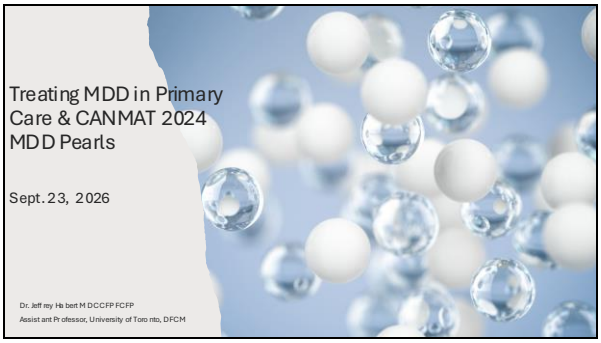

Treating MDD in Primary Care & CANMAT 2024 MDD Pearls

Sept. 23, 2026

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Speaker's Disclosures

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2

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3

Learning Objectives

- **Review** the updated **CANMAT 2023/2024 guidelines** for diagnosing and managing Major Depressive Disorder (MDD), including evidence-based treatment pathways.
- **Understand and apply** the principles of **early optimized treatment** and **measurement-based care** to improve functional outcomes and remission rates in MDD.
- **Identify strategies** for **managing inadequate response** to initial therapy, including antidepressant switching, adjunctive treatments, psychotherapy, and neuromodulation options.

MDD Unmet Needs

Early & Urgent 101

MDD is a highly prevalent disorder and a serious public health problem[1,2]

Burden

of Canadians will experience a major depressive episode in their lifetime[1]

Stigma

Stigma surrounding mental illness is prevalent in society, **and presents a large barrier to treatment**[2]

Primary care practitioners have the first opportunity to intercept and optimally treat depression earlier, potentially reducing the substantial morbidity, mortality, and functional impairment associated with MDD.[3]

Unmet Needs in the Treatment of MDD

Early & Urgent 101

Untreated MDD	Non-adherence	Treatment failure	Recurrence/relapse	Subsequent episode
Up to **50%** of cases[1,2]	Up to **70%** of cases overall[3] **60%** stop antidepressant therapy before 6 months[4] **28%** of primary care patients stop antidepressant therapy at 1 month[4]	**40–60%** of cases[5]	Up to **80%** of cases[5]	**50%** probability of a 2nd episode[6] **80–90%** probability of a 3rd episode[6]

Residual symptoms are associated with risk of relapse and recurrence[6,7]

Diagnosing MDD With DSM-5-TR

≥5 of the following symptoms:

- Depressed mood
- Markedly diminished interest or pleasure
- Weight or appetite changes
- Insomnia or hypersomnia
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness, or excessive or inappropriate guilt
- Executive dysfunction
- Recurrent thoughts of death or suicidal ideation/attempt

Symptoms present during same **2-week period** and represent a **change from previous functioning**

2 weeks

≥1 symptom must be "**depressed mood**" or "**markedly diminished/loss of interest or pleasure**"

MDD can cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

8

What is this Concept of Early optimized treatment

Functional Recovery in Major Depressive Disorder:
Focus on Early Optimized Treatment

Jeffrey Habert, MD, CCFP, FCFP[a,*]; Martin A. Katzman, MD, FRCPC[b]; Oloruntoba J. Oluboka, Roger S. McIntyre, MD[d]; Diane McIntosh, MD, FRCPC[e]; Glenda M. MacQueen, MD, PhD[f]; Atul Khullar, MD, FRCPC[g]; Roumen V. Milev, MD, PhD, FRCPC[h]; Kevin D. Kjernisted, MD[e]; Pratap R. Chokka, MD[g]; and Sidney H. Kennedy, MD, FRCPC[i]

Early Optimized Treatment in MDD: Making Your First Shot the Best Shot

"Shortening the time between onset of depression and providing optimized treatment may result in better clinical outcomes, increasing the likelihood of achieving full functional recovery from the depressive episode."[1]

Applying the Urgency to Treat Mindset in MDD

Recognize — Understand the consequences of NOT using the Early Optimized Treatment approach

Implement — Adopt a mindset that ensures patients are treated as fast and as assertively as possible until treatment yields positive results

Apply — Ensure patients do not remain on ineffective or poorly tolerated treatment, which may:
- Delay recovery
- Heighten the risk of residual symptoms and functional deficits
- Negatively impact patient mindset about disease and treatment

What are some of the reason(s) you would treat MDD with a greater sense of urgency?

Habert et al. Prim Care Companion CNS Disord. 2016; 18(5)10.4088/PCC.15r01926.

10

Inadequate Treatment of MDD Is Associated With Neurogenerative Changes

Untreated MDD can lead to loss of volume in various brain regions, including:
- Hippocampus[1-3]
  More severe volume loss with a longer duration of untreated depression[2-4]
- Prefrontal cortex[5]
- Orbitofrontal cortex[6]
- Subgenual cingulate cortex[7]
- Amygdala[8]

MDD treatment is generally associated with a reversal or reduction of changes to these brain regions[9]

Delaying effective treatment may reduce the likelihood of asymptomatic remission and functional recovery, and also increase the time to achieve remission.[10-13]

1. Videbech P, Ravnkilde B. Am J Psychiatry. 2004;161:1957-1966. 2. McKinnon et al. J Psychiatry Neurosci. 2009;34:41-54. 3. MacQueen G, Frodl T. Mol Psychiatry. 2011;16:252-264. 4. Sheline et al. Am J Psychiatry. 2003;160:1516-1518. 5. Si et al. Neuropsychopharmacology. 2004;29(11):2088-2096. 6. Scheuerecker et al. J Psychiatry Neurosci. 2010;35(5):311-320. 7. Drevets et al. CNS Spectr. 2008;13(8):663-681. 8. Hamilton et al. Mol Psychiatry. 2008;13(11):993-1000. 9. Oluboka et al. Int J Neuropsychopharm. 2018;21(2):128-144. 10. Gormley et al. J Affect Disord. 1999;54:49-54. 11. Okuda et al. Psychiatry Clin Neurosci. 2010;64:268-273. 12. Bukh et al. J Affect Disord. 2013;145:42-48. 13. Ghio et al. J Affect Disord. 2014;152-154:45-51.

