

Evidence-Based Treatment of Geriatric Anxiety Disorders

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Until the last decade, anxiety disorders were a relatively unrecognized public health problem among older adults. Recent emerging data have suggested a high prevalence and significant impact of anxiety in later life. A growing body of literature provides evidence-based guidelines for care, although the data still lag far behind what is known about the treatment of depression in later life. Treatment studies of late-life anxiety and clinical standards of care in this arena have focused largely on the impact of pharmacologic and cognitive behavioral approaches, following the large body of work in younger adults with anxiety. This article presents an overview of what is known about the prevalence and impact of late-life anxiety, followed by a more detailed, critical review of the available treatment outcome literature.

Community prevalence rates for anxiety disorders in older adults range from 3.5% [1] to 10.2% [2], suggesting a higher prevalence than late-life depression. The prevalence of late-life anxiety disorders is even higher among homebound elderly [3], nursing homes residents [4], older medical patients [5], and patients who have chronic medical illness [6,7]. Of all the anxiety disorders in later life, generalized anxiety disorder (GAD) is one of the most frequently diagnosed, with community prevalence ranging from 1.9% [8] to 7.3% [2]. GAD also seems to be the most frequently diagnosed anxiety disorder in primary care, where older adults most often present

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for assistance, with rates ranging from 3.1% [9] to 11.2% [5]. Anxiety symptoms that do not necessarily meet criteria for a psychiatric diagnosis occur even more often, with rates as high as 15% to 20% in general community and primary care samples [9–11] and over 40% in patients who have disability or chronic medical illnesses [6,12]. Many available prevalence rates, however, are likely serious underestimates, given the tendencies of older adults to underreport or deny psychologic symptoms [13] and difficulties with recognition of anxiety in older medical patients [8].

Among older people, anxiety symptoms and disorders are associated with decreased physical activity and functional status, poorer self-perceptions of health, decreased life satisfaction, and increased loneliness, even with adjustments for demographic variables and severity of chronic disease [14,15]. Anxiety in later life also is associated with increased physical disability [16,17], decreased quality of life [18–20], and increased service use [21]. Rates of coexistent depressive disorders are high [22,23], and anxiety has been associated with increased mortality in men [24,25].

Despite the relatively high prevalence and significant impact, however, anxiety symptoms and disorders frequently remain unrecognized and undertreated among older adults. Although anxiety disorders are particularly prevalent in medical settings, naturalistic data from ambulatory medical care settings suggest that anxiety disorders are diagnosed during only a small percentage of office visits made by older adults (1.3%) [21]. The recognition of anxiety in older patients is complicated by the presence of coexistent medical illness and treatments as well as a symptom presentation characterized more often by a somatic picture and the reluctance to acknowledge psychologic difficulties [8]. Nevertheless, anxiety is clearly a serious public health problem for older adults.

Anxiety in older adults has traditionally been treated pharmacologically, often with benzodiazepines [26]. However, the clinical recommendations for pharmacologic treatment actually have been much broader, including suggestions to consider serotonergic antidepressants, buspirone, and venlafaxine, given efficacy data from younger adults and a small body of emerging studies with older anxious patients [27,28]. Another growing body of literature has examined the impact of cognitive-behavioral therapy (CBT) treatments for late-life anxiety [29]. These studies follow from the body of efficacy data resulting from studies conducted with younger adults [30], the increased risk of adverse drug reactions in older patients [28], data suggesting the acceptability or preference for nonmedication interventions among older adults [31,32], and the time-limited, directive, and collaborative nature of a CBT approach [33].

Method

MEDLINE and PsychINFO searches were conducted using the population term “aged” and keywords “anxiety disorders,” “treatment,” and

“therapy.” The citation index in PsychINFO also was used to locate articles that cited relevant articles on the topic of treatment of anxiety in older adults. Reference lists from review articles and chapters on the treatment of geriatric anxiety also were examined, and investigators working in the field were contacted to solicit unpublished or in-press manuscripts.

Inclusion criteria consisted of reports in which (1) participants were at least 55 years old, with a principal or co-principal diagnosis of any anxiety disorder diagnosed according to criteria of the Diagnostic and Statistical Manual of Mental Disorders III-R or IV; (2) the study design was either a randomized controlled trial in which the intervention was compared with a waiting list, usual care, or a pill or attention placebo, or it was an open-label trial or a case series of more than five participants; and (3) data were reported on at least one outcome measure, either self-reported or interviewer-rated. Studies focusing on open trials with fewer than five participants or on patients who had anxiety symptoms rather than disorders were excluded.

The studies included and the associated statistically significant findings are reported in Tables 1 and 2 [34–54]. To compare clinical significance across studies, effect sizes were calculated where possible for each outcome measure within each study using the formula for Cohen’s $d = (\text{mean}_{\text{treatment}} - \text{mean}_{\text{control}}) / \text{standard deviation}_{\text{pooled}}$. For reports of case series, the pretreatment mean for the control group mean was substituted.

Results

Cognitive behavioral interventions

Generalized anxiety disorder

Most psychotherapy studies of late-life anxiety have focused on GAD. The first such study [34] compared 14 weeks of group-administered CBT with supportive psychotherapy (SP) in a sample of 48 GAD patients who were at least 55 years of age. Participants were required to discontinue psychotropic medications before enrolling in the study. CBT consisted of education about anxiety, its symptoms, and its triggers; symptom monitoring; progressive, passive, and cue-controlled relaxation training; cognitive restructuring, in which participants were taught to challenge their thoughts about the likelihood of negative events and catastrophic consequences; and imaginal and in vivo exposure to anxiety cues and triggers using systematic desensitization. SP emphasized empathic listening. In this investigation, CBT and SP were equally effective in decreasing symptoms of anxiety and depression. Effect sizes for CBT immediately after treatment ranged from $-.06$ to $.62$, with a mean of $.20$. Post-treatment response rates, defined by an improvement of at least 20% on three of four measures of anxiety and worry, were 28% in CBT and 54% in SP. Gains were maintained or enhanced in both conditions at 6-month follow-up, and response rates at

