

# Most effective, least worrisome therapies for late-life anxiety

## Work-up of memory concerns calls for excluding cognitive impairment and depression

**M**s. W, a 73-year-old widow with no psychiatric history, visits her primary care physician because she is concerned about her memory. She denies impairment in other cognitive domains—such as executive function—or activities of daily living.

Ms. W relates prominent worries about her health and finances and those of her grandchildren. She describes daily restlessness, sleep-onset insomnia, difficulty concentrating, and mild episodic dysphoria. She says she's always been a "worry wart" but her worry and other symptoms have become increasingly intrusive over the past 5 years with a series of deaths in her family. Ms. W's medical history includes hypertension and type 2 diabetes. Unsure how to treat her, the physician refers Ms. W to a psychiatrist.

Older adults with anxiety symptoms often are dissatisfied with treatment because they believe they receive insufficient help. This complaint is probably valid because limited data support pharmacologic interventions for anxiety in older adults, and therapy is often based on inferences from studies in younger subjects. Moreover, many anxious older patients are treated with benzodiazepines, which increases their risk for cognitive impairment and injuries.<sup>1,2</sup>

Fortunately, growing evidence points to 2 treatment modalities for anxiety disorders in patients age  $\geq 65$ :

- pharmacotherapy with antidepressants, benzodiazepines, and (perhaps) buspirone
- cognitive-behavioral therapy (CBT) for generalized anxiety disorder (GAD), panic disorder (PD), and mixed anxiety syndromes.

continued



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## Late-life anxiety

### Clinical Point

Anxiety disorders in older adults might be complicated by comorbid dementia, depression, or other psychiatric disorders

### Table 1 Is it GAD? Common features in older adults

Demographics
More prevalent at age <75 years
More common in women
Medical
Frequent visits to primary care
Low satisfaction with medical care
≥2 chronic physical illnesses
≥1 adaptive behavior limitations
Cognitive impairment, particularly verbal memory
Psychiatric
History of GAD symptoms (5 to ≥20 years)
Physiologic anxiety symptoms: restlessness, fatigue, muscle tension
Depressive symptoms
Prescribed a benzodiazepine
Presence of anxiety disorders
Suicidal ideation, particularly if depressed
Psychological
External locus of control
Neuroticism
Psychosocial
Limited social network
Perceived low instrumental support
Recent losses and traumatic life events
Loss of partner
GAD: generalized anxiety disorder Source: References 1,3-12

### A common, debilitating problem

Anxious older adults report diminished perceived health, physical activities, and quality of life and increased loneliness compared with their nonanxious counterparts.<sup>1</sup> The prevalence of anxiety disorders in older patients ranges from 0.4% for obsessive-compulsive disorder to 11.5% for GAD.<sup>3</sup>

Older adults with GAD present with a constellation of medical, psychiatric, psychological, and psychosocial features (Table 1).<sup>1,3-12</sup> Anxiety disorders in older adults also may co-occur with major

depressive disorder, other psychiatric conditions, or dementia, which can complicate diagnosis and treatment.

### CASE CONTINUED

#### Anxious, not depressed

You screen Ms. W with the Geriatric Depression Scale (short form; GDS) and Beck Anxiety Inventory (BAI). Her scores indicate no depression and moderate anxiousness. A neuropsychological screen finds no cognitive impairments. Based on the clinical interview and screening, Ms. W meets DSM-IV-TR criteria for GAD.

Psychopharmacologic interventions are first-line treatment for older adults with anxiety disorders, but you might consider other strategies because:

- Older patients may have increased vulnerability to medication side effects.
- Few randomized, placebo-controlled trials have examined psychopharmacologic interventions specifically for anxious older adults.

Evidence supports using psychotherapy as an alternative or adjunct to pharmacotherapy for treating anxiety symptoms. A meta-analysis of 15 studies that included 495 adults (mean age 69.5 years) with late-life anxiety symptoms and 20 psychotherapeutic interventions indicated that psychotherapy was reliably more effective than no treatment.<sup>13</sup>

### First-line pharmacotherapies

When selecting pharmacotherapy for an older adult with anxiety, take into account:

- physiologic changes in drug metabolism (older patients metabolize drugs more slowly than younger patients)
- comorbid medical problems
- polypharmacy (many older patients are taking multiple medications for multiple conditions, which increases the risk of drug-drug interactions).

Also consider prior treatment response and symptom severity when choosing the medication you feel will be most tolerable. “Start low and go slow” to avoid side effects while titrating the medication to the optimal dosage (Table 2, page 89).