11

MDD Should be Treated With a Greater Sense of Urgency

Many patients with MDD receive **inadequate treatment**[1,2]

- Subtherapeutic doses
- Inadequate duration of treatment
- Poor adherence

Prolonged illness[3,4]
- Delayed symptom remission
- Worsened functional, social, and economic burden of MDD

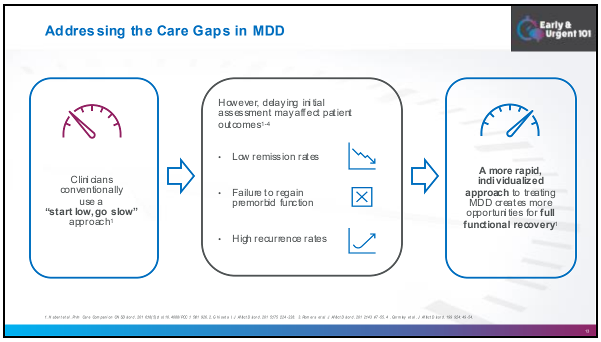
Reduced likelihood of future success

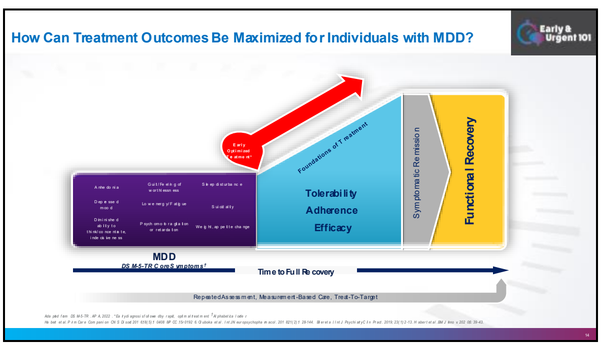
Multiple courses of treatment over prolonged periods are associated with a progressive decrease in the likelihood of treatment success[5]

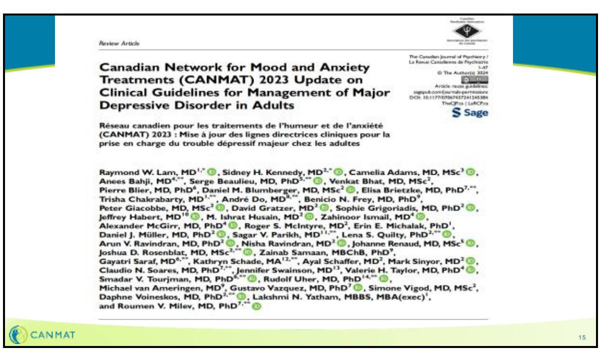
Successful management of MDD necessitates development of a personalized treatment plan that allows individuals to achieve full functional recovery in the most effective and efficient manner.[6,7]

1. Kennedy et al. Can J Psychiatry. 2016;61:540–560. 2. Robertson et al. J Clin Psychiatry. 2016;77:359-362. 3. McIntyre et al. Can J Psychiatry. 2004;49(suppl 1):10S–16S. 4. Götzner et al. Psychiatry Res. 2019;271:343–350. 5. Rush et al. Am J Psychiatry. 2006;163:1905–1917. 6. Habert et al. Prim Care Companion CNS Disord. 2016;18(5)10.4088/PCC.15r01926. 7. Oluboka et al. Int J Neuropsychopharmacol. 2018;21(2):128-144.

12






Review Article

Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults

Réseau canadien pour les traitements de l'humeur et de l'anxiété (CANMAT) 2023 : Mise à jour des lignes directrices cliniques pour la prise en charge du trouble dépressif majeur chez les adultes

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Sage

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15

CANMAT 2023 Guidelines for Major Depressive Disorder

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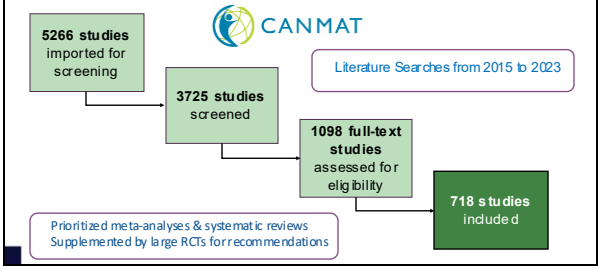
CANMAT Depression Guidelines 2024



CANMAT 2023 Update on Guidelines for Major Depressive Disorder

CANMAT Definitions for Level of Evidence and Line of Treatment

Level of Evidence Ratings

Level	Evidence Criteria
1	Meta-analysis with narrow confidence interval or replicated double-blind (DB), randomized controlled trial (RCT) that includes a placebo or active control comparison (n≥30 in each active treatment arm)
2	Meta-analysis with wide confidence interval or one DB-RCT with placebo or active control comparison condition (n≥30 in each active treatment arm)
3	At least one DB-RCT with placebo or active control comparison condition (n=10-29 in each active treatment arm) or health system administrative data
4	Uncontrolled trial, anecdotal reports, or expert opinion

Line of Treatment Recommendations

Line of Treatment	Evidence level
1st Line	Level 1 or Level 2 evidence for efficacy plus clinical support* for safety / tolerability / feasibility
2nd Line	Level 3 or higher evidence for efficacy plus clinical support* for safety / tolerability / feasibility
3rd Line	Level 4 evidence or higher for efficacy plus clinical support* for safety / tolerability / feasibility

* Instances where lack of clinical support for safety/tolerability/feasibility has impacted recommendations have been highlighted in the text and table.

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CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Primary Questions

8 primary questions representing a patient's care journey from assessment through treatment to maintenance

1. What are important issues for assessment and diagnosis?
2. What are principles for depression management?
3. How are treatments selected?
4. What is the role of digital health interventions?
5. How do you monitor treatment?
6. What do you do when a patient is better?
7. What do you do when a patient is not better?
8. What neuromodulation treatments are available?

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Question 2: Principles for MDD Management

- Collaborative Decision Making is essential
- Psychoeducation and self-management are integral to MD management
  - Psychoeducation refers to knowledge and information about the symptoms, coping strategies and treatment options for depression,
  - whereas self-management uses techniques (e.g., problem-solving, lifestyle changes, and behavioural activation [BA]) to empower patients to actively manage their illness and live well
- Symptom remission remains a crucial clinical target for acute treatment, as substantial evidence supports a lower risk of relapse in those who achieve remission compared with those who do not
  - In contrast, failure to achieve remission is associated with continuing symptom burden and poor functional outcomes. Evidence supports symptomatic remission as a realistic goal of acute phase treatment for most patients both in psychiatric and primary care settings

21

Risk Factors for Depression

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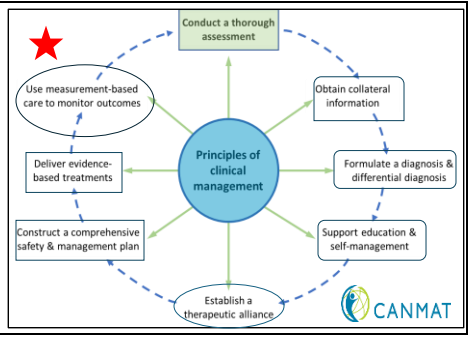
Non-modifiable	Dynamic (modifiable)
• Female sex and gender issues • Early age of onset • Family history • Adverse childhood events / maltreatment • Prior history of MDD, anxiety, mental health comorbidity • Death of a spouse	• Chronic physical disease • Substance use disorders • Insomnia, night work, later chronotype • Bullying / Cyberbullying • Stressful life events • Job strain / Income inequality • Lifestyle / Screen time

Principles of Clinical Assessment and Management of MDD



Lifestyle Interventions in the Treatment of Depression

Line of Treatment	Lifestyle Intervention	Level of Evidence
First Line	Supervised exercise (low to moderate intensity, for 30 to 40 minutes at a time, three to four times a week, for a minimum of nine weeks) for MDE of mild severity.	●
	Light therapy (10,000 lux white light for 30 minutes daily) for MDEs with seasonal (winter) pattern.	●
Second Line	Light therapy for mild severity nonseasonal MDE.	◔
	Adjunctive exercise for moderate severity MDE.	◔
	Adjunctive light therapy for moderate severity nonseasonal MDE.	◔
	Adjunctive sleep hygiene and cognitive-behavioural therapy for insomnia (CBT-I).	◐
Third Line	Adjunctive healthy diet (varied diet with high content of fruit, vegetables, and fibre, and low content of saturated fat and carbohydrates).	◐
	Adjunctive Mediterranean diet.	◐
	Adjunctive sleep deprivation (wake therapy).	◐
Insufficient Evidence	Probiotics.	n/a

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Primary Questions

8 primary questions representing a patient's care journey from assessment through treatment to maintenance

1. What are important issues for assessment and diagnosis?
2. What are the principles for depression management?
3. **How are treatments selected?**
4. What is the role of digital health interventions?
5. How is treatment monitored?
6. What should be done when a patient is better?
7. What should be done when a patient is not better?
8. When should neuromodulation treatments be used?

