BHICCI

Major Depression Practice Guideline

General

The following guideline is based on the American Psychiatric Association (APA) treatment guideline for major depression, last updated in 2010. The APA guideline is exhaustive and intended for psychiatrists. This guideline is intended for primary care providers and more focused on initial treatment options and practical monitoring resources that will be useful for treating patients with major depression.

Diagnosis and Monitoring Using the PHQ-9

The APA treatment guideline recommends the use of validated rating scales to help providers screen for major depression and monitor response to treatment. IEHP encourages the use of the PHQ-9 for its ease of use and documented validity for use in primary care settings. The PHQ-9 is a 10 item self-report scale and can be completed by the patient in less than five minutes. Free and downloadable version of the PHQ-9 is available at:

http://www.phqscreeners.com/

However, rating scales such as the PHQ-9 should not be the sole basis of diagnosing major depression. Positive screens on the PHQ-9 should be confirmed by the clinical interview. The differential diagnosis of major depression should be considered which includes:

- Substance intoxication or withdrawal
- Acute depressive phase of bipolar disorder
- Side effect of a medication
- Normal bereavement
- Adjustment disorder

Treatment: Acute Phase

Treatment options

The choice of initial treatment modality for patients with major depression include depression focused psychotherapies and pharmacotherapy. Patients should be provided with information on the various treatment options including the strengths and limitations of each.

Psychotherapy avoids potential side effects, safety issues and drug interactions of medications but requires regular attendance (generally weekly), availability of reliable transportation and availability of therapists to see patients within a reasonable amount of time (within several weeks). Psychotherapy may be particularly helpful for patients with significant psychosocial stressors and patients with more chronic, severe depression. **Pharmacotherapy** may be more convenient for patients with transportation difficulties or limitations in therapy availability. However pharmacotherapy requires good adherence to be effective and may cause side effects.

Severity of the current episode is another consideration when discussing treatment modalities with your patient. For mild or moderate depression, pharmacotherapy *or* psychotherapy monotherapy is appropriate. However, for severe depression a combination of psychotherapy and pharmacotherapy is recommended. Psychotherapy should not be the only modality in severe depression. On the PHQ-9, a severity of severe would correspond to a score of ≥ 20.

Severity of Depression per PHQ-9	Pharmacotherapy Alone	Psychotherapy Alone	Combination of Pharmacotherapy and Psychotherapy
Mild to Moderate	Yes, antidepressant	Yes	Optional
Severe without Psychotic Features	Yes, antidepressant	No	Yes
Severe with Psychotic Features	Yes, antidepressant + antipsychotic	No	Yes

Adapted from APA treatment Guidelines (2010)

Psychotherapy Options

For patients with mild depression, exercise alone is a reasonable initial intervention for a few weeks. If there is no significant improvement, psychotherapy or an antidepressant should be recommended.

There is no definitively superior type of psychotherapy for major depression. Psychotherapies with demonstrated acute efficacy for major depression include cognitive-behavioral therapy (CBT) and interpersonal psychotherapy (ITP).

Pharmacotherapy Options

The effectiveness of antidepressants is comparable between and within classes. Therefore, consideration between antidepressants is largely determined by patient preference, cost, safety, side effect profile, potential drug interactions, co-occurring psychiatric or general medical conditions and history of previous response to an antidepressant. Based on these considerations, the following antidepressants and classes of antidepressants are optimal initial options for most patients: Selective Serotonin Reuptake Inhibitors (SSRIs), Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), Bupropion, Mirtazapine.

In addition to the usual information on when, how often to take the medication and common side effects, it is important to review the following with patients:

1) The medication will need to be taken for several weeks before beneficial effects may be noticed.
2) Antidepressants need to be taken even if they are feeling better and not to “double up” on days they are feeling worse. In other words, they are not “as needed” medications

Dosing and properties of preferred initial first-line antidepressants:					
SSRI's	**Starting Dose (mg)**	**Therapeutic Dose Range (Max dose)**	**P450 Enzyme Inhibition**	**Notes**	**Side Effects**
Fluoxetine (Prozac)	20 daily	20-40 daily (max 60)	Strong 2D6 Mod 1A2	long half-life, slightly activating Lowest risk of discontinuation syndrome among SSRI's	Common: initial activation, nausea, diarrhea and headaches. (**if anxious, start with ½ starting dose x 1-2 weeks**) Can also cause decreased libido, erectile dysfunction, insomnia, akathisia, increased risk of falls. Increase GI bleed risk with NSAIDs
Paroxetine (Paxil)	20 bedtime	20-40 bedtime (max 60)	Strong 2D6	Weight gain, sedating, greatest risk of discontinuation syndrome among SSRI's	
Citalopram (Celexa)	20 daily	20-40 daily (max 40)	--	No drug interactions	
Escitalopram (Lexapro)	10 daily	10-20 daily (max 20)	Mild 2D6	S-enantiomer of citalopram	
Sertraline (Zoloft)	50 daily	50-200 daily (max 200)	Mild 2D6	Take with food	
SNRI's	**Starting Dose (mg)**	**Therapeutic Dose Range (Max dose)**	**P450 Enzyme Inhibition**	**Notes**	**Side Effects**
Venlafaxine ER (Effexor XR)	37.5 daily	75-150 daily (max 375)	--	Discontinuation syndrome risk similar to paroxetine	Same as SSRI + dry mouth, activation, constipation, tachycardia and elevated blood pressure, especially at doses > 150 daily
Duloxetine (Cymbalta)	30 daily	60 daily (max 120)	Mod 2D6	Also approved for fibromyalgia, diabetic peripheral neuropathy	Same as SSRI + dry mouth, activation, constipation, tachycardia and elevated blood pressure, especially at doses > 60 daily

