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Venlafaxine extended-release treatment of hoarding disorder

Sanjaya Saxena and Jennifer Sumner

Hoarding disorder, classified as a separate disorder in *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. (DSM-5), is a common, chronic, and potentially disabling syndrome that can be difficult to treat. Only one previous study prospectively measured response to pharmacotherapy in compulsive hoarders, finding that hoarders responded as well to paroxetine as did nonhoarding obsessive-compulsive disorder patients. However, paroxetine was not tolerated well in that study, and the overall response was moderate. Therefore, we conducted an open-label trial of venlafaxine extended-release for hoarding disorder. Twenty-four patients fulfilling the DSM-5 criteria for hoarding disorder were treated with venlafaxine extended-release for 12 weeks. All patients were free of psychotropic medications for at least 6 weeks before the study. No other psychotropic medications, cognitive-behavioral therapy, organizers, or cleaning crews were permitted during the study. To measure the severity of hoarding, the Saving Inventory-Revised (SI-R) and the UCLA Hoarding Severity Scale (UHSS) were administered before and after treatment. Twenty-three of the 24 patients completed treatment. Hoarding symptoms improved significantly, with a mean 36% decrease in UHSS scores and a mean 32% decrease in SI-R scores. Sixteen of the 23 completers (70%) were classified as responders to venlafaxine extended-release. These results suggest that venlafaxine extended-release may be effective for the treatment of hoarding disorder. *Int Clin Psychopharmacol* 29:266–273 © 2014 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

Hoarding is defined as the acquisition of and inability to discard items even though they appear (to others) to have no value (Frost and Gross, 1993). Frost and Hartl (1996) developed the first systematic definition and diagnostic criteria for clinically significant compulsive hoarding: (a) the acquisition of and failure to discard a large number of possessions that appear (to others) to be useless or of limited value, (b) living or work spaces are sufficiently cluttered so as to preclude activities for which those spaces were designed, and (c) significant distress or impairment in functioning is caused by the hoarding behavior or clutter. Hoarding and saving symptoms are part of a discrete clinical syndrome that includes the core symptoms of difficulty in discarding, urges to save, excessive acquisition, and clutter, as well as indecisiveness (Samuels *et al.*, 2008), perfectionism, procrastination, disorganization, and avoidance (Frost and Hartl, 1996). In addition, many compulsive hoarders are quite slow in completing tasks, are frequently late for appointments, and show circumstantial, overinclusive language. Patients with prominent hoarding and saving who show these other associated features are thus considered to have the 'compulsive hoarding syndrome' (Saxena *et al.*, 2002; Steketee and Frost, 2003). The bulk of evidence indicates that hoarding is a separate clinical syndrome, quite distinct from obsessive-compulsive disorder (OCD) (Saxena, 2007; Pertusa *et al.*, 2010). Therefore, formal diagnostic criteria were developed for 'hoarding disorder' (Mataix-Cols *et al.*, 2010) and are now included in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th ed. (DSM-5) (American Psychiatric Association, 2013). These diagnostic criteria have been found in a clinical field trial to have excellent sensitivity, specificity, inter-rater reliability, and validity (Mataix-Cols *et al.*, 2013).

Compulsive hoarding is driven by an exaggerated perceived need to keep and save items, often related to obsessional fears of losing items that the patient believes are valuable or may be needed later, or making the 'wrong' decision about what to keep or discard (Saxena *et al.*, 2002; Steketee and Frost, 2003). These fears cause considerable distress and lead to compulsions to save items. Hoarders also frequently have excessive emotional attachments to possessions and distorted beliefs about the importance of possessions (Frost and Gross, 1993). Excessive acquisition behaviors, including acquisition of free items, excessive buying, and stealing, are quite common, found in 65–85% of all compulsive hoarders (Frost *et al.*, 2009; Mueller *et al.*, 2009; Timpano *et al.*, 2011). The consequent clutter often causes significant social and occupational impairment (Frost *et al.*, 2000; Saxena *et al.*, 2002, 2011; Tolin *et al.*, 2008b) and adverse effects on the family members of compulsive hoarders (Tolin *et al.*, 2008a). In severe cases, it can produce health risks from infestations, falls, fires, and inability to cook or eat in the home (Steketee and Frost, 2003). Avoidance is prominent and includes behavioral avoidance of discarding

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or storing items, and cleaning, as well as cognitive avoidance of making decisions or even thinking about the clutter.

