

# Anxiety disorders in late life: A comprehensive review

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## Abstract

Anxiety disorders are not uncommon in late life. These disorders are associated with greater rates of comorbidities with other psychiatric and medical disorders. Anxiety disorders are also associated with greater morbidity and mortality in late life. These disorders are often under- and misdiagnosed in older individuals given their symptomatic overlap with other medical disorders and drug side effects. Additionally, the diagnostic criteria for anxiety disorders have been developed for younger individuals and not for older adults. Although limited, data from controlled studies indicate that both psychotherapeutic and pharmacotherapeutic modalities are beneficial in the treatment of anxiety disorders in late life.

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## Introduction

Anxiety disorders are the most prevalent group of psychiatric disorders in the United States [1] and cause significant social and functional impairments for those suffering from these disorders [2]. Although older epidemiological studies have suggested that anxiety disorders are less common in older versus younger individuals, emerging data indicate a higher prevalence of these disorders than previously thought [3, 4]. In this article, we review the data on anxiety disorders in the late life and their treatments.

## Epidemiology

The prevalence of anxiety disorders is greater in older adults than previously acknowledged [5]. Anxiety disorders are less common than anxiety symptoms, but are still the most prevalent psychiatric disorder [6]. The rates of anxiety symptoms in older adults are generally 15% to 20%, but are over 40% in individuals who have a disability or chronic medical illness [4]. In one study, clinically significant anxiety

symptoms occurred in approximately 17.1% of older men and 21.5% of women [7]. A review of anxiety disorders in late life found that the prevalence of phobias was 3.1% to 10% [3].

In the Longitudinal Aging Study Amsterdam (LASA) the overall prevalence of anxiety disorders was estimated at 10.2% [5]. Generalized anxiety disorder (GAD) was the most common disorder (7.3%) followed by phobic disorders (3.1%). A population-based study of older adults found that the 6-month prevalences of post-traumatic stress disorder (PTSD) and sub-threshold PTSD were 0.9 and 13.1%, respectively [8].

The National Comorbidity Survey Replication (NCS-R) found that among adults 45-59 years in age, the chance of having any anxiety disorder was 30.8% [1]. Specific phobia was the most common with a prevalence rate of 14.1%. This was followed by social phobia (12.4%), PTSD (9.2%), GAD (7.7%), panic disorder (5.9%), agoraphobia without panic (1.6%), and obsessive-compulsive disorder (OCD) (1.3%).

Among adults 60 years or older, the prevalence of any anxiety disorder was 15.3%. Specific phobia was the most prevalent (7.5%) followed by social phobia (6.6%), GAD (3.6%), PTSD (2.5%), panic disorder (2%), agoraphobia without panic (1%) and OCD (0.7%).

The Enquête sur la Santé des Aînés (ESA) study of French-speaking, community-dwelling older adults showed that the 12-month prevalence rate of any anxiety problem varied from 5.6% using the DSM-IV criteria to 26.2% when all subthreshold symptoms of anxiety were considered [9]. Specific phobia was the most common (2%) followed by OCD (1.5%), GAD (1.2%), social phobia (0.7%), panic disorder (0.6%) and agoraphobia (0.3%). However, prevalence rose to 26.2% when sub-threshold or threshold (DSM-IV) anxieties were included. The highest prevalence was for specific phobia at 9.8% followed by agoraphobia (4.5%), GAD (4.1%), panic (3.2%), OCD (3.0%) and social phobia (1.4%).

## Risk factors

An epidemiological study divided risk factors for late life anxiety into external and internal [5]. External factors, or stress factors, included chronic medical illnesses, disability, and major illness in spouse. Internal factors, or vulnerability factors, included personality traits of neuroticism and low self-efficacy. In a longitudinal study, anxiety onset was best predicted by having a partner who developed a major illness [10]. The effects of stress and vulnerability factors were additive.

## Consequences

Anxiety is an evolutionary response to stressful stimuli [11]. However, pathologic anxiety can be debilitating and harmful [12]. Among older adults, anxiety is associated with reduced physical activity and functional status, poorer self-perceptions of health, decreased life satisfaction, increased loneliness, decreased quality of life, increased service use and greater cost of care [13-17].

In a community-based study, 26.1% of older adults with anxiety disorders also met criteria for major depressive disorder while 47.5% of those individuals

with major depressive disorder also met criteria for anxiety disorders [18]. In LASA, late life anxiety disorder was associated with significantly more major depression, benzodiazepine use and chronic somatic diseases [19].

