A randomized controlled trial of the effectiveness of cognitive-behavioral therapy and sertraline versus a wait-list control group for anxiety disorders in older adults.

Schuurmans, J.; Comijs, H.; Emmelkamp, P.M.; Gundy, C.M.; Weijnen, I.J.C.; van Hout, M.A.

published in
American Journal of Geriatric Psychiatry
2006

DOI (link to publisher)
10.1097/01.JGP.0000196629.19634.00

document version
Publisher's PDF, also known as Version of record

A Randomized, Controlled Trial of the Effectiveness of Cognitive–Behavioral Therapy and Sertraline versus a Waitlist Control Group for Anxiety Disorders in Older Adults

Josien Schuurmans, M.Sc., Hannie Comijs, Ph.D., Paul M. G. Emmelkamp, Ph.D., Chad M. M. Gundy, M.Sc., Ingrid Weijnen, M.Sc., Marcel van den Hout, Ph.D., Richard van Dyck, Ph.D., M.D.

Objective: *This study is the first to investigate the relative effectiveness of cognitive–behavioral therapy (CBT) compared with a selective serotonin reuptake inhibitor (SSRI; sertraline) in a randomized, controlled trial on the treatment of anxiety disorders in older adults.* **Method:** *Eighty-four patients 60 years of age and over with a principal diagnosis of generalized anxiety disorder, panic disorder, agoraphobia, or social phobia were randomly assigned to one of three conditions: 15 sessions of CBT, pharmacologic treatment with an SSRI (sertraline; maximum dosage 150 mg), or a waitlist control group. Participants completed measures of primary outcome (anxiety) and coexistent worry and depressive symptoms at baseline, posttreatment, and at three-month follow up.* **Results:** *Attrition rates were high in both treatment groups. Consequently, findings are based on a relatively small sample of completers (N = 52). Although both CBT and sertraline led to significant improvement in anxiety, worry, and depressive symptoms both at posttreatment and at three-month follow up, sertraline showed superior results on worry symptoms. Effect size estimates for CBT were in the small to medium range both at posttreatment (mean d = 0.42) and at three-month follow up (mean d = 0.35), whereas effect sizes for sertraline fell into the large range (posttreatment mean d = 0.94 and three-month follow up mean d = 1.02). The waitlist condition showed virtually no effects (posttreatment mean d = .03).* **Conclusions:** *Our findings strongly suggest that the pharmacologic treatment of late-life anxiety with SSRIs has not been given the proper attention in research to date.* (Am J Geriatr Psychiatry 2006; 14:255–263)

Key Words: Anxiety disorders, aged, randomized controlled trial, sertraline, cognitive therapy

Received September 4, 2004; revised September 29, 2005; accepted October 28, 2005. From the Department of Psychiatry and Institute for Research in Extramural Medicine, VU Medical Centre, Amsterdam (JS, RvD); GGZ Buitenamstel, Amsterdam, The Netherlands (HC); the Department of Clinical Psychology, University of Amsterdam, Amsterdam, The Netherlands (PMGE); the Department of Clinical Epidemiology and Biostatistics, VU Medical Centre, Amsterdam (CMG); Riagg Maastricht, Maastricht, The Netherlands (IW); and the Department of Social Sciences, University of Utrecht, Utrecht, The Netherlands (MvdH). Send correspondence and reprint requests to Dr. Josien Schuurmans, Free University, Department of Clinical Psychology, van der Boechorststraat 1, 1081 BT Amsterdam. e-mail: j.schuurmans@psy.vu.nl

Anxiety disorders are highly prevalent in older adults[1] and are associated with increased disability, a great negative impact on quality of life,[2]and an inadequate use of healthcare services and psychotropic medication.[3] Hersen and van Hasselt[4]have argued for the development of psychosocial interventions, because the prescription of benzodiazepines or even of safer psychotropic drugs such as selective serotonin reuptake inhibitors (SSRIs) might be problematic in older adults as a result of comorbidity with physical illness and potential negative interactions with other drugs. Although this is a valid argument, a pharmacologic approach should not be discarded too hastily. In fact, randomized, controlled trials of SSRIs in older adults with depression, although limited in number, have provided evidence for the effectiveness and tolerability of these drugs in older adults,[5] even in the "older old."[6] Recently, the first randomized, placebo-controlled trial evaluating the effectiveness of an SSRI (citalopram) in the treatment of late-life anxiety has been published,[7] providing preliminary evidence for the effectiveness and tolerability of this drug in anxious older adults. However, this study awaits replication in a larger sample.