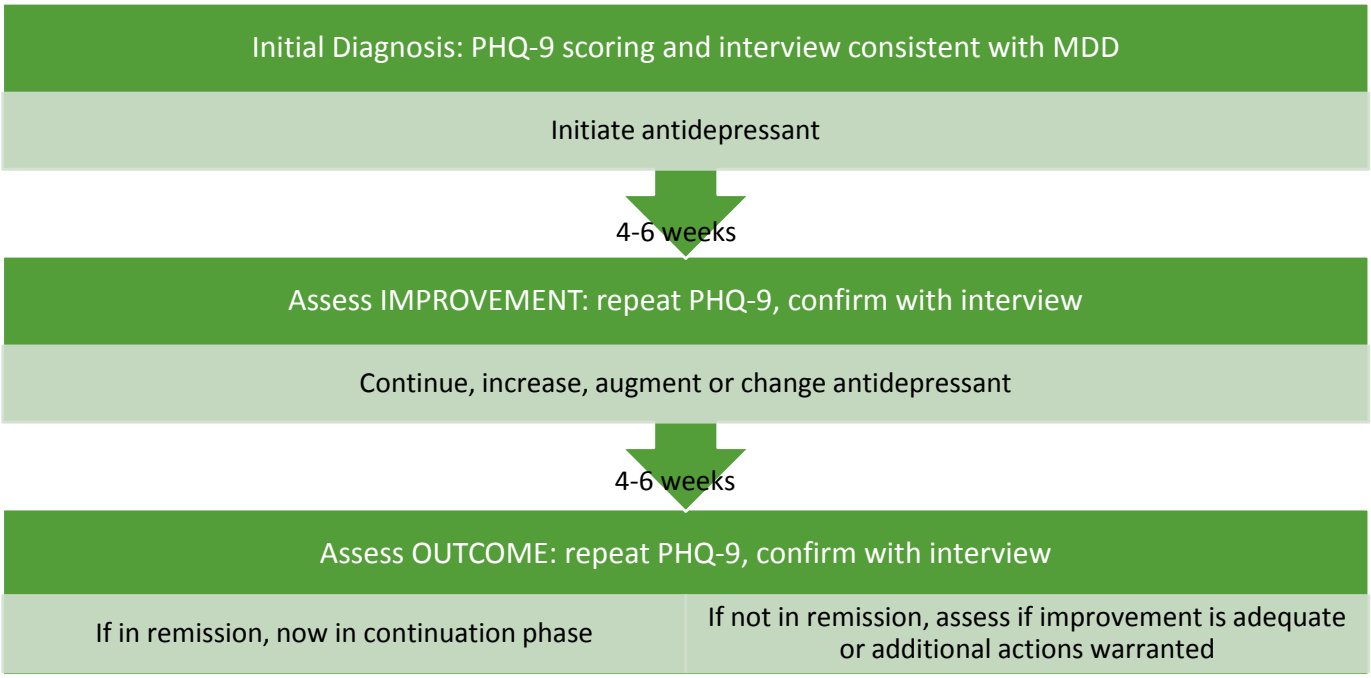
Dopamine Reuptake Inhibitors	Starting Dose (mg)	Therapeutic Dose Range (Max dose)	P450 Enzyme Inhibition	Notes	Side Effects
Bupropion, SR, XL (Wellbutrin SR, ER)	150 morning	SR: 150 morning and midday (max 400) XL/ER: 300 morning (max 450)	Strong 2D6	Avoid with history of seizures or eating disorder No decrease in libido or erectile dysfunction.	Activating, constipation, dry mouth, irritability, insomnia, headache
Nonadrenergic Antagonist	**Starting Dose (mg)**	**Therapeutic Dose Range (Max dose)**	**P450 Enzyme Inhibition**	**Notes**	**Side Effects**
Mirtazapine (Remeron)	15 bedtime	15-30 bedtime (max 45)	--	No decrease in libido or erectile dysfunction. Monitor cholesterol	Sedation, weight gain, dry mouth

Adapted from APA treatment Guidelines (2010)

Note: Some antidepressants can be started at the target dose without titration while other antidepressants are titrated to the target dose over 1-2 weeks. This will depend on the development of side effects and co-occurring medical or psychiatric conditions, especially very anxous patients. Also, older patients and those with a decreased ability to metabolize or clear antidepressants should be started on a lower initial dose and titrated to 50% of the usual therapeutic dose.