Table 1
Summary of cognitive behavioral interventions for geriatric anxiety disorders

Study	Study design	Model/conditions	Sample (size, setting, diagnosis, age, gender, other)	Follow-up (duration and completion rate)	Outcome measures and results	Limitations/comments
Barrowclough et al [45] 2001	RCT	8–12 sessions of individual, home-delivered (1) CBT; (2) SC	55 patients (27 CBT, 28 SC) with panic disorder, social phobia, GAD, or anxiety NOS; mean age 72y; 77% women All patients stabilized on psychotropic medications for at least 3 mo before enrollment in study (58% on anxiolytics, 51% on antidepressants, 9% on both) Exclusions: certain medical conditions and cognitive impairment	43 patients completed treatment (19 CBT, 24 SC); 39 completed 12-month follow-up (16 CBT, 23 SC)	BAI, GDS: CBT > SC at post, 12 mo BDI: CBT = SC at post, 12 mo HAMA, STAI-T: CBT = SC at post, CBT > SC at 12 mo	Attrition, results not reported separately by diagnosis.
Carmin et al [42] 1998	Case series based on chart review	Inpatient multidisciplinary treatment including at least 2 h/d of exposure and response prevention; education about OCD, anxiety management skills training, family therapy, group CBT	11 patients with OCD from inpatient psychiatric unit; mean age 69y; gender not reported; some patients received concurrent pharmacotherapy Exclusions: psychosis, mental retardation, gross neurological impairment	Information not reported	Patient-rated improvement: mean 7/10 Staff-rated responder (50% reduction in symptoms): 72%	No standard objective outcome measures; multifaceted inpatient intervention; retrospective case series design.

Gorenstein et al [46] 2005	RCT	13 individual sessions of (1) CBT plus MM; (2) MM alone	42 patients (23 CBT + MM, 19 MM) with GAD, panic disorder, or anxiety NOS, and on anxiolytic medication for at least 8 wk; mean age 68y; 50% women Exclusions: major depression, history of bipolar disorder or psychosis, substance abuse, recent suicidality, serious medical condition, and cognitive impairment	28 patients completed treatment (14 CBT + MM, 14 MM); 11 CBT patients completed 6 monthly booster sessions and 6-mo follow-up	Medication use, CGI, STAI-T, PSWQ, BDI, SCL-Anxiety: CBT + MM = MM SCL Phobia, OC, Som, GS: CBT + MM > MM Gains in medication use, CGI, SCL Anxiety, and SCL Phobia maintained at follow-up	Attrition, results not reported separately by diagnosis.
King and Barrowclough [44] 1991	Case series	3–12 individual sessions of CBT; 6 patients were seen in their own homes	10 patients with panic disorder, GAD, or agoraphobia; mean age 73y; 80% women; 7 patients on psychotropic medications Exclusions: organic impairment and psychosis	10 patients completed treatment; 9 patients completed 3–6-mo follow-up	Self-reported panic, dizziness, headaches, agoraphobic avoidance, hypochondriacal beliefs: 7/10 patients showed no symptoms and 9/10 decreased symptoms at post, 8/9 showed no symptoms, 9/9 showed decrease at follow-up BAI: 6/8 improved at post, 5/7 maintained gains at follow-up BDI: 6/7 improved at post, 3/7 maintained gains at follow-up	No comparison group, variability of treatment

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Table 1 (continued)

Study	Study design	Model/conditions	Sample (size, setting, diagnosis, age, gender, other)	Follow-up (duration and completion rate)	Outcome measures and results	Limitations/comments
Ladouceur <i>et al</i> [40] 2004	Case series	14 individual sessions CBT.	8 GAD patients; mean age 64y; 7 women, 1 man; 5 patients stabilized on psychotropic medications for at least 8 wk Exclusions: suicidal intent, substance dependence, history of schizophrenia, bipolar disorder, or organic mental disorder	8 patients completed treatment, 6-and 12-mo follow-ups	PSWQ $d = 2.4$; WAQ $d = 1.6$; WDQ $d = 1.6$; BAI $d = 1.0$; BDI $d = 1.1$ Gains maintained at follow-up	No comparison group, young sample (oldest patient was 71y).
Mohlman <i>et al</i> [37] 2003	RCT	Study 1: (1) 13 individual sessions of CBT; (2) WL Study 2: (1) 13 individual sessions of enhanced CBT (ECBT); (2) WL	Study 1: 27 GAD patients (14 CBT, 13 WL); mean age 66y; 70% women Study 2: 15 GAD patients (8 ECBT; 7 WL); mean age 68y; 60% women Exclusions, both studies: use of psychotropic medications, active suicidality, major depression, psychosis, organic brain disease, use of medications with anxiety-like effects, cognitive impairment	Study 1: 21 patients completed treatment, 6 monthly booster sessions, and 6-mo follow-up (11 CBT, 10 WL) Study 2: 15 patients completed treatment, booster sessions, and follow-up (8 ECBT, 7 WL)	Study 1: BAI, BDI, PSWQ, STAI-T, SCL Anxiety, SCI GS: CBT = WL Study 2: BAI, PSWQ, SCL Anxiety, SCI GS: ECBT > WL BDI, STAI-T: ECBT = WL Gains maintained at follow-up	Small sample; no direct comparison between CBT and ECBT; WL rather than alternative treatment.

