Primary Care Networks
EDMONTON AND AREA

Evidence-based treatment options for depressive disorders

(like Major Depressive Disorder)

Guidance for Psychiatrists, Family Physicians, and Nurse Practitioners

Developed by:

MANOR CLINIC

Evidence-based treatment options for depressive disorders (like MDD)

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According to the Canadian According to the Canadian Network for Mood and Anxiety Treatments (CANMAT) 2023 Update on Clinical Guidelines for Management of Major Depressive Disorder in Adults, the following psychological and pharmacological approaches could be beneficial for individuals with Major Depressive Disorder (MDD):

I. Psychological treatment:

First-line psychological treatment recommendations include cognitive-behavioral therapy (CBT), interpersonal therapy (IPT), and behavioral activation (BA). Second-line recommendations include Cognitive behavioral analysis system of psychotherapy (CBASP), Mindfulness-based cognitive therapy (MBCT), Problem-solving therapy (PST), Short-term psychodynamic psychotherapy (STPP) and Transdiagnostic psychological treatment of emotional disorders.

The optimal treatment strategies for improving individual outcomes in MDD should be based on patient preference, evidence-based treatments, and clinician/system capacity.

II. Pharmacological treatment:

a. First-line recommended medications for the treatment of MDD include

SSRI (Selective Serotonin Reuptake Inhibitors) medications like

- SSRI (Selective Serotonin Reuptake Inhibitors) medications like
- Escitalopram 10-20 mg
- Citalopram 20-40 mg
- Fluoxetine 20-60 mg
- Paroxetine 50-200 mg
- Sertraline 50-200 mg

SNRI (Serotonin and Norepinephrine Reuptake Inhibitors) medications like Newer medications: vortioxetine (Trintellix)

- Duloxetine 60 – 120 mg
- Venlafaxine XR 75-225 mg
- Desvenlafaxine 50-100 mg
- Levomilnacipran 40–120 mg

NDRI (Norepinephrine and Dopamine Reuptake Inhibitors) medication like

- Bupropion 150–450 mg

Newer medications like
Vortioxetine (Trintellix) 10–20 mg - Serotonin Reuptake Inhibitor; 5-HT1A, 5-HT1B agonist; 5-HT1D,

- 5-HT3A, 5-HT7 antagonist
- Vilazodone 20–40 mg - Serotonin Reuptake Inhibitor; 5-HT1A agonist

b. Second-line recommended medications for the treatment of MDD include:

- Tricyclic antidepressants like
- Amitriptyline 75–300 mg
- Clomipramine 150–300 mg
- Desipramine 100–300 mg
- Doxepin 75–300 mg
- Imipramine 75–300 mg
- Nortriptyline 75–150 mg
- Protriptyline 30–60 mg
- Trimipramine 75–300 mg

Reversible Monoamine Oxidase Inhibitor (MAOI) selective for isoform A (RIMA)

- Moclobemide 150–450 mg

Other medications:

- Trazodone 150–400 mg - Serotonin Reuptake Inhibitor; 5-HT2 antagonist
- Quetiapine 150-300 mg – Dopamine, 5-HT, α1 & α2 antagonist; Norepinephrine Reuptake Inhibitor

c. Third-line recommended medications for the treatment of MDD include:

- Phenelzine 45–90 mg MAO inhibitor
- Tranylcypromine 30–60 mg MAO inhibitor

Adjunctive treatments: For individuals who do not respond to first-line and/or second-line recommended medications, the following adjunctive treatments can be considered:

a. First-line adjunctive treatment:

- Aripiprazole (2 to 10 mg daily)
- Brexpiprazole 0.5–2 mg

b. Second-line adjunctive treatment:

- Bupropion 150–450 mg
- Intranasal esketamine 56–84 mg intranasally
- IV racemic ketamine 0.5–1.0 mg/kg IV
- Olanzapine 2.5–10 mg
- Quetiapine-XR 150–300 mg
- Risperidone 1–3 mg
- Lithium 600–1200 mg (therapeutic serum level: 0.5–0.8 mmol/L)
- Cariprazine 1.5–3 mg
- Mirtazapine/Mianserin 30–60 mg/30–90 mg
- Modafinil 100–400 mg
- Triiodothyronine 25–50 mcg

c. Third-line adjunctive treatment:

- Stimulants like Vyvanse
- Lamotrigine 100–300 mg
- Non-IV racemic ketamine

- Pramipexole 1–2 mg twice daily
- Ziprasidone 20–80 mg twice daily

d.Not recommended

- Cannabis (insufficient evidence for efficacy; risk of harm)

III. Neurostimulation treatments:

Repetitive Transcranial Magnetic Stimulation (rTMS): If individuals have failed at least one antidepressant treatment, they can be considered for rTMS.

Electroconvulsive treatment (ECT): This can be considered a first-line treatment for severe depression.

Newer treatment for the treatment of depression:

Esketamine/Ketamine treatment:

Esketamine is authorized in Canada under the brand name Spravato as a nasal spray for the treatment of moderate to severe major depressive disorder where patients have not responded to other antidepressants. The evidence base indicates a very good response rate of Esketamine/ Ketamine in the treatment of treatment-resistant depression.

Specific recommendations for most commonly prescribed medications:

SSRI step:

Escitalopram: Consider prescribing Escitalopram 10 mg every morning. The dose of Escitalopram can be increased by 5 mg every 2 to 4 weeks to a maximum dose of 20 mg daily, depending on their response and tolerability.

SNRI step:

Venlafaxine XR: Consider starting Venlafaxine XR at 37.5 mg or 75 mg every morning dose. Venlafaxine XR is a is a SNRI (Serotonin and Norepinephrine Reuptake Inhibitor). Depending on the patient's response and tolerability, the dose can be increased by 37.5 mg to 75 mg every 2 to 4 weeks to a maximum of 375 mg a day.

Duloxetine: Consider Duloxetine 30 mg every morning. Duloxetine is an SNRI (Serotonin and Norepinephrine Reuptake Inhibitor) medication

Adjunctive treatment step:

Aripiprazole: Consider starting on Aripiprazole as an adjunctive treatment to address their depressive symptoms if there is a limited response to the trial of an SSRI/SNRI treatment at a therapeutic dose for a reasonable period. Consider starting Aripiprazole 2 or 2.5 mg daily dose. The dose of Aripiprazole can be increased by 2 to 2.5 mg every 2 to 4 weeks to a maximum dose of 15 mg a day, depending on their response and tolerability.

Quetiapine: Consider prescribing quetiapine 25 mg nightly as an adjunct medication if there is a limited response to the trial of an SSRI/SNRI treatment at a therapeutic dose for a reasonable period and in circumstances when the patient has insomnia. Consider increasing the dose of quetiapine by 25 to 50 mg every 2 to 4 weeks to a maximum of 150-300 mg a day, depending on their response and tolerability. Quetiapine is a first-line adjunctive treatment for depression when individuals do not respond adequately to first-line and/or second-line medications.