

# Depression in older adults: How to treat its distinct clinical manifestations

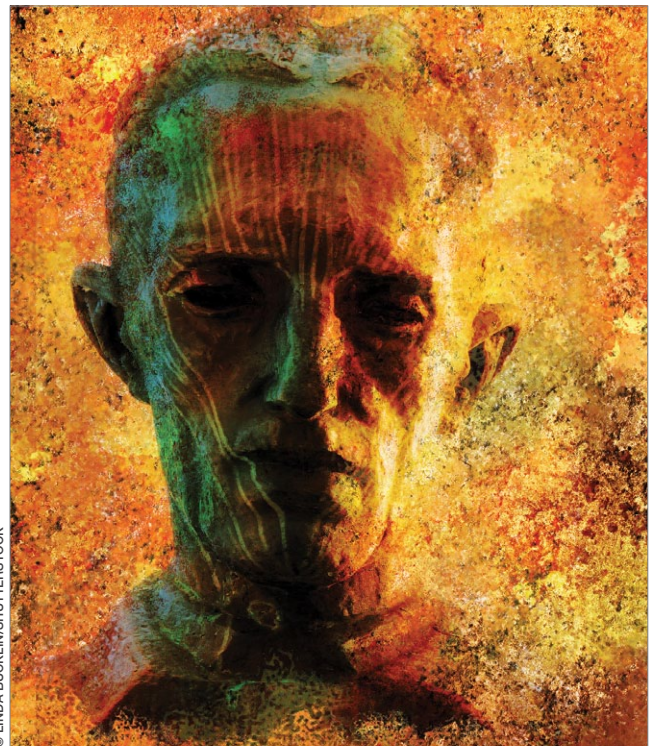
Algorithms help you select the most efficacious clinical tools for your patient

**D**epression in older adults (age  $\geq 65$ ) can devastate their quality of life and increase the likelihood of institutionalization because of behavioral problems.<sup>1</sup> Depression is a primary risk factor for suicide, and suicide rates are highest among those age  $\geq 65$ , especially among white males.<sup>2</sup> The burden of geriatric depression can extend to caregivers.<sup>1</sup> Prompt recognition and treatment of depression could help minimize morbidity and reduce suffering in older adults and their caregivers.

Although geriatric depression varies in severity and presentation, common categories include:

- major depressive disorder (MDD)
- vascular depression
- dysthymia
- depression in the context of dementias, psychosis, bipolar disorder, and executive dysfunction.

Diagnoses in this population generally correspond with DSM-IV-TR criteria, but geriatric depression has distinct clinical manifestations.<sup>1,2</sup> Compared with younger depressed patients, older adults are less likely to endorse depressed mood and more likely to report a lack of emotions.<sup>1,2</sup> Older patients report feelings of irritability and fearfulness more often than sadness.<sup>1,2</sup> Mood symptoms tend to be transient, reoccur frequently, and display either a diurnal pattern or multiple fluctuations in a single day.<sup>1,2</sup> Other common presentations include loss of interest in usual activities, lack of motivation, social withdrawal, and decline in activities of daily living.<sup>1,2</sup>



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**Nabil Kotbi, MD**

Assistant professor of psychiatry

**Nahla Mahgoub, MD**

Instructor in psychiatry

**Anna Odom, PhD**

Instructor of psychology in psychiatry

••••

Weill Medical College of Cornell University  
New York-Presbyterian Hospital  
White Plains, NY