In community-based population samples, clinically significant compulsive hoarding is common, with a population prevalence of 1.5–5.8% (Samuels *et al.*, 2008; Iervolino *et al.*, 2009; Mueller *et al.*, 2009; Timpano *et al.*, 2011; Nordsletten *et al.*, 2013). Initial onset of compulsive hoarding symptoms is usually around 12–13 years of age (Frost and Gross, 1993; Samuels *et al.*, 2002; Grisham *et al.*, 2006; Ayers *et al.*, 2010; Tolin *et al.*, 2010b). The course tends to be chronic and progressive, with severe levels of hoarding starting in the mid-thirties, and symptoms often worsening with age (Grisham *et al.*, 2006; Ayers *et al.*, 2010; Tolin *et al.*, 2010b).

Some retrospective studies investigating the influence of OCD symptom factors on treatment response found that hoarding and saving symptoms in patients with OCD were associated with poor response to pharmacotherapy with serotonin reuptake inhibitor (SRI) medications (Black *et al.*, 1998; Mataix-Cols *et al.*, 1999; Winsberg *et al.*, 1999; Stein *et al.*, 2007, 2008; Salomoni *et al.*, 2009), but many others have failed to replicate this association (Saxena, 2011). Several studies found that hoarding/saving symptoms had no significant effect on response to treatment in OCD patients (Alonso *et al.*, 2001; Erzegovesi *et al.*, 2001; Shetti *et al.*, 2005; Ferrao *et al.*, 2006; Landeros-Weisenberger *et al.*, 2010). In addition, a family study that compared a large group of hoarding OCD patients with nonhoarding OCD patients found that a very similar proportion of patients in the two groups reported moderate response or total remission with SRI treatment, as well as for behavioral therapy (Samuels *et al.*, 2007). Thus, hoarding is clearly not a consistent predictor of poor response to SRI medications.

Unfortunately, all previous studies except those by our group examined only patients who fulfilled diagnostic criteria for OCD, and most used diagnostic or screening instruments such as the Structured Clinical Interview for DSM-IV (SCID; First *et al.*, 1995), which exclude patients who have compulsive hoarding, but no other OCD symptoms (who comprise >80% of all hoarding disorder patients); thus, they may not be generalizable to the broader population of compulsive hoarders (Saxena, 2007). Moreover, none of the retrospective studies monitored, focused on, or measured hoarding symptoms apart from nonhoarding OCD symptoms; therefore, they could not determine whether hoarding symptoms improved or responded as well as nonhoarding OCD symptoms.

Only one study to date (Saxena *et al.*, 2007) has prospectively and quantitatively measured response to standardized pharmacotherapy in patients with the compulsive hoarding syndrome, irrespective of whether they had other OCD symptoms. Patients with the compulsive hoarding syndrome ($n = 32$) and nonhoarding OCD patients ($n = 47$) were treated openly with the SRI, paroxetine, for 12 weeks (mean dose 41.6 ± 12.8 mg/day), according to a standardized protocol. No other medications or cognitive-behavioral therapy (CBT) were allowed during the treatment period. Compulsive hoarders responded equally as well to paroxetine as nonhoarding OCD patients, with significant and almost identical improvements in OCD symptoms, depression, anxiety, and overall functioning (Saxena *et al.*, 2007). A similar proportion of hoarders and nonhoarding OCD patients were full responders (28 vs. 32%) and partial responders (22 vs. 15%). Hoarding/saving symptoms improved as much as nonhoarding OCD symptoms. The proportion of dropouts was also similar. Compulsive hoarders who completed treatment showed a mean 31% decrease in symptom severity. No correlation was found between hoarding severity and treatment response. Both the overall mean reduction in the YBOCS score (– 6.1 points) and the overall categorical response rate of 49% (39 of 79 patients were classified as responders) were very similar to those reported in the Cochrane review of SRI trials for OCD (Soomro *et al.*, 2008). These results suggested that SRI medications were just as effective for compulsive hoarders as for nonhoarding OCD patients (Saxena *et al.*, 2007).