Despite the argument for the development of psychosocial interventions for the treatment of anxiety in older adults, randomized, controlled trials in this area are scarce. In mixed-age populations, empiric evidence suggests that cognitive behavior therapy is the most effective form of psychotherapy for anxiety disorders.[8] In recent years, several research efforts have been made, providing some evidence for the effectiveness of CBT in anxious older adults,[9–12] but the evidence is limited and not unequivocal.[13]

Our study is one of the first to investigate the effectiveness of an SSRI (sertraline) in a randomized, controlled trial of the treatment of anxiety disorders in older adults. Sertraline was chosen because it has been found to be effective and well tolerated both in anxious mixed-age populations,[14] and in depressed older adults, even in case of comorbid medical illness.[15] Also, in contrast to most research efforts in this area, our study examines the effectiveness of individual rather than group CBT in anxious older adults, and it includes other anxiety disorders than generalized anxiety disorder (GAD), namely panic disorder, agoraphobia, and social phobia. Furthermore, the current investigation is the first to compare CBT with a SSRI and a waitlist control group among older adults with an anxiety disorder. This study was approved by the Medical Ethical Review Board of the University Medical Centre of Maastricht.

METHOD

Participants

Participants included 84 adults, aged 60 years and over, with a principal *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*[16] diagnosis of GAD, panic disorder (either with or without agoraphobia), agoraphobia without a history of panic disorder, or social phobia. Exclusion criteria were the presence of an organic condition that provided a contraindication for the use of SSRIs, current use of antidepressant medication, a comorbid diagnosis of alcohol dependency, current participation in psychotherapy, a history of psychosis or cognitive impairment as indicated by clinical impression, and a score of less than 26 on the Mini-Mental State Examination.[17] Individuals stabilized on benzodiazepines and their therapists were instructed not to change their dose or type of medication for the duration of the study. Individuals with comorbid depression, dysthymia, or other anxiety disorders were not excluded from participation as long as their principal diagnosis was GAD, panic disorder, agoraphobia, or social phobia. Principal diagnosis was defined as the most severely disabling disorder at the present time. Participants were recruited from 2000 to 2003 through media announcements, distribution of information leaflets in pharmacies, and clinics for general practice and among referrals for treatment to community mental health centers and outpatient clinics in five cities in the western and southern part of The Netherlands. All participants were selected on the basis of a structured diagnostic interview (SCID 2.0[18]) administered by psychologists who had received extensive training in this instrument.

Over a 3.5-year recruitment period, 160 subjects received a diagnostic interview, of whom 115 people (72%) fit the inclusion criteria and were invited to participate in the research. Thirty-one patients (27%) refused before providing preliminary data. Eighty-four participants remained who were randomized

into the study. Table 1 presents demographic and diagnostic information about the sample.

Procedures

All participants read and signed an informed consent form before being randomly assigned to one of three conditions: 15 weeks of CBT (N = 42), sertraline (N = 29), or a 15-week waiting period (N = 13). Randomization procedures were as follows: One envelope was filled with 62 labels stating "CBT," 62 labels stating "sertraline," and 26 labels stating "waitlist." Based on the assumption that the waitlist condition would show no effects, as is the case in comparable treatment studies,[10] we planned for fewer subjects in the waitlist condition. This distribution would yield maximum power to detect differences between CBT and sertraline while still allowing for enough power to differentiate between the active treatment conditions and the waitlist condition.[19] When a participant had completed the screening procedure, the principal researcher would then blindly take one label out of the envelope, which would then be excluded from further randomization procedures. However, although we allowed for a lengthy recruitment period and great efforts were made to contact potential participants, we could only assign 84 participants and the remaining 66 labels were not used in the randomization procedure, which is why sample sizes are unequal.