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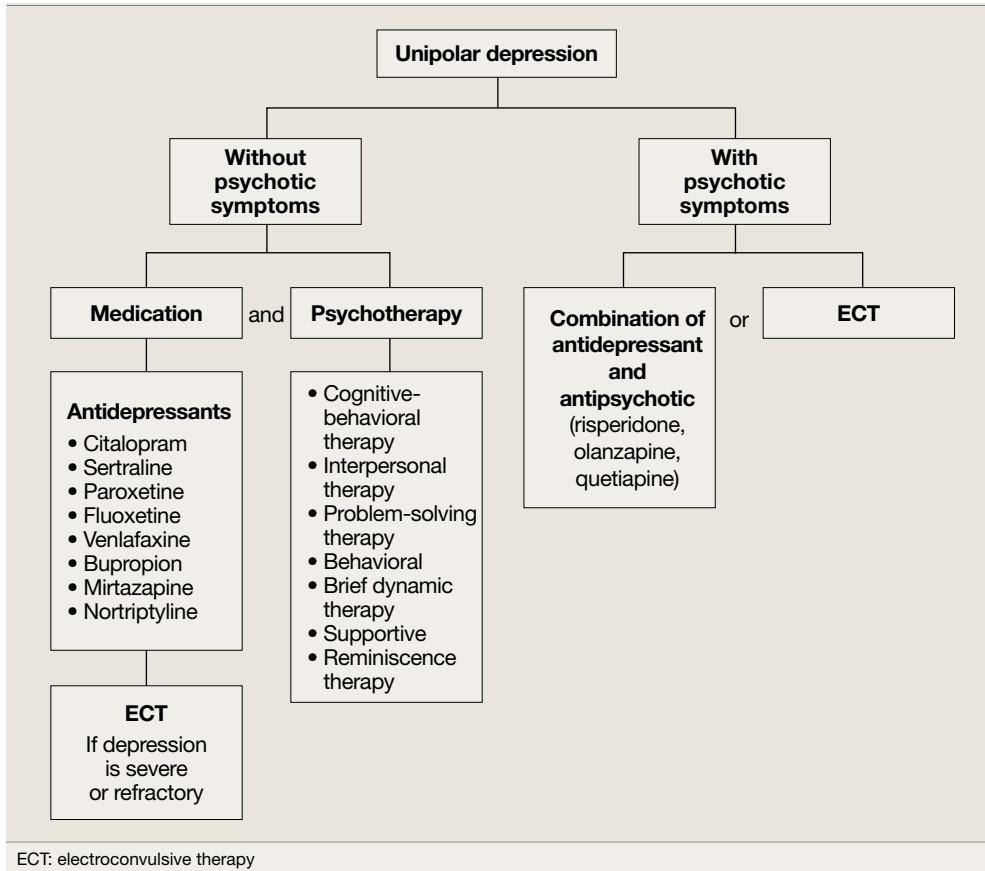
## Geriatric depression

### Clinical Point

Older patients report feelings of irritability and fearfulness more often than sadness

### Algorithm 1

## Treatment for unipolar depression in geriatric patients



### Summary of recommendations

Age-specific recommendations for assessing and treating geriatric depression can be generated in part from evidence-based reviews, meta-analyses,<sup>3</sup> and geriatric expert consensus guidelines.<sup>4</sup> Such guidelines and recommendations often do not take into account the marked heterogeneity of medical, cognitive, and overall functioning in patients age  $\geq 65$ , however, because they are based on studies of younger populations and patients with complicated issues often are excluded from studies. The recommendations in this article are based largely on findings from a National Institutes of Health (NIH)-sponsored project by Alexopoulos et al to develop consensus guidelines for managing geriatric depression and expert opinion from clinicians who treat geriatric patients.<sup>4</sup>

During your initial clinical evaluation, confirm the diagnosis and type, duration, and severity of depression. Seek to understand the biopsychosocial context of each

patient's presentation. Carefully consider your patient's suicide risk. Hospitalization may be required if he or she is at high risk for suicide or has complex medical and social circumstances that cannot be managed adequately in an outpatient setting.<sup>5</sup>

