IntegrationSteps.org

Guiding Principles for Initiating Antidepressant Medications

1. **Differential diagnosis for Depressed Mood**:

The differential diagnosis for depressive symptoms includes (see DSM V for precise definitions):

- *Adjustment Disorder with Depressed Mood*—Depressed mood that occurs in response to an identifiable psychosocial stressor that took place within the last three months.
- *Depression secondary to Medical Condition*: Many medical illnesses can give rise to depression, including hypothyroidism, multiple sclerosis, obstructive sleep apnea, Parkinson disease, stroke, systemic lupus erythematosus, traumatic brain injury, or vitamin B12 insufficiency. Typically the depression arises within a month of the medical condition and doesn't respond to typical depression treatment.
- *Medication effect*—glucocorticoids are particularly implicated; there are mixed data on others such as beta-blockers.
- *Substance Use*—depressive symptoms can be related to active use, withdrawal or early recovery. If symptoms persist after one or more months following cessation of use or withdrawal, a diagnosis of depression is more likely. Additionally, a diagnosis of depression is more likely if the patient had previous depressive symptoms during a prolonged period of being substance free.
- *Persistent Depressive Disorder (Dysthymia*)---At least 2 yrs of persistent depressive symptoms that may or may not meet MDD criteria (can have both)
- *Bipolar Depression*—This is important to rule out as antidepressants alone can be destabilizing for patients with bipolar disorder. Tools to rule out Bipolar Disorder include:
    - DIGFAST Criteria: ttp://www.drabboudassaf.com/Psychiatric%20Disorders/bipolar-disorder.html
    - Composite International Diagnostic Interview (CIDI): *Best Tool**
      http://www.cqaimh.org/pdf/tool_cidi.pdf

2. **Medication selection**: Familiarize yourself with at least 2 SSRI's, 1 SNRI, mirtazapine, and bupropion
    - Consider personal and family history of response
    - Consider presence or absence of neurovegetative symptoms, medical comorbidities, potential side effects, drug interactions and any relative contraindications.

Antidepressant Medication Classes

Antidepressant class	Medications
Serotonin Reuptake Inhibitors (SSRI)	• Citalopram (Celexa)* • Escitalopram (Lexapro) • Fluoxetine (Prozac)* • Paroxetine (Paxil) * • Paxil CR • Sertraline (Zoloft)*
Serotonin and Norepinephine Reuptake Inhibitors (SNRI)	• Venlafexine (Effexor)* • Effexor XR • Duloxetine (Cymbalta)
Norepineprhine and Dopamine Reuptake Inhibitors	• Buproprion (Wellbutrin SR)* • Wellbutrin XL
Antagonizes Alpha 2 and 5 HT2/3 receptors (NaSSA)	• Mirtazapine (Remeron)
Primarily Norepinephrine Reuptake Inhibitor (TCA)	• Desipramine (Norpramin, Pretofrane)* • Norpriptyline (Pamelor)*

Antidepressant medication selection and initiation

Prescribing Tips: In general, serotonin reuptake inhibitors (SSRIs) are effective for both depression and anxiety and are typically first-line treatment.

However, other classes of antidepressant medications can provide specific additional benefits. The following table gives a list of commonly-used SSRIs and non-SSRI antidepressants and specific benefits or precautions that may influence initial medication selection. For additional details including more comprehensive side effects, see UpToDate article, "Unipolar major depression in adults: Choosing initial treatment"

Medication and typical starting dose*	Medication class	Additional conditions for which medication may be helpful	Precautions specific to this medication
Sertraline 25 mg	Serotonin reuptake inhibitor (SSRI)		Most likely to cause GI side effects
Escitalopram oxalate 10 mg	SSRI		Risk of QTC prolongation (though less than citalopram)
Fluoxetine 20 mg	SSRI		May be activating
Duloxetine 20 mg	Serotonin and norepinephrine reuptake inhibitor (SNRI)	Chronic pain	
Venlafaxine XR 75 mg	SNRI	Vasomotor symptoms associated with menopause	Risk of elevated blood pressure

Mirtazapine 15 mg	SNRI	Insomnia, loss of appetite, weight loss	May be sedating, may be associated with weight gain.
Bupropion 75 mg	Norepinephrine and dopamine reuptake inhibitor	Assists with smoking cessation	Lowers seizure threshold; can be activating and worsen anxiety

*Start at half of this dose for elderly or those sensitive to side effects.

