Therapeutics in Late-Life Anxiety Disorders—An Update

Gert-Jan Hendriks, PhD, MD^{1,2,3}

Address

¹Centre for Anxiety Disorders “Overwaal”, Institute for Integrated Mental health Care “Pro Persona”, Pastoor van Laakstraat 48, 6663 CB, Lent, The Netherlands
E-mail: g.hendriks@propersona.nl

²Behavioral Science Institute, Radboud University Nijmegen, Nijmegen, The Netherlands

³Department of Psychiatry, Radboud University Medical Centre, Nijmegen, The Netherlands

Published online: 7 January 2014

© Springer International Publishing AG 2014

Keywords Anxiety disorders · Elderly · Aged · Panic disorder · Agoraphobia · Generalized anxiety disorder · Social anxiety disorder · Obsessive compulsive disorder · Posttraumatic stress disorder · Treatment · Cognitive behavioral therapy · Psychotherapy · Pharmacologic treatment · Antidepressants · Benzodiazepines

Opinion statement

The first choice treatments for all anxiety disorders (ADs) are cognitive behavioral therapy (CBT), pharmacological treatment with antidepressants, or their combination. However, empirical findings for these treatments in elderly suffering from ADs are still scarce. The scarcity of empirical research in this age group may be attributable to the fact that late-life anxiety is generally viewed as a minor health problem, and therefore, that we are dealing with a population that tends to go largely underdiagnosed and hence un(der)treated. From a mental-health perspective, both the material and immaterial costs of this unmet need are substantial. If left untreated, late-life anxiety has a tendency to become chronic and is associated with a substantial risk of major depression, increases in health-care utilization, reduced quality of life, more disability, and increased relative mortality risk. Additionally, most elderly suffering from ADs remain in primary care. This is partly complicated by their worries about stigmatization and reluctance to be referred to specialized mental health care. Therefore, the main issue to solve is how to increase both the detection rate and proper treatment of late-life anxiety in primary care. The following signals in elderly patients may indicate an anxiety disorder: frequent visits to the primary care physician with fluctuating, unexplained somatic symptoms, chronic and non-specific stress-related symptoms (nervousness, irritability, sleep disorder, concentration problems, emotional instability, apathy), hyperventilation, palpitation, dizziness, frequent request for tranquilizers, alcohol abuse, depression, avoidance of (social) activities. Although far from conclusive, the available evidence suggests efficacy, although limited, for CBT in late-life ADs compared with CBT for ADs in younger adults. In the treatment of late-life generalized anxiety disorder there is no difference between CBT or alternative psychological treatments like supportive counseling or a discussion group. The efficacy of antidepressant treatment

with selective serotonin re-uptake inhibitors (SSRIs) or tri-cyclic antidepressants (TCAs) seems to be comparable in both younger and older adults. However, one has to keep in mind that direct comparisons of CBT or pharmacological treatment between younger and older adults suffering from ADs have not yet been conducted. Therefore, the main treatment options in late-life ADs are comparable with those in younger adults with ADs.

Introduction

Anxiety disorders (ADs) are the most prevalent psychiatric disorders in the elderly, although an onset in later life is uncommon [1]. As a result of conceptual and methodological differences between studies, prevalence rates differ widely. Most studies showed a prevalence of late-life ADs between 6 and 10 % [2]. Generalized anxiety disorder (GAD) is frequently cited as the most common AD in elderly; see e.g. [3, 4••]. However, the National Comorbidity Survey Replication (NCS-R) revealed social anxiety disorder and specific phobias as the most prevalent ADs across the life span, with a life-time prevalence in later life of 6.6 % and 7.5 %, respectively. Additionally, the prevalence rates in later life were 2.0 % for panic disorder (PD), 1.0 % for agoraphobia, 0.7 % for obsessive-compulsive disorder, 2.5 % for posttraumatic stress disorder, and 3.6 % for GAD [1]. Belonging to an older age group is a risk factor for not receiving adequate treatment [5]. This is associated with more disability, decline in functioning, reduced quality of life and increase of health care utilization; see e.g. [6–8].