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Pharmacologic management of anxiety typically has included benzodiazepines, tricyclic antidepressants, barbiturates, and antihistamines. Newer antidepressants have emerged as first-line treatment for several anxiety disorders and mixed anxiety-depression syndromes, however, because of their more tolerable side-effect profiles, especially when used long-term.<sup>14</sup> These antidepressants include:

- selective serotonin reuptake inhibitors (SSRIs)
- serotonin/norepinephrine reuptake inhibitors (SNRIs).

**SSRIs** are useful for treating anxiety disorders in young and middle-aged adults, as shown in randomized, placebo-controlled clinical trials. Much less evidence exists, however, on the use of SSRIs in anxious older adults.

Citalopram—started at 10 mg/d and titrated to 30 mg/d as tolerated—was used in the only prospective, double-blind, randomized, controlled trial of an SSRI in older patients with anxiety disorders. In this 8-week trial, Clinical Global Impression scale scores and Hamilton Anxiety scale scores improved.<sup>15</sup> In other investigations:

- Paroxetine, averaging approximately 28 mg/d, produced a similar response in older and younger adults with PD in terms of efficacy and tolerability in a naturalistic follow-up trial.<sup>16</sup>
- Sertraline, started at 25 mg/d and titrated to 100 mg/d (maximum 150 mg/d), when combined with CBT was effective for treating older adults with anxiety disorders in a randomized, placebo-controlled trial<sup>17</sup> and specifically for those with PD in an open-label trial.<sup>18</sup>
- Fluvoxamine, median 200 mg/d, reduced anxiety symptoms in an open-label study of 12 older adults with various anxiety disorders. Most patients with GAD (57%) responded to fluvoxamine, but 3 patients with PD did not.<sup>19</sup>

• We found no studies of fluoxetine for anxiety symptoms in older adults.

An important caveat to these findings is data suggesting older adults with mixed anxiety and depression (MAD) may take longer to respond to pharmacologic and

**Table 2**  
**Recommended dosages for treating anxiety in older adults**

Medication	Starting dosage	Maximum dosage
<b>Selective serotonin reuptake inhibitors</b>		
Citalopram	10 mg/d	30 mg/d
Escitalopram	5 mg/d	10 mg/d
Fluvoxamine	25 mg/d	100 mg/d
Paroxetine	10 mg/d	20 mg/d
Sertraline	12.5 mg/d	50 mg/d
<b>Serotonin/norepinephrine reuptake inhibitors</b>		
Duloxetine	30 mg/d	60 mg/d
Venlafaxine	37.5 mg/d	150 mg/d
<b>Benzodiazepines</b>		
Lorazepam	0.5 mg/d divided bid	1 to 3 mg/d, divided bid or tid
Oxazepam	30 mg/d divided tid	45 to 60 mg/d divided tid or qid
<b>Azapirone</b>		
Bupirone	10 to 15 mg/d divided bid or tid	30 to 60 mg/d, divided bid or tid

psychotherapeutic interventions than older adults with anxiety or depression alone.<sup>20,21</sup> On the other hand, Lenze et al<sup>22</sup> found no evidence of a lower or slower response to paroxetine in depressed older adults with or without anxiety. In an open-label, flexible-dose study, escitalopram, 10 to 20 mg/d, reduced comorbid anxiety and depression symptoms and improved social functioning in 17 older outpatients.<sup>23</sup>

**SNRIs.** In a retrospective, pooled analysis of 5 randomized, placebo-controlled trials<sup>24</sup> venlafaxine ER, 37.5 to 225 mg/d, was significantly more effective than placebo in treating older adults with GAD. Several studies suggest duloxetine may be effective for treating GAD in adults, but none examined efficacy specifically for older adults.

### Clinical Point

**SSRIs and SNRIs are considered first-line therapy for anxious older adults with panic disorder and generalized anxiety disorder**



## Late-life anxiety

### Clinical Point

When short-term benzodiazepines are indicated for acute anxiety, use short half-life medications such as lorazepam or oxazepam

**Benzodiazepines'** primary benefits are rapid onset and minimal cardiovascular effects. They remain the mainstay of pharmacologic therapy for acute anxiety and can be useful as initial, short-term adjunctive therapy with SSRIs and SNRIs.