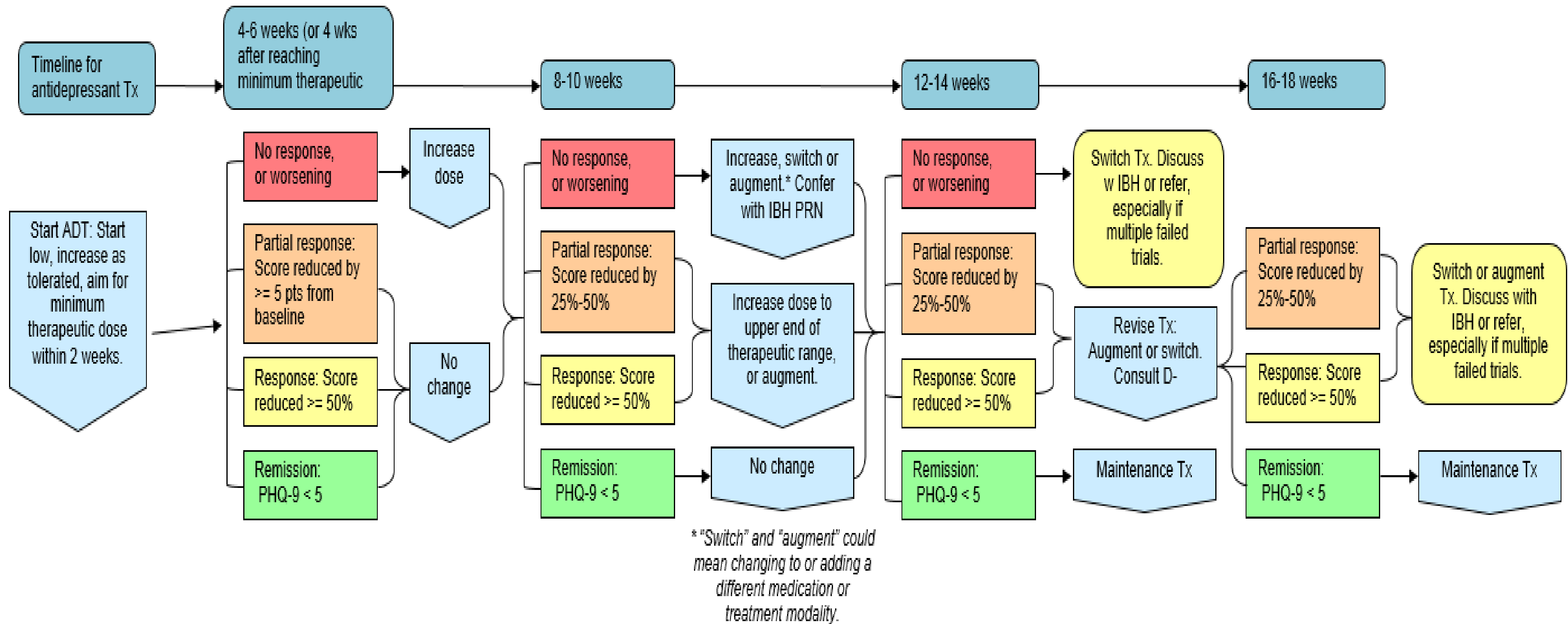
*There are more antidepressants than those listed on this table. However, the list provides a reasonable variety of medications that have different neurotransmitter mechanisms and different side effect profile

** Generally, start at the beginning of the therapeutic range. If side effects are bothersome, reduce dose and increase slowly. For patients sensitive to sideffects, start at lower doses.

Titrating Antidepressant Medication

1. See protocol below for details. Take home messages include:
   - Full response at any one dose can take 4-6 weeks
   - Titrate dose up monthly as needed based on response
     - If no response to first medication (usually an SSRI), try an alternative medication(usually another SSRI);If no response to 2nd SSRI, change drug class
   - If partial response: Use an adjunctive mediation such as antidepressant from another class, buspirone, aripiprazole, or lithium can be utilized if partial response
   - Psychotherapy is an important adjunct. Combine medication and therapy for the highest risk patients and most robust response
   - Advice to patients (increases adherence)
     - Take every day and take with food
     - Most SE resolve within a week. If not too bad stick with the medication.
     - Can take 4-6 weeks for full result (many patients respond earlier)
     - If at all possible do not stop drug abruptly (can have discontinuation syndrome)

Prescribing Protocol:



*adapted from Trina Chang, MD