Managing depression in older patients
A guide to the most current evidence
Depression is common in older people, but is not a normal part of aging

**TABLE 1.** Depression occurs in up to one in ten older adults seen in primary care, with much higher rates in medical and institutional settings.\(^1\)\(^-\)\(^3\)

<table>
<thead>
<tr>
<th></th>
<th>Major depressive disorder</th>
<th>Minor depression symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRIMARY CARE</td>
<td>5-10%</td>
<td>25%</td>
</tr>
<tr>
<td>HOSPITAL</td>
<td>≥20%</td>
<td>17-30%</td>
</tr>
<tr>
<td>LONG-TERM CARE</td>
<td>≥20%</td>
<td>33-61%</td>
</tr>
</tbody>
</table>

Patients with depression in late life have worse health outcomes than patients without depression, including:

- increased mortality in patients with comorbid coronary heart disease\(^4\)
- elevated risk of suicide\(^5\)
- stroke and all-cause mortality\(^6\)

The U.S. Preventive Services Task Force recommends screening all adults for depression.\(^7\)

Only 1 in 3 adults who screen positive for depression receives treatment.\(^8\)

Effectively treating depression can reduce disability and improve quality of life.
Identifying the problem, and managing it

**FIGURE 1. Algorithm to screen for, evaluate, and treat depression symptoms**

1. Screen all patients with 2-item tool (PHQ-2).

   **If screen is positive:**

   2. Diagnose depression using DSM-5 criteria.

   3. Establish baseline severity with the PHQ-9.*

   **If patient has other factors:**

   - At risk of harming self or others:
     Evaluate the patient’s safety, and hospitalize if risk is significant. See page 9 for more.
   - Bipolar disorder, psychosis, or substance abuse problems:
     Refer to mental health professional

   4. Minimal symptoms
      PHQ-9 score: ≤4
      Educate patient about self-help options (e.g., exercise).
      Psychotherapy

   5. Mild to moderate
      PHQ-9 score: 5-14
      Educate patient about self-help options (e.g., exercise).
      Psychotherapy
      Psychotherapy **OR** antidepressants

   6. Moderately severe to severe
      PHQ-9 score: 15-27
      Regularly reassess symptoms, treatment response, and adverse effects.
      Psychotherapy **AND** antidepressants

**PHQ:** Patient Health Questionnaire, 2- and 9-item versions

**DSM-5:** Diagnostic and Statistical Manual, 5th edition

*The Geriatric Depression Scale (GDS), developed specifically for older adults, is another validated option. See AlosaHealth.org/Depression for more information about these tools and criteria.*
Psychotherapy is an effective first line treatment for depression

**FIGURE 2.** In older adults, cognitive behavioral therapy (CBT) improved the likelihood of treatment response and remission compared to patients randomized to usual care or wait-list controls.\(^{11}\)

Referral to a psychotherapist can help many older patients with depression.

Evidence in younger patients with moderate depression suggests CBT produces the same results as antidepressants,\(^ {12}\) but comparative data are not available for older adults or for severe depression.

Psychotherapy can encompass many evidence-based interventions.

**FIGURE 3.** Problem solving therapy achieves remission for a larger fraction of patients than supportive therapy.\(^ {13}\)
Trial data can guide drug choices

A recent meta-analysis found that all antidepressants were more effective at achieving a response or remission than placebo in adults with moderate to severe depression.¹⁴

**FIGURE 4.** An evidence-based approach to drug therapy based on findings of the large multi-year NIH-funded STAR*D trial¹⁵

Prescribe a trial of escitalopram (5-10 mg) or sertraline (25-50 mg) for 4-6 weeks.

- **Remission**
  - Double the dose of initial medication for 4-6 weeks.
  - **Remission**
  - **Partial response**

- **Partial response**
  - Add a first line augmentation strategy. *
  - **Remission**
  - **Partial or NO response**

- **NO response**
  - Switch to another SSRI, SNRI, or mirtazapine
  - **Partial or NO response**
  - **Remission**

- **Partial response**
  - **NO response**
  - Refer to a specialist. †
  - **Partial or NO response**
  - **Remission**

Continue with successful treatment for 12 months and reassess.

