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Updated 7/2026

SSRI Basics and Beyond

SSRIs and SNRIs remain the workhorses of psychopharmacology. Knowing how to use them well can get you surprisingly far in treating depression and anxiety.

1) **Choice of initial antidepressant**
   -What worked before.
   -Not what didn't work before.

   -**For depression – 1st Line – SSRI** or **bupropion** (if no comorbid anxiety disorder)
   -choose bupropion if pt won't accept risk of weight gain or sexual side effects fr SSRI, if there are contraindications to SSRIs (thrombocytopenia or recent GI bleed, hyponatremia) and no risk factors for seizures.

   - Exceptions - Comorbid chronic pain – consider SNRI (venlafaxine, duloxetine)
   -If weight gain and sedation would be helpful or patient not tolerating SSRI/SNRIs, consider mirtazapine

   -**For anxiety** (GAD, social anxiety disorder, panic disorder), OCD, PTSD – **an SSRI**

https://psychsnaps.com/how-do-you-choose-an-antidepressant/

2) **Which SSRI?** https://psychsnaps.com/which-ssri-should-i-choose/
   a. 1st line - **escitalopram** or **sertraline** – escitalopram is slightly more sedating with slightly higher risk of clinically significant weight gain than sertraline.
      sertraline is slightly more likely to cause diarrhea
   b. 2nd line – **fluoxetine** most activating of SSRIs, has a very long half life (>1 week) so SSRI of choice in someone who can't take a pill every day, med treatment of choice for bulimia, many drug-drug interactions
   c. 3rd line – **paroxetine** – most sedating SSRI, more weight gain and anticholinergic side effects than the other SSRIs, higher risk of severe SSRI withdrawal symptoms, drug-drug interactions
      -Citalopram – the racemic mixture of escitalopram + R-citalopram. Has a black box warning for QTc prolongation at higher doses, which are often necessary for the psych treatment. Escitalopram 10mg = citalopram 20mg, and escitalopram doesn't have this warning, so start escitalopram instead. If pt stable on citalopram 60mg or 80mg, no need to change it, just get an EKG to be sure Qtc is ok

      https://psychsnaps.com/which-ssri-should-i-choose/

3) **Dosing** – For most SSRIs, split the first 3 pills in half so they take 6 days at a lower dose, then increase to a full pill (equivalent of low-dose) if tolerating. Generally, start in the morning

(because they can cause insomnia) with food (to limit GI side effects), and switch to bedtime if they find it sedating.

Estimated dose equivalence of commonly used antidepressants

	Low-dose	Moderate-dose	High-dose	FDA Max
SSRIs				
Sertraline	50mg	100mg	150-200mg	200mg
Escitalopram	10mg	20mg	30mg	20mg
Fluoxetine	20mg	40mg	60-80mg	80mg
Citalopram	20mg	40mg	---	20-40mg
Paroxetine	20mg	35mg (30-40mg)	50mg	50mg
SNRIs				
Venlafaxine XR	75mg	150mg	225-375mg	225mg
Duloxetine	30mg	60mg	90-120mg	120mg
Other				
Bupropion XL	150mg	300mg	450mg	450mg
Mirtazapine	30mg	45mg	60mg	45mg

Start at ½ normal starting doses in geriatric pts, current panic attacks, people who have not tolerated multiple SSRIs previously. There are also liquid formulations so you can start even lower if necessary for tolerability (fluoxetine 1mg, for example).

https://psychsnaps.com/how-do-you-individualize-antidepressant-prescribing-part-1/

https://psychsnaps.com/wp-content/uploads/2026/06/Dosing-Antidepressants-for-Major-Depression-and-GAD-ESJ-2.pdf

4) **Initial Patient Education** - In addition to how to take the pill, information about diagnosis and rationale for antidepressants, and expected duration of treatment (at least 6 months from the point that you feel like yourself (for a first episode of major depression), don't stop abruptly). To see the specific initial instructions that I use to get people started, please see Addendum 1. They are particularly important for people with anxiety who are more likely to be alarmed by new somatic side effects of SSRIs than people with depression.

   https://psychsnaps.com/wp-content/uploads/2024/01/patient-instructions-for-starting-ssri.pdf

5) **Titration** - You are balancing the potential for side effects if you go to fast vs. delayed efficacy if go to slow. I usually go up every 3-4 weeks in the same increment as starting dose until there

evidence of some notable response, then stay there for at least 4 weeks. Full response takes 8-12 weeks at a given dose for anxiety, 6-8 weeks for major depression.

Target dose for depression – low-to-moderate dose
Target dose for anxiety (SSRI/SNRI/mirtazapine) – moderate-to-high dose

For depression, switch meds if pt is at a moderate dose for 4-6 weeks without any response. **Moderate dose = fluoxetine 40mg, paroxetine 35mg, escitalopram 20mg, citalopram 40mg, sertraline 100mg, bupropion xl 300mg.** For anxiety, switch meds if 4-6 weeks at max FDA dose without a response, because doses needed for anxiety treatment may be higher than for depression treatment. Also stop if side effects limit titration, or patient is in remission.

https://psychsnaps.com/when-should-you-stop-an-ssri-trial-for-depression-due-to-lack-of-efficacy/

https://psychsnaps.com/how-do-you-individualize-antidepressant-prescribing-part-2/

6) **Managing Chronic Side Effects of SSRIs**
https://psychsnaps.com/how-do-you-manage-the-side-effects-of-ssris/