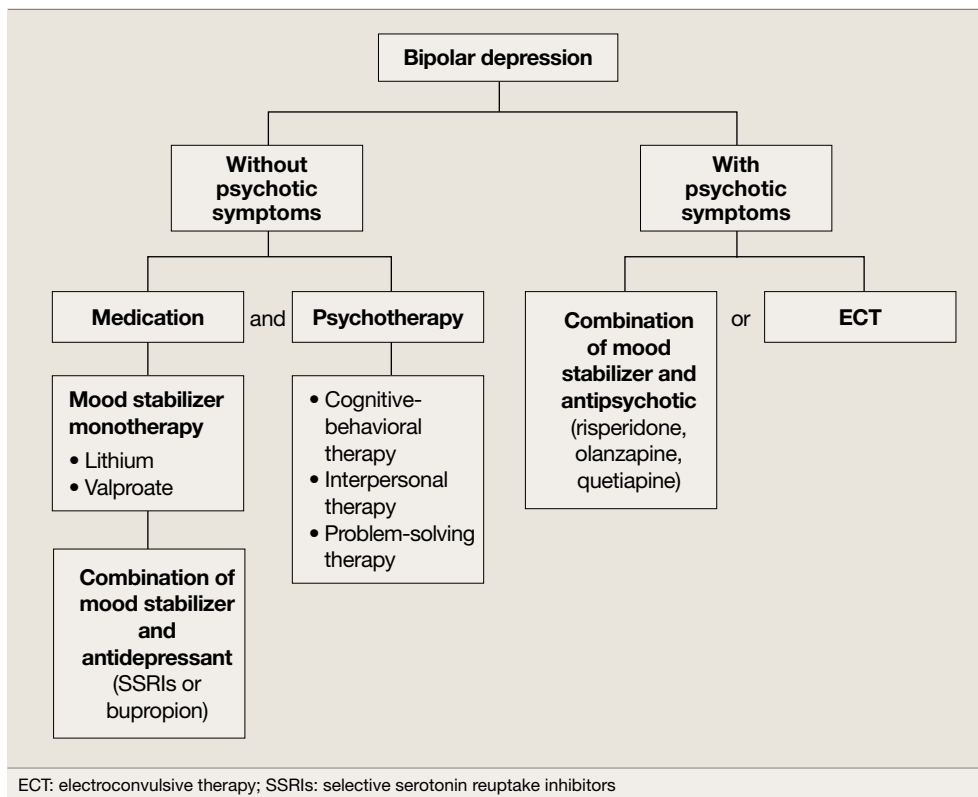
### Unipolar major depression

For unipolar, nonpsychotic geriatric depression, the NIH-Alexopoulos et al guidelines emphasize a combination of antidepressants and psychotherapy (*Algorithm 1*).<sup>4</sup> Selective serotonin reuptake inhibitors (SSRIs) and venlafaxine are first-line options.<sup>4,6,7</sup> Tricyclic antidepressants (TCAs), bupropion, and mirtazapine are alternatives.<sup>4</sup> Among SSRIs, citalopram, escitalopram, and sertraline are preferred initial antidepressants. Fluoxetine is used less frequently.<sup>4</sup> Paroxetine also is less commonly used because of its anticholinergic effects and because the drug inhibits cytochrome P4502D6,<sup>2</sup> which

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## Bipolar depression: Options for combination therapy



## Clinical Point

Paroxetine is not frequently used because of its anticholinergic effects and inhibition of cytochrome P4502D6

metabolizes several medications commonly prescribed for older adults. Among TCAs, nortriptyline is preferred.<sup>4</sup> Studies have shown that duloxetine improves depression and is safe and well-tolerated in older adults with recurrent MDD.<sup>8</sup> Electroconvulsive therapy (ECT) is an option for treating severe or treatment-resistant unipolar major depression.<sup>9</sup>

For unipolar depression with psychotic symptoms, guidelines recommend a combination of an antidepressant and an antipsychotic or ECT.<sup>4</sup> Atypical antipsychotics are preferred over typical antipsychotics<sup>4</sup>; risperidone, olanzapine, and quetiapine are most frequently used.<sup>4</sup> Clinical data on aripiprazole and ziprasidone in older adults are limited. Many geriatric experts recommend continuing an antipsychotic for 6 months after symptom remission, then gradually tapering the dose.<sup>4</sup>

During acute illness, administer an antidepressant for 6 to 12 weeks at the individually determined dose required to achieve symptom remission.<sup>6</sup> For an older adult ex-

periencing a first lifetime episode of major depression, continue antidepressant treatment for 1 year after remission.<sup>4</sup> If your patient has had 2 lifetime episodes of major depression, continue the antidepressant at the same dose used to achieve remission for at least 3 years. For patients who have had  $\geq 3$  episodes of depression or whose index episode was particularly severe or involved significant suicidal thoughts or behaviors, continue maintenance treatment indefinitely.

## Bipolar depression

Mood stabilizers such as lithium or valproate—as monotherapy or in combination with an antidepressant—are recommended to treat bipolar depression without psychotic symptoms in older adults (*Algorithm 2*).<sup>10</sup> For bipolar depression with psychotic symptoms, a combination of a mood stabilizer and an atypical antipsychotic or ECT is recommended.<sup>10</sup>

Older adults' increased sensitivity to side effects and reduced ability to tolerate

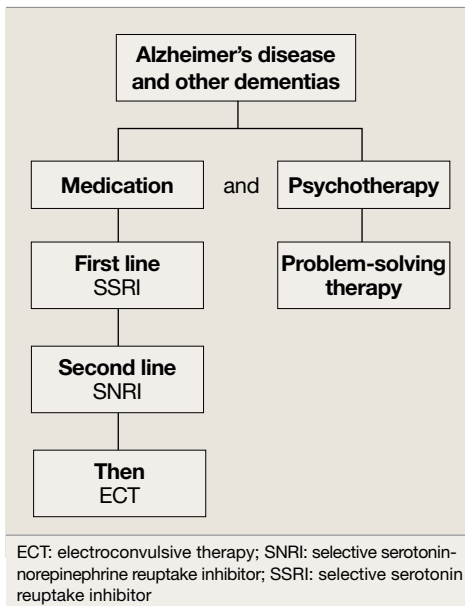


## Geriatric depression

### Clinical Point

ECT for depressed patients with dementia often is modified to twice-a-week, unilateral stimulus because of increased delirium risk