SSRI: selective serotonin reuptake inhibitor; SNRI: serotonin norepinephrine reuptake inhibitor

* First line augmentation strategy: bupropion (avoid in seizure risk); buspirone; psychotherapy

† Specialist referral is indicated if: treatment resistance; psychotic features; substance abuse; suicidal risk
Managing antidepressants in older adults

**Start low, go slow, don’t stall.**

- Increase to a therapeutic dose.

- Provide adequate time for effect. Older adults may take up to 10-12 weeks to respond to treatment.¹⁶

- Antidepressants are effective in older adults, but response rates may be lower for those 55 and over.¹⁷

- Switching medications may be preferable in frail older adults to avoid the polypharmacy that results from augmentation.

- Be aware that treatment for other coexisting conditions may be affected by antidepressants.

---

**Older patients are at higher risk of serious antidepressant side effects such as:**

- **Hyponatremia** (serum sodium <135 mmol/L)
- **Bleeding** (e.g., gastrointestinal)
- **Falls**
- **Fractures**

**SSRIs and TCAs can prolong QTc.** Obtain an ECG prior to starting these medications in older adults at high cardiovascular risk.¹⁸
### Medication characteristics impact selection

**TABLE 2. Summary of the doses and side effects of antidepressants**

<table>
<thead>
<tr>
<th>DRUG</th>
<th>STARTING DOSE</th>
<th>THERAPEUTIC DOSE</th>
<th>Anticholinergic effects</th>
<th>Drowsiness</th>
<th>Agitation</th>
<th>GI distress</th>
<th>QTc prolongation</th>
</tr>
</thead>
<tbody>
<tr>
<td>citalopram (Celexa)(^a)</td>
<td>10 mg</td>
<td>20 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>escitalopram (Lexapro)</td>
<td>5-10 mg</td>
<td>10-20 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>fluoxetine (Prozac)(^b)</td>
<td>10 mg</td>
<td>40-60 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>fluvoxamine (Luvox)</td>
<td>50 mg</td>
<td>100-200 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>paroxetine (Paxil; Paxil CR)(^c)</td>
<td>10 mg; 12.5 mg</td>
<td>50 mg; 62.5 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>sertraline (Zoloft)</td>
<td>25-50 mg</td>
<td>50-200 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>duloxetine (Cymbalta)</td>
<td>20-30 mg</td>
<td>60 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>levomilnacipran (Fetzima)(^d)</td>
<td>20 mg</td>
<td>40-120 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>venlafaxine (Effexor)(^d)</td>
<td>37.5-75 mg</td>
<td>150 mg-225 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>desvenlafaxine (Pristiq)(^d)</td>
<td>25-50 mg</td>
<td>50-100 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>bupropion XL (Wellbutrin XL)(^e)</td>
<td>150 mg</td>
<td>300 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>mirtazapine (Remeron)</td>
<td>7.5 mg</td>
<td>30 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>vilazodone (Viibryd)</td>
<td>10 mg</td>
<td>20 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>vortioxetine (Trintellix)</td>
<td>5 mg</td>
<td>5-20 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>amitriptyline (Elavil)</td>
<td>25 mg</td>
<td>100-300 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>nortriptyline (Pamelor)</td>
<td>25-50 mg</td>
<td>75-100 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
<tr>
<td>buspirone (Buspar)(^f)</td>
<td>15-20 mg</td>
<td>10-60 mg</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
<td>IFICATE</td>
</tr>
</tbody>
</table>

\(^a\) Black box warning caps dose at 20 mg per day  
\(^b\) Long half life may lead to accumulation  
\(^c\) Anticholinergic effects limit use in older patients  
\(^d\) Monitor for increases in blood pressure  
\(^e\) Avoid in patients with seizure risk  
\(^f\) Used for augmentation  
\(^g\) FDA-approved doses may exceed therapeutic dose  


= infrequent;  
= frequent;  
= very frequent or treatment limiting
Most patients respond to treatment, but those who don’t require other options

Depression that doesn’t respond to several medications from at least two different classes may benefit from referral to a specialist.