As less than 14 % of the older adults suffering from ADs are offered appropriate care [9], it is obvious that there are major obstacles both in diagnosing and in treating these patients. Most elderly people with ADs tend to attribute their symptoms to physical causes [10]. Approximately 20 % of the elderly suffering from an AD consult health care services as a result of perceived dysfunctional anxiety symptoms [11]. General practitioners (GPs) have great difficulty recognizing the condition. Separating ADs from ‘normal’ anxiety induced by medical problems like cardiovascular or obstructive pulmonary diseases may be difficult [12, 13]. This is worrying as ADs are both more prevalent in and associated with increased complications in older adults with existing medical conditions [14, 15]. As GPs will likely be targeting diagnostic procedures for the somatic symptoms, which may also cover specific physical anxiety symptomatology, the diagnosis of a comorbid AD may easily be missed [16–19].

Additionally, the current generation of elderly may be less open in sharing psychological problems, as well as have a lack in necessary skills to recognize and verbalize anxiety symptoms compared to younger generations, and may therefore have been struggling with anxiety symptoms for many years without ever receiving adequate treatment [20]. This is partly complicated by their worries about stigmatization and reluctance to be referred to specialized mental health care [21]. Also, the level of agreement between targeted screening for anxiety and depression in older patients and the diagnostic findings of GPs is low [22, 23]. Chronic somatic comorbidity and the absence of earlier mental problems also decreases the chance of a proper diagnosis [16–18, 24].

There has been extensive research into the management of ADs in populations aged between 18 and 65 years, which has led to evidence-based guidelines stipulating cognitive behavioral therapy (CBT) and antidepressants as the two treatments of choice. In addition, the few findings from randomized controlled trials (RCTs) focusing exclusively on elderly patients also tentatively indicated that both regimens may also be the optimal treatments for the management of late-life ADs; see e.g. [25, 26]. Although it was believed that CBT should be adapted to the specific needs of the elderly [27], there is no or very little actual evidence for these assumptions. Two trials showed enhancement of CBT by age-specific adaptations for GAD in older adults [28, 29]. In essence, the adaptations referred to a distinct focus on education, a frequent use of reminders and repetition of the treatment rationale, offering frequent help with the homework assignments, and the exploitation of adherence enhancement strategies. Additionally, Wetherell and colleagues [30] found efficacy for a personalized type of CBT, modular CBT, which was adapted to the preferences of the elderly patient, compared to community enhancement in the treatment of late-life GAD. In one small study, acceptance and commitment therapy (ACT) was directly compared with CBT in the treatment of late-life GAD. Although there

was no difference in efficacy between both treatments, ACT seemed more feasible for older GAD patients [31]. However, to date, there is no systematic research that has investigated which adaptations are needed to improve the effects of CBT for late-life ADs, nor studies that determined the extent to which modifications improve efficacy. However, as these trials were small and the adapted protocolized CBT was not directly compared to standard CB, except in one study [31], these findings are premature. Moreover, although Gould and colleagues [32••] confirmed the efficacy of CBT in older adults with ADs, a lower efficacy compared to younger adults was suggested. Therefore, research into new treatment approaches, e.g. enhancement strategies, is urgently needed.

In stark contrast to the volume of RCTs testing pharmacological agents for major depression in later life, psychopharmacological interventions for late-life ADs have hardly been systematically studied. The data on late-life depression showed selective serotonin reuptake inhibitors (SSRIs) and tri-cyclic antidepressants (TCAs) to be comparably effective [33, 34]. Although the tolerability of both groups of agents was satisfactory, the classical TCAs (e.g. imipramine and clomipramine) were associated with significantly more side effects and dropout than the SSRIs (24 % vs. 18 %; [33, 35]). As to the pharmacological treatment of late-life ADs, Pinquart and Duberstein [21] conducted a meta-analytic review of all available naturalistic studies and RCTs, and recommended antidepressants as the treatment of choice for late-life anxiety. The findings warrant a more balanced interpretation, however. Although all 23 reviewed studies tested pharmacological treatments, only four were RCTs evaluating specific late-life ADs. One of these showed venlafaxine to be superior to placebo in the treatment of late-life GAD [36], while two reported large effect sizes for SSRIs in the management of mixed ADs [37, 38], with the distinction that in these latter two trials over 70 % of the patients were diagnosed with GAD. And lastly, in the fourth study, both alprazolam and imipramine showed large effect sizes compared to placebo in the treatment of late-life PD. This was, however, a small-scale pilot-study [39]. With a total number of 324 participants and cohorts ranging from 25 to 184 patients, the majority of these four RCTs were too small-scale to found the recommendations on. Recently, Gonçalves and Byrne published a meta-analysis of RCTs in late-life GAD and found similar efficacy in both pharmacological and psychological treatments [40••]. In the past six years, five more RCTs with pharmacological treatment in late-life ADs have appeared [41, 42•, 43–45]. Compared to placebo, efficacy was showed for duloxetine as well as quetiapine in late-