### Algorithm 3 Treating comorbid depression and dementia



lithium may limit its use and may prompt you to consider atypical antipsychotics as alternatives to other mood stabilizers. Although quetiapine and fluoxetine-olanzapine combination are well studied in younger patients,<sup>11,12</sup> there is a lack of data to support their clinical effectiveness and tolerability in older adults. Among antidepressants, SSRIs or bupropion are preferred over TCAs to prevent a switch to mania.<sup>10</sup> Lamotrigine is an effective maintenance treatment for bipolar depressive episodes in older adults.<sup>13</sup>

Although optimal mood stabilizer and antidepressant dosing for this population has not been adequately assessed, pharmacotherapy that has been effective generally should be continued without modification for at least 6 to 12 months.<sup>10</sup> After the patient achieves remission, gradually discontinue antidepressants while maintaining the mood stabilizer.<sup>10</sup>

### Depression in dementia

Managing depression in dementia patients is similar to treatment in older adults without dementia,<sup>5,14</sup> although pharmacologic agents must be carefully selected

because of increased risk of side effects (Algorithm 3). American Psychiatric Association practice guidelines recommend considering antidepressants for depressed patients with dementia even if their mood disturbances do not meet DSM-IV-TR criteria for MDD.<sup>5</sup>

SSRIs' lower side effect profile make them the preferred treatment; the selective serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine is a second-line option.<sup>4,14</sup> Avoid TCAs and other agents with anticholinergic side effects because of potential cardiovascular complications and cognitive side effects, unless SSRIs or SNRIs are ineffective or contraindicated.<sup>14</sup> Recently clinicians have been reluctant to use antipsychotics in patients with dementia, because of the FDA's "black-box" warning regarding the increased mortality risk associated with their use in this population.

When using ECT to treat depression in patients with dementia, the treatment protocol often is modified to twice-a-week, unilateral stimulus because of these patients' increased risk of delirium.<sup>14</sup> The safety of ECT to treat depression in patients with dementia has not been adequately assessed.<sup>14</sup>

### Vascular depression

The "vascular depression hypothesis" proposes that accumulation of subcortical white matter hyperintensities can disrupt frontostriatal pathways, resulting in depressive symptoms.<sup>15</sup> This hypothesis is supported by the confluence of depression and vascular risk factors.<sup>15</sup> Sertraline, citalopram, nortriptyline,<sup>16</sup> and trazodone<sup>15</sup> have been shown to reduce depressive symptoms after a stroke.

### Minor depression and dysthymia

Although the efficacy of antidepressants in minor depression—depression that does not meet criteria for MDD—is not well established, expert consensus guidelines recommend SSRIs and psychotherapy, separately or in combination, for minor depression and dysthymia in older adults (Algorithm 4, page 44).<sup>4</sup> Depression in executive dysfunction re-

sponds poorly to SSRI treatment<sup>2</sup>; however, behaviorally oriented psychotherapeutic interventions such as problem-solving therapy (PST) show promise.<sup>2</sup>

### Comorbid medical conditions

When an older adult has a medical problem that likely contributes to depression—such as hypothyroidism—treat the condition and prescribe antidepressants simultaneously.<sup>2</sup> However, if the medical problem likely causes depression—such as substance withdrawal—treat the condition first and prescribe antidepressants only if mood symptoms persist.<sup>2</sup>

### Refractory depression

If your patient does not respond to an antidepressant trial of adequate dosage and duration, first make sure he or she is taking it correctly (*Algorithm 5, page 45*). After ruling out poor adherence, screen for comorbid psychiatric or medical con-

ditions or psychosocial stressors and reassess the principal diagnosis.<sup>5</sup>

If these steps don't address your patient's depressive symptoms, expert consensus guidelines suggest switching to a different antidepressant:<sup>4</sup>

- If you first prescribed an SSRI, consider venlafaxine XR or bupropion SR.<sup>4,17</sup>
- If your patient initially received a TCA or bupropion, an SSRI or venlafaxine XR would be appropriate.<sup>4</sup>
- If venlafaxine XR was the first antidepressant, a SSRI is recommended.<sup>4</sup>