Trained psychologists and a trained research assistant performed assessment interviews at pretest, posttest, and at three-month follow up. Participants in the CBT condition were treated individually by a certified behavior therapist in 15 weekly one-hour sessions. CBT consisted of relaxation training, cognitive restructuring, and exposure. Treatment protocols for CBT were derived from prevailing treatment protocols of panic disorder,[20] GAD,[21] and social phobia[22] in mixed-age populations, which were adapted for use with older adults (our CBT protocol consisted of 15 sessions, allowing more attention to psychoeducation and repeated explanation and revision of new information and newly learned coping skills). Participating therapists took part in regular supervision meetings, which were led by certified supervisors for behavior therapy. Therapists were repeatedly and explicitly instructed to contact their project supervisor if they felt that they needed to deviate from the protocol. Their supervisor would then talk through the problem at hand to ensure that therapists would adhere to the protocol.

In the sertraline condition, patients were treated by a psychiatrist or a resident–psychiatrist in eight 20-minute sessions over a period of 15 weeks. The

TABLE 1. Descriptives of the Sample (before attrition)

Variable		Cognitive–Behavioral Therapy (N = 42)	Sertraline (N = 29)	Waitlist (N = 13)	Total (N = 84)
Age	M (SD)	70.71 (6.58)	69.79 (5.49)	66.85 (5.96)	69.80 (6.20)
Duration of anxiety (years)	M (SD)	23.33 (23.46)	29.86 (22.86)	27.22 (25.52)	26.16 (23.46)
Female	N (%)	31 (73.8)	22 (75.9)	9 (69.2)	62 (73.8)
Married	N (%)	23 (54.8)	18 (64.3)	6 (46.2)	47 (56.6)
Education					
Low	N (%)	19 (45.2)	12 (41.4)	5 (38.5)	36 (42.9)
Medium	N (%)	8 (19.0)	10 (34.5)	5 (38.5)	23 (27.4)
High	N (%)	15 (35.7)	7 (24.1)	3 (23.1)	25 (29.8)
Main diagnosis					
Generalized anxiety disorder	N (%)	14 (33.3)	10 (34.5)	5 (38.5)	29 (34.5)
Panic disorder*	N (%)	17 (40.5)	16 (55.2)	5 (38.5)	38 (45.2)
Agoraphobia†	N (%)	7 (16.7)	1 (3.4)	0 (0)	8 (9.5)
Social phobia	N (%)	4 (9.5)	2 (6.9)	3 (23.1)	9 (10.7)
Comorbid diagnosis					
Specific phobia	N (%)	17 (40.5)	5 (17.2)	2 (15.4)	24 (28.6)
Other anxiety disorder	N (%)	22 (52.4)	11 (37.9)	5 (38.5)	36 (42.9)
Depression	N (%)	7 (16.7)	8 (27.6)	2 (15.4)	17 (20.2)

*With or without agoraphobia.
†Without a history of panic disorder.
M: mean; SD: standard deviation.

protocol for sertraline included a dosage schedule adapted for older adults, in which the starter dose was lower (25 mg) and the dosage was built up more gradually than in the customary procedure (up to a minimum dose of 100 mg, which had to be reached within four weeks, and a maximum dose of 150 mg on the basis of tolerability and lack of clinical response). Medication was maintained during three-month follow up.

Measures

Outcome was assessed at posttreatment and at three-month follow up. Pre- and posttreatment measures consisted of self-report measures and a structured interview. The interview consisted of the Hamilton Anxiety Rating Scale (HARS,[23] Cronbach alpha = 0.82). The HARS was performed by two members of the research group. Interrater agreement on the HARS was measured in the initial stages of the project. Weighted kappa was 0.58, constituting moderate interrater agreement. Self-report measures included the Beck Anxiety Inventory (BAI[24]; Cronbach alpha = 0.93) and the Dutch adaptation of the Worry Domain Questionnaire (WDQ[25]; Cronbach alpha = 0.92). Items related to work situations in the WDQ were omitted because they were not considered appropriate for an older population. Depressive symptoms were measured with the Center for Epidemiological Studies Depression Scale (CES-D[26]; Cronbach alpha = 0.90). The BAI and the HARS should be considered as the primary outcome measures of this study. Assessment at three-month follow up consisted solely of self-report measures, which were distributed by mail (thereby excluding the HARS) unless participants preferred a personal interview with the researcher. Adverse effects in the sertraline condition were measured with the Fawcett checklist[27] at the last session of the sertraline protocol.

