesky		Mind over Mood: Change How Your Feel by the Way You Think
Diane Mcintosh		This is Depression: A comprehensive, Compassionate Guide for Anyone Who Wants to Understand Depression
Jeffrey E. Young		Reinventing Your Life: The Breakthrough Program to End Negative Behavior…and Feel Great Again
Sleep Hygiene		
Anxiety Canada		https://www.anxietycanada.com/sites/default/files/SleepHygiene.pdf
Dalhousie University		https://mysleepwell.ca/
Health Link BC		https://www.healthlinkbc.ca/healthwise/insomnia-improving-your-sleep
Psychotherapy Supports		
Access Mental Health		Phone number: 403-943-1500, fax 403-943-9044
Alberta College of Social Workers		https://www.acsw.ab.ca/
Calgary Counselling Centre		Phone number: 403-265-4980; https://calgarycounselling.com/
Catholic Family Services		Phone number: 403-233-2360; https://www.ementalhealth.ca/index.php?m=record&ID=13861
Community Connect YYC		https://www.communityconnectyyc.ca/
Employee, Family Assistance Programs		Depending on your employer, this may be available through your benefits
Jewish Family Services		Phone number: 403-287-3510; https://www.jfsc.org/
Owlpod (physician referral required)		https://www.owlpod.org/
PCN Supports, including: BHC, MH Assist, MH Nurse		Dependent on the PCN your doctor is a part of
Private psychologist		https://psychologistsassociation.ab.ca/
University of Calgary Psychology Clinic		Phone number: 403-220-7731; https://arts.ucalgary.ca/psychology-clinic
Women's Health Resources		Phone number: 403-944-2260
Urgent Services		
Urgent Counselling Services		
Eastside Community Mental Health Service		Phone number: 403-299-9699. https://www.woodshomes.ca/eastside-community-mental-health-services/
Sheldon Chumir		https://www.albertahealthservices.ca/findhealth/Service.aspx?id=10641 60&serviceAtFacilityID=1099658

South Calgary Health Centre	Phone number: 403-943-9374; https://www.albertahealthservices.ca/findhealth/service.aspx?serviceAt FacilityId=1018206#contentStart
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