Mohlman and Gorman [38] 2005	RCT	(1) 13 individual sessions of CBT for patients with intact EF, improved EF, and impaired EF; (2) WL	32 GAD patients (10 intact EF, 5 improved EF, 7 impaired EF, 10 WL); mean age 69y; 53% women Exclusions: current major depression, recent suicidality, history of psychotic symptoms, use of anxiolytic or antidepressant medications	30 patients completed treatment (8 intact EF, 5 improved EF, 7 impaired EF, 10 WL); 15 CBT patients (5 intact EF, 5 improved EF, 5 impaired EF)	BAI: intact EF = improved; EF = impaired; EF = WL BDI: improved EF > WL PSWQ: intact EF = improved; EF > WL STAI-T: Improved EF > impaired; EF = WL; SCL-GSI: improved; EF > WL = impaired EF Improved EF group completed 12-mo follow-up	Small group sizes.
Radley et al [43] 1997	Multiple baseline design	4-wk no-treatment control period followed by 8 group sessions of CBT	9 patients with specific phobia, agoraphobia, social phobia, or GAD; mean age 71y; 7 women, 2 men; 1 on psychotropic medication for 4 wk prior to enrollment	6 patients completed treatment	HADS-A $d = .37$; HAMA $d = .88$; GAS $d = 1.1$; STAI-T $d = 1.0$; STAI-S $d = .39$; FI $d = 0$; PSI $d = .51$; CAQ $d = .26$; ELI $d = -.17$	Attrition; no comparison group; no follow-up.
Stanley et al [34] 1996	RCT	14 group sessions of (1) CBT; (2) SP	48 GAD patients (26 CBT, 20 SP; 2 dropped before randomization); mean age 68y; 71% women; patients required to discontinue psychotropic medications Exclusions: current psychotherapy, serious medical conditions, substance abuse, psychosis, and cognitive impairment	31 patients completed treatment and 6-mo follow-up (18 CBT, 13 SP)	GAD severity, percent worry, PSWQ, WS, STAI-T, HAMA, DBI, HAMD, FQ: CBT = SP Gains maintained at follow-up	Attrition; assessors not blind to treatment condition.

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Table 1 (*continued*)

Study	Study design	Model/conditions	Sample (size, setting, diagnosis, age, gender, other)	Follow-up (duration and completion rate)	Outcome measures and results	Limitations/comments
Stanley <i>et al</i> [35] 2003	RCT	(1) 15 group sessions of CBT; (2) MCC	85 GAD patients (39 CBT, 41 MCC); 5 dropped before randomization; mean age 66y; 75% women; patients required to discontinue psychotropic medications Exclusions: current psychotherapy, substance abuse, serious medical conditions, psychotic symptoms, and cognitive impairment	66 patients completed treatment (29 CBT, 35 MCC); 27 CBT patients completed 12-mo follow-up	GAD severity, PSWQ, STAI-T, HAMA, BDI, GDS, HAMD, QOLI, LSI-Z: CBT > MCC WS: CBT = MCC Gains maintained at follow-up	Attrition; MCC rather than alternative treatment.
Stanley <i>et al</i> [39] 2003	RCT	(1) 8 individual sessions of CBT; (2) usual care (UC)	12 medical patients with GAD (6 CBT, 6 UC); mean age 71y; 83% women; 50% on psychotropic medications Exclusions: suicidality, psychosis or bipolar disorder, substance abuse, and cognitive impairment excluded	9 patients completed treatment (5 CBT, 4 UC)	GAD severity, PSWQ, BDI, SF-36 VT: CBT > UC BAI, QOLI, SF-36 MH, RE, GH, PF, RP, BP, SF: CBT = UC	Small sample; no follow-up; UC rather than alternative treatment.

Swales et al [41] 1996	Open-label trial	10 individual sessions of CBT	20 panic disorder patients; mean age 63y; 80% women Exclusions: bipolar disorder, psychosis, borderline personality disorder, OCD, substance abuse within past 6 mo, current use of anxiolytics or other anxiety treatment, cognitive impairment, and unstable cardiopulmonary conditions	15 patients completed treatment and 3-mo follow-up	ACQ $d = 1.0$; BSQ $d = 1.1$; TPRPS $d = .7$; MI $d = .6$; FQ $d = .9$; BAI $d = 1.6$; Panic attacks $d = 1.0$ Gains maintained at follow-up	No comparison group.
Wetherell et al [36] 2003	RCT	12 group sessions of (1) CBT; (2) DG focused on common topics of worry among older adults; (3) WL	75 GAD patients (26 CBT, 26 DG, 23 WL); mean age 67y; 80% women; 40% on psychotropic medications Exclusions: history of mania or psychosis, cognitive impairment, current psychotherapy, substance abuse, and lack of recent medical check-up	57 patients completed treatment (18 CBT, 18 DG, 21 WL); 18 CBT patients and 17 DG patients completed 6-mo follow-up	GAD severity: CBT = DG > WL; DG = WL Percent worry: CBT > DG; CBT = WL; DG = WL PSWQ: CBT = DG > WL HAMA, BAI, HAMD, SF-36 SF: CBT = DG = WL BDI, SF-36 RE, VT: CBT > WL; DG = WL, CBT = DG CBT = DG on all measures at 6 mo	Attrition; attention placebo rather than alternative treatment.

Abbreviations: ACQ, Agoraphobia Cognitions Questionnaire; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BP, SF-36 Bodily Pain; BSQ, Body Symptoms Questionnaire; CAQ, Cognitive Anxiety Questionnaire; CGI, Clinical Global Impression; ECBT, enhanced CBT; ELI, Effects on Life Inventory; FI, Fear Inventory; FQ, Fear Questionnaire; GDS, Geriatric Depression Scale; GH, SF-36 General Health; GSI, Global Severity Index; HADS-A, Hospital Anxiety and Depression Scale-Anxiety; HAMA, Hamilton Anxiety Scale; LSI-Z, Life Satisfaction Index; MH, SF-36 Mental Health; MI, Mobility Inventory for Agoraphobia; NOS, not otherwise specified; PF, SF-36 Physical Functioning; PSI, Physical Symptom Inventory; PSWQ, Penn State Worry Questionnaire; QOLI, Quality of Life Index; RE, SF-36 Role Functioning - Emotional; RP, SF-36 Role Functioning - Physical; SCL, Hopkins Symptom Checklist; SF, SF-36 Social Functioning; SF-36, Medical Outcomes Study 36-item Short Form Health Survey; STAI-T, Spielberger State-Trait Anxiety Inventory-Trait; TPRPS, Texas Panic-Related Phobia Scale; TPRPS, Texas Panic-Related Phobia Scale; WAQ, Worry and Anxiety Questionnaire; WDQ, Worry Domains Questionnaire.