If your patient experienced a partial response but not full remission with the initial antidepressant, consider adding a second antidepressant or an augmenting agent:<sup>4</sup>

- If your patient first received an SSRI, adding bupropion, lithium, or nortriptyline is recommended.
- If the initial antidepressant was a TCA or bupropion, consider adding lithium or an SSRI.
- Augmenting venlafaxine XR with lithium is recommended.<sup>4</sup>

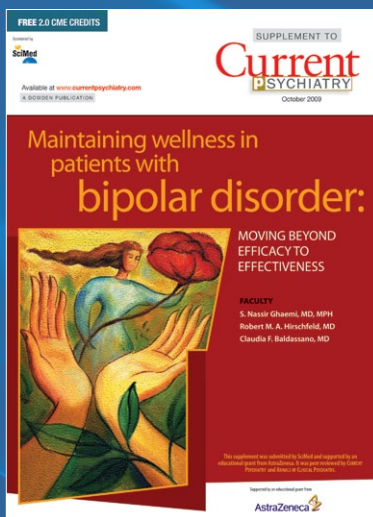
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### Clinical Point

If a medical problem likely causes depression, treat the condition first and offer antidepressants if mood symptoms persist

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### PARTICIPATING FACULTY

#### S. Nassir Ghaemi, MD, MPH

Director, Mood Disorders  
and Psychopharmacology  
Programs  
Professor of Psychiatry  
Tufts Medical Center  
Boston, Massachusetts

#### Robert M. A. Hirschfeld, MD

Titus H. Harris Chair  
Harry K. Davis Professor  
Professor and Chairperson  
Department of Psychiatry  
and Behavioral Sciences  
University of Texas Medical Branch  
Galveston, Texas

#### Claudia F. Baldassano, MD

Assistant Professor of Psychiatry  
Director, Bipolar Outpatient  
Program  
Hospital of the University  
of Pennsylvania  
Philadelphia, Pennsylvania

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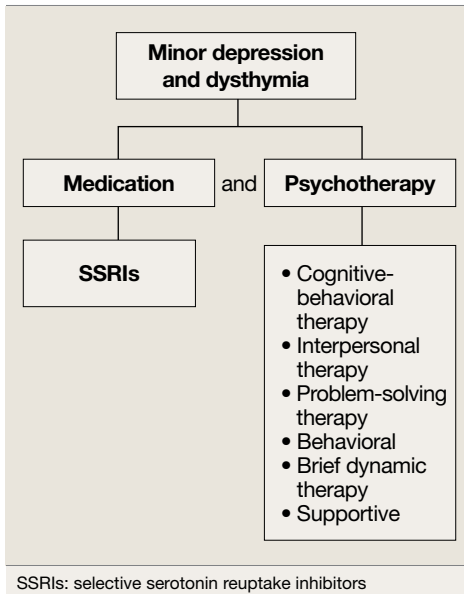
## Geriatric depression

### Clinical Point

ECT can be administered to many older depressed adults with relatively low complication rates

#### Algorithm 4

### Minor depression: SSRIs plus psychotherapy



The National Institutes of Mental Health-sponsored Sequenced Treatment Alternatives to Relieve Depression (STAR\*D) study of treatment-resistant depression in mixed-age groups reported that patients who do not attain remission with an initial SSRI may respond to switching to bupropion SR or venlafaxine XR.<sup>17</sup> Augmenting an SSRI with bupropion SR has been shown to be effective.<sup>18</sup> In addition, consider mirtazapine augmentation,<sup>19</sup> especially if your patient experiences insomnia or anorexia. A combination of mirtazapine and venlafaxine have better efficacy and tolerability compared with the monoamine oxidase inhibitor tricyclic promine.<sup>19</sup> Some studies have shown augmenting SSRIs with buspirone in patients with severe depression is efficacious and safe in younger adults,<sup>20</sup> but this practice is not well studied in older patients.