How Do You Choose the Initial Treatment?

Considerations for selecting treatment(s)

- Collaborative decision-making
- Patients' attitudes and preferences
- Informed awareness of treatments
- Quality of evidence
- Availability of treatments
- Risk from delay in treatment initiation
- Severity of depression

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Depression Severity	Recommendations for Initial Treatment [1]
Mild, with low risk	• Psychotherapy (preferred) or pharmacotherapy • Exercise, certain CAM treatments, guided DHIs can be considered as monotherapies*

[1] There is stronger evidence for efficacy and safety of pharmacotherapy and psychotherapy compared to exercise, complementary and alternative medicine treatments, and digital health interventions.

The level of evidence refers to the choice of treatment, not to the treatments themselves.

*Especially if preferred by patients.

How Do You Choose the Initial Treatment?

Considerations for selecting treatment(s)

- Collaborative decision-making
- Patients' attitudes and preferences
- Informed awareness of treatments
- Quality of evidence
- Availability of treatments
- Risk from delay in treatment initiation
- Severity of depression

Depression Severity	Recommendations for Initial Treatment [1]
Mild, with low risk	• Psychotherapy (preferred) or pharmacotherapy • Exercise, certain CAM treatments, guided DHIs can be considered as monotherapies*
Moderate to severe, with low-moderate risk	• Pharmacotherapy or psychotherapy (consider combination) • Adjunctive treatment with exercise, certain CAM treatments, DHIs*

[1] There is stronger evidence for efficacy and safety of pharmacotherapy and psychotherapy compared to exercise, complementary and alternative medicine treatments, and digital health interventions.

The level of evidence refers to the choice of treatment, not to the treatments themselves.

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CAM: Complementary and Alternative Medicine; DHIs: digital health interventions; ECT: electroconvulsive therapy

Lam RW, Kennedy SH, et al. Can J Psychiatry 2024.

30

How Do You Choose the Initial Treatment?

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Moderate to severe, with low-moderate risk	• Pharmacotherapy or psychotherapy (consider combination) • Adjunctive treatment with exercise, certain CAM treatments, DHIs*
Severe or high risk	• Without psychotic symptoms: use sequential pharmacotherapy-psychotherapy • With psychotic symptoms: use combination antidepressant + antipsychotic • For very severe or life-threatening situations, consider ECT

[1] There is stronger evidence for efficacy and safety of pharmacotherapy and psychotherapy compared to exercise, complementary and alternative medicine treatments, and digital health interventions.

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CANMAT

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31

Psychotherapy

Psychotherapy can be recommended alone for mild-to-moderate depression, or in conjunction with medication for moderate and severe depression.[1]

Various forms of psychotherapy for depression exist. **The first-line options are described below:**[9]

- **Cognitive-behavioural therapy (CBT):** focuses on identifying negative cognitions and behaviours, substituting more realistic thinking and promoting behavioural activation. Usually 12 to 16 weekly sessions.
- **Interpersonal therapy:** focuses on identifying and dealing with interpersonal conflicts and problems. Usually 14 to 16 weekly sessions.
- **Behavioural activation**: focuses on increasing and reinforcing activities, scheduling and monitoring, and problem solving. Usually six to eight weekly sessions.

Recommendation	LoE	Psychological Treatment
1st Line	●●●	• Cognitive-behavioural therapy (CBT) • Interpersonal therapy (IPT) • Behavioural activation (BA)
2nd Line	◐	• 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
3rd Line	◐	• Acceptance & commitment therapy (ACT) • Long-term psychodynamic psychotherapy (PDT) • Metacognitive therapy (MCT) • Motivational interviewing (MI)

LoE, Level of Evidence ● Level 1 ◐ Level 2 ◐ Level 3 ◐ Level 4

Red indicates new since 2016.

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Lam RW, Kennedy SH, et al. Can J Psychiatry 2024.

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Recommendations for Medication Treatments

1st Line

- Citalopram (SSRI)
- Escitalopram (SSRI)
- Fluoxetine (SSRI)
- Fluvoxamine (SSRI)
- Paroxetine (SSRI)
- Sertraline (SSRI)
- Desvenlafaxine (SNRI)
- Duloxetine (SNRI)
- **Levomilnacipran (SNRI)**
- Venlafaxine (SNRI)
- Bupropion (NDRI)
- Mirtazapine (α2-adrenergic & 5-HT2 antagonist)
- **Vilazodone (in ultimo dal)**
- Vortioxetine (in ultimo dal)
- Agomelatine* (MT1 & MT2 agonist; 5-HT2 antagonist)
- Mianserin* (α2-adrenergic & 5-HT2 antagonist)
- Milnacipran* (SNRI)

2nd Line

- Amitriptyline, clomipramine, nortriptyline, others (TCAs)
- Moclobemide (reversible inhibitor MAO-A)
- Trazodone (SRI; 5-HT2 antagonist)
- Quetiapine (DA, 5-HT α1 & α2 antagonist; NRI)
- **Dextromethorphan-bupropion* (NMDA antagonist; SNRI; NDRI)**
- Nefazodone* (SRI, 5-HT2 antagonist)
- **Selegiline transdermal* (irreversible inhibitor MAO-B)**

3rd Line

- Phenelzine* (irreversible inhibitor MAO)
- Tranylcypromine
- Reboxetine* (NRI)

MT, melatonin; 5-HT, serotonin; MAO, monoamine oxidase; NDRI, noradrenaline and dopamine reuptake inhibitor; NMDA, N-methyl-D-aspartate receptor; SNRI, serotonin and noradrenaline reuptake inhibitor; SRI, serotonin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic agent.

All agents have Level 1 evidence

* Not available in Canada.

Red indicates new since 2016.