life GAD [41, 44], whereas both sertraline and buspirone were similar effective [45]. Both paroxetine and CBT were effective in the treatment of late-life PD [42•]. Lenze and colleagues reported modest efficacy of escitalopram compared to placebo in late-life GAD [43]. Augmentation or combination studies of antidepressants and psychotherapy in late-life ADs are scarce. To date, one study showed enhanced response with modular CBT in the acute treatment phase of late-life GAD with escitalopram. At the long term, both escitalopram and CBT prevented relapse. Adding modular CBT to elderly GAD-patients with no or not sufficient response on escitalopram is a useful strategy in increasing response rates [4••].

In contrast to guidelines, elderly patients are prescribed benzodiazepines three times more often compared to antidepressants (43 % versus 14 %, [9]). Frequent use of prescription benzodiazepines is, however, associated with serious drug-related hazards, such as an increased risk of falls and fractures and possible aggravation of cognitive difficulties [46, 47]. But what are the underlying reasons for prescribing benzodiazepines, then? First of all, the agents are highly effective in the management of late-life anxiety [26]. Furthermore, many older adults resist the use of antidepressants based on a fear of dependence, prior negative experiences, a resistance to viewing their symptoms as a medical illness, and concern that antidepressants will prevent natural feelings [48]. Moreover, especially in older adults, the use of both SSRIs and TCAs is not without risk. The high prevalence of somatic syndromes such as cardiovascular diseases and arthrosis and the subsequent use of medications in this population increase the risk of interaction with SSRIs. The concurrent use of SSRIs and aspirin or nonsteroidal anti-inflammatory drugs (NSAIDs), for example, raises the risk of gastrointestinal bleeding [49, 50]. Furthermore, previous findings showed that in elderly patients using either benzodiazepines or antidepressants the risk of falls and fractures was comparable; see e.g. [51••, 52]. Even the preferred SSRIs and other antidepressants (e.g. venlafaxine) showed a higher hazard ratio compared to the TCAs [51••].

In conclusion, although CBT is effective in late-life ADs, the results of both protocolized CBTs and enhanced CBTs reported so far are modest, when compared with CBT outcome in younger adults. No differences were found between CBT and alternative psychological treatments in late-life GAD [32••, 40••, 53]. Differential age-effects are observed in the treatment of ADs, with a suggested lower efficacy in older adults; see e.g. [32••, 43, 54, 55•]. A major part

of the mentioned RCTs, both psychological and pharmacological trials, were hampered by recruitment difficulties and high attrition rates (> 20–25 %) and concerned community-dwelling, relatively younger and relatively healthy participants. Research into the available psychopharmacological approaches to ADs to date indicates that the tolerability and effectiveness of antidepressants is comparable in younger and elderly adults. However, the benefits should be weighed carefully against the preferences of the elderly patients themselves, the relative risks of antidepressants, the severity of the anxiety symptoms, as well as the available alternative, behavioral approaches like CBT. Additionally, although preliminary, it is suggested that in late-life PD with a late disease onset or shorter du-

ration of illness, CBT is to be preferred over paroxetine, whereas paroxetine might be the first choice in patients with an early onset and long duration of illness. [56]. Depending on the availability of CBT, in mild to moderate late-life ADs, CBT might be preferred compared to pharmacological treatment. In severe ADs, especially with comorbid depression, combined treatment with CBT and antidepressants is the first choice, with SSRIs as the preferred antidepressants. However, GAD is by far the most studied AD in later life. Evidence is predominantly limited to GAD, leaving most other anxiety syndromes underinvestigated, and thus preventing generalization of the results to “older” (e.g. 75-plus) elderly patients and populations suffering from specific ADs.