Using benzodiazepines for more than a few weeks in older adults is not recommended, however.<sup>14</sup> Potential complications of long-term benzodiazepine use in these patients include:

- excessive daytime drowsiness
- cognitive and psychomotor impairment
- confusion
- risk of falls
- depression
- paradoxical reactions
- amnesic syndromes
- respiratory problems
- potential for abuse/dependence
- breakthrough withdrawal reactions.<sup>2,25,26</sup>

For older patients, short half-life benzodiazepines—such as lorazepam (maximum 1 to 3 mg/d divided bid or tid) or oxazepam (maximum 45 to 60 mg/d divided tid or qid)—are preferred because they require only phase II metabolism and are inactivated by direct conjugation in the liver, mechanisms minimally impacted by aging.<sup>27</sup>

**Buspirone.** Investigations of anxious older adults have suggested that buspirone is effective for addressing anxiety symptoms.<sup>28,29</sup> Our experience, however, indicates that response to buspirone is inconsistent.

**Recommendations.** Based on this evidence and our clinical practice, we recommend using SSRIs or SNRIs as first-line treatment for most anxiety disorders in older adults (Table 3).

To minimize nonadherence associated with antidepressants' delayed onset of action and initial transient "jitters":

- provide patient education about medication onset and side effects
- add a short half-life benzodiazepine for the first few weeks of treatment only
- start with small doses and increase gradually.

## Psychotherapy as an alternative or adjunct

Researchers have compared the efficacy of CBT—which is effective for depression in older adults<sup>30</sup>—with that of other psychotherapies for mixed and specific anxiety disorders, including GAD and PD.

**For GAD.** Multicomponent CBT for GAD typically includes:

- psychoeducation
- thought monitoring
- cognitive restructuring
- progressive muscle relaxation and similar techniques
- breathing retraining
- problem solving
- exposure (imaginal, in vivo, worry)
- time management
- problem solving.

CBT treatment helps older adults with GAD improve on short-term measures of anxiety, worry, depression, and fear. In a clinical trial of 85 older patients with GAD who participated in 15 weekly CBT group sessions, Stanley et al<sup>31</sup> rated 45% of CBT group patients as responders, compared with 8% of a control group that received minimal contact. Additionally, 55% of CBT participants met DSM-IV-TR diagnostic criteria for GAD, compared with 81% of control patients. CBT group patients maintained improvements across measures of worry, anxiety, depression, fears, and quality of life at 3-, 6-, and 12-month assessments.

Six months of group CBT or nondirective supportive psychotherapy have shown similar efficacy in reducing worry, anxiety, and depression scores in older adults with GAD.<sup>32</sup> In a randomized trial,<sup>33</sup> group CBT produced slightly greater improvements in anxiety, depression, and pathologic worry among 75 older adults with GAD, compared with a worry discussion group (DG). CBT's only statistically significant advantage, however, was that patients spent less time worrying immediately after treatment, compared with DG patients. This difference disappeared at 6 months.

**For PD.** Evidence supports using CBT for older adults with PD. CBT for PD typically

Table 3

## Anxiety in older adults: Recommended interventions

Disorder	First-line treatment(s)	Second-line treatment(s)
<b>Generalized anxiety disorder</b>	SSRIs, SNRIs, buspirone, and/or CBT	Other newer antidepressants*
<b>Panic disorder, with or without agoraphobia</b>	SSRIs, SNRIs, and/or CBT	Other newer antidepressants*
<b>Mixed anxiety and depression</b>	SSRIs or SNRIs	Buspirone, CBT
<b>Anxiety and medical disorders</b>	Identify and treat medical cause, use SSRIs or SNRIs for primary anxiety disorder	Benzodiazepines

\* Novel agents such as mirtazapine  
CBT: cognitive-behavioral therapy; SNRIs: serotonin/norepinephrine reuptake inhibitors; SSRIs: selective serotonin reuptake inhibitors

includes interventions used for GAD but also integrates interoceptive exposure and tailored psychoeducation regarding panic symptom onset and maintenance. Older adults with PD who received 10 sessions of CBT over 12 weeks improved significantly on all symptoms measured—cognitive, behavioral, physiologic, and depression—in a study by Swales et al.<sup>34</sup> These improvements were seen immediately after treatment and at 3-month follow-up. In a separate study, a sample of 43 older adults—most of whom were diagnosed with PD—were randomly assigned to receive CBT or individual, in-home supportive therapy.<sup>35</sup> The CBT group reported greater reductions in anxiety and depression.

**For mixed anxiety disorders.** Several investigations have assessed the efficacy of CBT for older adults with mixed anxiety diagnoses and symptoms.

In one randomized trial, 84 older adults with a principal anxiety disorder diagnosis—GAD, PD, agoraphobia, or social phobia—were assigned to CBT, sertraline (maximum dosage 150 mg/d), or a waitlist.<sup>17</sup> Compared with patients assigned to the waitlist, those in the CBT and sertraline groups improved on measures of anxiety and worry immediately after treatment and at 3-month follow-up. Patients receiving sertraline worried slightly less than those who received CBT. The sertraline and CBT groups did not differ in percentage of subjects who responded to treatment or end-state functioning.