A longitudinal study of community-living older adults found that when compared to baseline at 3-year follow-up, anxiety often progressed to depression or depression with GAD [20]. Additionally, onset of pure depression and depression with co-existing GAD was predicted by loss events, ill health, and functional disability. Remission rates at follow-up were 41% for individuals with depression only, 48% for pure GAD and 27% for depression with co-existing GAD, indicating that comorbid anxiety and depression are poor prognostic indicators.

The National Epidemiologic Survey on Alcohol and Related Conditions found that among older adults, the majority of individuals with GAD had a co-morbid mood or anxiety disorder [21]. Approximately 25% also had a personality disorder. Additionally, individuals with GAD were more likely to have various chronic health problems and poorer health-related quality of life.

Higher levels of anxiety and vulnerability to stress have been associated with increased risk of Alzheimer's disease and a more rapid decline in global cognition [22]. In a prospective cohort study of community-dwelling older adults, incident cognitive impairment was associated with baseline anxiety disorders in men, and anxiety symptoms in women [23]. Anxiety symptoms in women were associated with incident amnesic cognitive impairment, whereas anxiety disorders in men were associated with incident non-amnesic cognitive impairment. In a community-based cohort study, cognitive impairment no dementia (CIND) was associated with subclinical GAD in men [23]. In men, but not women, CIND was related to clinical/subclinical GAD whether depression was present or absent.

In a recently published RCT, 55.2% of individuals  $\geq 60$  years in age with GAD reported alcohol use in the past month, with a mean weekly frequency of drinks of 5.38 [24]. Approximately 41.7% of participants drank moderately ( $\leq 7$  drinks per week), 8.5% participants reported at-risk drinking (8–14 drinks per week) and 4.9% indicated heavy drinking ( $> 14$  drinks

per week). Alcohol use in this study was higher than what has been reported in a previous study of older veterans [25].

One study found that anxiety disorders in late life are also associated with chronically painful conditions and other commonly occurring diseases [26], which can result in poorer self-rated physical and/or mental health.

In a longitudinal study a baseline diagnosis of an anxiety disorder in older men, but not women, was associated with an adjusted mortality risk [27]. However, another study found that in older individuals with GAD and mixed anxiety-depression, there was no increase in mortality risk [28].

## Assessment

Anxiety disorders in late life are often under-recognized and poorly treated among older adults [4]. In one study, primary care physicians correctly made the diagnosis of GAD or any anxiety disorder in only 1.5% and 9% of the older individuals, respectively [29]. In contrast, in younger individuals, primary care physicians correctly diagnosed GAD in 34.4% [30]. The physical symptoms associated with anxiety/anxiety disorders often overlap with medical disorders that often occur in older adults [29]. Moreover, the current diagnostic criteria for anxiety disorders were developed in younger adults and may not be sensitive in older adults [31]. Furthermore, anxiety disorders in late life are often co-morbid with depression, substance use disorders and cognitive disorders resulting in greater diagnostic complexity [31].

The first step in diagnosing an anxiety disorder in late life is through a thorough history [31] corroborated by a well-informed family member or significant other [32]. A mental status examination, formal cognitive testing, ruling out or treatment of comorbid psychiatric disorders, physical examination and laboratory testing should also be performed.

The use of standardized assessment scales will help qualify and quantify the anxiety symptoms [33]. These can be divided into self-reported [33-35] and clinician-rated scales [33, 34]. Neuropsychological

testing may be useful for co-morbid personality disorders and /or cognitive disorders.