### Nonpharmacologic treatments

ECT is an important therapeutic intervention because of its safety, efficacy, and faster clinical response.<sup>6,7,9,21</sup> Consider ECT for older adults with severe or psychotic major depression, acute suicidality, catatonia, or severe malnutrition caused by refusal to eat. Patients who remain significantly

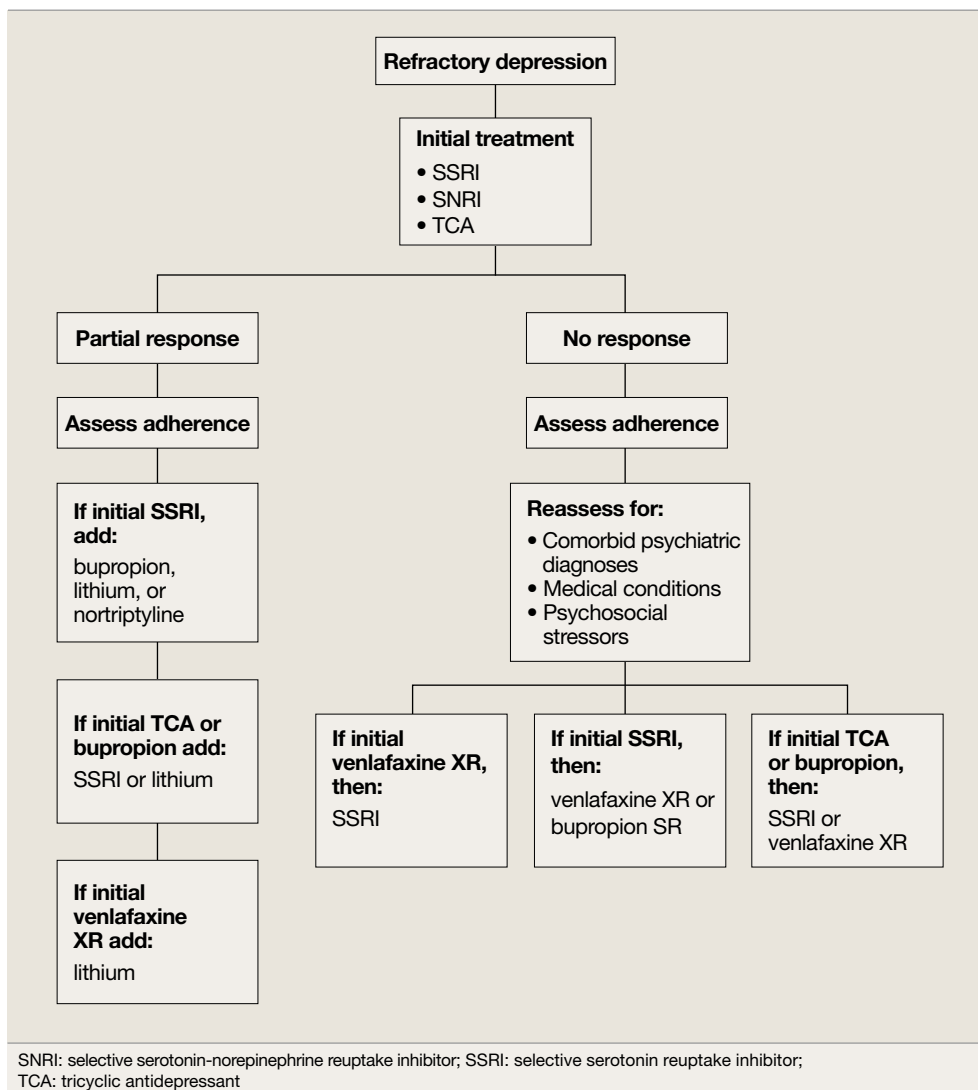
symptomatic after multiple medication trials, do not tolerate medications well, or have comorbid medical conditions that preclude antidepressant use also are potential candidates for ECT.<sup>5,22</sup>

ECT can be administered to many older depressed adults with relatively low complication rates. Pretreatment clinical and laboratory evaluations and consultation with medical colleagues may minimize the risk of adverse effects, including cardiovascular instability, delirium, and falls.<sup>9</sup> Anterograde memory loss—a common concern for clinicians and patients—usually is temporary and can be reduced by modifying the ECT administration parameters, such as switching from bilateral to unilateral stimulus and spacing treatments.<sup>9</sup> Use caution when considering ECT for patients with cardiovascular or neurologic conditions—such as myocardial infarction or cerebrovascular accident within 6 months of treatment—that may increase the risk of adverse effects. Some pharmacologic agents, such as benzodiazepines and anti-convulsant mood stabilizers, may decrease ECT's efficacy by inhibiting seizure.<sup>22</sup>

Depressive relapse after ECT is a major clinical concern.<sup>21</sup> Continuation ECT—within the first 6 months of remission—aims to prevent relapse of the same episode, whereas maintenance ECT—beyond the first 6 months—helps avert occurrence of new episodes.<sup>4,21</sup> Relapse and recurrence also can be prevented with continuation or maintenance pharmacotherapy,<sup>4,21</sup> which should be initiated immediately after the index course of ECT.<sup>21</sup> Typically, ECT continuation/maintenance treatments are provided weekly, then gradually spaced out to once a month based on the minimum frequency that is effective for an individual patient.<sup>21</sup>