Table 2
Summary of psychopharmacological interventions for geriatric anxiety disorders

Study	Study design	Model/conditions	Sample (size, setting, diagnosis, age, gender, other)	Follow-up (duration and completion rate)	Outcome measures and results	Limitations/comments
Bresolin et al [52] 1988	Prospective randomized controlled trial	Ketazolam vs placebo	63 outpatients; multicenter; aged 66–85 (mean 74y) with GAD for at least 1 mo and HAMA \geq 18	15 d of placebo or ketazolam for 15 d Nonresponders in both conditions received an additional dose of ketazolam Responders continued with the same treatment 60 completed first phase, 59 completed the study	At 15 days: HAMA: ketazolam > placebo Response rates: HAMA \geq 25%; 83% ketazolam vs 43% placebo ($P \leq 0.01$)	Short trial with unusual study design making second phase results hard to characterize. Ketazolam is not available in the US. 25% reduction in HAMA is not usually considered response. Current GAD criteria are 6 mo not 1 mo. Nevertheless, these data support acute efficacy of benzodiazepines for late-life GAD.
Frattola et al [53] 1992	Prospective randomized controlled trial	Alpidem vs placebo	40 outpatients at two sites; aged 65–80 (mean 70y), with GAD (n = 33) or adjustment disorder with anxious mood (n = 7) of at least 1 mo duration	3 wk; 37 completed	HAMA, STAI, VAS: alpidem > placebo Response rates: HAMA \geq 25%; 55% alpidem vs 15% placebo ($P = .02$)	Alpidem is not available in the US. Short trial. 25% reduction in HAMA is not usually considered response.

Katz et al [55] 2002	Pooled secondary analysis of 5 phase III randomized controlled trials	Venlafaxine XR vs placebo	184 outpatients; multisite; aged 60+ (mean 66y) with GAD	8 wk (2 studies provided 24-wk data), 134 completed 8 wk	<p>Completer analysis: HAMA, CGI, HAD: venlafaxine > placebo</p> <p>Response rates: HAMA \geq 50%: 65% venlafaxine vs 39% placebo ($P \leq .05$); CGI 1 or 2: 77% venlafaxine vs 48% placebo ($P \leq .01$)</p> <p>ITT analysis: HAD: venlafaxine > placebo; HAMA, CGI: venlafaxine = placebo</p> <p>Response rates: HAMA \geq 50%: 53% venlafaxine vs 38% placebo (ns); CGI 1 or 2: 66% venlafaxine vs 41% placebo ($P < .01$)</p> <p>Response rates and tolerability were comparable to younger adults.</p>	Limited by retrospective nature of data and industry sample. Nevertheless, this study provides evidence that venlafaxine is efficacious for late-life GAD.
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Table 2 (continued)

Study	Study design	Model/ conditions	Sample (size, setting, diagnosis, age, gender, other)	Follow-up (duration and completion rate)	Outcome measures and results	Limitations/comments
Koepke et al [54] 1982	Prospective randomized controlled trial	Oxazepam vs placebo	220 outpatients; multicenter; "all but one" aged ≥ 60 (mean age 67.5y) with anxiety neurosis ($n = 201$); adjustment reaction with anxiety ($n = 7$) or anxiety reaction with depression ($n = 12$)	4 wk; 182 completed (roughly equivalent dropouts in drug and placebo groups)	Completer analysis: HAMA, Physician's Target Symptom Scale, Hopkins 35-item Symptom Checklist, and Global Improvement Scale: oxazepam > placebo	Completer-only analysis (although roughly equivalent dropouts); short trial. "Anxiety neurosis" is non-specific diagnosis. Nevertheless this trial demonstrates benzodiazepine efficacy for late-life anxiety disorders.
Lenze et al [56] 2005 ^a	Prospective randomized controlled trial	Citalopram vs placebo	34 outpatients; single site; aged 60+ (mean 69y) with GAD ($n = 31$), panic disorder ($n = 2$), or PTSD ($n = 1$) and HAMA ≥ 17	8 wk; 29/34 completed	HAMA: citalopram > placebo ($d = .52$) Response rates: (HAMA $\geq 50\%$ reduction or CGI = 1 or 2) 65% citalopram compared with 24% placebo ($P < .02$)	Small study with some diagnostic heterogeneity (though mainly GAD). This study provides preliminary evidence that SSRIs are efficacious for geriatric anxiety disorders, particularly GAD.
Sheikh et al [57] 2004	Open-label trial	Sertraline	10 outpatients; single site; mean age 72.5, with panic disorder	12 wk; Completion rate unknown	90% panic-free in week before last visit HAMA $d = .96$ CGI $d = 3.17$	Small open-label study. Nevertheless, data are promising for SSRIs in late-life panic disorder.

Sheikh and Swales [58] 1999	Pilot randomized controlled trial	Imipramine vs alprazolam vs placebo	25 outpatients; single site; age 55–73 (mean 61y) with panic disorder	8 wk; 18/25 completed (dropout = 0% in alprazolam; 10% in imipramine; 86% in placebo)	No group comparisons conducted due to small sample sizes HAMA: imipramine $d = 1.6$; alprazolam $d = 1.5$; placebo $d = .5$ HAMD: imipramine $d = 1.6$; alprazolam $d = 1.4$; placebo $d = .6$	Study was terminated early because of concerns that imipramine was causing adverse events. On unblinding, this concern was not substantiated.
Wylie et al [59] 2000	Open-label trial	Fluvoxamine	19 outpatients; single site; aged 50+ (mean 67y), with GAD (n = 11), panic disorder (n = 3), GAD and panic (n = 3), or OCD (n = 2)	21 wk; 12/19 completed	Completer analysis: HAMA $d = 1.02$ Response rates: HAMA $\geq 50\%$, 67%; CGI 1 or 2: 58% ITT analyses: response rates: HAMA $\geq 50\%$: 42%; CBI 1 or 2: 37%	Small open-label study with diagnostic heterogeneity. Large dropout rate limits efficacy.

