# Antidepressants in the Older Adult

*Last updated May 2024*

**Medication Classes (in order of preference)**

1. SSRIs
    a. SSRIs are the first-line treatment for LLD because of their favorable side effect profiles and because they also help with cooccurring anxiety.
    b. Start with:
        i. Sertraline at 25 mg daily and titrate up to 100 mg per response.
        ii. Escitalopram at 5 mg daily and titrate up to 20 mg. Although citalopram has more efficacy data, we avoid it due to its boxed warning for QTc prolongation at doses > 20 mg/day in OAs.
    c. All serotonergic antidepressants can cause:
        i. Bleeding especially in those also taking NSAIDs, anticoagulants, or antiplatelet agents. For patients prescribed blood-thinners, I recommend clearing the SSRI/SNRI with the patient's PCP.
        ii. Decreased bone density can result in a higher risk of fractures. If a patient has a history of falls or fractures, I'll choose mirtazapine or bupropion first-line.
        iii. Rates of hyponatremia with SSRIs/SNRIs are relatively high in older adults. Hyponatremia often occurs within 14 days of medication initiation. Monitor sodium levels closely when starting or changing dosages. Bupropion, mirtazapine, and TCAs have lower rates of hyponatremia than SSRIs (Nelson JC, *Handb Exp Pharmacol* 2019;250:389–413).
    d. Drug-Drug Interactions
        i. For patients taking other medications, I will use escitalopram, mirtazapine, sertraline, or venlafaxine, as they're the least likely to interact.

2. SNRIs
    a. SNRIs cause more side effects than SSRIs, including falls (Sobieraj DM et al, *J Am Geriatr Soc* 2019;67(8):1571-1581), so are second line treatments.

3. Other Antidepressants
    a. Mirtazapine is a popular choice. In the past, it was often my first choice, but a recent article showed it had the highest risk of adverse outcomes compared with sertraline. So, now it's third line in my repertoire (Ishtiak-Ahmed K et al, *Am J Psychiatry* 2024;181:47–56). Its side effects (sedation and appetite stimulation) can be used to address insomnia and weight loss, which are common issues for OAs who are depressed.
    b. Bupropion is a stimulating antidepressant that can also assist with anhedonia, apathy, and smoking cessation.
    c. Vortioxetine holds promise in LLD due to its pro-cognitive benefits extending beyond its antidepressant effects.
    d. Vilazodone has excellent safety and tolerability profiles and may also treat anxiety.

4. TCAs have good efficacy in LLD but, along with MAOIs, are not recommended due to their potential for drug-drug interactions and poor side effect profiles (Allan CL & Ebmeier KP, *Adv Psychiat Treatment* 2013;19(4):302–309).
5. Other treatments include ECT, TMS, ketamine, or esketamine.

**Augmentation**

1. For partial responders, augment, in order, with aripiprazole, mirtazapine, bupropion XL, quetiapine (Lenze EJ & Oughli AH, *J Am Geriatr Soc* 2019;67(8):1555–1556), or methylphenidate.
2. Aripiprazole augmentation of 2 mg to 15 mg/day can result in remission in 44% of patients compared to 29% taking placebo. However, aripiprazole causes significantly more akathisia (26% vs 12%) and parkinsonism (17% vs 2%) than placebo (Lenze EJ et al, *Lancet* 2015;386(10011):2404–2412).
3. Methylphenidate augmentation of 5 mg to 40 mg/day can improve mood, boost well-being, and lead to higher remission rates. It appears to be a safe strategy, though you should first consult with a cardiologist for patients with cardiac risk factors. We don't have much data on methylphenidate's long-term use, so consider prescribing it short-term to help "jump-start" recovery (Lavretsky H et al, *Am J Psychiatry* 2015;172(6):561–569).

**If Antidepressant Treatment Fails Consider the Following**

1. **Adherence**- A common reason for low antidepressant effectiveness is that many patients never take them, stop them early, or take them intermittently.
2. **Suboptimal trial duration**- OAs may respond to antidepressants more slowly than younger adults, possibly requiring 10 to 12 weeks before effects are seen.
3. **Suboptimal dose**- While the adage is to "start low", don't forget to keep going and use the full dosage range of the drug (Lenze EJ & Oughli AH, *J Am Geriatr Soc* 2019;67(8):1555–1556).
4. **Too long on an ineffective treatment**- If the first treatment is unsuccessful, switch to the next option (Srifuengfung M et al, *Ther Adv Psychopharmacol* 2023;13:1–14).

**Treatment Algorithm:**

1. Mild Depression: Psychotherapy OR Pharmacotherapy
2. Moderate Depression: Psychotherapy AND Pharmacotherapy
3. Severe Depression without Psychotic Features: (Psychotherapy AND Pharmacotherapy) OR ECT
4. Severe Depression with Psychotic Features: (Pharmacotherapy with Antidepressant AND Antipsychotic) OR ECT
5. Treatment Resistant Depression: Augmentation OR Switching Drug Classes OR ECT OR TMS OR Other Treatments

| Drug Class/Drug | Starting Dose | Dose Range | Comments |
|---|---|---|---|
| **SSRIs** | | | |
| **Escitalopram** | 5 mg daily | 5 mg to 20 mg daily | Bleeding risk<br>Hyponatremia<br>Few drug-drug interactions |
| **Sertraline** | 12.5 mg to 25 mg daily | 50 mg to 200 mg daily | Bleeding risk<br>Drug-drug interactions at doses > 150 mg/day<br>Hyponatremia |
| **SNRIs** | | | |

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| **Duloxetine** | 20 mg daily | 20 mg to 60 mg daily | Activating<br>Bleeding risk<br>Discontinuation syndrome<br>Dose-dependent increases in blood pressure and heart rate<br>Hyponatremia<br>Useful for co-occurring pain |
| **Venlafaxine ER** | 37.5 mg qAM | 75 mg to 225 mg daily | Same as for duloxetine<br>Few drug-drug interactions |
| **Other antidepressants** | | | |
| **Bupropion** | 75 mg qAM | 150 mg BID in the morning and early afternoon with SR formulation or 150 mg to 300 mg qAM with the ER formulation | Activating<br>Don't use if history of seizures, eating disorders, or alcohol use disorder<br>May worsen anxiety or insomnia<br>Might improve apathy<br>Smoking cessation |
| **Mirtazapine** | 7.5 mg qHS | 15 mg to 30 mg qHS | Caution with renal/hepatic impairment<br>Sedation<br>Weight gain |
| **Vortioxetine** | 5 mg daily | 5 mg to 20 mg daily | Bleeding risk<br>Fewer sexual side effects<br>Hyponatremia<br>Nausea<br>Potential cognitive-enhancing effects |
| **Vilazodone** | 10 mg daily | 10 mg to 40 mg daily | Bleeding risk<br>Hyponatremia<br>Less weight gain and sexual side effects<br>Nausea<br>Take with food |
| **Augmentation** | | | |
| **Aripiprazole** | 2 mg qAM to 5 mg qAM | 2 mg qAM to 15 mg qAM | Akathisia<br>Increased risk of stroke and death in patients with dementia-related psychosis<br>Parkinsonism |
| **Methylphenidate** | 2.5 mg qAM to 5 mg qAM | 2.5 mg qAM to 20 mg BID (morning and noon) | Clear with cardiology if cardiac risk factors<br>Weight loss |

**Deprescribing**

- **Review Regularly:** The necessity of continued pharmacotherapy should be reviewed regularly, with an aim to reduce and stop medications, if possible, to minimize polypharmacy.