Additional approaches that may be recommended by a psychiatrist include:

- other medications such as lithium, liothyronine (T₃), antipsychotic medications (APMs), or other combinations of antidepressants
- neuromodulation treatments such as electroconvulsive therapy (ECT) or transcranial magnetic stimulation (TMS)

Benefits and risks of APMs

**FIGURE 5.** APMs are more effective than placebo for improving response and remission rates in adults when added to antidepressant therapy.¹⁹,²⁰

<table>
<thead>
<tr>
<th>Patients remitting on treatment (%)</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
<th>40</th>
<th>50</th>
</tr>
</thead>
<tbody>
<tr>
<td>placebo + venlafaxine ER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>aripiprazole + venlafaxine ER</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Patients were twice as likely to remit on aripiprazole than placebo (OR 2.0; 95% CI: 1.1-3.7).

Risks of APMs include:

- **Extrapyramidal symptoms** (e.g., akathisia, parkinsonism, dystonia)
- **Tardive dyskinesia:** While lower with atypical APMs, the risk of tardive dyskinesia is real with these drugs as well, and increases with duration of use.²¹
- **Metabolic changes** can lead to weight gain, hyperglycemia, and type 2 diabetes.
- **An increased risk of death of >50% in older patients with dementia.** While there are little data on mortality risk associated with APM use in depression, caution is needed when prescribing these drugs in older adults.
Don’t forget to ask about suicidal thoughts to identify those at greatest risk

Older men, especially over age 85, have the highest rate of completed suicide.⁵

- 50-70% of elderly patients who commit suicide have had contact with their primary care physician within the preceding month.²²
- Access to a firearm increases the odds of suicide by three-fold.²³

For patients who express thoughts of self-harm or that they’d be better off dead:

1. **Identify risk factors** (e.g., untreated mood, anxiety, psychotic or substance use disorders, access to lethal methods).

2. **Identify protective factors** (e.g., ability to cope with stress, family or social relationships, responsibility to children or beloved pets).

3. **Ask about suicidal ideation**, plan, behaviors, and intent.

4. **Determine risk level** and select **one or more** interventions:

<table>
<thead>
<tr>
<th>RISK LEVEL</th>
<th>SUICIDALITY</th>
<th>INTERVENTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>Suicide attempt or persistent ideation with strong intent or suicide rehearsal</td>
<td>Hospitalization likely indicated; suicide precautions</td>
</tr>
<tr>
<td>MODERATE</td>
<td>Suicide ideation with plan, but no intent or behavior</td>
<td>Hospitalization, depending on risk factors. Develop a crisis plan and provide crisis resources.</td>
</tr>
<tr>
<td>LOW</td>
<td>Thoughts of death; no plan, intent, or behavior</td>
<td>Outpatient referral, symptom reduction. Provide crisis resources.</td>
</tr>
</tbody>
</table>

5. **Document safety plan.** Provide patients with resources, support, and a plan for how to manage suicidal thoughts and intents at home.

Resources include the National Suicide Prevention Lifeline:
1-800-273-8255 or 1-800-799-4889 (deaf/hard of hearing) | suicidepreventionlifeline.org
FIGURE 6. Price of a 30-day supply of selected antidepressant medications