Abbreviations: CGI, Clinical Global Impression; HAD, Hospital Anxiety and Depression; HAMA, Hamilton Anxiety Scale; ITT, Intent-to-treat; ns, not significant; SSRI, selective serotonin reuptake inhibitor; STAI, Spielberger State-Trait Anxiety Inventory; VAS, Visual Analogue Scale.

^a Lenze et al [51] reported an effect size of .79.

this time were 50% (CBT) and 77% (SP), a difference that was not significant. Although this study was the first randomized controlled psychotherapy trial among older adults with a diagnosed anxiety disorder, a number of serious limitations warrant caution in the interpretation of results, namely, the absence of an inactive control condition, the relatively young age and demographic homogeneity of the sample, the use of nonblind raters to assess outcomes, and the relatively brief follow-up interval.

In a follow-up study designed to address some of these limitations, 85 adults with GAD who were at least 60 years old were withdrawn from psychotropic medications (when appropriate) and offered 15 weeks of group-administered CBT or a minimal contact control (MCC) condition [35]. The CBT protocol in this investigation was similar to the one described earlier. The effects of CBT on measures of worry, anxiety, depression, and quality of life were superior by comparison with MCC, with effect sizes ranging from $-.05$ to 1.1 (mean, $.71$). Gains were maintained over a 1-year follow-up period. Post-treatment response rates, defined as in the previous trial, were 45% (CBT) and 8% (MCC). By the 12-month follow-up, the response to CBT was 63%. Strengths of the study included the relatively large sample size, the attention to quality of life outcomes, and 12-month follow-up. However, the study sample was still relatively young and demographically restricted. The absence of an alternative active treatment condition also limited conclusions about the specific benefits of CBT.

Another team of investigators [36] compared interventions consisting of 12 weeks of group-administered CBT, an attention placebo consisting of a discussion group (DG) focused on worry-provoking topics, and a waiting list (WL), using a sample of 75 older adults with GAD, 40% of whom were taking psychotropic medications. This CBT protocol was similar to the one described earlier. CBT participants did better than WL participants on five measures of anxiety, depression, and quality of life. DG was superior to WL on two measures of anxiety. However, CBT was superior to DG only on one measure of anxiety, and this difference was no longer significant at the 6-month follow-up. Effect sizes for CBT relative to WL ranged from $.39$ to 1.4 , with a mean of $.71$. Effect sizes for CBT relative to DG ranged from $-.11$ to $.45$, with a mean of $.24$. In both active treatment groups, patients tended to maintain or enhance their gains over time. Post-treatment response rates, defined as in earlier studies, were 33% in CBT, 33% in DG, and 5% in WL. By the 6-month follow-up, response rates were 50% in CBT and 53% in DG. This study is the only one to date that has compared CBT simultaneously with active and inactive control conditions. However, as in the previous studies, patients included in this trial were relatively young, healthy, well educated, and mainly white, and thus were not representative of more heterogeneous groups of older adults.

Another independent investigation [37] compared standard, individually administered CBT with WL in a sample of 27 older adults with GAD and also compared an enhanced form of individually administered CBT with

WL in a sample of 15 older adults with GAD. None of the patients in any condition was taking psychotropic medications. Enhanced CBT included the standard CBT elements of relaxation training, cognitive therapy, prevention of overly cautious behaviors, problem-solving skills training, daily structure, and sleep hygiene, as well as additional attention to at-home practice assignments, reminder telephone calls, and weekly reviews of concepts and techniques. No significant group differences were found between standard CBT and WL on any outcome measure. Effect sizes ranged from .09 to 1.0, with a mean of .43. However, enhanced CBT participants did significantly better than WL participants on two outcome measures, and significantly fewer enhanced CBT participants than WL participants met GAD criteria after the intervention. Effect sizes ranged from .04 to 1.6, with a mean of .81. The response rate to enhanced CBT (defined as in previous trials) was 75%, relative to 40% in standard CBT, and 9% to 14% in WL. Gains were maintained in the enhanced CBT condition at 6-month follow-up after monthly booster sessions. Overall, results suggest that CBT enhancements to counteract cognitive changes associated with aging may help to improve the response of anxious older adults. Unfortunately, enhanced and standard CBT were not directly compared in this study, and sample sizes were small. As in other studies, patients also were relatively young, largely white, and high functioning.

A follow-up investigation compared CBT with a WL among 32 older GAD patients who had intact executive function (EF), impaired EF, and those who initially showed impaired EF but also demonstrated improvement in cognitive function along with anxiety symptoms [38]. CBT in this study followed the enhanced format described above, with reminder telephone calls and feedback on at-home practice assignments. Results suggest that individuals with impaired EF did not respond to CBT (mean effect size .31 relative to WL, and no patients classified as responders), whereas those with intact and improved EF were more likely to respond (mean effect sizes of .78 and 1.3 and response rates of 50% and 67%, respectively, compared with WL). This study makes a unique contribution in exploring predictors of response to CBT in older adults with GAD and the possible impact of cognitive limitations, although samples were quite small and replication of study findings is necessary.

In an effort to examine the value of CBT for a broader and more representative sample of older adults, a small sample of 12 primary care patients who had GAD, half of whom were taking psychotropic medication, were assigned to receive eight sessions of individually administered CBT or usual care (UC). The response to CBT was superior to UC on measures of anxiety and depression [39]. CBT in this protocol included psychoeducation, symptom monitoring, relaxation training, cognitive therapy, exposure, problem-solving skills training, and guidelines for good sleep. Effect sizes ranged from .41 to 3.7, with a mean of 1.3, and all five patients who completed CBT (100%) were classified as responders. In the UC group, 25% of patients were classified similarly. However, sample sizes were very small, and

conclusions await completion of a larger clinical trial. Nevertheless, this investigation was an important initial effort to disseminate anxiety treatment to the primary care setting, where most older adults with GAD present for treatment. Patients in this trial also were somewhat older, less well educated, and more ethnically diverse than in previous studies.