However, paroxetine was not well tolerated in that study. Only 16 of the 79 patients in the study could tolerate the target dose of paroxetine, 60 mg/day. Fewer than half of the sample achieved a dose of 40 mg/day and 12 patients could not tolerate more than 30 mg/day. The most common side effects limiting dose increases were sedation, fatigue, constipation, headaches, and sexual side effects (Saxena *et al.*, 2007). Compulsive hoarders in both clinical and research settings tend to be middle-aged and older adults, predominantly women (Steketee and Frost, 2003; Tolin *et al.*, 2008a, 2008b; Steketee *et al.*, 2010; Pertusa *et al.*, 2010), and the anticholinergic side effects of paroxetine can be more problematic for such populations. Therefore, we sought to test a medication better tolerated in older populations, which would allow higher doses, known to be more effective for the treatment of OCD (Bloch *et al.*, 2010). In addition, the paroxetine study was initiated before specific rating scales for measuring hoarding severity were available; hence, most participants in that study could not have their hoarding/saving symptoms measured separately from nonhoarding OCD symptoms. Hence, we sought to assess and quantify the specific response of hoarding symptoms to pharmacotherapy using more recently developed hoarding symptom rating scales.

We conducted an open-label trial of venlafaxine extended-release for hoarding disorder. We chose venlafaxine extended-release primarily for its superior tolerability in middle-aged and older patients as well as its potential efficacy in patients who have not responded well to more selective SRI's. Venlafaxine has been tested extensively in

older populations and has been found to be safe and well tolerated (Staab and Evans, 2000; Mazeh *et al.*, 2007; Ibor *et al.*, 2008). Venlafaxine appears to be as effective as paroxetine or clomipramine for OCD (Albert *et al.*, 2002; Denys *et al.*, 2003) and is less likely to cause these side effects than those medications. Moreover, venlafaxine may be efficacious for SSRI-refractory OCD (Hollander *et al.*, 2003; Marazziti, 2003). We hypothesized that patients with hoarding disorder would tolerate venlafaxine extended-release well and show significant symptom improvement in both the core symptoms and the associated features of compulsive hoarding, as well as comorbid depression, anxiety, and OCD symptoms.

Methods

This study was approved by the UCSD Institutional Review Board, in accordance with the Declaration of Helsinki. All participants enrolled provided written informed consent to participate after the procedures and possible side effects were explained to them.

Participants

Participants were recruited from the San Diego area with flyers, print, and Internet advertisements, as well as referrals from local clinicians. Twenty-four patients with hoarding disorder (21 women, three men; mean age = 51.8 ± 8.1 years; age range 33–61 years) were enrolled. Nineteen participants were Caucasian, three were Hispanic, and two were Asian-American. To be enrolled, participants had to fulfill the DSM-5 diagnostic criteria for hoarding disorder as their primary, most distressing, or impairing condition. All participants were diagnosed by clinical interview, followed by administration of the MINI International Neuropsychiatric Interview (MINI; Sheehan *et al.*, 1998). For additional identification of comorbid OCD and related 'OC spectrum disorders', all participants were also administered the OCD spectrum module from a revision of the Structured Clinical Interview for DSM-IV (First *et al.*, 1995) developed by C. Lochner, P.L. du Toit, J. Van Kradenburg, D.J. Stein (in preparation). Patients with primary psychotic disorders, bipolar disorder, panic disorder, post-traumatic stress disorder, substance abuse/dependence, eating disorders, dementia, or mental retardation were excluded. All participants were free of psychotropic medication and any other medication that could affect brain function for at least 6 weeks before starting venlafaxine extended-release.

To measure the severity of the component symptoms of hoarding disorder, every participant was administered both the UCLA Hoarding Severity Scale (UHSS; Saxena *et al.*, 2007) and the Saving Inventory-Revised (SI-R; Frost *et al.*, 2004) immediately before and after the 12-week treatment period. The UHSS is a 10-item, clinician-administered scale that assesses the presence and severity of various components of the compulsive hoarding syndrome, including extent of clutter, urges to save items, excessive acquisition, difficulty discarding, social and occupational impairment, slowing, perfectionism, indecisiveness, and procrastination. Scores reflect the average occurrence of each symptom over the 1 week before and including the time of the interview. Its maximum score is 40. The UHSS is a semistructured interview that allows additional questions for clarification, which helps improve accuracy when assessing patients who may be prone to confusion on the meaning of specific questions. Scores are based on the patient's report, but may also include information obtained from family members or others, and the final rating depends on the clinical judgment of the interviewer, which is especially important when assessing patients with poor insight. Use of a clinician-administered rating scale is especially important in assessing patients with hoarding disorder because many compulsive hoarders have poor insight into their condition and symptoms (Steketee and Frost, 2003; Pertusa *et al.*, 2010; Neziroglu *et al.*, 2012) and tend to under-report their specific hoarding symptoms, while over-reporting their overall global impression of hoarding severity (Dimauro *et al.*, 2013).