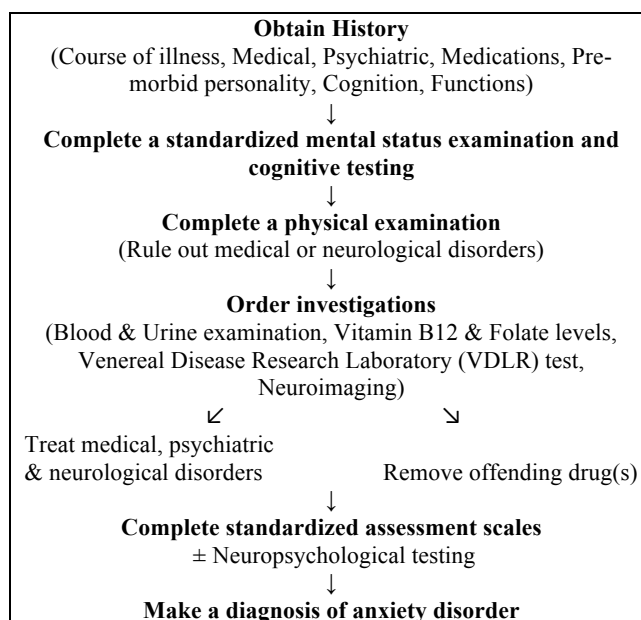


Figure 1. Assessment of anxiety disorders in late life

## Prevention

In a RCT, 170 individuals  $\geq 75$  years-old with sub-threshold depression or anxiety symptoms were randomly assigned to a preventive stepped-care program ( $n = 86$ ) or usual care ( $n = 84$ ) [36]. The participants sequentially received a watchful waiting approach, cognitive behavior therapy-based bibliotherapy, cognitive behavior therapy-based problem-solving treatment and a referral to a primary care clinician for medication if required. The 12-month incidence of depressive and anxiety disorders was 50% of the usual care. The stepped-care program was successful in halving the incidence rate of depression and anxiety at 563 euros (412 British pounds) per recipient and 4,367 euros (3,196 British pounds) per disorder-free year gained when compared with routine primary care [37].

In a follow-up to the aforementioned randomized controlled trial, the cumulative incidence rate of DSM-IV major depression or anxiety disorders during 24 months was one-half in the intervention group when compared to the usual care group [38].

## Treatments

There is a growing body of literature that both non-pharmacological and pharmacological treatment strategies are beneficial to older adults with anxiety disorders [4, 33, 39] (Tables 1 and 2).

### Non-pharmacological

#### Randomized controlled trials

In a trial by Barrowclough et al., 55 individuals with anxiety disorder (mean age: 72 years) were randomized to receive 8-12 sessions of individual and home-delivered CBT or Supportive Counseling (SC) [40]. CBT was superior to SC on the Beck Anxiety Inventory (BAI). On the Hamilton Anxiety Scale A (HAM-A) and State Trait Anxiety Inventory (STAI-T), CBT was equal to SC at the end of treatment and better than SC at 12-month follow-up.

**Table 1.** Summary of psychotherapeutic trials for anxiety disorders in late life

Reference number	Population under study	Comparisons	Outcomes
[40]	Anxiety disorders	CBT Vs. SC	CBT > SC on BAI All others scales CBT = SC
[41]	GAD	CBT Vs. DG Vs. WPG	CBT = DG > WPG
[42]	GAD	CBT Vs. MCC	CBT > MCC
[43]	Anxiety disorders	CBT-MM Vs. MM	CBT-MM > MM
[44]	Anxiety disorders	CBT Vs. Sertraline Vs. WLC	CBT < Sertraline and Sertraline > WLC
[45]	GAD	CBT Vs. EUC	CBT > EUC
[46]	GAD or other Anxiety disorders	MP Vs. EnCT	MP = EnCT

BAI: Beck Anxiety Inventory; CBT: cognitive behavioral therapy; CBT-MM: CBT plus medical management; DG: discussion group; EnCT: enhanced community treatment; EUC: enhanced usual care; GAD: generalized anxiety disorder; MP: modular psychotherapy; SC: supportive counseling; WLC: waitlist control group; WPG: waiting period group

In the study by Wetherell et al., 70 older adults with GAD (mean age: 67.1) were randomly assigned to be in a CBT, a discussion (DG) or a waiting period group (WPG) [41]. Participants in both active treatment groups improved compared to the WPG. Although individuals in the CBT group improved on more measures than the DG participants immediately after treatment, there were no differences noted at 6-month follow-up.

In a study by Stanley et al., 85 individuals  $\geq 60$  years-old with GAD were randomized to receive 15 CBT group sessions or minimal contact-controls (MCC) [42]. There were significant improvements in worry, anxiety, depression and quality of life in the CBT vs. MCC group post-treatment. Forty-five percent of individuals in the CBT group were classified as responders compared to 8% in the MCC group, but still did not reach normative functioning.