Treatment

Diet and lifestyle

- Some lifestyle accommodations could be helpful in the management of late-life ADs.
 - Responsible alcohol use.
 - Engagement in social activities.
 - Engagement in physical activities.
 - Increasing self-reliance.
 - Consuming healthy foods, avoiding fast food.

Pharmacologic treatment

- Pharmacologic treatment is initiated if late-life anxiety interferes with daily functioning and reduces quality of life substantially [26, 42•, class I]. The aim is to decrease dysfunctional cognitive, emotional and physiological anxiety and accompanying avoidance behaviors as well, in order to restore self-control and self-reliance. The preferred adage for starting drug therapy compared to younger adults is to “start low and go slow”. From a clinical point of view, beginning drug therapy with 50 % of the normal dosage compared to younger adults is a good starting point, and dosage is increased at slower pace, e.g. with 50 % of the normal dosage.
- Wetherell and colleagues showed that adding modular CBT to elderly GAD patients with no or not sufficient response on escitalopram is a useful strategy in increasing response rates [4••, class II].

- In case of frail elderly patients with somatic comorbidity, it is advised to use lower therapeutic dosages.
- It is important to keep in mind that in order to assess efficacy properly, patients have to continue medication at a therapeutic dosage for at least 4 to 12 weeks (depending on the type of AD).
- SSRIs, serotonin norepinephrine reuptake inhibitors (SNRIs) and TCAs are associated with an increased risk of falls and fractures. The hazard ratio is more unfavorable for SSRIs/SNRIs compared to TCAs [51••, class II].
- Concurrent use of SSRIs and serotonergic drugs (e.g. buspirone, St. John's wort) increases the risk of the serotonin syndrome.
- Most studies point out that both the SSRIs and the TCAs are well tolerated [26, 42•].
- The risk of side effects of SSRIs and buspirone is increased by the concurrent use of St. John's wort.

Serotonin Re-uptake inhibitors (SSRIs) / Serotonergic noradrenergic re-uptake inhibitors (SNRIs)

Standard dosage	Table 1 includes the standard dosage of SSRIs and SNRIs.
Contraindications	No absolute contraindications.
Main drug interactions	SSRIs are metabolized via Cytochrome P450. The involved enzymes and SSRIs are: <ul style="list-style-type: none"> – fluvoxamine and 1A2: theophyllin, clozapine, duloxetine – paroxetine/fluoxetine and 2D6: nortriptyline, IC-anti-arrhythmics, haloperidol, phenothiazines – fluoxetine/fluvoxamine and 2C (possible): carbamazepine, diazepam, phenytoine – fluoxetine/fluvoxamine/sertraline and 3A4 (possible): alprazolam, statines, ergotamine, carbamazepine, diazepam, midazolam
Main side effects	Nausea/gastrointestinal upset, fatigue, headache, sleep disturbance, somnolence, perspiration, sexual dysfunction, loss of weight, increase of weight, hyponatraemia. Sometimes increased anxiety and/or panic attacks during the first weeks of drug therapy. (Es-)citalopram may extend the QT-interval.

Table 1. Dosage of SSRIs and SNRIs

	Starting dosage	Therapeutic dosage
SSRI		
citalopram	5 mg	10–40 mg
escitalopram	5 mg	10–20 mg
fluoxetine	5 mg	10–40 mg
fluvoxamine	25 mg	75–150 mg
paroxetine	5 mg	10–40 mg
sertraline	25 mg	50–150 mg
SNRI		
venlafaxine xr	37.5 mg	75–150 mg
duloxetine	30 mg	60–120 mg

- Special points** The combination of SSRIs with non-steroid anti-inflammatory drugs increases the risk of gastrointestinal bleeding. The combination of SSRIs with anti-platelet drugs (e.g. after myocardial infarction) increases the risk of cerebrovascular bleeding. Those risks have to be weighed against the advantage of SSRI use, considering alternative treatments. As the use of SSRIs in older people is associated with hyponatraemia, it is important to check. SSRIs are indicated for panic disorder, social anxiety disorder, obsessive-compulsive disorder, posttraumatic stress disorder and generalized anxiety disorder.