The UHSS is internally consistent and shows convergent, discriminant, and known groups validity (Saxena *et al.*, 2013). It shows good internal reliability (Ayers *et al.*, 2014a) and is strongly correlated with the SI-R across both hoarding and healthy control samples (Saxena *et al.*, 2013; Ayers *et al.*, 2014a). Principal component factor analysis of the UHSS shows three factors, representing (a) associated features and functional impairment, (b) clutter and social impairment, and (c) excessive acquisition, distress with discarding, and need to save possessions, which account for 58% of the variance (Saxena *et al.*, 2013). The UHSS has been found to differentiate compulsive hoarders from healthy controls with no psychiatric disorders, as well as from patients with OCD who have other symptom domains as their predominant problems, even if they also have some hoarding/saving symptoms (Saxena *et al.*, 2007). The UHSS has also been shown to detect clinically significant changes in hoarding symptom severity with treatment (Saxena *et al.*, 2007; Ayers *et al.*, 2014b). In addition, the UHSS has been found to be a slightly stronger predictor of disability in geriatric hoarding disorder patients than the SI-R, uniquely correlating with both the extent of limitation and the frequency of disability (Ayers *et al.*, 2014a).

The SI-R is a well-validated, 23-item self-report questionnaire with three-factor analytically defined subscales for difficulty discarding, excessive clutter, and compulsive acquisition (Frost *et al.*, 2004). It shows good internal consistency and test–retest reliability, as well as known group validity and concurrent and divergent validity in clinical and nonclinical samples. The SI-R has been found to distinguish hoarders from nonhoarding populations. Its maximum score is 92, and a score of at least 36 has been used as a cutoff for inclusion in studies of compulsive hoarders (Grisham *et al.*, 2006). To be

enrolled, participants had to score more than 40 on the SI-R and more than 17 on the UHSS. The SI-R cutoff was based on the results of previous studies that constructed receiver operating characteristic curves to distinguish patients with hoarding disorder from controls and other diagnostic groups with maximal sensitivity and specificity (Tolin *et al.*, 2010a; Frost and Hristova, 2011).

Participants were also assessed immediately before and after treatment with the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960), Hamilton Anxiety Scale (Ham-A; Hamilton, 1959), Global Assessment Scale (GAS; Endicott *et al.*, 1976), and Clinical Global Impression/Improvement (CGI) scale. Despite the fact that it is not adequate for assessment of the severity or extent of hoarding symptoms, the Yale-Brown Obsessive-Compulsive Scale (YBOCS; Goodman *et al.*, 1989) was also administered to assess changes in both hoarding and nonhoarding symptoms, to allow for comparison with older studies that grouped hoarding and nonhoarding symptoms together. 'Response' was defined as a more than 30% decrease in UHSS and SI-R scores, and at least 'much improved' on the CGI-Improvement scale. These response criteria were based on those found to be optimally predictive of clinical response in OCD (Tolin *et al.*, 2005).

Treatment

All participants were treated with venlafaxine extended-release for 12 weeks, according to a standardized protocol, but with some flexibility in dosing, on the basis of side effects. Participants were started on venlafaxine extended-release 37.5 mg orally every day for the first 4 days. The dose was then increased by 37.5 mg increments every 4 days to a target of 225 mg/day (reached by the end of 3 weeks) as tolerated. Participants then remained on that dose until week 8, at which time, if they had not shown significant improvement in compulsive hoarding symptoms, the dose was increased to 300 mg orally every day as tolerated for weeks 9–12. Dosages could be maintained or reduced if a participant could not tolerate higher doses. No other psychotropic medications were permitted during the study. Participants also could not receive CBT, assistance from professional organizers or cleaning crews, or other interventions from third parties during the treatment period.

Statistical analyses

The data were first statistically screened for distributional properties, outliers, and missing values. No variables were rejected by this process. Because rating scale data were not normally distributed, nonparametric Wilcoxon's signed-rank tests were used on pretreatment and post-treatment standardized symptom rating scale scores. Paired-samples *t*-tests were used on pretreatment and post-treatment SI-R and UHSS component factor scores. To determine whether pretreatment hoarding severity was associated with treatment response, Spearman's rho correlations between age, final venlafaxine extended-release dose, baseline symptom rating scale scores, baseline UHSS and SI-R factor scores, and pretreatment to post-treatment changes on the UHSS and SI-R were performed.