**Psychotherapy** for geriatric depression generally is effective.<sup>23</sup> One-half of older patients prefer psychotherapy over pharmacotherapy.<sup>24</sup> Efficacious psychotherapies include behavioral therapy, cognitive-behavioral therapy (CBT), PST, brief dynamic therapy, interpersonal therapy, supportive therapy, and reminiscence therapy.<sup>23</sup> CBT has the most empiric sup-

## Treatment-resistant geriatric depression: Partial vs no response



## Clinical Point

Among psychotherapies, cognitive-behavioral therapy has the most empiric support for treating geriatric depression

port for treating geriatric depression.<sup>5,6</sup>

Psychotherapy alone is appropriate for mild-to-moderate depression, although severe depression requires adding medication.<sup>25</sup> The combination of pharmacotherapy and psychotherapy appears to be more effective than either intervention alone in preventing recurrent major depression, especially when a specific psychosocial stressor has been identified.<sup>5,6</sup> CBT, interpersonal therapy, and family-focused therapy enhance pharmacotherapy outcomes in bipolar disorder.<sup>13</sup>

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study found that in mixed-age patients, pharmacotherapy plus psychotherapy is

more beneficial than medication alone in stabilizing bipolar depression.<sup>26</sup> For older adults with executive dysfunction, research suggests that PST is more effective than other psychotherapies.<sup>27</sup> Psychosocial interventions—such as psychoeducation for the family and caregivers, family counseling, and participation in senior citizen centers and services—are strongly recommended for many patients.<sup>4</sup>

## References

1. Lyketsos CG, Lee HB. Diagnosis and treatment of depression in Alzheimer's disease. A practical update for the clinician. *Dement Geriatr Cogn Disord*. 2004;17(1-2): 55-64.
2. Alexopoulos G. Late-life mood disorders. In: Sadavoy J, Jarvik LF, Grossberg GT, et al, eds. *Comprehensive textbook of geriatric psychiatry*. 3rd ed. New York, NY: W.W. Norton and Company; 2004:609-653.



## Geriatric depression

### Clinical Point

For older adults with executive dysfunction, problem-solving therapy is more effective than other psychotherapies

## Related Resources

• Blazer DG, Steffens DC, Koenig HG. Mood disorders. In: Blazer DG, Steffens DC, eds. *The American Psychiatric Publishing textbook of geriatric psychiatry*. 4th ed. Arlington, VA: American Psychiatric Publishing, Inc.; 2009:275-300.

• American Association for Geriatric Psychiatry. [www.aagponline.org](http://www.aagponline.org).

### Drug Brand Names

Aripiprazole • Abilify	Nortriptyline • Aventyl,
Bupropion • Wellbutrin,	Pamelor
Zyban	Olanzapine • Zyprexa
Buspirone • Buspar	Paroxetine • Paxil
Citalopram • Celexa	Quetiapine • Seroquel
Duloxetine • Cymbalta	Risperidone • Risperdal
Escitalopram • Lexapro	Sertraline • Zoloft
Fluoxetine • Prozac	Tranylcypromine • Parnate
Fluoxetine-olanzapine	Trazodone • Desyrel
• Symbyax	Valproate • Depakote
Lamotrigine • Lamictal	Venlafaxine • Effexor
Lithium • Eskalith, Lithobid	Ziprasidone • Geodon
Mirtazapine • Remeron	

### Disclosure

The authors report no financial relationship with the manufacturer of any product mentioned in this article or with manufacturers of competing products.

3. Shanmugham B, Karp J, Drayer R, et al. Evidence-based pharmacologic interventions of geriatric depression. *Psychiatr Clin North Am*. 2005;28(4):821-835,viii.
4. Alexopoulos GS, Katz IR, Reynolds CF III, et al. The expert consensus guidelines series. Pharmacotherapy of depressive disorders in older patients. *Postgrad Med*. 2001; *Spect No Pharmacolotherapy*:1-86.
5. American Psychiatric Association practice guidelines for the treatment of psychiatric disorders. Arlington, VA: American Psychiatric Association; 2006:793-794.
6. Bartels SJ, Dums AR, Oxman TE, et al. Evidence-based practice in geriatric mental health care. *Psychiatr Serv*. 2002;53(11):1419-1431.
7. Bartels SJ, Dums AR, Oxman TE, et al. Evidence-based practices in geriatric mental health care: an overview of systematic reviews and meta-analyses. *Psychiatr Clin North Am*. 2003;26(4):971-990,x-xi.
8. Raskin J, Wiltse CG, Siegal A, et al. Efficacy of duloxetine on cognition, depression, and pain in elderly patients with major depressive disorder: an 8-week, double-blind, placebo-controlled trial. *Am J Psychiatry*. 2007;164(6):900-909.
9. Alexopoulos GS, Young RC, Abrams RC. ECT in the high-risk geriatric patient. *Convuls Ther*. 1989;5(1):75-87.
10. Young RC, Gyulai L, Mulsant BH, et al. Pharmacotherapy of bipolar disorder in old age: review and recommendations. *Am J Geriatr Psychiatry*. 2004;12:342-357.