Serotonergic agonist—Buspirone

- Standard dosage** 5 mg/ day, increase by 5 mg per week to 10–15 mg/day on an administration regime of three times daily.
- Contraindications** Severe liver or kidney insufficiency, epilepsy.
- Main drug interactions** As inhibiting drugs of CYP3A4 (e.g. diltiazem, verapamil, itraconazole, erythromycin) may increase the plasma concentration of buspirone, the concurrent use of grapefruit juice has to be avoided. Decrease the dose of buspirone in the case of concurrent use of HIV-protease inhibitors or ketoconazole. Rifampicine potentiates the metabolism of buspirone.
- Main side effects** Dizziness, drowsiness, headache, nausea, perspiration, nervousness, agitation, sleep disturbance, confusion.
- Special points** Buspirone is indicated for the treatment of GAD.

Tricyclic antidepressants (TCAs)

- Standard dosage** Table 2 contains the standard dosage of TCAs.
- Contraindications** Absolute contraindication is a recent myocardial infarction. Relative contraindications are urine retention, prostate hyperplasia, cardiovascular diseases and epilepsy.
- Main drug interactions** TCAs are metabolized via Cytochrome 450. TCAs may extend the QT interval. The concurrent use of antipsychotics or cimetidine may increase the plasma concentration of TCAs. Phenobarbital may decrease the plasma concentration of TCAs. TCAs may potentiate the action of both anti-arrhythmic and sympathetic drugs, and may undo the action of methyl dopa or clonidine.
- Main side effects** Dry mouth, dizziness, constipation, sexual dysfunction, urinary problems, sweating, glaucoma, blurred vision, cognitive dysfunctioning, confusion, agitation, orthostatic hypotension, electro-cardiographic changes (e.g. abnormal QT interval), sedation, weight gain.
- Special points** Imipramine is indicated for the treatment of panic disorder; clomipramine is indicated for the treatment of obsessive compulsive disorder.

Table 2. Dosage of TCAs

	Start	Therapeutic
clomipramine	25 mg	100–150 mg
imipramine	25 mg	100–150 mg

Benzodiazepines

Special points Benzodiazepines are effective in the treatment of panic disorder, social anxiety disorder and generalized anxiety disorder [26, class I]. The use of benzodiazepines increases the risk of dependency, cognitive disturbance, amnesia, falls and fractures. Therefore, they are not considered as first choice drugs in the treatment of late-life ADs.

Antipsychotics/ Anti-convulsants /Mono-amine Oxidase Inhibitors (MAOIs)

Special points Drug-therapy with antipsychotics, anti-convulsants or MAOIs are a third or later step in the pharmacologic treatment of obsessive compulsive disorder, posttraumatic stress disorder and social anxiety disorder, respectively. However, empirical data are scarce in the treatment of those ADs in the elderly. To date, one RCT showed effectiveness of quetiapine compared to placebo in late-life GAD [44, class III]. However, this trial was rated as “low quality” [40••].

Cognitive behavioral therapy (CBT)

- CBT is initiated if late-life anxiety interferes with daily functioning and reduces quality of life substantial. The aim is to decrease dysfunctional cognitive, emotional and physiological anxiety, and accompanying avoidance behaviors as well. CBT is characterized by a modular strategy and is offered in 45–90 minute sessions once or twice a week. The nature of CBT is to train patients in skills to reduce dysfunctional beliefs, attitudes and behaviors in order to restore self-control and self-reliance. During the treatment, symptoms are monitored in order to evaluate treatment progress and outcome [25, 26, 32••; class I].
- The usual CBT modules are:
 - Psycho-education.
 - Relaxation training.
 - Cognitive restructuring of irrational thoughts, irrational worrying, agoraphobic or social phobic cognitions, and obsessive thoughts.
 - Exposure to anxiety provoking situations, activities and/or thoughts in order to reduce avoidance behaviors.
 - Response prevention of unnecessary, compulsive behaviors.
 - Relapse prevention.
- Psychotherapy research in older patients suffering from ADs consists mainly of CBT trials in GAD or mixed AD-disorders (mostly GAD, panic disorder, agoraphobia, and social anxiety disorder). In one (well-designed although small) study, CBT was compared with paroxetine in older patients with panic disorder [42•, class II]. Both CBT and paroxetine were effective and no difference was found between the two treat-