Data Analysis

Analyses of variance and chi-squared tests were used to compare participants assigned to the three conditions on pretreatment demographic and clinical variables, including number of coexistent diagnoses, number of chronic diseases, and baseline anxiety measurements.

Paired *t*-tests were used to establish improvement within each condition. When data were not normally distributed, Wilcoxon signed rank tests were performed instead of paired *t*-tests. A random coefficient regression analysis was performed to establish between-group differences with regard to improvement over time.

Two measures of clinically significant change were assessed: treatment response for anxiety, defined as an improvement of 20% on two measures of anxiety (BAI and HARS) and end-state functioning for anxiety, defined as a score of less than 10 on both the BAI and the HARS (which equals a score within the normal range). The 20% reduction criterion of treatment response in a composite measure of self-report and interview-rated instruments is frequently used in the treatment literature of anxiety in older adults.[10–12] Rates of treatment response and end-state functioning were only available for posttreatment measurements.

RESULTS

Attrition

Ten (12%) of 84 patients refused participation in the trial immediately after randomization, four of whom were assigned to sertraline, three to CBT, and three to the waitlist condition. Seventeen (23%) of the remaining 74 participants dropped out of the trial before completing CBT (N = 9), sertraline (N = 7), or waitlist conditions (N = 1), culminating in a total attrition rate of 32% (27 of the initial sample of 84 participants). There were no significant differences in attrition rates across treatment groups. One participant randomized to sertraline switched to venlafaxine in one of the first weeks of treatment as a result of adverse side effects and was excluded from outcome analysis. For completer analyses, data from 56 participants were available who completed CBT (N = 30), sertraline (N = 17), and waitlist conditions (N = 9). Another four participants failed to turn in their pretreatment questionnaires, although they did complete the HARS interview, one of which was assigned to sertraline, two to CBT, and one to the waitlist condition. Reasons mentioned for dropout from CBT included: treatment was found to be too

straining or confronting (N = 2) or too time-consuming (N = 2); participants did not agree with the treatment rationale (N = 5); and spontaneous remission of symptoms (N = 4). Reasons mentioned for dropout from sertraline included: long-term illness (N = 1), deceased before starting medication (N = 1), side effects (N = 4), anticipated side effects before actually starting medication (N = 1), and spontaneous remission of symptoms (N = 1).

No significant differences between dropouts and completers were found for sex, age, marital status, level of education, main psychiatric diagnosis, medication use, chronic illness, or duration of symptoms. Noncompleters were found to have a higher score at pretreatment on the HARS ($t = 2.33$, $df = 79$, $p < 0.05$), but not on any of the other outcome variables.

At three-month follow up, four participants (9%) refused to fill in their questionnaires. During follow up, three participants (two CBT and one sertraline participant) were given an alternative psychopharmacologic treatment because their symptoms had not sufficiently improved. These participants were excluded from follow-up analyses, leaving a sample of 39 participants (25 CBT and 14 sertraline) who were included in follow-up analyses. Waitlist participants were not included in follow-up analyses, because they were reassigned to one of the active treatment conditions after completing the 15-week waiting period.

Differences Between Therapy Groups at Pretreatment

A comparison on all pretreatment demographic and clinical variables, including the distribution of principal diagnosis and severity of anxiety symptoms at baseline using χ^2 tests and analyses of variance, demonstrated no significant differences (Table 1). After attrition, sertraline participants had a higher rate of comorbid depression at baseline than CBT or waitlist participants ($\chi^2 = 7.18^2$, $p < 0.05$). Therefore, the rate of comorbid depression was entered into completer analyses as a confounder.

Treatment Outcome

Paired *t*-tests were performed to assess within-treatment effects for each group between pretreatment and posttreatment and between pretreatment and three-month follow up. Results from Wilcoxon signed rank tests showed the same results. Table 2 presents *t* and p values, effect size estimates, and percentage of change over time by condition.

At posttreatment, both CBT and sertraline participants had improved significantly on every outcome measure. Improvement was largely maintained during three-month follow up. Participants in the waitlist condition did not show significant change on any of the outcome measures. Effect size estimates were calculated as the difference between mean pre- and posttreatment scores divided by the pooled standard deviations from the baseline and posttreatment scores (Cohen's d[28]). In general, effect sizes for CBT were in the small to medium range both at posttreatment (mean $d = 0.42$) and at three-month follow up (mean $d = 0.35$), whereas effect sizes for sertraline were in the large range (posttreatment mean $d = 0.94$ and three-month follow up mean $d = 1.02$). The waitlist condition showed virtually no effects (posttreatment mean $d = 0.03$).