A recent promising case series presented data on a form of CBT based on intolerance of uncertainty as a key feature of GAD [40]. In this study, eight older adults with GAD received 14 weekly sessions of individual CBT consisting of awareness training, increasing tolerance of uncertainty using behavioral experiments (eg, driving to an event at an unknown location without taking the route the day before), reevaluating beliefs about the usefulness of worry, problem-solving skills training, exposure to worrisome thoughts using a looped tape, prevention of behaviors used to distract attention or neutralize the worry, and relapse prevention by reviewing skills learned and distinguishing between normal and pathologic worry. Seven of the eight participants no longer met diagnostic criteria for GAD after treatment, and these gains were maintained at 6- and 12-month follow-ups. The mean effect size was 1.7. Future investigations will need to compare this protocol with an alternative condition in a randomized trial.

Panic disorder

To date, no randomized controlled psychosocial intervention trials have been conducted exclusively among older adults with panic disorder. In an open-label trial, 20 older adults whose symptoms met criteria for panic disorder with or without agoraphobia, none of whom was taking anxiolytic medication, received 10 individual 90-minute sessions of CBT consisting of education, challenging inappropriate or maladaptive thoughts, muscle relaxation, breathing, and exposure to panic cues and triggers. Results showed large and clinically significant gains on measures of panic, anxiety, and depression [41]. Effect sizes ranged from .6 to 1.6, with a mean of 1.0. Although this study suggests that older adults can be treated successfully for panic disorder using exposure to internal sensations and external triggers without adverse cardiac or other consequences, the lack of any control condition seriously limits the conclusions that can be drawn.

Obsessive-compulsive disorder

The only report [42] on the treatment of geriatric obsessive-compulsive disorder (OCD) that met criteria for inclusion in this review was a retrospective chart review of 11 older patients who received treatment in an inpatient behavioral medicine unit. Treatment was multidisciplinary and included at least 2 hours per day of exposure to obsessional thoughts and situations combined with the prevention of ritualized, compulsive responses. Additional treatment components included education about OCD, anxiety management training, family therapy, and group CBT. Some patients also received adjunctive pharmacotherapy, but no details were reported. Information on

the duration of treatment also was not reported. Outcomes included self-reported improvement on 11-point scales (0 to 10) for the frequency of obsessions and time spent engaging in compulsive rituals. Patients were classified as treatment responders if they experienced a 50% reduction in targeted OCD symptoms, as rated by staff. Self-reported improvement and staff-rated response rates were both high. No long-term follow-up data were reported. Weaknesses of this investigation include the retrospective chart review methodology, lack of a comparison condition, and lack of follow-up.

Mixed anxiety disorders

In a small open trial, nine patients who had specific phobias, agoraphobia, social phobia, or generalized anxiety symptoms were evaluated before and after a 4-week baseline control period and then received 8 weeks of group-administered CBT, consisting of relaxation and breathing training, avoidance reduction, increasing self-confidence, strategies for coping with anxiety, and cognitive therapy [43]. Patients also received booster sessions 4 and 12 weeks after treatment. There was a significant increase in a measure of cognitive anxiety during the baseline control period. After treatment, patients improved significantly on several measures of anxiety symptoms, with a mean effect size of .56. The use of a baseline no-treatment period in this study was a creative method for controlling for the effects of time passage without resorting to a WL condition. However, the small sample size and lack of longer-term follow-up restrict the ability to generalize the findings.

In a case series of 10 patients who had panic disorder, GAD, or agoraphobia, individual CBT was offered over 3 to 12 sessions [44]. CBT in this trial included self-monitoring, reinterpretation of physical sensations as nonthreatening, controlled breathing, and behavioral experiments. Some patients had comorbid conditions such as depression and hypochondriasis. Most patients improved, and most maintained their gains at 3- to 6-month follow-up. Because of differences in outcome measures, however, it was not possible to calculate effect sizes. Limitations included diagnostic heterogeneity and the lack of a comparison condition.

A randomized trial with 55 anxious older adults compared 8 to 12 sessions of individual, home-delivered CBT to supportive counseling (SC) [45]. Most of the sample (51%) had panic disorder, whereas 2% had social phobia, 19% had GAD, and 28% had anxiety disorder not otherwise specified (NOS). Specific CBT elements varied by disorder but included education, cognitive restructuring, and, for the panic patients, exposure to bodily sensations associated with panic attacks as well as to external triggers. The SC condition focused on empathic listening. One of the strengths of this investigation was that all participants had failed at least one 3-month trial of psychotropic medication before enrollment in the study and also failed to recover after an additional 6-week baseline period following

enrollment but before the initiation of psychotherapy. Results provided some evidence for the superiority of CBT on self-ratings of anxiety and depression immediately after treatment, with better performance for CBT on most measures across a 12-month follow-up period. Effect sizes for CBT immediately after treatment ranged from 0.1 to .74, with a mean of .38. Response rates, defined by a 20% reduction on two measures of anxiety, were 71% in CBT and 39% in SC. One major limitation of this study was the failure to report results separately by diagnosis, at least for the panic disorder patients.