CANMAT 2023 Recommendations: Antidepressants

Summary Recommendations for Antidepressants: First Line

Antidepressant	Daily dose[1]	Mechanism	Level of evidence
Citalopram	20-40 mg	SSRI	1
Escitalopram	10-20 mg	SSRI	1
Fluoxetine	20-60 mg	SSRI	1
Fluvoxamine	100-300 mg	SSRI	1
Paroxetine	20-50 mg	SSRI	1
Sertraline	50-200 mg	SSRI	1
Desvenlafaxine	50-100 mg	SNRI	1
Duloxetine	60-120 mg	SNRI	1
Levomilnacipran*	40-120 mg	SNRI	1
Venlafaxine-XR	75-225 mg	SNRI	1
Bupropion	150-450 mg[2]	NDRI	1
Mirtazapine	30-60 mg	α2 antagonist; 5-HT2 antagonist	1
Vilazodone*	20-40 mg	SRI; 5-HT1A agonist	1
Vortioxetine	10-20 mg	SRI; 5-HT1A, 5-HT1B agonist; 5-HT1D, 5-HT1A, 5-HT7 antagonist	1
Agomelatine*	25-50 mg	MT1, MT2 agonist; 5-HT2a antagonist	1
Mianserin*	30-90 mg	α2 antagonist; 5-HT2a antagonist	1
Milnacipran*	50-200 mg	SNRI	1

Level 1
Not available in Canada.

[1]Dose ranges are taken from product monographs; individuals doses below and above the range may be used.

[2]Daily doses above 300 mg should be given in divided doses.

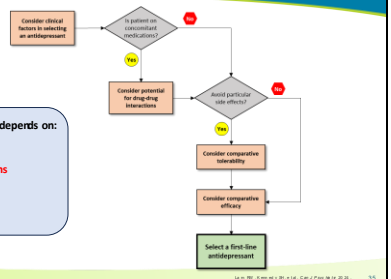
By convention, the order of recommendations within each line of treatment is based first by availability in Canada, then by class, and then by alphabetical order.

* Star red items indicate changes since CANMAT 2016 guidelines, based on updated evidence.

5-HT, 5-hydroxytryptamine receptor; α2 = alpha-2 adrenergic receptor; MT, melatonin receptor; NDRI, norepinephrine-dopamine reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor; SRI, serotonin reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Algorithm for selecting an antidepressant



Selection of an antidepressant depends on:

- **Efficacy**
- **Tolerability**
- **Concomitant medications**
- Clinical presentation
- Past medication history
- Cost
- Patient preference

Table 3.6. Summary Medication Recommendations for DSM-5-TR Episode Specifiers and Symptom Dimensions.

	DSM-5-TR Episode Specifiers				Symptom Dimensions		
Line of Treatment	➢ Anxious distress ➢ Atypical features ➢ Melancholic features	➢ Mixed features	➢ Psychotic features	➢ Catatonic features	➢ Cognitive dysfunction	➢ Sleep disturbance	➢ Somatic symptoms
First Line	Any first-line antidepressant from Table 3.2	Any first-line antidepressant* from Table 3.2	Any first-line antidepressant from Table 3.2 + atypical antipsychotic	Benzodiazepine and any first-line antidepressant from Table 3.2	Vortioxetine	Agomelatine	Duloxetine (pain) Bupropion (fatigue)
Second Line	Any second-line antidepressant from Table 3.2	Lurasidone**			Bupropion Duloxetine SSRIs**	Mirtazapine Quetiapine-XR Trazodone	Duloxetine** (fatigue) Other SNRIs (pain) SSRIs** (fatigue)

Level 1 Level 2 Level 3 Level 4

* When initiating medications, monitor for activating side effects (e.g., agitation, increase in suicidal ideation) and potential switch to (hypo)mania.

** Comparisons only with placebo

SSRI, selective serotonin reuptake inhibitor; SNRI, serotonin-norepinephrine reuptake inhibitor.

Lam RW, Kennedy SH, et al. *Can J Psychiatry* 2024

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

First-line Antidepressants: Consensus Comparative Ratings

Based on evidence from varied sources and expert consensus

More favourable
Less favourable
Neutral[6]

	Efficacy and drug-specific issues			
Antidepressant	Efficacy[1]	Acceptability[2]	Drug interactions	Discontinuation
SSRIs				
Citalopram			QTc[4]	
Escitalopram				
Fluoxetine				
Fluvoxamine				
Paroxetine				
Sertraline				
SNRIs				
Desvenlafaxine				
Duloxetine				
Levomilnacipran				
Venlafaxine-XR				
Others				
Bupropion				
Mirtazapine				
Vilazodone				
Vortioxetine				
Not available in Canada				
Agomelatine			LFTs[5]	
Mianserin				
Milnacipran				

[1] Efficacy refers to response rates in meta-analyses; [2] Acceptability refers to all-cause discontinuation rates in meta-analyses; [3] Other Tolerability refers to side effects other than sedation, weight gain, and sexual dysfunction. [4] Indicates recommended monitoring for prolongation of QTc interval; [5] Indicates recommended monitoring of liver function tests; [6] Clear squares indicate neutral ratings and do not imply intermediate or favourability ratings.

Lam RW, Kennedy SH, et al. *Can J Psychiatry* 2024

CANMAT 37

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

First-line Antidepressants: Consensus Comparative Ratings

Based on evidence from varied sources and expert consensus

More favourable
Less favourable
Neutral[6]

	Efficacy and drug-specific issues				Tolerability issues			
Antidepressant	Efficacy[1]	Acceptability[2]	Drug interactions	Discontinuation	Sedation	Weight gain	Sexual dysfunction	Other Tolerability[3]
SSRIs								
Not available in Canada								
Agomelatine			LFTs[5]					
Mianserin								
Milnacipran								

For most adults with MDD, the choice of the first antidepressant is based on the balance of efficacy and tolerability.[1]

The table to the right summarizes efficacy and tolerability for the first-line antidepressants.[1]

Per the CANMAT guidelines, agomelatine, escitalopram, and vortioxetine showed advantages over other antidepressants when considering both efficacy and acceptability.[1]

[1] Efficacy refers to response rates in meta-analyses; [2] Acceptability refers to all-cause discontinuation rates in meta-analyses; [3] Other Tolerability refers to side effects other than sedation, weight gain, and sexual dysfunction. [4] Indicates recommended monitoring for prolongation of QTc interval; [5] Indicates recommended monitoring of liver function tests; [6] Clear squares indicate neutral ratings and do not imply intermediate or favourability ratings.

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CANMAT 38

Nausea		Somnolence	
Greater than 20% (>30% *)		**Greater than 20%**	
• Citalopram • Paroxetine • Desvenlafaxine • Fluoxetine • Milnacipram)*	• Sertraline • Venlafaxine XR* • Vilazodone • Vortioxetine • Duloxetine	• Fluvoxamine • Paroxetine	
Less than 20%		**Less than 10%**	
• Agomelatine • Bupropion • Escitalopram (15%)		• Agomelatine • Bupropion XL • Desvenlafaxine • Escitalopram • Vilazodone • Vortioxetine	

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Primary Questions

8 primary questions representing a patient's care journey from assessment through treatment to maintenance

1. What are important issues for assessment and diagnosis?
2. What are the principles for depression management?
3. How are treatments selected?
4. What is the role of digital health interventions?
5. **How is treatment monitored?**
6. What should be done when a patient is better?
7. What should be done when a patient is not better?
8. When should neuromodulation treatments be used?