ments. CBT is not studied in obsessive-compulsive disorder, social anxiety disorder and posttraumatic stress disorder. Overall, CBT is an effective psychological treatment in late-life ADs. However, compared with younger adults, its efficacy seems limited [e.g. 32••, 54, 55•; class I].

Alternative psychological interventions

- Modular psychotherapy (MP) was developed as an alternative psychological treatment for late-life GAD. The rationale was to offer a more personalized type of psychotherapy for the typical heterogeneous older AD-patients in primary care, and to tailor it to specific symptoms and needs. MP includes psycho-education about the AD, monitoring symptoms, relaxation training, cognitive restructuring, thought stopping, exposure, behavioral activation, guidelines for improving sleep disturbance, problem-solving skills, life review, acceptance and mindfulness exercises, assertiveness training, time management, pain management and relapse prevention. Both therapist and patient discussed, according to a problem list, which modules were chosen. Patients received on average seven to eight modules. In one small study, MP was found effective compared with enhanced community treatment [30, class II].
- Acceptance and commitment therapy (ACT) focuses on accepting symptoms, noticing dysfunctional thoughts and emotions in a non-judgmental way and increasing meaningful activities. In a small pilot study ($n=16$) with older GAD patients, ACT was compared with CBT. Both CBT and ACT were effective; however, 50 % of the CBT-patient dropped out, suggesting that ACT may be more feasible [31, class III].

Compliance with Ethics Guidelines

Conflict of Interest

Gert-Jan Hendriks declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with animal subjects performed by the author.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Kessler RC et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):593–602.
2. Bryant C, Jackson H, Ames D. The prevalence of anxiety in older adults: methodological issues and a review of the literature. *J Affect Disord*. 2008;109(3):233–50.