Another recently completed study investigated the efficacy of CBT plus medication management (MM) versus MM alone in 42 older adults who wished to discontinue their use of anxiolytic medication [46]. At enrollment, patients had been taking medications, including benzodiazepines (62%), meprobamate (12%), antidepressants (17%), opiates (5%), valerian (2%), and diphenhydramine (2%), for at least 8 weeks. Patients had GAD (55%), panic disorder (17%), comorbid panic disorder and GAD (9%), or anxiety disorder NOS (19%). CBT was conducted in 13 individual 50-minute sessions, with components that included education about anxiety, monitoring anxiety symptoms, diaphragmatic breathing, progressive muscle relaxation, cognitive restructuring, prevention of overly cautious behaviors, exposure to internal and external anxiety cues, problem-solving skills training, daily structure, guidelines for managing medication withdrawal, and sleep hygiene. MM involved 13 weekly 15-minute sessions and included medication taper, discussing symptoms, and monitoring efficacy and side effects. Results indicated that CBT plus MM was more effective than MM alone in reducing scores on several Hopkins Symptom Checklist-90 subscales, with equivalent efficacy in reducing dependence on anxiolytic medications. However, there was no differential efficacy on worry, state or trait anxiety, or depression. CBT effect sizes ranged from -0.3 to $.95$, with a mean of $.40$. Gains tended to erode by the 6-month follow-up, despite the fact that patients received monthly booster sessions. However, response rates at post-treatment, defined according to global clinician rating, were 64% in CBT and MM and 36% in MM alone. The greatest strength of this investigation was the focus on patients wishing to discontinue psychotropic medications, particularly benzodiazepines, the long-term use of which is often contraindicated in older adults because of adverse effects on cognition and balance. Limitations included an attrition rate of 39% from CBT and the failure to report results separately by diagnostic group.

Pharmacologic intervention

Given that older adults with anxiety disorders present most often for care to medical settings, it is no surprise that pharmacologic intervention is the most frequently used avenue of care. Naturalistic data, in fact, demonstrate that approximately half of the patients assigned an anxiety disorder

diagnosis in primary care were prescribed an anxiolytic or antidepressant [21]. However, very few treatment trials have addressed the impact of pharmacologic treatment for anxiety disorders in older patients. Consequently, clinical recommendations are often derived from clinical trials with younger adults, even though outcome data from these studies may not generalize to older samples, given the differential pharmacokinetic properties of medications, the greater potential impact of adverse events among older patients, and the increased frequency of coexistent medical problems that complicate treatment. The literature in this area that met inclusion criteria for this report has focused largely on the use of benzodiazepines and antidepressant medications. Other medications with potential benefit (eg, buspirone, a typical antipsychotic) warrant further investigation [47,48].

Benzodiazepines

Benzodiazepines continue to be the medications most frequently prescribed for anxiety in later life, with epidemiologic data suggesting general prevalence rates of 10% [49] to 12% [50] and as high as 43% for individuals with persistent anxiety [51]. However, only three randomized controlled trials have investigated the impact of benzodiazepines for anxiety disorders in later life [52–54]. Two of these trials have focused on GAD [52,53], and one trial has studied an earlier, potentially comparable category of anxiety neurosis [54]. In all of these studies, medication was efficacious relative to placebo, with treatment effects evident within as early as 7 days [53]. Only one study [53] provided sufficient data for the calculation of effect size, with d ranging from 0.79 to 0.95 (mean d , .85). Response rates to medication ranged from 57% to 83% [52,53], but the definition of response in these trials was more liberal than in more recent studies [55,56]. Attrition rates were generally low ($\leq 17\%$). Overall, the data from these trials suggest the value of benzodiazepines for treating anxiety disorders in older adults, although only one of the medications investigated (oxazepam) is commonly used or even available in the United States [54].

The treatment duration across all benzodiazepine trials was brief, ranging from 3 to 6 weeks. Although this treatment interval is typical and expected for acute pharmacologic trials with these types of medications, studies with longer treatment intervals are of value given the chronic nature and serious impact of anxiety disorders, particularly GAD, in later life. However, longer-term treatment with benzodiazepines generally is not recommended, particularly for older adults, given the potential for more serious adverse events. Benzodiazepines can affect cognitive functioning and psychomotor performance, leading to an increased risk of hip fractures caused by falls, a decreased ability to drive, and an increase in memory problems. As such, clinical recommendations for the use of benzodiazepines with older adults suggest that lower doses of compounds with shorter half-lives be used over a briefer interval than might be the case for younger patients [28].

Antidepressant medications

Five pharmacotherapy studies of late-life anxiety disorders have examined the value of antidepressant medications. Two of these studies focused on patients who had panic disorder [57,58], one study focused on a mixed group of patients who had GAD, panic disorder, or OCD [59], and two studies focused on GAD [55,56].

Panic disorder. Sheikh and Swales [58] compared the effects of imipramine, alprazolam, and placebo for the treatment of panic disorder in 25 older patients. This study was stopped prematurely because of concerns about adverse events and high attrition, resulting in sample sizes that were too small to generate solid conclusions regarding the efficacy of either medication. Nevertheless, the calculation of effect sizes suggests equivalent effects of imipramine and alprazolam relative to placebo for anxiety and depressive symptoms. In a subsequent small open-label trial of sertraline [57], 10 patients who had panic disorder were treated over the course of 12 weeks. Results at post-treatment suggest significant improvement in anxiety symptoms according to the Hamilton anxiety scale and ratings of global severity. Of course, the small sample size and lack of controlled design seriously limit the conclusions that can be drawn from this report. Nevertheless, the data from these two preliminary studies are encouraging with regard to the potential pharmacologic treatment of late-life panic disorder.

Mixed anxiety disorders. In an open trial with 19 patients whose symptoms met criteria for GAD, panic disorder, or OCD, Wylie and colleagues [59] demonstrated some potential value of fluvoxamine. Response rates ranged from 37% to 67%, with variation based on the measure used and the evaluation of completer or intent-to-treat samples. Response rate among the GAD subgroup was 57%, but interestingly, none of the three patients who had panic disorder responded. These data highlight the need for attention to diagnostic heterogeneity. Although the cut-off age for study inclusion was only 50 years, data analyses suggest comparable response for patients who are 50 to 64 years and those who are 65 years or older. Nevertheless, the mean age of the study sample was still relatively young. The small sample size, high attrition rate (37%), and uncontrolled nature of the trial also limit conclusions that can be drawn.