Random coefficient regression analysis of patients completing treatment revealed significant group*time interactions on the WDQ ($\chi^2 = 14.54$, $df = 3$, $p < 0.001$) and the HARS ($\chi^2 = 13.82$, $df = 2$, $p < 0.01$), but not on the BAI ($\chi^2 = 5.81$, $df = 3$, $p = 0.12$) or the CES-D ($\chi^2 = 7.05$, $df = 3$, $p = 0.07$). Specific group*time interactions were calculated after the removal of main effects. These analyses showed that both CBT (mean difference [MD]: -5.97, standard error [SE]: 2.16, $df = 37$, $p < 0.01$) and sertraline completers (MD: -9.26, SE: 2.36, $df = 24$, $p < 0.001$) showed greater improvement than waitlist completers on the HARS. Sertraline completers showed greater improvement on the WDQ than waitlist completers (MD: -12.85, SE: 4.50, $df = 24$, $p < 0.01$), whereas CBT completers did not (MD: -4.12, SE: 4.24, $df = 37$, $p = 0.34$). Furthermore, sertraline completers showed greater improvement on the WDQ than CBT completers, both from pre- to posttreatment (MD: -8.73, SE: 3.04, $df = 45$, $p < 0.01$) and from pretreatment to follow up (MD: -10.11, SE: 3.13, $df = 45$, $p < 0.01$). Sertraline completers did not show greater improvement on the HARS than CBT completers (MD: -3.29, SE: 1.76, $df = 45$, $p = 0.07$).

An intent-to-treat analysis revealed significant group*time interactions on the HARS ($\chi^2 = 8.44$, $df = 2$, $p < 0.05$), but not on any of the other outcome measures. Specific group*time interaction analyses

TABLE 2. Paired *t*-Tests and p Values, Effect Size Estimates, and Percentage Change Over Time by Condition

	CBT									Sertraline							Waitlist				
	Pre–Posttreatment (N = 30)				Pretreatment–Three-Month Follow Up (N = 25)					Pre–Posttreatment (N = 17)				Pretreatment–Three-Month Follow Up (N = 14)			Pre–Posttreatment (N = 9)				
	t	p	d	%	df	t	p	d	%	df	t	p	d	%	df	t	p	d	%	df	t	p	d	%	df
BAI	3.47	<0.01	0.44	29	26	2.43	<0.05	.36	25	23	3.98	<0.01	0.86	47	13	3.25	<0.01	0.82	42	13	0.97	0.37	0.24	14	6
CES-D	2.48	<0.05	0.31	18	26	2.06	0.05	.34	17	23	3.66	<0.01	0.85	33	13	3.61	<0.01	0.94	33	12	0.00	1.00	0.00	0	6
HARS	4.39	<0.01	0.58	30	28						4.30	<0.01	0.96	43	15						−0.90	0.40	−0.37	−12	8
WDQ	5.45	<0.01	0.36	14	27	2.89	<0.01	0.35	12	24	4.36	<0.01	1.08	28	15	3.87	<0.01	1.30	30	13	1.09	0.32	0.22	7	6

d was calculated as $(M_{pre\text{-}treatment}-M_{post\text{-}treatment})/standard\ deviation_{pooled}$.
CBT: cognitive–behavioral therapy; BAI: Beck Anxiety Inventory; CES-D: Center for Epidemiological Studies Depression Scale; HARS: Hamilton Anxiety Rating Scale; WDQ: Worry Domain Questionnaire.

revealed that sertraline participants showed greater improvement on the HARS than waitlist participants (MD: -5.92, SE: 2.41, df = 39, p <0.05) but not CBT participants (MD: -2.97, SE: 1.80, df = 68, p = 0.10). CBT participants did not show greater improvement than waitlist participants on the HARS (MD: -2.95, SE: 2.24, df = 53, p = 0.19).