3. Beekman AT et al. Anxiety disorders in later life: a report from the Longitudinal Aging Study Amsterdam. *Int J Geriatr Psychiatry*. 1998;13(10):717–26.
 - 4.●● Wetherell JL et al. Antidepressant medication augmented with cognitive-behavioral therapy for generalized anxiety disorder in older adults. *Am J Psychiatry*. 2013;170(7):782–9.
- This is the first augmentation study in the treatment of late-life GAD, and it showed faster and sustained response by enhancement with CBT.
5. Wang PS et al. Failure and delay in initial treatment contact after first onset of mental disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):603–13.
 6. Beekman AT et al. Anxiety and depression in later life: co-occurrence and communality of risk factors. *Am J Psychiatry*. 2000;157(1):89–95.
 7. Porensky EK 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(6):473–82.
 8. Wetherell JL et al. Quality of life in geriatric generalized anxiety disorder: a preliminary investigation. *J Psychiatr Res*. 2004;38(3):305–12.
 9. Schuurmans J et al. The outcome of anxiety disorders in older people at 6-year follow-up: results from the Longitudinal Aging Study Amsterdam. *Acta Psychiatr Scand*. 2005;111(6):420–8.
 10. Sheehan B, Philpot M, Banerjee S. Attributions of physical symptoms in patients of an old age psychiatry service. *Int J Geriatr Psychiatry*. 2002;17(1):61–4.
 11. Grenier S 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(4):316–26.
 12. Kim HF et al. Functional impairment in COPD patients: the impact of anxiety and depression. *Psychosomatics*. 2000;41(6):465–71.
 13. Kim HF, Braun U, Kunik ME. Anxiety and depression in medically ill older adults. *J Clin Geropsychol*. 2001;7(2):117–30.
 14. Bryant C, Jackson H, Ames D. Depression and anxiety in medically unwell older adults: prevalence and short-term course. *Int Psychogeriatr*. 2009;21(4):754–63.
 15. Huffman JC et al. Anxiety, independent of depressive symptoms, is associated with in-hospital cardiac complications after acute myocardial infarction. *J Psychosom Res*. 2008;65(6):557–63.
 16. Chou KL. Panic disorder in older adults: evidence from the national epidemiologic survey on alcohol and related conditions. *Int J Geriatr Psychiatry*. 2010;25(8):822–32.
 17. Chung MC et al. Posttraumatic stress disorder and general health problems following myocardial infarction (Post-MI PTSD) among older patients: the role of personality. *Int J Geriatr Psychiatry*. 2006;21(12):1163–74.
 18. Todaro JF et al. Prevalence of anxiety disorders in men and women with established coronary heart disease. *J Cardiopulm Rehabil Prev*. 2007;27(2):86–91.
 19. Wetherell JL, Maser JD, van Balkom A. Anxiety disorders in the elderly: outdated beliefs and a research agenda. *Acta Psychiatr Scand*. 2005;111(6):401–2.
 20. Wetherell JL et al. Older adults are less accurate than younger adults at identifying symptoms of anxiety and depression. *J Nerv Ment Dis*. 2009;197(8):623–6.
 21. Sirey JA et al. Perceived stigma as a predictor of treatment discontinuation in young and older outpatients with depression. *Am J Psychiatry*. 2001;158(3):479–81.
 22. Volkers AC et al. The problem of diagnosing major depression in elderly primary care patients. *J Affect Disord*. 2004;82(2):259–63.
 23. Watts SC et al. Mental health in older adult recipients of primary care services: is depression the key issue? Identification, treatment and the general practitioner. *Int J Geriatr Psychiatry*. 2002;17(5):427–37.
 24. Nuyen J et al. Accuracy of diagnosing depression in primary care: the impact of chronic somatic and psychiatric co-morbidity. *Psychol Med*. 2005;35(8):1185–95.
 25. Hendriks GJ et al. Cognitive-behavioural therapy for late-life anxiety disorders: a systematic review and meta-analysis. *Acta Psychiatr Scand*. 2008;117(6):403–11.
 26. Pinquart M, Duberstein PR. Treatment of anxiety disorders in older adults: a meta-analytic comparison of behavioral and pharmacological interventions. *Am J Geriatr Psychiatry*. 2007;15(8):639–51.
 27. Stanley MA, Beck JG. Anxiety disorders. *Clin Psychol Rev*. 2000;20(6):731–54.
 28. Mohlman J et al. Standard and enhanced cognitive-behavior therapy for late-life generalized anxiety disorder: two pilot investigations. *Am J Geriatr Psychiatry*. 2003;11(1):24–32.
 29. Stanley MA et al. Cognitive-behavioral treatment of late-life generalized anxiety disorder. *J Consult Clin Psychol*. 2003;71(2):309–19.
 30. Wetherell JL et al. Modular psychotherapy for anxiety in older primary care patients. *Am J Geriatr Psychiatry*. 2009;17(6):483–92.
 31. Wetherell JL et al. Acceptance and commitment therapy for generalized anxiety disorder in older adults: a preliminary report. *Behav Ther*. 2011;42(1):127–34.
 - 32.●● Gould RL, Coulson MC, Howard RJ. Efficacy of cognitive behavioral therapy for anxiety disorders in older people: a meta-analysis and meta-regression of randomized controlled trials. *J Am Geriatr Soc*. 2012;60(2):218–29.
- This article described the most recent meta-analysis in CBT for late-life ADs.