Results

Of the 24 participants, seven had comorbid major depressive disorder (MDD), five had compulsive buying, four had comorbid attention deficit/hyperactivity disorder (ADHD), three had comorbid generalized anxiety disorder (GAD), and one had comorbid social anxiety disorder. Although we did not attempt to exclude participants with comorbid nonhoarding OCD, only one participant in this study fulfilled the diagnostic criteria for nonhoarding OCD, and four had subclinical OC symptoms. None had hoarding behavior related to other, 'typical' OCD obsessions. Baseline pretreatment hoarding symptom severity was in the moderate to severe range, with a mean UHSS score of 24.4 ± 3.9 and a mean SI-R score of 68.8 ± 9.9.

Twenty-three of the 24 participants (96%) completed treatment with venlafaxine extended-release for 12 weeks, and one dropped out of the study after 10 weeks because she moved out of state. No patients dropped out of the study because of side effects or lack of efficacy. The mean final dose was 204 ± 72 mg/day. Twenty of the 23 patients could tolerate at least 150 mg/day, 16 tolerated at least 225 mg/day, and four reached a final dose of 300 mg/day.

Compulsive hoarding symptoms improved significantly. The mean UHSS score decreased by 36% ($Z = -4.20$, $P < 0.0001$), and the mean SI-R score decreased 32% ($Z = -4.02$, $P < 0.001$). The effect sizes for reduction in hoarding symptom severity with venlafaxine extended-release treatment were large (1.98 for the UHSS, 1.68 for the SI-R). Significant pretreatment to post-treatment decreases were found for all three UHSS component factors ($t = 10.76$, $d.f. = 22$, $P < 0.001$ for associated features and functional impairment; $t = 5.01$, $d.f. = 22$, $P < 0.001$ for core symptoms; and $t = 11.69$, $d.f. = 22$, $P < 0.001$ for clutter and social impairment). All three SI-R component factors also showed significant pretreatment to post-treatment improvements ($t = 6.63$, $d.f. = 22$, $P < 0.001$ for clutter; $t = 7.37$, $d.f. = 22$, $P < 0.001$ for difficulty discarding; and $t = 6.92$, $d.f. = 22$, $P < 0.001$ for excessive acquisition). Sixteen of the 23 completers (70%) were classified as responders to treatment, on the basis of at least 30% reduction of UHSS and SI-R scores, as well as a rating of at least 'much improved' on the CGI-I (Table 1).

Depression, anxiety, OCD symptoms, and overall functioning also improved significantly, with a 48% decrease in the mean HDRS score ($Z = -3.34$, $P = 0.001$), a 43%

Table 1 Symptom rating scale scores before and after treatment

Symptom rating scale	Pretreatment score	Post-treatment score	Wilcoxon's signed-rank test	
			Z	*P*
UHSS	24.4±3.9	15.5±4.9	−4.20	<0.001
SI-R	68.8±9.9	46.5±15.4	−4.02	<0.001
HDRS (17)	11.0±6.3	5.7±3.5	−3.34	0.001
HAM-A	11.0±5.6	6.3±3.7	−3.54	<0.001
YBOCS	22.3±4.2	13.7±5.5	−4.03	<0.001
GAS	52.9±6.0	63.0±6.4	−4.20	<0.001

GAS, Global Assessment Scale; HAM-A, Hamilton Anxiety Scale; HDRS, Hamilton Depression Rating Scale; SI-R, Saving Inventory-Revised; UHSS, UCLA Hoarding Severity Scale; YBOCS, Yale-Brown Obsessive-Compulsive Scale.

decrease in the mean HAM-A score ($Z = -3.54$, $P < 0.001$), a 39% decrease in the mean YBOCS score ($Z = -4.03$, $P < 0.001$), and a 19% increase in the mean GAS score ($Z = -4.20$, $P < 0.001$).