CANMAT

Measurement-Based Care in MDD: General Principles

- Use of routine outcome measurements and feedback to support clinical decisions
- Measurement-based care (MBC) has been demonstrated to improve medication adherence and outcomes, especially in the pharmacological treatment of MDD

Three components:

- Regularly using validated outcome scales during patient encounters
- Reviewing the scale scores with patients
- Using the scales alongside clinical assessment to support collaborative decision-making

- **The use of scales for MBC is similar to the use of laboratory tests in that the results must be considered within the context of clinical assessment and care**

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Meta-analysis of measurement-based care (MBC) for depression

THE JOURNAL OF CLINICAL PSYCHIATRY

JCP CME: META-ANALYSIS

The Efficacy of Measurement-Based Care for Depressive Disorders: Systematic Review and Meta-Analysis of Randomized Controlled Trials

Maria Zhu, MSc[a]; Ran Ha Hong, BSc[a]; Tao Yang, MD, PhD[b]; Xiaorui Yang, MD[b]; Xing Wang, MD[b]; Jing Liu, MHA[a]; Jill K. Murphy, PhD[a]; Erin E. Michalak, PhD[a]; Zuowei Wang, MD, PhD[b]; Lakshmi N. Yatham, MBBS, MBA/Exec[a]; Jun Chen, MD, PhD[b]; and Raymond W. Lam, MD[a,*]

- PRISMA methodology
- Literature search of databases to July 1, 2020
- Comprehensive search terms
- 67 studies identified
  (5 in English literature, 2 in Chinese)
- Only pharmacotherapy studies were identified

Zhu M et al. J Clin Psychiatry 2021;82:21r14084

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Tools to Monitor Course of Treatment

Outcome	Clinician-Rated	Patient-Rated
Symptoms/ severity	• Hamilton Depression Rating Scale (HAM-D, HAM-7) • Montgomery Åsberg Depression Rating Scale (MADRS) • Inventory for Depressive Symptomatology (IDS) • Columbia Suicide Severity Rating Scale (C-SSRS)	• Beck Depression Inventory-II (BDI-II) • Clinically Useful Depression Outcome Scale (CUDOS) • Patient Rated Outcome Measurement Information System (PROMIS) • Patient Health Questionnaire (PHQ-9) • Quick Inventory for Depressive Symptomatology, Self-Rated (QIDS-SR) • Suicidality Scale
Functioning	• Multidimensional Scale of Independent Functioning (MSIF) • Social and Occupational Functioning Assessment Scale (SOFAS) • WHO Disability Assessment Scale (WHO-DAS)	• Lam Employment Absence and Productivity Scale (LEAPS) • Sheehan Disability Scale (SDS) • WHO-DAS, self-rated • Work and Social Adjustment Scale (WSAS)
Quality of Life	• Quality of Life Interview (QOLI)	• EuroQoL-5D (EQ-5D) • Quality of Life, Enjoyment and Satisfaction Questionnaire (QLESQ)
Side Effects	• UKU Side Effect Rating Scale • Toronto Side Effects Scale	• Frequency, Intensity and Burden of Side Effects Rating (FIBSER)

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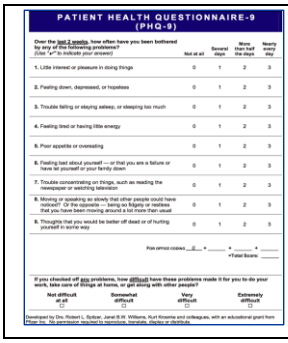


PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

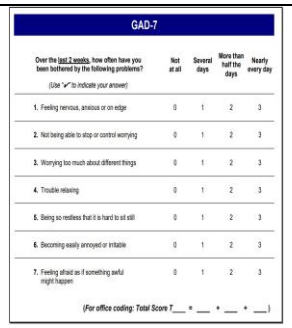
Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✓" to indicate your answer)

	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 figgety 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: ___

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



GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems? (Use "✓" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

(For office coding: Total Score T___ = ___ + ___ + ___)

Interpretation of Self-rated scales

PHQ-9 Interpretation

Score	Interpretation
5 - 9	Mild
10 – 14	Moderate
15 - 19	Moderately severe
20 - 27	Severe

GAD-7 Interpretation

Score	Interpretation
5 - 9	Mild
10 – 15	Moderate
15 - 21	Severe

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What laboratory tests do you monitor during treatment?

- No routine tests are necessary, but CBC and TSH are low-cost blood tests to rule out medical conditions that present with depressive symptoms
- Other baseline tests (blood, imaging, ECG) should only be considered if history or physical examination indicates clinical suspicion
- No routine lab tests are recommended to monitor antidepressant treatment, except in specific situations (e.g., LFTs in liver disease, electrolytes in elderly patients, bloodwork during lithium treatment)
- Metabolic monitoring (weight, glucose, lipid profiles) is recommended because weight gain is common in depression (as a symptom, a medication side effect, or both).

CBC, complete blood count;
TSH, thyroid stimulating hormone;
LFTs, liver function tests.

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Lam RW, Kennedy SH, et al. Can J Psychiatry 2024

SUMMARY

- Use MBC routinely to guide decision-making
- Incorporate MBC tools (paper-pencil, mobile, internet)
- Incorporate MBC in EMR
- Integrate MBC into pathways (stepped, stratified, collaborative care)
- Laboratory or imaging tests should be ordered case-by-case
- MBC should include basic metabolic monitoring

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Table 5.1. Summary Recommendations for Monitoring Treatment*.

Summary Recommendations for Monitoring	Level of Evidence
Use validated rating scales for measurement-based care.	
Obtain laboratory and imaging tests only when clinically indicated.	
Monitor weight, glucose, and lipid profiles at baseline and every 6 months when prescribing medications associated with weight gain.	

Level 1 Level 2 Level 3 Level 4

* Recommendations for principles of care generally have Level 3 or Level 4 evidence.

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Primary Questions

8 primary questions representing a patient's care journey from assessment through treatment to maintenance

1. Who should be treated for depression?
2. What are principles for depression management?
3. How do you select the initial treatment?
4. What is the role of digital health interventions?
5. How do you monitor treatment?
6. **What do you do when a patient is better?**
7. What do you do when a patient is not better?
8. What neuromodulation treatments are available?

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When a person achieves remission

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- ☐ Confirm Remission using MBC
- ☐ Continue Psycho/Pharmaco- therapy for 6-12 months after achieving remission
- ☐ If history of previous relapses/ recurrences suggest- maintain treatment for 2 years or longer
- ☐ Taper medication gradually
- ☐ Psychological therapies may be initiated during taper of medication
- ☐ Reinforce lifestyle interventions as part of daily routine

2

Who needs longer duration of MaintenanceTherapy (2 Years +)

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Major Risk Factors

- History of Childhood maltreatment
- Residual symptoms
- Higher number of previous episodes
- Comorbid anxiety

Other Risk Factors

- Early age of onset
- Longer duration of depressive episodes
- Greater severity of depressive episodes

Managing Discontinuation Symptoms by Antidepressant

High Risk	Moderate risk	Low Risk	Minimal/No Risk
• Desvenlafaxine • Paroxetine • Venlafaxine	• Citalopram • Duloxetine • Escitalopram • Fluvoxamine • Levomilnacipran • Milnacipran • Sertraline • Vilazodone • TCAs • MAOIs	• Bupropion • Mirtazapine	• Agomelatine • Fluoxetine • Vortioxetine

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CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Primary Questions