- **weight gain** (5-20%) – if ongoing and unable to control with lifestyle changes, switch meds, even in the same class. Consider bupropion if treating depression.
- **sexual dysfunction** (30-40%) – delayed orgasm/anorgasmia or decreased libido most common. Could be problems with arousal (erectile dysfunction / lubrication). Wait for tolerance to develop (4-6 weeks). Reduce antidepressant dose. Drug-holidays (skip 1-2 days to lower blood levels temporarily which can help sexual functioning. Take medication Sun – Thurs, sex on Fri/Sat, for example). Addition of bupropion xl 300mg may help with libido. Phosphodiesterase inhibitors for erectile dysfunction. Use bupropion or mirtazapine instead of SSRIs. Switching to another antidepressant, even within the class, can also help.

https://psychsnaps.com/how-do-you-manage-ssri-snri-induced-sexual-side-effects/

https://psychsnaps.com/how-do-you-manage-ssri-snri-induced-sexual-side-effects-part-2/

- **emotional numbing or apathy** – often dose-dependent. Lower the dose. Switch to a non-SSRI antidepressant.
- **"meds stop working,"-** try raising the dose as a first step
- **nightsweats or excessive daytime sweating,** wait for tolerance, minimize dose, glycopyrrolate (peripheral anticholinergic) 1-2mg can help – dose in AM if daytime sweating, at night if nighttime sweating.
- **bruxism**- reduce dose, addition of buspar can sometimes help

7) **If ineffective despite adequate trial**, confirm diagnosis (undiagnosed bipolar, PTSD, substance use, med adherence problem, IPV or other ongoing severe psychosocial stressor), and then **switch** to the next option.
-SSRI #1 (or bupropion)
- SSRI #2 (or bupropion, SNRI, mirtazapine)

-treatment resistant depression – consider referral to psychiatry, TMS, ketamine/esketamine, or augmentation strategies

***If partial response to any of the above, consider augmentation strategies** once the dose of the initial medication is optimized. These could include low-dose atypical antipsychotic (recommend aripiprazole as first option among these), lithium, or T3. Combinations of multiple antidepressants (ie SSRI + bupropion or mirtazapine) have not been shown to be more effective than treatment with a single antidepressant.

https://psychsnaps.com/is-adding-bupropion-to-an-ssri-snri-an-effective-depression-augmentation-strategy/
https://psychsnaps.com/how-do-you-use-low-dose-aripiprazole-for-depression-augmentation/

8) **Switching between antidepressants** – Different people do this differently, but I recommend a cross-taper -- there is probably some incomplete cross-tolerance between the SSRIs, so a cross taper may decrease the likelihood of withdrawal symptoms, and of start-up symptoms as well. If a patient cannot handle the complexity of multiple changing med doses, simplify it to something that they can do.

In general, pick the dose "equivalent" to the one you're going to stop (see table above), and aim to cross-titrate to that within at most 2-3 weeks. For example, if my patient is on sertraline 100mg without benefit, I might decide to switch to escitalopram. Sertraline 100mg is about escitalopram 20mg, so Week 1: escitalopram 10mg + sertraline 50mg, Week 2: escitalopram 20mg. Low-to-mid dose SSRIs can usually be switched within 1-2 weeks, higher doses might take 2-3 weeks.

https://psychsnaps.com/how-do-you-switch-from-one-antidepressant-medication-to-another/

9) **Stopping SSRIs** – You should stop antidepressants when they are no longer necessary. Taper the medications for somewhere between 4 weeks and 3 months to avoid SSRI withdrawal. Err towards the longer-side if they are on higher dose antidepressant, have a history of SSRI withdrawal symptoms, or are on paroxetine or venlafaxine.
https://psychsnaps.com/how-do-you-stop-an-ssri/

10) **SSRI/SNRI withdrawal** can occur in setting of missing doses, stopping abruptly, or less commonly, reducing the dose of an SSRI or SNRI. The symptoms include dizziness, nausea, lethargy, headache, agitation, sleep disturbance. **Sensations like electric shocks ("brain zaps") or feeling brief bursts of dizziness when moving head are relatively specific.** Paroxetine and venlafaxine have the highest risk of more severe withdrawal, but it is relatively common with all of them.

- Timing – sudden onset, usually within a few days of stopping the med. Can last from ~5 days to many months.
- 25% of people stopping antidepressants describe withdrawal effects that are severe
- Sx resolve fully within 24 hours if original antidepressant is restarted, or sometimes if a pharmacologically similar one is started. This is a key to confirming the diagnosis.

If patient develops symptoms, go back to the previous dose and wait longer before resuming taper. Slow taper even further at the end if patient has had symptoms with dose reduction. Can use liquid

SSRI formulations to slow tapers further if necessary. If pt still has severe symptoms despite very gradual taper, can cross-taper to fluoxetine 10mg, then taper the fluoxetine over several months.

If you made it to this point and have questions or feedback for me, I'd be happy to hear from you at esjones@stanford.edu. Also, check out Psychsnaps.com for more information about SSRIs, including counseling patients about antidepressants in pregnancy, use of SSRIs in patients with anxiety disorders, PTSD, dementia, PMDD, among others.

Addendum 1:

Patient Instructions for Taking SSRIs

1) This medication usually takes 2-3 weeks to begin to have a therapeutic effect.

2) Side effects can start, however, after the first dose. While your body adjusts to the medication, you may experience side effects such as nausea, diarrhea, decreased appetite, trouble sleeping, sedation, dizziness, headaches, increased anxiety or agitation. These early side effects are temporary and will generally go away within 7-10 days if you continue to take the medication.

3) This medication is generally well tolerated, but sometimes people experience weight gain, problems with sexual functioning, or increased sweating. These side effects may last for the duration of treatment, but can often be managed, and will go away if the medication is stopped. Be sure to let me know if you experience any of these side effects.

4) This medication can rarely be associated with an increase in suicidal thinking in children and young adults (<age 25). If you experience an increase in suicidal thinking, stop the medication and contact me.

**If you experience any side effect in the first two weeks of treatment that makes you want to stop the medication, please contact me.