In a RCT by Gorenstein et al., 42 individuals with anxiety disorders who were  $\geq 60$  years in age were randomized to receive 13 sessions of CBT plus medical management (MM) for medication taper (CBT-MM) and MM only [43]. The investigators found that CBT-MM was superior to MM group in reducing scores on several Hopkins Symptom Checklist-90 subscales. Both groups were similar in reducing the use of anxiolytic medications and scores for worry, state, or trait anxiety and depression. Despite monthly booster sessions, there were losses of treatment gains at 6 months follow-up. Post-treatment response rates on the CGI were better in CBT-MM group compared to the MM group.

In a randomized, controlled trial, 84 individuals  $\geq 60$  years of age with a diagnosis of generalized anxiety disorder, panic disorder, agoraphobia or social phobia were randomized to be in a 15 sessions of CBT, sertraline, or waitlist control group (WLC) [44]. Although both the CBT and sertraline groups had significant improvements in anxiety, worry and depressive symptoms both at post-treatment and at three-month follow-up, the sertraline group showed superior results on worrying.



**Table 2.** Summary of pharmacotherapeutic trials for anxiety disorders in late life

Reference number	Population under study	Comparisons	Outcomes
[49]	Anxiety disorders	Oxazepam or placebo	Oxazepam > Placebo
[50]	GAD	Ketazolam or Placebo	Ketazolam > Placebo
[51]	Anxiety disorders	Alpidem or Placebo	Alpidem > placebo
[52]	Anxiety disorders	Abecarnil or Placebo	Abecarnil > Placebo
[53]	Panic disorder	Alprazolam, Imipramine or Placebo	Alprazolam = Imipramine > Placebo
[54]	GAD	Venlafaxine XR or Placebo	Venlafaxine XR > Placebo
[55]	Anxiety disorder (mainly GAD)	Citalopram or Placebo	Citalopram > Placebo
[56]	GAD	Duloxetine or Placebo	Duloxetine > Placebo

GAD: generalized anxiety disorder

In a trial by Stanley et al., older adults who were receiving treatment for GAD were randomized to receive either CBT or enhanced usual care (EUC) for three months [45]. Individuals receiving CBT had less worry and depressive symptoms and better general mental health when compared to the EUC group. Response rates defined by worry severity were higher in the CBT vs. EUC group.

In a pilot study, 31 older adults with GAD or unspecified anxiety disorder were randomized to receive either modular psychotherapy (MP) or enhanced community treatment (EnCT) [46]. The investigators found substantial improvements in anxiety symptoms, worry, depressive symptoms and mental health-related quality of life in both treatment groups. Most individuals in the enhanced community treatment group also reported receiving medications or some other form of professional treatment for their anxiety. The individuals who reported major life events or stressors and those who used involvement in

activities as a coping strategy made smaller gains than those who did not use these interventions.

### Meta-analyses

A meta-analysis of non-pharmacological interventions for late-life anxiety included a total of 15 outcome studies [47]. These studies included 495 participants (mean: 69.5 years) and provided 20 separate treatment interventions. Psychological interventions were more effective than no treatment on self-rated and clinician-rated measures of anxiety with an effect size of 0.55.

In a meta-analysis to evaluate the efficacy of cognitive behavior therapy [CBT] alone, CBT with relaxation training [RT] and RT alone for late life anxiety, data from 19 trials were reviewed [48]. The investigators found that treatments for older adults with anxiety symptoms were, on average, more effective than active control conditions. The effect sizes were comparable to CBT for anxiety in the general population or for pharmacotherapy in anxious older adults. CBT (alone or augmented with RT) did not seem to add anything beyond RT alone. The effects on depressive symptoms were smaller, with no differences among treatment types.

### Pharmacotherapy

#### Benzodiazepines

There are only four published RCTs of benzodiazepines in anxiety disorders in late life, the last of which was completed in 1997. In this section, the trials are arranged in chronological order of publication.

In a multicenter trial, 220 older outpatients with a primary diagnosis of anxiety disorders were randomized to receive oxazepam (n = 108) or placebo (n = 112) over a four-week study period [49]. Oxazepam reduced symptoms of anxiety more than placebo based on four different clinical scales.

In a double-blind trial, 63 older adults with GAD were randomly assigned to receive 15 mg of ketazolam or placebo daily for 15 days [50]. At the end of this period, if their total HAM-A scores had decreased by at least 25%, treatment was continued unchanged for an additional 15 days. For unresponsive individuals,

the ketazolam dose was increased to 30 mg daily. During the initial 15 days, 83% of the ketazolam-treated and 43% of the placebo-treated individuals responded to treatment. During the second 15 days, anxiety scores in ketazolam-treated individuals continued declining with no improvements in the placebo group.