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Brand Name</th>
<th>Dosage</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>citalopram 20 mg</td>
<td></td>
<td>$4</td>
</tr>
<tr>
<td></td>
<td>escitalopram 10 mg</td>
<td></td>
<td>$78</td>
</tr>
<tr>
<td></td>
<td>fluoxetine 20 mg</td>
<td></td>
<td>$4</td>
</tr>
<tr>
<td></td>
<td>fluvoxamine 100 mg</td>
<td></td>
<td>$57</td>
</tr>
<tr>
<td></td>
<td>paroxetine 20 mg</td>
<td></td>
<td>$4</td>
</tr>
<tr>
<td></td>
<td>sertraline 50 mg</td>
<td></td>
<td>$34</td>
</tr>
<tr>
<td><strong>SNRIs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>desvenlafaxine 50 mg</td>
<td></td>
<td>$215</td>
</tr>
<tr>
<td></td>
<td>duloxetine 60 mg</td>
<td></td>
<td>$135</td>
</tr>
<tr>
<td></td>
<td>levomilnacipran (Fetzima) 40 mg</td>
<td></td>
<td>$427</td>
</tr>
<tr>
<td></td>
<td>venlafaxine ER 150 mg</td>
<td></td>
<td>$109</td>
</tr>
<tr>
<td><strong>Atypical antidepressants</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>bupropion SR (12 hr) 300 mg</td>
<td></td>
<td>$77</td>
</tr>
<tr>
<td></td>
<td>bupropion XL (24 hr) 300 mg</td>
<td></td>
<td>$88</td>
</tr>
<tr>
<td></td>
<td>mirtazapine 30 mg</td>
<td></td>
<td>$53</td>
</tr>
<tr>
<td><strong>Serotonin modulators</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>vilazodone (Viibryd) 20 mg</td>
<td></td>
<td>$298</td>
</tr>
<tr>
<td></td>
<td>vortioxetine (Trintellix) 10 mg</td>
<td></td>
<td>$425</td>
</tr>
<tr>
<td><strong>TCAs</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>amitriptyline 75 mg</td>
<td></td>
<td>$4</td>
</tr>
<tr>
<td></td>
<td>nortriptyline 75 mg</td>
<td></td>
<td>$21</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>buspirone 30 mg</td>
<td></td>
<td>$33</td>
</tr>
</tbody>
</table>

Prices from goodrx.com, October 2018. Listed doses are based on Defined Daily Doses by the World Health Organization and should not be used for dosing in all patients. All prices shown are for generics when available, unless otherwise noted. These prices are a guide; patient costs will be subject to copays, rebates, and other incentives.
Key messages

- Depression is not a normal part of aging, and is treatable in older patients.
- Screen for depression in all patients with a simple two-question tool (PHQ-2). If the screen is positive, confirm the diagnosis with DSM-5 criteria and establish severity using a validated tool such as the PHQ-9.
- Offer treatment based on depression severity and patient preference.
  - Refer to psychotherapy, such as CBT.
  - Prescribe an antidepressant, such as escitalopram or sertraline.
- Monitor response to treatment, watch for side effects, titrate doses upward as needed, or switch therapy if inadequate response.
- In patients at risk of suicide, evaluate the risk and develop a plan for intervention.
- Refer to a specialist for continuing treatment resistance or safety concerns.

More information is available at AlosaHealth.org/Depression

References:
(9) Unutzer J, Park M. Older adults with severe, treatment-resistant depression. JAMA. 2012;308(9):909-918.
About this publication

These are general recommendations only; specific clinical decisions should be made by the treating physician based on an individual patient’s clinical condition. More detailed information on this topic is provided in a longer evidence document at AlosaHealth.org.

The Independent Drug Information Service (IDIS) is supported by the PACE Program of the Department of Aging of the Commonwealth of Pennsylvania.

This material is provided by Alosa Health, a nonprofit organization which is not affiliated with any pharmaceutical company. IDIS is a program of Alosa Health.

This material was produced by Elizabeth LaSalvia, M.D., Instructor in Psychiatry; Dae Kim, M.D., M.P.H., Sc.D., Assistant Professor of Medicine (principal editor); Michael A. Fischer, M.D., M.S., Associate Professor of Medicine; Niteesh K. Choudhry, M.D., Ph.D., Professor of Medicine; Jerry Avorn, M.D., Professor of Medicine; Jing Luo, M.D., M.P.H., Instructor in Medicine; all at Harvard Medical School, and Ellen Dancel, PharmD, M.P.H., Director of Clinical Materials Development at Alosa Health. Drs. Avorn, Choudhry, Fischer, and Luo are physicians at the Brigham and Women’s Hospital, Dr. LaSalvia practices at the Beth Israel Deaconess Medical Center and Dr. Kim at Hebrew Senior Life, all in Boston. None of the authors accepts any personal compensation from any drug company.

Medical writer: Jenny Cai