Treatment Monitoring

Improvement from antidepressants can be seen as early as 1-2 weeks but allow for 4-6 weeks before assessing improvement. Patients continue to accrue benefit for an additional 4-6 weeks so allow 8-12 weeks before concluding on the outcome of an antidepressant trial. The following is a visual summary of a typical antidepressant trial. 4-6 weeks



IMPROVEMENT after 4-6 weeks (assuming adequately dosed and adherent) using the PHQ-9

PHQ-9 score drop from baseline	Improvement	Antidepressant Plan	Psychotherapy Plan*
≥ 5 points	Adequate	Continue current dose	No change
2-4 points	Probably Inadequate	Consider ↑ Dose vs Augment** OR Switch if not tolerating	Consider adding antidepressant if not already taking
1 point or increase	Inadequate	↑ Dose vs Augment** OR Switch if not tolerating	Strongly consider antidepressant if not already taking Contact therapist re: PHQ-9 score

*Reasonable time to improvement may vary depending on the type of psychotherapy
**Augment is defined as adding an additional agent to the regimen

Potential reasons for inadequate improvement:

- Inaccurate diagnosis
- Nonadherence to treatment
- Unaddressed co-occurring medical, psychiatric or substance use disorders
- Inadequate dose of medication or frequency of therapy
- Inadequate duration of treatment
- Pharmacokinetic/pharmacodynamic factors affecting medication action
- Complicating psychosocial or psychological factors

Factors favoring augmentation vs switch

AUGMENT →	• Partial Response on target dose • Minimal side effects • Patient ok with two medications
SWITCH →	• No Response on target dose • Intolerable side effects • Patient hesitant about two medications

Augmentation Options

Another antidepressant with different mechanism of action

- SSRI + Bupropion
- SSRI or SNRI + Mirtazapine

Non Antidepressant augmentation

- Buspirone (BusPar)
- Second Generation Antipsychotics
  - Aripiprazole (Abilify)*
  - Quetiapine (Seroquel)*
- Lithium
- Thyroid Hormone (triiodothyronine)

*FDA approved options

Switch Options

If the initial antidepressant was a SSRI, there is no compelling evidence that would favor changing to a different SSRI, versus switching to a different class of antidepressant. Important to consider if there is a co-morbid anxiety disorder since sertonergic antidepressants are more likely to be effective for co-morbid anxiety and depression.

OUTCOME after 8-12 weeks (assuming adequately dosed and adherent) using the PHQ-9

Patient Condition	PHQ-9	Antidepressant Management
Remission	Total PHQ-9 score ≤ 5	At GOAL! Continue AD and/or PT
Response	> 50% drop from baseline, but not remission	Continue AD vs Augment*
Partial Response	25-49% drop from baseline	Consider ↑ dose vs Augment*
No Response	< 25% drop from baseline	Switch*

The goal of treatment is remission. Remission is defined as the absence or near absence of symptoms for at least 3 weeks. On the PHQ-9, this would correspond to a score of < 5 and a rating of "not difficult at all" on the function question.

*For patients with significant psychiatric and or medical co-morbidity, or ongoing severe psychosocial stressors, complete remission may take longer or be difficult to achieve. For such patients, a 50% drop from the baseline PHQ-9 score or < 10 on the PHQ-9 may be reasonable goals of treatment. The decision to escalate treatment intensity in such settings is one made between provider and patient in alignment with goals defined by the patient.

Treatment: Continuation Phase

Patients who have recovered from an acute major depressive episode should continue pharmacotherapy of the same dose and frequency for an additional 4-9 months to prevent relapse.

At the end of the continuation phase, patients should be considered for proceeding into the maintenance phase versus discontinuation of treatment. Factors in favor of proceeding to the maintenance phase include:

- Persistence of subthreshold depressive symptoms
- History of ≥ 3 episodes of major depressive disorder
- Greater severity of initial and any subsequent episodes
- Earlier age at onset
- Presence of a co-occurring psychiatric condition
- Presence of a chronic general medical disorder
- Family history of psychiatric illness, particularly mood disorder
- Ongoing psychosocial stressors or impairment
- Negative cognitive style
- Persistent sleep disturbances

Treatment: Maintenance Phase

Patients proceeding to the maintenance phase are generally continued on the same pharmacotherapy and at the same dose as in the acute and continuation phases. If there are side effects at this dose, attempts should be made to at least remain at the lowest known therapeutic dose of the medication.

Patients in psychotherapy proceeding to the maintenance phase may reduce the frequency of therapy from approximately once weekly to once monthly (depending on the type of psychotherapy).

Discontinuation of Treatment

Patients proceeding to discontinuation of pharmacotherapy after the continuation phase should be monitored closely after treatment discontinuation as the highest risk of relapse is in the first two months. Early signs of relapse should be reviewed with the patient and if possible, with a family member. A plan should be developed and agreed upon in case of depressive relapse.

Discontinuation of pharmacotherapy should be done over several weeks or longer depending on the dose of the medication. If that patient is on multiple medications for depression, they should be tapered one at a time.

References

Full American Psychiatric Association Guideline available at: http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf

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