**For withdrawal support.** Gorenstein et al.<sup>36</sup> assessed withdrawal from anxiolytic medications among 42 patients age >60 with GAD, PD, comorbid GAD and PD, or anxiety disorder, not otherwise specified. Patients were randomly assigned to CBT plus medical management for medication taper or to medical management alone. Because of a high attrition rate, researchers used data only from subjects who completed the study. Compared with patients receiving medical management only, those who underwent CBT plus medical management had greater declines in anxiety and depressive symptoms from baseline. Many treatment gains were maintained at 6-month follow-up.

### CASE CONTINUED

#### Combination pharmacotherapy, CBT

You explain to Ms. W that depressed and anxious older adults frequently perceive memory difficulties. You further relate that it is possible that anxious older adults may experience memory changes because of medication side effects (particularly benzodiazepines) or interference of cognitive functioning by negative mood states. You prescribe sertraline, which is titrated to and maintained at 50 mg/d. Ms. W also participates in 10 psychotherapy sessions, which focus on psychoeducation about symptoms of GAD, relaxation strategies, sleep hygiene, grieving, and cognitive restructuring regarding her worries.

**Modifying CBT for older adults.** The quality of older adults' cognitive functioning

### Clinical Point

Some data show buspirone relieves anxiety, but our experience suggests older patients' response to this drug may be inconsistent



## Late-life anxiety

### Clinical Point

Enhance older adults' adherence to CBT by providing weekly psychoeducation, graphing symptom changes, and making reminder phone calls

may affect their response to CBT,<sup>37</sup> particularly if they exhibit impaired executive functioning.<sup>38</sup> Modifying CBT to meet the needs of older adults has not been systematically investigated.

Mohlman et al<sup>39</sup> evaluated the use of modified CBT in 8 older adults with GAD who were randomly assigned to enhanced individual CBT or a waiting list. Strategies used to enhance adherence with cognitive-behavioral procedures included:

- weekly readings of psychoeducational materials that emphasized the relationship between cognitions, behaviors, physiological functioning, and emotions
- graphing symptom changes
- reminder/troubleshooting phone calls.

Using these strategies was associated with lower anxiety and worry symptoms as well as fewer symptoms of GAD or comorbid disorders. The enhanced CBT resulted in improvement on more measures and produced large effect sizes than standard CBT when each intervention was compared with a control group assigned to a waiting list.

### CASE CONTINUED

#### Follow-up evaluation

You refer Ms. W to her primary care physician for follow-up. After 12 weeks of treatment, she reports declining anxiety symptoms. A repeat BAI indicates mild anxiousness, which she describes as minimally affecting her day-to-day activities. She continues sertraline and participation in individual psychotherapy with a particular focus on recent losses in her life.

**Delivering CBT in primary care.** Integrating CBT into anxious older patients' primary care may be desirable because:

- Older adults prefer to receive psychiatric care in this setting.<sup>40</sup>
- Collaborative-care models for depressed and anxious older adults have been successful.<sup>41</sup>

In collaborative-care models, psychiatrists may supervise a specialized case manager who may identify patients with depression and provide assessment findings and antidepressant treatment support to the patient's primary care physician. The

specialized case manager also may provide psychoeducational information, support, and limited psychotherapy to patients.

A small pilot study that provided CBT in a primary care setting for older adults who met DSM-IV-TR criteria for GAD found statistically and clinically significant declines in self-reported worry, depression, and GAD symptom severity compared with patients receiving care as usual.<sup>42</sup>

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## Related Resources

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### Drug Brand Names

Buspirone • BuSpar	Lorazepam • Ativan
Citalopram • Celexa	Mirtazapine • Remeron
Duloxetine • Cymbalta	Oxazepam • Serax
Escitalopram • Lexapro	Paroxetine • Paxil
Fluoxetine • Prozac	Sertraline • Zoloft
Fluvoxamine • Luvox	Venlafaxine • Effexor

### Disclosure

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## Clinical Point

Older patients often prefer to receive treatment for anxiety and other psychiatric disorders in a primary care setting

## Bottom Line

Selective serotonin reuptake inhibitors and serotonin/norepinephrine reuptake inhibitors are considered first-line pharmacologic interventions for treating anxiety in older adults because of their efficacy and relative tolerability. Cognitive-behavioral therapy (CBT) can be efficacious for older adults with anxiety disorders as an alternative or adjunct to pharmacotherapy. CBT may be most effective when modified to improve compliance among older patients and delivered in a primary care setting.