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1. What are important issues for assessment and diagnosis?
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Poor Response to Initial Treatment

Patient Factors

- Wrong diagnosis
- Older age, female sex, greater severity, younger age of onset
- Psychiatric comorbidities
- Medical comorbidities
- Obesity
- Substance use
- Acute or chronic stressors
- Poor adherence
- Pharmacogenetic variability

Medication Factors

- Dose is too high/low
- Duration is too short
- Adherence is sporadic
- Side effects are intolerable;

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Lam RW, Kennedy SH, et al. Can J Psychiatry 2024

Importance of Recognizing Inadequate Response Quickly

If improvement (a 20% or greater reduction in scores on a symptom rating scale) is not seen by 4 weeks, there is a low likelihood of response or remission at 8 to 12 weeks.[1]

Consequences of Not Achieving Remission of Depression[2]

Disease Course	Costs
• Higher risk of relapse • More rapid relapse • Increased rate of recurrence • Shorter course of well intervals • Fewer symptom-free weeks • Increased risk of suicide	• Medical, psychiatric, emergency care • More psychiatric hospitalizations • Increased welfare or disability insurance benefits • Associated work impairment

Adapted from:
1. Lam RW, et al. *Can J Psychiatry* 2024;1-47; doi:10.1177/07067437241245384; 2. Culpepper L et al. *Am J Med* 2015;128(9A):S1-15

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Antidepressant Dose Optimization in MDD

Early & Urgent 101

Optimizing the antidepressant dose is essential for success in treating MDD[1]

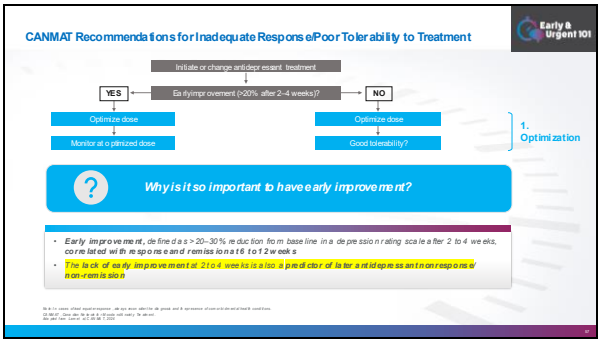
? *What does dose optimization mean in MDD treatment?*

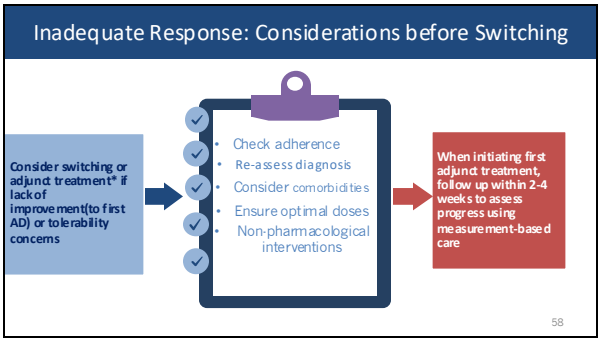
Optimization means using medications that patients can tolerate at doses sufficient for achieving remission and recovery[1,2]

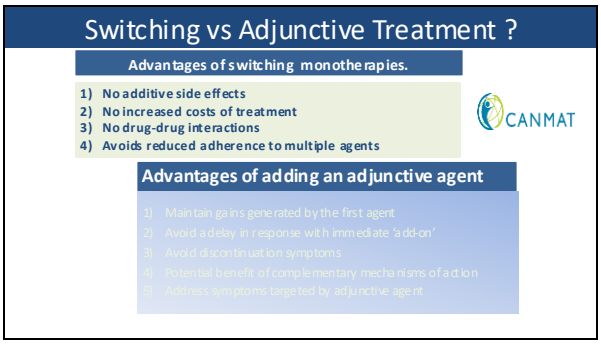
Most antidepressants have starting doses that are lower than the average dose required for full response. Thus, the target dose is reached over time, and an optimized dose is achieved when therapeutic efficacy and patient tolerance are balanced.[1]

1. Manning JS. J Clin Psychiatry 201 071(suppl 1):10-15. 2. Rush et al. UpToDate. Unipolar major depression in adults: Choosing initial treatment. Available from [illegible]

56


CANMAT Recommendations for Inadequate Response/Poor Tolerability to Treatment
Early & Urgent 101
Initiate or change antidepressant treatment
YES
Early improvement (>20% after 2-4 weeks)?
NO
Optimize dose
Monitor at optimized dose
Optimize dose
Good tolerability?
1. Optimization
Why is it so important to have early improvement?
Early improvement, defined as >20–30% reduction from baseline in a depression rating scale after 2 to 4 weeks, correlated with response and remission at 6 to 12 weeks
The lack of early improvement at 2 to 4 weeks is also a predictor of later antidepressant non-response/non-remission


Inadequate Response: Considerations before Switching
Consider switching or adjunct treatment* if lack of improvement(to first AD) or tolerability concerns
Check adherence
Re-assess diagnosis
Consider comorbidities
Ensure optimal doses
Non-pharmacological interventions
When initiating first adjunct treatment, follow up within 2-4 weeks to assess progress using measurement-based care
58


Switching vs Adjunctive Treatment ?
Advantages of switching monotherapies.
1) No additive side effects
2) No increased costs of treatment
3) No drug-drug interactions
4) Avoids reduced adherence to multiple agents
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Advantages of adding an adjunctive agent
1) Maintain gains generated by the first agent
2) Avoid a delay in response with immediate 'add-on'
3) Avoid discontinuation symptoms
4) Potential benefit of complementary mechanisms of action
5) Address symptoms targeted by adjunctive agent

Switching vs Adjunctive Treatment ?

Advantages of switching monotherapies.

1) No additive side effects
2) No increased costs of treatment
3) No drug-drug interactions
4) Avoids reduced adherence to multiple agents

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Advantages of adding an adjunctive agent

1) Keep gains generated by the first agent
2) Avoid a delay in response with immediate 'add-on'
3) Avoid discontinuation symptoms
4) Potential for complementary mechanisms of action
5) Address symptoms targeted by adjunctive agent

CANMAT 2023 Update on Guidelines for Major Depressive Disorder

New Evidence for Medication Strategies for Poor Initial Antidepressant Response

Dose-Response

- Higher than minimal therapeutic doses are more effective but less well-tolerated
- There is little evidence that high doses of antidepressants (especially SSRIs) lead to better response (exceptions of note are Venlafaxine, Sertraline and Vortioxetine)

Switching antidepressants

- RCTs show that switching the antidepressant does not lead to better response
- Response rates diminish with each successive switch

LoE, Level of Evidence Level 1 Level 2 Level 3 Level 4

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CANMAT 2023 Update on Guidelines for Major Depressive Disorder

Medication Strategies for Difficult to Treat Depression (DTD)
(poor response to initial AD)

- **Consider:** Re-evaluate diagnosis, co-morbidities (ADHD, substance abuse, anxiety) and tolerance/adherence ……..
- **Optimize** – one dose increase usually adequate (notable exceptions sertraline, venlafaxine)
- **Switch** – for non-response (one switch): evidence limited and typically for lack of tolerability
- **Add Adjunctive/augmentation agents - Consider earlier** (greater efficacy and shorter time to response/remission)
- **Stop:** Medications that have uncertain benefit (e.g., sleep meds, OTC meds)
- (Consider Psychotherapy or Neuromodulation)

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Choosing Between Switching and Adjunctive Treatment

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CONSIDER A SWITCH WHEN:

- First antidepressant trial
- Poorly tolerated side effects to the initial antidepressant
- <25% improvement to the initial antidepressant*
- More time to wait for a response (less severe, less functional impairment)†
- Patient prefers to switch to another antidepressant
  - Suggest only ones switch before moving to adjunct
  - When switching, consider AD with different MOA*

CONSIDER AN ADJUNCT WHEN:

- ≥2 antidepressant trials
- Initial antidepressant is well tolerated
- >25% improvement to the initial antidepressant
- Specific residual symptoms or side effects to the initial antidepressant that can be targeted
- Less time to wait for a response (more severe, more functional impairment)†
- Patient prefers to add on another medication

How can I apply measurement-based care approaches when considering switching or adding on therapy?