Treatment Response and End-State Functioning

At posttreatment, 44% of CBT participants, 57% of sertraline participants, and one waitlist participant (11%) could be classified as treatment responders. Separate χ^2 analyses of the three group comparisons revealed significant differences in treatment response rates between sertraline and waitlist ($\chi^2 = 4.87^1$, p <0.05), but not between CBT and waitlist ($\chi^2 = 3.25^1$, p = 0.08) or between CBT and sertraline ($\chi^2 = 0.60^1$, p = 0.33).

Before treatment, χ^2 analyses did not reveal any significant differences between conditions with regard to level of functioning for anxiety. After treatment, 48% of CBT participants, 47% of sertraline participants, and none of the waitlist participants fit criteria for high end-state functioning ($\chi^2 = 6.88^2$, p <0.05).

Adverse Effects in the Sertraline Group

Adverse effects that were reported by medication completers (N = 17) and that were deemed moderate to very severe by the (resident) psychiatrist at the last session of treatment were anorexia (N = 1; 5.9%), tinnitus (N = 1; 5.9%), stiffness (N = 1; 5.9%), ataxia (N = 1; 5.9%), dry mouth (N = 1; 5.9%), hypertension (N = 1; 5.9%), heart palpitations (N = 2; 11.8%), miction problems (N = 2; 11.8%), agitation (N = 2; 11.8%), increase in appetite (N = 2; 11.8%), tremors (N = 2; 11.8%), nausea/vomiting (N = 2; 11.8%), drowsiness (N = 2; 11.8%), fatigue (N = 3; 17.6%), headache (N = 3; 17.6%), anxiety and nervousness (N = 3; 17.6%), transpiration (N = 3; 17.6%), insomnia (N = 3; 17.6%), reduction of frequency of sex (N = 4; 23.5%), problematic erection or lubrication (N = 4; 23.5%), absence of orgasm (N = 4; 23.5%), lessened intensity of orgasm (N = 4; 23.5%) reduction of libido (N = 5; 29.4%), depression (N = 5; 29.4%), and pain (N = 5; 29.4%).

DISCUSSION

Implications of Our Findings

Our study was the first to compare the effectiveness of a SSRI with CBT for the treatment of anxiety disorders in older adults. We found that although both treatments led to significant improvement on all measures of outcome, sertraline completers showed greater improvement on symptoms of worry as measured with the WDQ. Moreover, effect sizes for CBT were relatively small (0.31−0.58), whereas effect sizes for sertraline fell into the large range (0.85−1.08). However, treatment response rates and rates of high end-state functioning were not significantly different between treatment groups. Some of our findings run contrary to what one might expect on the basis of results from similar studies in mixed-age populations. In most randomized, controlled trials of the treatment of anxiety disorders, SSRIs and CBT are found to be equally effective.[8]

Our findings indicate that the reluctant attitude of both researchers and general practitioners toward the use of SSRIs in late life may be unjustified. Given the fact that four participants (14%) did report adverse effects to sertraline as a reason for dropping out of the trial, which is comparable to dropout rates resulting from side effects in studies of sertraline for depression in late life (11%–19%[15,29,30]), patients should be closely monitored and better informed on what to expect from an SSRI by their physician to increase treatment adherence.

In concordance with most other treatment studies in late-life anxiety,[9,10,12] effect sizes for CBT were substantially lower and attrition rates for both CBT and sertraline were considerably higher than those found in comparable treatment studies in mixed-age populations (mean attrition rate approximately 10%).[31] These findings imply that it is important that we find ways to increase treatment adherence in anxious older adults.

CBT did not perform as well as expected on the basis of similar treatment studies in older adults. The only comparable trial that investigated individual format CBT in anxious older adults (with mixed anxiety disorders) was the study by Barrowclough et al.,[11] which yielded more positive results for CBT than our study. However, participants in Barrowclough's study were mostly treated in their own homes, which may have positively influenced both the effectiveness of treatment as well as treatment adherence. Also, 51% of participants in the Barrowclough study used antidepressants during the treatment phase, which may well have biased the results. Although treatment response rates were higher in the Barrowclough study (71% at 12-month follow up), effect sizes were also in the small to medium range at 0.34. Also, participants in other treatment studies[9,10,12] were mostly well educated, whereas in our study, 45% of CBT participants had only finished primary school.

Finally, problems with homework completion may play an important role in the moderate outcome of CBT in our study. Although we did not measure homework completion in a standardized manner, we do recall that one of the topics that came up frequently in our supervision meetings was the trouble that therapists encountered in getting participants to complete the homework. Reasons for this phenomenon were related to participants' disbelief in the usefulness of homework assignments, insecurity and difficulties in dealing with assignments, and lack of time.