Generalized anxiety disorder. Katz and colleagues [55] conducted a secondary analysis of data from patients aged 60 years and older who participated in five randomized clinical trials of venlafaxine for the treatment of GAD. Results suggest a significant impact of treatment relative to placebo for older adults, although findings were less robust in intent-to-treat analyses. Response rates were generally comparable across older and younger samples. Attrition rates from venlafaxine (older adults, 23% and younger adults, 27%) and placebo (older adults, 31% and younger adults, 28%)

also were equivalent across age subgroups. As such, these data support the potential value of venlafaxine for the treatment of late-life GAD. However, little attention was given to the maintenance of gains over long-term follow-up. The power to detect significant age effects also was limited, and the replication of these findings is necessary in a prospective study with a larger sample of older adults. Older patients in these studies also were relatively young and likely more healthy and functional than older patients seen in primary care.

In the only prospective, randomized clinical trial of a serotonergic antidepressant conducted to date, Lenze and colleagues [56] examined the effect of citalopram versus placebo in a sample of 34 patients, 31 of whom were diagnosed with GAD. Results demonstrate significant improvement in Hamilton anxiety ratings, with an effect size of 0.52, calculated according to the formula used in this review. Response rates were 65% after citalopram and 27% after placebo. Again, however, no data addressed long-term maintenance of gains, and patients were recruited largely through the media, limiting generalizability to more representative samples of older adults with mental health needs.

Discussion

Overall, the available data suggest the potential value of both CBT and pharmacologic treatments for late-life anxiety disorders, most notably GAD. The CBT literature consistently documents a positive response relative to no treatment, although response rates are lower than is evident for younger adults and there is no consistent evidence of a significant CBT benefit relative to other psychosocial treatment options (eg, supportive therapy). The response to pharmacologic treatment may be more robust [60], although differential definitions of response across psychologic and pharmacologic studies and the lack of direct comparisons of these two forms of treatment make this kind of comparison very difficult. However, there remains room for significant future advances in both treatment arenas.

Across the majority of clinical trials conducted to date, samples of patients are relatively homogeneous and often are not representative of older adults in general with regard to age, functional status, ethnicity, education, or medical health. For the most part, treatment trials also have been conducted in academic mental health settings where older patients do not present routinely for clinical care. Relatively few data have addressed the value of treatment in more real-world settings, with patients who represent a broad range of demographic and clinical characteristics. Future research will need to examine more closely the outcomes of treatment for late-life anxiety in primary care and other community-based settings where older adults typically often receive services. A number of efforts are ongoing in this domain and data from these trials will provide more evidence related to the translational value of available efficacy data.

Another serious limitation of the research literature in both psychologic and pharmacologic domains is the predominant focus on late-life GAD. Although GAD is one of the most prevalent anxiety disorders among older adults, other common and potentially more disabling anxiety conditions, including agoraphobia and post-traumatic stress disorder (PTSD), have largely been neglected. The lack of attention to PTSD is particularly striking given the high prevalence among war veterans, Holocaust survivors, and disaster victims [61]. Specific phobias that interfere with necessary medical procedures, such as fear of injections and claustrophobia, also merit research and clinical attention.

In the psychologic research literature, the rates of attrition in many trials are higher among older adults (21%–39%) than among younger adults (approximate average of 10%) [62]. Attention needs to be given to this issue, perhaps with improved treatment strategies that better meet the needs of individual patients. In pharmacologic treatment studies, attrition is somewhat lower (15%–23%) [23,55] and comparable to what is seen in trials of younger adults with anxiety disorders.

One clear limitation of the CBT literature to date, particularly with regard to studies of GAD, is the focus on group interventions. A group intervention was selected for early trials in this area given the hypothesized importance of social support and reduced cost for older patients. However, meta-analytic work with data from younger adults has documented reduced outcomes for group versus individual interventions [62], which may explain some of the relatively modest response rates in early trials of CBT for late-life GAD. More recent work [39,46] and ongoing studies are focused on the use of individual treatments that allow for greater idiosyncratic tailoring of treatment to the clinical and personal needs of patients, with the goal of creating an intervention that is better suited to more heterogeneous populations seen in typical care settings.

Another limitation specific to CBT trials includes the emphasis of primary analyses on outcome data from completers. Pharmacologic trials, on the other hand, more often analyze data on an intent-to-treat basis. Completer analyses tend to inflate treatment effects. Furthermore, psychotherapy studies typically use a large number of outcome measures, often assessing the same construct, which complicates the interpretation of results when significant effects are found on some but not all measures. Finally, there is no psychotherapeutic comparison condition equivalent to a pill placebo. It is impossible to craft a double-blind psychotherapy study. So-called nonspecific therapeutic effects are associated with almost any credible intervention, making it difficult to find a significant effect for a comparison of a CBT with an alternative treatment or attention placebo. The comparison with wait list control conditions or usual care, however, not only raise ethical issues, they sometimes fail to deliver the critical component of equal expectancies for each condition.

Studies of both psychologic and pharmacologic treatment will need to focus further on the long-term maintenance of treatment gains. In studies of

CBT to date, follow-up is limited to 12 months or less, and no attention has been given to comparisons of methods for increasing response further over follow-up or to extension of gains beyond this time interval. Pharmacologic trials also have not yet attended to the nature and efficacy of various maintenance options. These issues are of critical importance given the enduring nature and significant impact of anxiety disorders in later life.

Summary

Available data point to the potential value of pharmacologic and cognitive-behavioral interventions for the treatment of late-life anxiety disorders, with modest improvement and response rates in most cases. Further efficacy work is needed to investigate the impact of improved psychosocial approaches that allow for more idiosyncratic attention to the needs of older patients and outcomes following a broader range of pharmacologic treatments. Attention in this work needs to be given to long-term outcomes and generalizability of findings to broader and more representative samples of older patients. Additional effectiveness work also is needed to address the value of various treatment options in the settings where older adults typically receive care (eg, primary care, community-based programs) and to the methods for optimal dissemination of evidence-based interventions.

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