In a RCT, 40 older individuals with anxiety disorder were randomized to receive either alpidem or placebo for three weeks after a 7-day placebo run-in period [51]. Alpidem reduced symptoms of anxiety on all rating scales when compared to placebo. The anxiolytic effect of the drug was evident from day 7 of the study.

Small and Bystritsky studied the tolerability and efficacy of abecarnil, a new partial benzodiazepine agonist, for the treatment of anxiety in older individuals [52]. After a 7-day placebo lead-in period, 182 outpatients were randomly assigned to receive high- or low dose-abecarnil or placebo for 6 weeks, followed by an abrupt discontinuation and a 2-week follow-up period. During the treatment period, the discontinuation rate from adverse events was greater for the group treated with high-dosage (44%) compared to low-dosage abecarnil (14%) or placebo (12%). The most frequently reported adverse effects were drowsiness and insomnia. The low-dosage abecarnil was superior to placebo in reducing anxiety at weeks 2, 3, 4 and 6, and was superior to high-dosage abecarnil at weeks 4, 5 and 6. More than half of the individuals in the placebo group showed at least moderate global improvement at weeks 3 and 6. One week after abecarnil discontinuation, the placebo-treated group had less anxiety than both active drug groups. The most common withdrawal effects were headache and insomnia.

Abecarnil, alpidem, and ketazolam not available in the US. The drugs reduced anxiety to a greater extent than placebo and were fairly well-tolerated. However, these studies were only conducted between 3 and 6 weeks.

### *Antidepressants*

Twenty-five older adults (55-73 years-old) with a DSM-III-R diagnosis of panic disorder were randomized to receive alprazolam, imipramine or

placebo for eight weeks [53]. There were no dropouts in the alprazolam group, 10% in imipramine group and 86% in placebo group. Both alprazolam and imipramine reduced the number of panic attacks per week and resulted in improved HAM-A and HAM-D scores compared to baseline. Both drugs were well-tolerated using half the normal adult dose daily.

In a pooled secondary analysis of five phase III randomized controlled trials, Katz et al. included 184 adults  $\geq 60$  years in age with a DSM-IV diagnosis of GAD and total scores of  $\geq 18$  on the HAM-A [54]. The participants received fixed or flexible doses of venlafaxine ER between 37.5-225 mg a day or matched placebo. On the Clinical Global Impression of Improvement (CGI-I), 66% of the individuals in the venlafaxine ER group responded when compared with 41% in the placebo group ( $P < 0.01$ ). Higher levels of depression were associated with decreased responses of anxiety symptoms. Twenty-three percent of older adults in the venlafaxine ER group discontinued treatment prematurely when compared to 31% of the individuals in the placebo group. The investigators concluded that venlafaxine ER is safe and well tolerated in older adults for the treatment of GAD.

In a RCT, 34 participants  $\geq 60$  years in age with a DSM-IV diagnosis of anxiety disorder (mainly GAD) and a HAM-A score of  $\geq 17$  were randomly assigned under double-blind conditions to receive either citalopram or placebo for eight weeks [55]. Eleven (65%) of the 17 citalopram-treated participants responded by 8 weeks when compared to four (24%) of the 17 placebo-treated participants. The response rates for the citalopram group were 10/15 participants (67%) when compared to 4/15 (27%) in the placebo group ( $P < 0.03$ ) for GAD. The most common problematic side effect of citalopram was sedation. Twelve of the 17 citalopram-treated participants complained of at least one side effect when compared to 9/17 placebo-treated participants. The most common side effects in both groups were dry mouth, nausea and fatigue. Side effects decreased in the citalopram group over time, but not in the placebo group. These results support the efficacy of citalopram in the treatment of late-life anxiety disorders.

Alaka et al. conducted a flexible-dosed study to evaluate the efficacy and safety of duloxetine 30-120 mg once daily for the treatment of GAD in older

adults [56]. Individuals with GAD who were  $\geq 65$  years in of age were randomly assigned to double-blind treatment with either duloxetine or placebo. At week 10, duloxetine was superior to placebo on mean changes from baseline in HAM-A total and Sheehan Disability Scale (SDS) global scores. Treatment-emergent adverse events occurred in  $\geq 5\%$  of duloxetine-treated individuals with a rate double of placebo including constipation, dry mouth and somnolence. The investigators concluded that treatment with duloxetine improved symptoms of anxiety and functioning in older adults with GAD with safety consistent with previous GAD studies.