Limitations

The main limitation to the present study was it is lack of power as a result of large attrition rates and the differences in sample size between conditions, which resulted from the fact that our randomization procedures were unsuccessful as a result of unforeseen recruitment problems. As a consequence, our study is not as persuasive as it might have been if other randomization procedures were used.

Also, the follow-up period of this study was relatively short (three months), considering the fact that in mixed-age populations, the outcome of CBT, tends to improve after termination of treatment.[31] However, our results showed no improvement of CBT outcome during three-month follow up.

Although completer analyses showed some significant differences in treatment effect between CBT and sertraline, it should be noted that intention-to-treat analyses did not yield the same results.

The fact that the use of sertraline was largely maintained during follow up may have biased the comparison with CBT, because evidence from younger

populations suggests that anxiety symptoms tend to recur after termination of pharmacologic treatment.[8]

Unfortunately, the Dutch review board for medical ethics did not grant us permission to allocate older adults to a placebo condition. As a consequence, we could not reliably establish whether treatment effect and reported side effects should be attributed to sertraline. The fact that treatment in our study lasted for 15 weeks (more than twice the length of most pharmacologic studies in younger populations) and the fact that treatment results were largely maintained during three-month follow up makes it less plausible that treatment effect is attributable to a placebo effect.

Relating to the inclusion of different anxiety disorders, the fact that we chose not to include measures on phobic avoidance or the frequency of panic attacks might be considered as a limitation. However, such measures would not have been appropriate for all subjects, which is why we chose two outcome measures for general anxiety symptoms, the BAI and the HARS, as the main outcome measures of this study. Also, the inclusion of different anxiety disorders might limit the generalizibility of our findings. The inclusion of agoraphobia without panic disorder in particular might induce comments on the fact that there is no specific evidence on the effectiveness of SSRIs for the treatment of this disorder. However, repeated outcome analyses excluding those with a main diagnosis of agoraphobia without panic disorder yielded similar results.

Finally, it should be noted that assessment was not blind and that follow-up assessments were solely based on self-report measures.

Recommendations and Conclusions

Future randomized, controlled trials might incorporate other psychologic interventions that might be more suitable for use with older adults (such as reminiscence therapy, which has shown positive results for the treatment of late-life depression[32]). More research is needed to firmly establish if and what modifications are needed for the appropriate use of CBT with an older population. Finally, our findings strongly suggest that the pharmacologic treatment of late-life anxiety with SSRIs has not been given the proper attention in research to date.

This research project was funded by a research grant from the Dutch Health Research and Development Council, project number 940–33-036.

Portions of the results from this study were presented at the 34th EABCT annual conference in Manchester, United Kingdom, September 2004.

The authors thank Edwin de Beurs, Ph.D., from the Department of Psychiatry at the LUMC in Leiden, The Netherlands, for his significant contribution to the initial phases of this investigation.

References

1. Beekman ATF, Bremmer MA, Deeg DJH, et al: Anxiety disorders in later life: a report from the longitudinal aging study Amsterdam. Int J Geriatr Psychiatry 1998; 13:717–726
2. Wetherell JL, Thorp SR, Patterson TL, et al: Quality of life in geriatric generalized anxiety disorder: a preliminary investigation. J Psychiatr Res 2004; 3:305–312
3. de Beurs E, Beekman ATF, van Balkom AJLM, et al: Consequences of anxiety in older persons: its effect on disability, well-being and use of health services. Psychol Med 1999; 2:583–593
4. Hersen M, van Hasselt VB: Behavioral assessment and treatment of anxiety in the elderly. Clin Psychol Rev 1992; 1:619–640
5. Schneider LS, Nelson JC, Clary CM, et al: An 8-week multicenter, parallel-group, double-blind, placebo-controlled study of sertraline in elderly outpatients with major depression. Am J Psychiatry 2003; 16:1277–1285
6. Gildengers AG, Houck PR, Mulsant BH, et al: Course and rate of antidepressant response in the very old. J Affect Disord 2002; 6: 177–184
7. 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; 16:146–150
8. Emmelkamp PMG: Behavior therapy with adults, in Bergin and Garfield's Handbook of Psychotherapy and Behavior Change. Edited by Lambert M. New York, John Wiley & Sons, 2004, pp 393–446
9. Stanley MA, Beck JG, Novy DM, et al: Cognitive–behavioral treatment of late-life generalized anxiety disorder. J Consult Clin Psychol 2003; 7:309–319
10. Wetherell JL, Gatz M, Craske MG: Treatment of generalized anxiety disorder in older adults. J Consult Clin Psychol 2003; 7:31–40
11. 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; 6:756–762
12. Stanley MA, Beck JG, Glassco JD: Treatment of generalized anxiety in older adults: a preliminary comparison of cognitive-behavioral and supportive approaches. Behavior Therapy 1996; 2:565–581
13. Mohlman J: Psychosocial treatment of late-life generalized anxiety