Improvement in hoarding severity was not correlated significantly with pretreatment UHSS, SI-R, HDRS, HAM-A, YBOCS, or GAS scores, or with the dose of venlafaxine extended-release. However, there was a significant negative correlation between age and improvement on the SI-R ($\rho = -0.53$, $P = 0.009$), and a trend toward a significant negative correlation between age and improvement on the UHSS ($\rho = -0.37$, $P = 0.08$), indicating that higher patient age was associated with less improvement in hoarding symptoms with treatment. Age was also significantly, negatively correlated with improvement in the UHSS core symptoms factor ($\rho = -0.51$, $P = 0.02$). As expected, pretreatment UHSS and SI-R scores were strongly correlated ($\rho = 0.76$, $P < 0.001$), as were the pretreatment to post-treatment changes in UHSS and SI-R scores ($\rho = 0.69$, $P < 0.001$).

Discussion

To our knowledge, this is the first study to prospectively and quantitatively assess response to standardized medication treatment of patients with hoarding disorder with specific measures of pretreatment and post-treatment hoarding symptom severity in all patients. The results of this open trial suggest that venlafaxine extended-release may be quite effective for the treatment of hoarding disorder, with a large effect size, and is well tolerated in these patients. The categorical responder rate (70%) and the effect sizes for reduction in hoarding symptom severity after treatment with venlafaxine extended-release (1.98 on the UHSS, 1.68 on the SI-R) were quite large, and they compare favorably with the effect sizes of many pharmacotherapy trials for OCD (Soomro *et al.*, 2008). Moreover, significant pretreatment to post-treatment decreases were observed on all SI-R and UHSS component factors, indicating that treatment with venlafaxine extended-release resulted in broad improvements in all major components of the compulsive hoarding syndrome – difficulty discarding, excessive acquisition, clutter, associated features, and functional impairment. There were no dropouts because of side effects or lack of efficacy. Taken together, the results of the current study of venlafaxine extended-release and the previous study of paroxetine treatment for compulsive hoarding (Saxena *et al.*, 2007) indicate that the 'conventional wisdom' that compulsive hoarding does not respond well to SRI treatment is wrong. SSRI/SNRI medications appear to be as effective for patients with hoarding disorder as for nonhoarding OCD patients. Randomized, double-blind, placebo-controlled trials of venlafaxine extended-release for hoarding disorder are now warranted.

Symptom improvement from pharmacotherapy of compulsive hoarding compares quite favorably with that resulting from CBT. In published CBT trials, improvement in compulsive hoarding symptoms, measured by decreases in the mean SI-R score, has ranged from 10–30% for group CBT (Steketee *et al.*, 2000; Muroff *et al.*, 2009, 2010, 2012; Gilliam *et al.*, 2011) to 27–28% for individual CBT (Tolin *et al.*, 2007; Steketee *et al.*, 2010). However, in the present study, treatment with venlafaxine extended-release resulted in a 32% mean improvement on the SI-R and 36% on the UHSS, whereas in the previous paroxetine study, the mean symptom improvement was 31% for completers and 24% for the entire sample in an intent-to-treat analysis (Saxena *et al.*, 2007). The effect sizes for reduction in hoarding severity with venlafaxine extended-release treatment in the present study were considerably larger than those found in the previous studies of CBT for hoarding with similar treatment duration (12 weeks) and similar to those found in recent studies of facilitated support group treatment of hoarding (Frost *et al.*, 2011a, 2012). Larger improvements have been found using the Hoarding Rating Scale (HRS; Tolin *et al.*, 2010a) and longer durations of treatment; Steketee *et al.* (2010) found a 39% decrease in HRS scores after 26 weeks of individual CBT for compulsive hoarding. The improvements in depression and anxiety symptoms with venlafaxine extended-release in this study were also larger than those achieved in most previous studies of CBT or facilitated support group treatment of hoarding.

Further, pharmacotherapy may lead to faster improvement in compulsive hoarding symptoms than CBT. In both the venlafaxine extended-release and the paroxetine trials, significant improvement was found after only 12 weeks of treatment, whereas the individual and group CBT trials required up to 26 weeks to achieve at least a 25% mean improvement on the SI-R and comparable effect sizes. Future trials of CBT or other therapies should control for the significant effects of medication treatment on hoarding symptoms and should require that medications not be started or adjusted during the treatment period; most previous CBT and support group studies have failed to control for potential medication treatment effects.