### *Other medications*

Although mood stabilizers, antipsychotics, prazosin and glutamatergic medications like riluzole and memantine have been used successfully in the treatment of anxiety disorders in younger adults, there are no RCTs of these medications in older individuals [57].

### *Combination treatments*

In a sequenced treatment combining pharmacotherapy and cognitive-behavioral therapy (CBT) for GAD, individuals who were  $\geq 60$  years of age initially received 12 weeks of open-label escitalopram [58] and were randomly assigned to: 16 weeks of treatment with escitalopram (10-20 mg/day) plus modular CBT, followed by 28 weeks of maintenance escitalopram; escitalopram alone, followed by maintenance escitalopram; escitalopram plus CBT, followed by pill placebo; or escitalopram alone, followed by placebo. Escitalopram augmented with CBT increased response rates on the Penn State Worry Questionnaire, but not HAMA, compared with escitalopram alone. Both escitalopram and CBT prevented relapse.

## **Conclusions**

Both psychotherapy and pharmacotherapy have been evaluated in controlled studies for the treatment for anxiety disorders in late life. Available data indicate that any psychotherapeutic treatment was better than no treatment for anxiety disorders in late life.

Benzodiazepines and antidepressants have shown benefit in treating anxiety disorders.

## **References**

1. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62:593-602.
2. Mendlowicz MV, Stein MB. Quality of life in individuals with anxiety disorders. *Am J Psychiatry*. 2000;157:669-82.
3. Flint AJ. Epidemiology and comorbidity of anxiety disorders in the elderly. *Am J Psychiatry*. 1994;151:640-9.
4. Wetherell JL, Lenze EJ, Stanley MA. Evidence-based treatment of geriatric anxiety disorders. *Psychiatr Clin North Am*. 2005;28:871-96.
5. Beekman AT, Bremner MA, Deeg DJ, et al. Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. *Int J Geriatr Psychiatry*. 1998;13:717-26.
6. Olsson M, Broadhead EW, Weissman MM, et al. Subthreshold psychiatric symptoms in a primary care group practice. *Arch Gen Psychiatry* 1996;53:880-6.
7. Himmelfarb S, Murrell SA. The prevalence and correlates of anxiety symptoms in older adults. *J Psychol*. 1984;116:159-67.
8. van Zelst WH, de Beurs E, Beekman AT, et al. Prevalence and risk factors of posttraumatic stress disorder in older adults. *Psychother Psychosom*. 2003;72:333-42.
9. Grenier S, Prévile M, Boyer R, et al. The impact of DSM-IV symptom and clinical significance criteria on the prevalence estimates of subthreshold and threshold anxiety in the older adult population. *Am J Geriatr Psychiatry*. 2011;19:316-26.
10. De Beurs E, Beekman A, Geerlings S, et al. On becoming depressed or anxious in late life: similar vulnerability factors but different effects of stressful life events. *Br J Psychiatry*. 2001;179:426-31.
11. Marks IM, Nesse RM. Fear and fitness: An evolutionary analysis of anxiety disorders. *Theology and Sociobiology*. 1994;15:247-61.
12. Lydiard RB. The role of GABA in Anxiety Disorders. *J Clin Psychiatry* 2003;64:21-7.
13. Tinetti ME, Inouye SK, Gill TM et al. Shared risk factors for falls, incontinence, and functional dependence. Unifying the approach to geriatric syndromes. *JAMA*. 1995;273:1381-3.
14. Dew MA, Karp JF, et al. The burden of late-life generalized anxiety disorder: effects on disability,