disorder: current status and future directions. Clin Psychol Rev 2004; 2:149–169
14. Allgulander C, Dahl AA, Austin C, et al: Efficacy of sertraline in a 12-week trial for generalized anxiety disorder. Am J Psychiatry 2004; 16:1642–1649
15. Sheikh JI, Cassidy EL, Doraiswamy PM, et al: Efficacy, safety, and tolerability of sertraline in patients with late-life depression and comorbid medical illness. J Am Geriatr Soc 2004; 5:86–92
16. Diagnostic and Statistical Manual of Mental Disorders–Text Revision, 4th Edition. Washington, DC, American Psychiatric Association, 1994
17. Folstein ME, Folstein SE, McHugh PR: Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 1:189–198
18. First MB, Spitzer RL, Gibbon M, et al: Structured Clinical Interview for *DSM–IV* Axis I Disorders–Patient Edition (SCID-I/P, Version 2.0). Lisse, The Netherlands, Swets & Zeitlinger BV, 1999
19. Woods SW, Sholomskas DE, Shear MK, et al : Efficient allocation of patients to treatment cells in clinical trials with more than two treatment conditions. Am J Psychiatry 1998; 15:1446–1448
20. Clark DM, Salkovskis PM: A Manual for the Cognitive Therapy of Panic Disorder. New York, Oxford University Press Inc, 1986
21. Borkovec TD, Costello E: Efficacy of applied relaxation and cognitive–behavioral therapy in the treatment of generalized anxiety disorder. J Consult Clin Psychol 1993; 6:611–619
22. Scholing A, Emmelkamp PMG: [Social Phobia]: Sociale fobie. Houten, Bohn Stafleu van Loghum, 1995
23. Hamilton M: The assessment of anxiety states by rating. Br J Med Psychol 1959; 3:50–55
24. Beck AT, Steer RA: Manual for the Beck Anxiety Inventory. San Antonio, TX, Psychological Corp, 1990
25. Rijsoort SV, Emmelkamp PMG, Vervaeke G: The Penn State Worry Questionnaire and the Worry Domains Questionnaire: structure, reliability and validity. Clin Psychol Psychother 1999; 6:297–307
26. Radloff LS: The CES-D scale: a self-report depression scale for research in the general population. Applied Psychological Measures 1977; 1:385–401
27. Fawcett S: Symptoms, signs, side effects checklist. Psychopharmacol Bull 1987; 2: 322–323
28. Cohen J: Statistical Power Analysis for the Behavioral Sciences, 2nd Edition. Hillsdale, NJ, Erlbaum, 1988
29. Bondareff W, Alpert M, Friedhoff AJ, et al: Comparison of sertraline and nortriptyline in the treatment of major depressive disorder in late life. Am J Psychiatry 2000; 15:729–736
30. Newhouse PA, Krishnan KR, Doraiswamy PM, et al: A double-blind comparison of sertraline and fluoxetine in depressed elderly outpatients. J Clin Psychiatry 2000; 6:559–568
31. Gould RA, Safren SA, Wash DO, et al: A meta-analytic review of cognitive–behavioral treatments, in Generalized Anxiety Disorder: Advances in Research and Practice. Edited by Heimberg RG, Turk CL, Mennin DS. New York, Guilford, 2004, pp 248–264
32. Bohlmeijer E, Smit F, Cuijpers P: Effects of reminiscence and life review on late-life depression: a meta-analysis. Int J Geriatr Psychiatry 2003; 1:1088–1094