33. Mottram P, Wilson K, Strobl J. Antidepressants for depressed elderly. *Cochrane Database Syst Rev*. 2006;1, CD003491.
 34. Pinquart M, Duberstein PR, Lyness JM. Treatments for later-life depressive conditions: a meta-analytic comparison of pharmacotherapy and psychotherapy. *Am J Psychiatry*. 2006;163(9):1493–501.
 35. Wilson K, Mottram P. A comparison of side effects of selective serotonin reuptake inhibitors and tricyclic antidepressants in older depressed patients: a meta-analysis. *Int J Geriatr Psychiatr*. 2004;19(8):754–62.
 36. Katz IR et al. 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(1):18–25.
 37. Lenze EJ 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(1):146–50.
 38. Schuurmans J 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 Psychiatr*. 2006;14(3):255–63.
 39. Sheikh JL, Swales PJ. Treatment of panic disorder in older adults: a pilot study comparison of alprazolam, imipramine, and placebo. *Int J Psychiatry Med*. 1999;29(1):107–17.
 - 40.●● Goncalves DC, Byrne GJ. Interventions for generalized anxiety disorder in older adults: systematic review and meta-analysis. *J Anxiety Disord*. 2012;26(1):1–11.
- In this meta-analysis, no differences were found between pharmacological and psychological treatments in late-life GAD.
41. Davidson J et al. Efficacy and tolerability of duloxetine in elderly patients with generalized anxiety disorder: a pooled analysis of four randomized, double-blind, placebo-controlled studies. *Hum Psychopharmacol*. 2008;23(6):519–26.
 - 42.● Hendriks GJ et al. A randomized controlled study of paroxetine and cognitive-behavioural therapy for late-life panic disorder. *Acta Psychiatr Scand*. 2010;122(1):11–9.
- Although small, this was the first report of CBT compared with a SSRI in late-life PD. No differences were found between CBT and paroxetine.
43. Lenze EJ et al. Escitalopram for older adults with generalized anxiety disorder: a randomized controlled trial. *JAMA*. 2009;301(3):295–303.
 44. Mezhebovsky I et al. Double-blind, randomized study of extended release quetiapine fumarate (quetiapine XR) monotherapy in older patients with generalized anxiety disorder. *Int J Geriatr Psychiatr*. 2013;28(6):615–25.
 45. Mokhber N et al. Randomized, single-blind, trial of sertraline and buspirone for treatment of elderly patients with generalized anxiety disorder. *Psychiatry Clin Neurosci*. 2010;64(2):128–33.
 46. Wang PS et al. Zolpidem use and hip fractures in older people. *J Am Geriatr Soc*. 2001;49(12):1685–90.
 47. Wang PS et al. Hazardous benzodiazepine regimens in the elderly: effects of half-life, dosage, and duration on risk of hip fracture. *Am J Psychiatry*. 2001;158(6):892–8.
 48. Givens JL et al. Older patients' aversion to antidepressants. A qualitative study. *J Gen Intern Med*. 2006;21(2):146–51.
 49. Weinrieb RM et al. Selective serotonin re-uptake inhibitors and the risk of bleeding. *Expert Opin Drug Saf*. 2005;4(2):337–44.
 50. Yuan Y, Tsoi K, Hunt RH. Selective serotonin reuptake inhibitors and risk of upper GI bleeding: confusion or confounding? *Am J Med*. 2006;119(9):719–27.
 - 51.●● Coupland C et al. Antidepressant use and risk of adverse outcomes in older people: population based cohort study. *BMJ*. 2011;343:d4551.
- In this large cohort the risks of SSRIs, SNRIs and TCAs in elderly patients are described. It is important to keep this in mind when treating older adults with antidepressants.
52. Hartikainen S, Lonnroos E, Louhivuori K. Medication as a risk factor for falls: critical systematic review. *J Gerontol A Biol Sci Med Sci*. 2007;62(10):1172–81.
 53. Thorp SR et al. Meta-analysis comparing different behavioral treatments for late-life anxiety. *Am J Geriatr Psychiatr*. 2009;17(2):105–15.
 54. Stanley MA et al. Cognitive behavior therapy for generalized anxiety disorder among older adults in primary care: a randomized clinical trial. *JAMA*. 2009;301(14):1460–7.
 - 55.● Wetherell JL et al. Age differences in treatment response to a collaborative care intervention for anxiety disorders. *Br J Psychiatry*. 2013;203(1):65–72.
- As most elderly are treated in primary care, it is worthwhile to realize that response to treatment is decreased in older compared to younger adults.
56. Hendriks GJ et al. Predictors of outcome of pharmacological and psychological treatment of late-life panic disorder with agoraphobia. *Int J Geriatr Psychiatr*. 2012;27(2):146–50.