No study has as yet compared CBT and pharmacotherapy for compulsive hoarding directly. The combination of antiobsessional pharmacotherapy and CBT for hoarding disorder may be more effective than either treatment alone, as has been found in systematic meta-analyses for major depression (Pampallona *et al.*, 2004), panic disorder and agoraphobia (Van Balkom *et al.*, 1997; Furukawa *et al.*, 2007), and in some studies of OCD (Hohagen *et al.*, 1998; Pediatric OCD Treatment Study (POTS) Team, 2004).

Age was the only pretreatment variable found to correlate significantly with response to venlafaxine extended-release in this study. Older age was correlated significantly with less improvement in hoarding symptoms, as measured by the SI-R (with a trend toward a significant correlation with less improvement on the UHSS as well). This finding is consistent with previous findings of poorer response to CBT in elderly hoarders, compared with younger and middle-aged compulsive hoarders (Ayers *et al.*, 2011). However, to our knowledge, age has not been reported to be a significant correlate or predictor of medication treatment response in previous treatment studies of hoarding disorder.

Limitations

This study is limited by its open-label design and relatively small sample size. Large, randomized, double-blind, placebo-controlled studies will be needed to establish the efficacy of venlafaxine extended-release treatment for hoarding disorder. The study population included only patients requesting treatment for compulsive hoarding and who were free from many confounds, such as other psychotropic medications, concurrent psychotherapies, and many comorbid neuropsychiatric disorders. Thus, it is possible that the results of this study might not be generalizable to the broader population of compulsive hoarders with various comorbid psychiatric disorders and variable motivation for treatment. However, similar limitations are present in most clinical drug efficacy trials. The study did include participants with several comorbid psychiatric disorders – MDD, ADHD, GAD, social anxiety disorder, compulsive buying, and OCD – found to commonly be comorbid with hoarding disorder (Frost *et al.*, 2011b), which supports its generalizability. The prevalence of comorbid psychiatric disorders in our sample of participants was similar to those reported in a large sample by Frost *et al.* (2011b), with MDD, compulsive buying, ADHD, and GAD being the most frequent. Unfortunately, the sample size was too small to assess the influence of these comorbidities on treatment response in this study. Another limitation was that we did not assess symptom severity more frequently during the 12-week treatment period; thus, we could not analyze the speed or the trajectory of symptom improvement quantitatively. Future studies may need to rate symptom severity every one to two weeks to determine the onset and pace of clinical response to treatment. Another important limitation was that no home visits were performed to assess clutter volume or hazards in the patients' living spaces.

Nevertheless, this study also had several strengths that add to the importance of its results. All participants were prospectively diagnosed with valid diagnostic instruments and assessed with specific symptom rating scales before and after standardized treatment. Both clinician-rated and self-report symptom rating scales were used, an important issue in assessing symptoms of a disorder known to be frequently characterized by poor insight (Pertusa *et al.*, 2010; Neziroglu *et al.*, 2012). The sample of participants had moderate to severe symptoms at baseline, with pretreatment UHSS scores (24.4 ± 3.9) similar to those found in the paroxetine study (Saxena *et al.*, 2007), and SI-R scores (68.8 ± 9.9) that were slightly higher than those of multiple previous samples of compulsive hoarding participants in CBT and support group studies, which have ranged from 59 to 67 (Steketee *et al.*, 2000, 2010; Tolin *et al.*, 2007; Muroff *et al.*, 2009, 2010, 2012; Frost and Hristova, 2011; Gilliam *et al.*, 2011; Frost *et al.*, 2012). Both self-report and clinician-administered hoarding severity rating scales showed clinically and statistically significant improvements in hoarding symptom severity with treatment. The average age (51.8 ± 8.1) and sex distribution (88% women) of the sample of participants was also very similar to those of previous studies of compulsive hoarding patients. Thus, the sample appears fairly representative of hoarding disorder patients in other clinical and research settings.

This present study also avoided any potential confound from other potentially active treatments. All other psychotropic drugs besides venlafaxine were disallowed, as were CBT and any other psychotherapy that addressed compulsive hoarding symptoms, as well as any assistance from professional organizers or cleaning crews, or other interventions from third parties during the treatment period. Thus, the significant clinical improvements in hoarding severity and comorbid conditions can reasonably be attributed to the effect of treatment with venlafaxine extended-release, to the extent possible in an open-label trial.

Moreover, the very low dropout rate and significant improvement in hoarding symptom severity, comorbid symptoms, and overall functioning suggest that extended-release venlafaxine is well tolerated and may be effective for the treatment of hoarding disorder.

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Conflicts of interest

There are no conflicts of interest.

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