- health-related quality of life, and healthcare utilization. *Am J Geriatr Psychiatry*. 2009;17:473-82.
15. de Beurs E, Beekman AT, van Balkom AJ, et al. Consequences of anxiety in older persons: its effect on disability, well-being and use of health services. *Psychol Med*. 1999;29:583-93.
16. Porensky EK, Dew MA, Karp JF, et al. The burden of late-life generalized anxiety disorder: effects on disability, health-related quality of life, and healthcare utilization. *Am J Geriatr Psychiatry*. 2009;17:473-82.
17. Vasiladis HM, Dionne PA, Prévile M, et al. The excess healthcare costs associated with depression and anxiety. *Am J Geriatr Psychiatry*. 2013;21:536-48.
18. Beekman AT, de Beurs E, van Balkom AJ, et al. Anxiety and depression in later life: Co-occurrence and communality of risk factors. *Am J Psychiatry*. 2000;157:89-95.
19. van Balkom AJ, Beekman AT, de Beurs E, et al. Comorbidity of the anxiety disorders in a community-based older population in The Netherlands. *Acta Psychiatr Scand*. 2000;101:37-45.
20. Schoevers RA, Deeg DJ, van Tilburg W, et al. Depression and generalized anxiety disorder: co-occurrence and longitudinal patterns in elderly patients. *Am J Geriatr Psychiatry*. 2005;13:31-9.
21. Mackenzie CS, Reynolds K, Chou KL, et al. Prevalence and correlates of generalized anxiety disorder in a national sample of older adults. *Am J Geriatr Psychiatry*. 2011;19:305-15.
22. Wilson RS, Begeny CT, Boyle PA, et al. Vulnerability to stress, anxiety, and development of dementia in old age. *Am J Geriatr Psychiatry*. 2011;19:327-34.
23. Potvin O, Forget H, Grenier S, et al. Anxiety, depression, and 1-year incident cognitive impairment in community-dwelling older adults. *J Am Geriatr Soc*. 2011;59:1421-8.
24. Ivan MC, Amspoker AB, Nadorff MR, et al. Alcohol use, anxiety, and insomnia in older adults with generalized anxiety disorder. *Am J Geriatr Psychiatry*. 2014;22:875-83.
25. Kirchner JE, Zubritsky C, Cody M, et al. Alcohol consumption among older adults in primary care. *J Gen Intern Med*. 2007;22:92-7.
26. El-Gabalawy R, Mackenzie CS, Shoostari S, Sareen J. Comorbid physical health conditions and anxiety disorders: a population-based exploration of prevalence and health outcomes among older adults. *Gen Hosp Psychiatry*. 2011;33:556-64.
27. van Hout HP, Beekman AT, de Beurs E, et al. Anxiety and the risk of death in older men and women. *Br J Psychiatry*. 2004;185:399-404.
28. Holwerda TJ, Schoevers RA, Dekker J, et al. The relationship between generalized anxiety disorder, depression and mortality in old age. *Int J Geriatr Psychiatry*. 2007;22:241-9.
29. Calleo J, Stanley MA, Greisinger A, et al. Generalized anxiety disorder in older medical patients: diagnostic recognition, mental health management and service utilization. *J Clin Psychol Med Settings*. 2009;16:178-85.
30. Wittchen HU, Kessler RC, Beesdo K, Krause P, Höfler M, Hoyer J. Generalized anxiety and depression in primary care: prevalence, recognition, and management. *J Clin Psychiatry*. 2002;63:S24-34.
31. Kogan JN, Edelstein BA, McKee DR. Assessment of anxiety in older adults: current status. *J Anxiety Disord*. 2000;14:109-32.
32. Seignourel PJ, Kunik ME, Snow L, et al. Anxiety in dementia: a critical review. *Clin Psychol Rev*. 2008;28:1071-82.
33. Stanley MA, Beck JG. Anxiety disorders. *Clin Psychol Rev*. 2000;20:731-54.
34. Beck JG, Stanley MA, Zebb BJ. Characteristics of generalized anxiety disorder in older adults: a descriptive study. *Behav Res Ther*. 1996;34:225-34.
35. Stanley MA, Beck JG, Zebb BJ. Psychometric properties of four anxiety measures in older adults. *Behav Res Ther*. 1996;34:827-38.
36. van't Veer-Tazelaar PJ, van Marwijk HW, van Oppen P, et al. Stepped-care prevention of anxiety and depression in late life: a randomized controlled trial. *Arch Gen Psychiatry*. 2009;66:297-304.
37. van't Veer-Tazelaar P, Smit F, van Hout H, et al. Cost-effectiveness of a stepped care intervention to prevent depression and anxiety in late life: randomised trial. *Br J Psychiatry*. 2010;196:319-25.
38. van't Veer-Tazelaar PJ, van Marwijk HW, van Oppen P, et al. Prevention of late-life anxiety and depression has sustained effects over 24 months: a pragmatic randomized trial. *Am J Geriatr Psychiatry*. 2011;19:230-9.
39. Blay SL, Marinho V. Anxiety disorders in old age. *Curr Opin Psychiatry*. 2012;25:462-7.
40. Barrowclough C, King P, Colville J, et al. A randomized trial of the effectiveness of cognitive-behavioral therapy and supportive counseling for anxiety symptoms in older adults. *J Consult Clin Psychol*. 2001;69:756-62.
41. Wetherell JL, Gatz M, Craske MG. Treatment of generalized anxiety disorder in older adults. *J Consult Clin Psychol*. 2003;71:31-40.
42. Stanley MA, Beck JG, Novy DM, et al. Cognitive-behavioral treatment of late-life generalized anxiety disorder. *J Consult Clin Psychol*. 2003;71:309-19.
43. Gorenstein EE, Kleber MS, Mohlman J, et al. Cognitive-behavioral therapy for management of anxiety and medication taper in older adults. *Am J Geriatr Psychiatry*. 2005;13:901-9.
44. Schuurmans J, Comijs H, Emmelkamp PM, et al. A randomized, controlled trial of the effectiveness of cognitive-behavioral therapy and sertraline versus a