11. Vieta E, Calabrese JR, Goikolea JM, et al. Quetiapine monotherapy in the treatment of patients with bipolar I or II depression and a rapid-cycling disease course: a randomized, double-blind, placebo-controlled study. *Bipolar Disord*. 2007;9(4):413-425.
12. Corya SA, Perlis RH, Keck PE Jr, et al. A 24-week open-label extension study of olanzapine-fluoxetine combination and olanzapine monotherapy in the treatment of bipolar depression. *J Clin Psychiatry*. 2006;67(5):798-806.
13. Sajatovic M, Gyulai L, Calabrese JR, et al. Maintenance treatment outcomes in older patients with bipolar I disorder. *Am J Geriatr Psychiatry*. 2005;13(4):305-311.
14. Lyketsos CG, Olin J. Depression in Alzheimer's disease: overview and treatment. *Biol Psychiatry*. 2002;52(3):243-252.
15. Alexopoulos GS, Meyers BS, Young RC, et al. 'Vascular depression' hypothesis. *Arch Gen Psychiatry*. 1997; 54(10):915-922.
16. Starkstein SE, Mizrahi R, Power BD. Antidepressant therapy in post-stroke depression. *Expert Opin Pharmacother*. 2008;9(8):1291-1298.
17. Rush AJ, Trivedi MH, Wisniewski SR, et al and STAR\*D Study Team. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *N Engl J Med*. 2006; 354(12):1231-1242.
18. Trivedi MH, Fava M, Wisniewski SR, et al and the STAR\*D Study Team. Medication augmentation after the failure of SSRIs for depression. *N Engl J Med*. 2006;354(12):1243-1252.
19. McGrath PJ, Stewart JW, Fava M, et al. Tranylcypromine versus venlafaxine plus mirtazapine following three failed antidepressant medication trials for depression: a STAR\*D report. *Am J Psychiatry*. 2006;163(9):1531-1541.
20. Appelberg BG, Syvälahti EK, Koskinen TE, et al. Patients with severe depression may benefit from buspirone augmentation of selective serotonin reuptake inhibitors: results from a placebo-controlled, randomized, double-blind, placebo wash-in study. *J Clin Psychiatry*. 2001;62(6): 448-452.
21. Greenberg RM, Kellner CH. Electroconvulsive therapy: a selected review. *Am J Geriatric Psychiatry*. 2005;13(4): 268-281.
22. Kaplan HI, Sadock BJ. Electroconvulsive therapy. In: Kaplan and Sadock's synopsis of psychiatry. 8th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 1998:1138-1143.
23. Gum A, Areán P. Current status of psychotherapy for mental disorders in the elderly. *Curr Psychiatry Rep*. 2004;6:32-38.
24. Unützer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in primary care settings: a randomized controlled trial. *JAMA*. 2002;288: 2836-2845.
25. Niederehe G, Schneider LS. Treatments for depression and anxiety in the aged. In: Nathan PE, Gorman JM, eds. *A guide to treatments that work*. New York, NY: Oxford University Press; 1998:270-287.
26. Miklowitz DJ, Otto MW, Frank E, et al. Psychosocial treatments for bipolar depression: a 1-year randomized trial from the Systematic Treatment Enhancement Program. *Arch Gen Psychiatry*. 2007;64:419-426.
27. Alexopoulos GS, Raue P, Areán P. Problem-solving therapy versus supportive therapy in geriatric major depression with executive dysfunction. *Am J Geriatr Psychiatry*. 2003;11:46-52.

## Bottom Line

Depression in patients age  $\geq 65$  is similar to that seen in younger adults, but comorbidities and varying presentations and severity may complicate assessment and management. Treatment often starts with antidepressants. Mood stabilizers, atypical antipsychotics, electroconvulsive therapy, and psychotherapy—alone or as adjuncts—also are options.