* expert consensus as evidence not supported

Follow-Up Visit – Recipe for Success: An Example Using the PHQ-9

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Follow-up after 2–4 weeks of treatment initiation:

<25% PHQ-9 score reduction (non-responder)	>25% PHQ-9 score reduction but not at remission (PHQ-9 score >5)	>25% PHQ-9 score reduction and remission (PHQ-9 score <5)
• Failure to achieve this at 2-4 weeks strongly suggests a need to **adjust** the **treatment plan** • Consider **increasing dose (if not optimized)** or **Switching AD (if first AD) or not tolerated** • **Consider adjunctive agent if non-response and failed 2 trials**	• **Maintain dose** if patient continues to improve • **Optimize dose** to maximum tolerated • **Consider add-on** (adjunct therapy) once dose is optimized and/or at clinical discretion	• **Maintain** current therapy and **assess recurrence risk** • Arrange additional **assessments for residual symptoms, side effects, and adherence** • Maintain current therapy for 6–9 months **AFTER** remission (if first episode)

PHQ: Patient Health Questionnaire

Recommendations for Adjunctive Medications

Recommendation	Adjunctive Agent	Level of Evidence	Target Dose
First Line	Aripiprazole	●	2-10 mg (new lower dose range)
	Brexpiprazole		1-2 mg
Second Line	Quetiapine		100-300 mg
	Bupropion		150 – 300 mg
	Intranasal Esketamine	●	56-84 mg intranasally
	IV Racemic Ketamine		0.5-1.0 mg/kg intravenously
	Cariprazine		1.5-3 mg
	Risperidone		1-3 mg
	Olanzapine		2.5-10 mg
	Lithium		600-1200 mg (therapeutic serum level: 0.5-0.8 mmol/L)
	Mirtazapine	◔	30-60 mg
	Modafinil		100-400 mg
	Triiodothyronine		25-50 mcg

Agents in red are new recommendations since the 2016 guidelines

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CANMAT First-line Recommendations for Adjunctive Medications for DTD

Adjunctive agent	Target dose*
Aripiprazole	2–15 mg
Brexpiprazole	0.5–2 mg

Indicated as adjunct to antidepressants for adult MDD patients **with inadequate response to prior antidepressant treatments**

DTD=difficult-to-treat depression

*Dose ranges are taken from product monographs; in clinical care, doses below and above the range may be used.

Lam RW, et al. *Can J Psychiatry*. 2016;61(9):541-567.

66

Efficacy of Adjunctive Treatment

Lam RH, et al. Clinical Psychopharmacology and Neuroscience 2018;16(2):170-175.; McIntyre RS, et al. *J Clin Psychopharmacol*. 2021;41(2):113-135. Thase ME, et al. NCT. 2018; Volume 15:37-43. McIntyre RS, et al. *Journal of Affective Disorders*. 2016;201:116-123.

Adjunctive
aripiprazole

Adjunctive aripiprazole was observed to be efficacious in routine clinical practice, for reducing scores on assessment scales including both Hamilton Anxiety Rating scale (HAMA) and Hamilton Depression Rating scale (HAMD)

Adjunctive
brexpiprazole

Adjunctive brexpiprazole is efficacious in reducing core depressive symptoms, and appetite, as well as improving functioning, in patients with MDD and anxious distress who have inadequate response to first-line antidepressants

67

Recommendations for Adjunctive Medications

Recommendation	Adjunctive Agent	Level of Evidence	Target Dose
Third Line	TCA's	◔	Various
	Lamotrigine		100-300 mg
	Other monotherapies for MDD	◐	Various
	Releasers (stimulants)		Various
	Non-IV racemic ketamine		Various
	Pramipexole		1-4 mg
	Ziprasidone		20-80 mg BID
Third Line in Subgroups	Estradiol (only during perimenopause)	◐	2 mg
	L-Methyl Folate (especially with MTHFR mutation)*		15-30 mg BID *associated with homocysteinuria
Experimental	Psychedelic-Assisted Therapy	◔	Moderate to high doses accompanied with psychotherapy
Not Recommended	Cannabis	Lack of efficacy; potential harm	Not Applicable

CANMAT — Agents in red are new recommendations since the 2016 guideline.

Lam RW, Kennedy SH, et al. *Can J Psychiatry* 2024

Anxiety Symptoms *Post hoc* Analysis: Definition of Anxious Distress

- The DSM-5 'with anxious distress' specifier defines anxious distress as the presence of at least two out of five listed symptoms during the majority of days of a major depressive episode[1]
- This *post hoc* analysis used proxies for the DSM-5 specifiers to determine the presence or absence of anxious distress at baseline (i.e., randomization)[2]
  - No proxy could be found for 'Feeling that the individual might lose control of himself or herself'; meaning that patients were classified as having anxious distress if they met criteria for at least two out of four symptoms (rather than two out of five symptoms)[2]

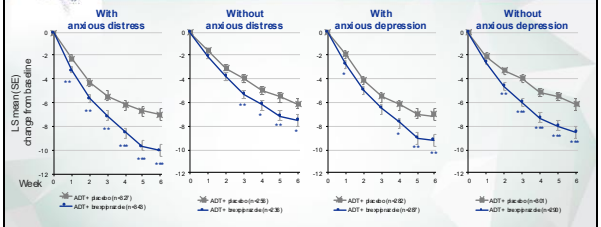
DSM-5 specifier	Proxy used in the post hoc analysis
Feeling keyed up or tense	MADRS item 3 (inner tension) score of ≥3
Feeling unusually restless	IDS-SR item 24 (feeling restless) score of ≥2
Difficulty concentrating because of worry	MADRS item 6 (concentration difficulties) score of ≥3
Fear that something awful may happen	HAM-D item 10 (psychic anxiety) score of ≥3
Feeling that the individual might lose control of himself or herself	No proxy could be found

"No proxy could be found for the DSM criterion 'Feeling that the individual might lose control of himself or herself.'"