- waitlist control group for anxiety disorders in older adults. *Am J Geriatr Psychiatry*. 2006;14:255-63.
45. Stanley MA, Wilson NL, Novy DM, et al. Cognitive behavior therapy for generalized anxiety disorder among older adults in primary care: a randomized clinical trial. *JAMA*. 2009;301:1460-7.
  46. Wetherell JL, Ayers CR, Sorrell JT, et al. Modular psychotherapy for anxiety in older primary care patients. *Am J Geriatr Psychiatry*. 2009;17:483-92.
  47. Nordhus IH, Pallesen S. Psychological treatment of late-life anxiety: an empirical review. *J Consult Clin Psychol*. 2003;71:643-51.
  48. Thorp SR, Ayers CR, Nuevo R, et al. Meta-analysis comparing different behavioral treatments for late-life anxiety. *Am J Geriatr Psychiatry*. 2009;17:105-15.
  49. Koepke HH, Gold RL, Linden ME, Lion JR, Rickels K. Multicenter controlled study of oxazepam in anxious elderly outpatients. *Psychosomatics*. 1982;23:641-5.
  50. Bresolin N, Monza G, Scarpini E, et al. Treatment of anxiety with ketazolam in elderly patients. *Clin Ther*. 1988;10:536-42.
  51. Frattola L, Piolti R, Bassi S, et al. Effects of alpidem in anxious elderly outpatients: a double-blind, placebo-controlled trial. *Clin Neuropharmacol*. 1992;15:477-87.
  52. Small GW, Bystritsky A. Double-blind, placebo-controlled trial of two doses of abecarnil for geriatric anxiety. *J Clin Psychiatry*. 1997;58:S24-9.
  53. Sheikh JI, Swales PJ. Treatment of panic disorder in older adults: a pilot study comparison of alprazolam, imipramine, and placebo. *Int J Psychiatry Med*. 1999;29:107-17.
  54. Katz IR, Reynolds CF 3rd, Alexopoulos GS, Hackett D. Venlafaxine ER as a treatment for generalized anxiety disorder in older adults: pooled analysis of five randomized placebo-controlled clinical trials. *J Am Geriatr Soc*. 2002;50:18-25.
  55. Lenze EJ, Mulsant BH, Shear MK, et al. Efficacy and tolerability of citalopram in the treatment of late-life anxiety disorders: results from an 8-week randomized, placebo-controlled trial. *Am J Psychiatry*. 2005;162:146-150.
  56. Alaka KJ, Noble W, Montejo A, et al. Efficacy and safety of duloxetine in the treatment of older adult patients with generalized anxiety disorder: a randomized, double-blind, placebo-controlled trial. *Int J Geriatr Psychiatry*. 2014;29:978-86.
  57. Koen N, Stein DJ. Pharmacotherapy of anxiety disorders: a critical review. *Dialogues Clin Neurosci*. 2011;13:423-37.
  58. Wetherell JL, Petkus AJ, White KS, et al. Antidepressant medication augmented with cognitive-behavioral therapy for generalized anxiety disorder in older adults. *Am J Psychiatry*. 2013;170:782-9.