

Question from the Clinic: Anti-depressant side effects

Question: I am treating a 39 year old person for depression. They are responding well to the SSRI, but struggling with some GI effects that are not improving. How do I choose a different agent within the same class, while being mindful of potential side effects?

Answer: Previous response (self or family) to a specific agent can be a good predictor of efficacy. However, side effects can often determine patient adherence more than efficacy. When choosing an antidepressant, interview the patient to target their individual characteristics, symptoms, priorities, and use a relative side effect chart such as one of the tables below.

- A general approach in someone without other major disease states/co-morbidities:
 1. Would they benefit more from an activating agent (to help overcome fatigue/low motivation), or a sedating agent (to overcome agitation)?
 2. What are the most troublesome symptoms of their depression? What is their priority in terms of side effects to avoid?

Table 1: Choosing an anti-depressant based on target symptoms:

Priority/Target symptoms	First-Line Options	Use with caution or avoid:
Insomnia, Agitation, Anxiety	<u>Neutral or sedating agents:</u> SSRIs (Paroxetine is most sedating) Mirtazapine Trazodone	<u>Initially Activating:</u> Bupropion Sertraline, Fluoxetine Venlafaxine (avoid w/HTN)
Fatigue or low motivation	<u>Activating agents:</u> Bupropion Fluoxetine, sertraline Venlafaxine	<u>Sedating agents:</u> Paroxetine, fluvoxamine Mirtazapine Trazodone
Gastro-intestinal Disorders (IBS, “touchy stomach”)	<u>Lowest GI effects:</u> Mirtazapine	<u>Highest risk of GI Distress:</u> Sertraline, Citalopram Venlafaxine
Overweight	<u>Potential weight loss:</u> Bupropion	<u>Potential weight gain:</u> Mirtazapine, Paroxetine, TCAs
Elderly	<u>Slow titration/low dose SSRI</u> See Beer’s List	<u>Anticholinergic effects:</u> TCAs, Paroxetine, fluvoxamine QT prolongation (interaction) Citalopram> Escitalopram
Need to avoid sexual side effects	Bupropion, Mirtazapine	Most SSRIs, SNRIs
Chronic Pain, Neuropathy	<u>Dual Action agents:</u> Venlafaxine, duloxetine	

Table 2 – on next page:

Table 2: Anti-depressant comparison chart: Side effect potential by Class and Drug

Drug	Class	Sedation	Anxiety or Insomnia	Weight Gain	Sexual Dysfunction	GI Distress	Anti-cholinergic	QT Prolongation
Citalopram	SSRI	Low	↓	Moderate	Moderate	High	Low	High
Escitalopram	SSRI	Low	↓	Neutral	High	Moderate	Low	Moderate
Fluoxetine	SSRI	Low	↑ early	Neutral	High	Moderate	Low	Low
Fluvoxamine	SSRI	Moderate	↑	Neutral	Moderate	Moderate	Moderate	Moderate
Paroxetine	SSRI	High	↓	Moderate	High	Moderate	High	Moderate
Sertraline	SSRI	Low	↑ early	Neutral	Moderate	High	Low	Moderate
SNRI								
Desvenlafaxine	SNRI	Low	Low	Neutral	Moderate	Moderate	Low	Moderate
Duloxetine	SNRI	Low	Low	Neutral	Moderate	Moderate	Low	Low
Levomilnacipran	SNRI	Low	Low	Neutral	Moderate	Moderate	Low	Low
Milnacipran	SNRI	Low	Low	Neutral	Moderate	Moderate	Low	Low
Venlafaxine	SNRI	Low	↑ early	Neutral	High	High	Low	Moderate
Atypical								
Bupropion	Atypical	Low	↑	Loss	Low	Moderate	Low	Low
Mirtazapine	Atypical	High	↓	High	Low	Low	Moderate	Low
Trazodone	Serotonin Modulator	High	↓	Neutral	Low	Moderate	Moderate	Moderate
Vilazodone	Serotonin Modulator	Low	↓	Neutral	Moderate	High	Low	Low
TCA								
Amitriptyline	TCA	High	↓	High	High	High	High	High
Nortriptyline	TCA	Moderate	↓	Moderate	Moderate	Moderate	High	Moderate

References: Accessed 7/25/25

- UptoDate: Comparison of Antidepressant Adverse Effects. Updated 7/10/25
- Dynamed: Drug Review: Adverse Effects of Antidepressant Medication. Updated Aug 29, 2024
- **American Psychiatric Association.** *Practice Guideline for the Treatment of Patients With Major Depressive Disorder*, 3rd ed.