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition; HAM-D, Hamilton Depression Rating Scale; IDS-SR, Inventory of Depressive Symptomatology Self-Report; MADRS, Montgomery-Åsberg Depression Rating Scale

1. APA. DSM-5. 2013
2. Thase et al. J Neuropsychiatr Dis Treat 2019;15:537–45

Anxiety symptoms *post hoc* analysis: Change in MADRS total score – all patient subgroups



*p<0.05, **p<0.01, ***p<0.001 versus placebo MMRM
Response defined as ≥50% reduction from baseline in MADRS total score
Anxious distress and anxious depression status measured at baseline
The maximum approved dose of brexpiprazole for MDD in Canada is 2 mg/day. No additional benefit was demonstrated at doses greater than 2 mg/day.
Thase et al. *Neuropsychiatr Dis Treat* 2019;15:537–45.

Acute TEAEs in pooled short-term trials (Pyxis, Polaris, Sirius, Delphinus)

n (%)	ADT + placebo (n = 819)	ADT + brexpiprazole (n = 1032)
At least one TEAE	399 (48.7)	595 (57.7)
Discontinuation due to TEAE	5 (0.6)	23 (2.2)
TEAEs occurring in ≥5% of patients in either treatment group		
Akathisia	21 (2.6)	83 (8.0)
Headache	49 (6.0)	60 (5.8)
Weight increased	13 (1.6)	60 (5.8)
Other TEAEs of interest		
Somnolence	10 (1.2)	50 (4.8)
Restlessness	6 (0.7)	41 (4.0)
Fatigue	11 (1.3)	29 (2.8)
Insomnia	17 (2.1)	29 (2.8)
Anxiety	10 (1.2)	24 (2.3)
Sedation	4 (0.5)	2 (0.2)

Safety population; presented for brexpiprazole 1–3 mg
ADT= antidepressant treatment; TEAE = treatment-emergent adverse event

Brexpiprazole dose 1–3 mg/day
The maximum approved dose of brexpiprazole for MDD in Canada is 2 mg/day. No additional benefit was demonstrated at doses greater than 2 mg/day.
Thase et al. *Expert Opin Pharmacotherapy* 2019; DOI:10.1080/14656566.2019.1689913

Conclusion (anxious distress)[1]

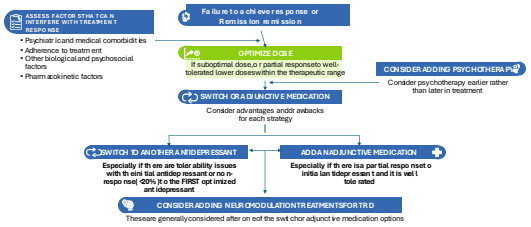
- **In patients with anxious distress at baseline, adjunctive brexpiprazole showed greater improvements than adjunctive placebo across various MADRS items**
- **In patients with anxious distress at baseline, adjunctive brexpiprazole showed greater improvement in functioning than adjunctive placebo (SDS Mean, SDS social life, and SDS family life)**
- Improvements with adjunctive brexpiprazole were generally larger in patients with anxious distress than in those without anxious distress
- Adjunctive brexpiprazole improved anxious distress versus adjunctive placebo, as shown by a reduced likelihood of patients still having anxious distress after 6 weeks of treatment

- Adjunctive brexpiprazole is efficacious in reducing core depressive symptoms, sleep, and appetite, and improving functioning, in patients with MDD and anxious distress who have inadequate response to ADTs
- Furthermore, adjunctive brexpiprazole reduces the likelihood of patients meeting anxious distress criteria following treatment

ADT=antidepressant treatment; MADRS=Montgomery-Åsberg Depression Rating Scale; MDD=major depressive disorder; SDS=Sheehan Disability Scale

1. McIntyre et al. J Clin Psychopharmacol 2024;44(2):133–140.

CANMAT algorithm for suboptimal response to initial antidepressant treatment



CANMAT, Canadian Network for Mood and Anxiety Disorders. Adapted from Lam RW et al. Can J Psychiatry 2024;69(9):641–87.

74

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CANMAT 2023 Update on Guidelines for Management of MDD p. 44 of 92

Line of Treatment	Complementary and Alternative Medicine (CAM) Treatment	Level of Evidence
First Line	St. John's wort for **MDE of mild severity**.	●
Second Line	Acupuncture for **mild severity MDE**.	◔
	St. John's wort for **moderate severity MDE**.	◔
	Adjunctive acupuncture for **moderate severity MDE**.	◔
	Adjunctive L-methylfolate for **mild-moderate severity MDE**.	◔
Third Line	Adjunctive S-adenosyl-L-methionine (SAM-e) for **mild to moderate severity MDE**.	◔
	Dehydroepiandrosterone (DHEA) for **mild severity** MDE.	◐
	Omega-3 fatty acids for **mild severity MDE**.	◐
	Saffron, lavender, or roseroot for **mild severity MDE**.	◐

● Level 1 ◔ Level 2 ◐ Level 3 ○ Level 4

Lam RW, Kennedy SH, et al. *Can J Psychiatry* 2024

Reasons Behind Lack of Remission

There are several potential reasons why patients may not achieve remission:[1-4]

Non-adherence issues	Inadequate dose	Patient is a non-responder	Alternative or comorbid diagnosis	Patient has treatment-resistant depression
• Choose drugs with better tolerability • Use fewest medications possible • Adjust dose/treatment to minimize side effects • Patient education	• Increase dose • Prolong treatment course	• Switch or add therapy, depending on clinical scenario	• Consider common differential diagnoses (e.g., ADHD, bipolar disorder, substance abuse, personality disorder) • Treat accordingly	• Consider other therapies (e.g., ECT, esketamine)

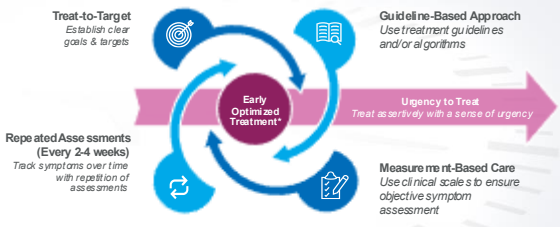
In the patient-centred Early Optimized Treatment approach, treatment decisions are made earlier, which can substantially improve patients' chances of a timely and long-lasting return to best possible functioning[3,4]

Quote from patient 26 yo female patient: Sept. 2025

"Prior to starting any medication for my mood, I really thought it wasn't that bad.
I was ruminating most of the time, constantly tired and moody, and feeling like
I could burst into tears at any second.
Since starting Trintellix and Rexulti, my whole life has changed.
I feel better about myself and I'm able to let things go more easily. I didn't realize that I was doing life the hard way."

Thank you

Early Optimized Treatment and Urgency to Treat in MDD: How to Implement This Strategy in My Clinical Practice



CLINICAL PEARLS

The Early Optimized Treatment CANMAT based approach to MDD management involves:

1. Using measurement-based care
2. Seeing patients ~2-3 weeks after treatment initiation to optimize the antidepressant dose
3. Considering a therapy switch if <20% early improvement (and first antidepressant used), as lack of early improvement ≥20% correlates with patients being unlikely to achieve remission
4. Using adjunctive therapy if >25% improvement and no remission can be effective, with dose optimization at 4-6 weeks
5. Considering medical/Psychiatric comorbidities that can complicate depression or explain non-response to therapy