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Mindfulness-Based Stress Reduction vs Escitalopram for the Treatment of Adults With Anxiety Disorders
A Randomized Clinical Trial

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IMPORTANCE Anxiety disorders are common, highly distressing, and impairing conditions. Effective treatments exist, but many patients do not access or respond to them. Mindfulness-based interventions, such as mindfulness-based stress reduction (MBSR) are popular and can decrease anxiety, but it is unknown how they compare to standard first-line treatments.

OBJECTIVE To determine whether MBSR is noninferior to escitalopram, a commonly used first-line psychopharmacological treatment for anxiety disorders.

DESIGN, SETTING, AND PARTICIPANTS This randomized clinical trial (Treatments for Anxiety: Meditation and Escitalopram [TAME]) included a noninferiority design with a prespecified noninferiority margin. Patients were recruited between June 2018 and February 2020. The outcome assessments were performed by blinded clinical interviewer at baseline, week 8 end point, and follow-up visits at 12 and 24 weeks. Of 430 individuals assessed for inclusion, 276 adults with a diagnosed anxiety disorder from 3 urban academic medical centers in the US were recruited for the trial, and 208 completed the trial.

INTERVENTIONS Participants were 1:1 randomized to 8 weeks of the weekly MBSR course or the antidepressant escitalopram, flexibly dosed from 10 to 20 mg.

MAIN OUTCOMES AND MEASURES The primary outcome measure was anxiety levels as assessed with the Clinical Global Impression of Severity scale (CGI-S), with a predetermined noninferiority margin of −0.495 points.

RESULTS The primary noninferiority sample consisted of 208 patients (102 in MBSR and 106 in escitalopram), with a mean (SD) age of 33 (13) years; 156 participants (75%) were female; 32 participants (15%) were African American, 41 (20%) were Asian, 18 (9%) were Hispanic/Latino, 122 (59%) were White, and 13 (6%) were of another race or ethnicity (including Native American or Alaska Native, more than one race, or other, consolidated owing to low numbers). Baseline mean (SD) CGI-S score was 4.44 (0.79) for the MBSR group and 4.51 (0.78) for the escitalopram group in the per-protocol sample and 4.49 (0.77) vs 4.54 (0.83), respectively, in the randomized sample. At end point, the mean (SD) CGI-S score was reduced by 1.35 (1.06) for MBSR and 1.43 (1.17) for escitalopram. The difference between groups was −0.07 (0.16; 95% CI, −0.38 to 0.23; P = .65), where the lower bound of the interval fell within the predefined noninferiority margin of −0.495, indicating noninferiority of MBSR compared with escitalopram. Secondary intent-to-treat analyses using imputed data also showed the noninferiority of MBSR compared with escitalopram based on the improvement in CGI-S score. Of patients who started treatment, 10 (8%) dropped out of the escitalopram group and none from the MBSR group due to adverse events. At least 1 study-related adverse event occurred for 110 participants randomized to escitalopram (78.6%) and 21 participants randomized to MBSR (15.4%).

CONCLUSIONS AND RELEVANCE The results from this randomized clinical trial comparing a standardized evidence-based mindfulness-based intervention with pharmacotherapy for the treatment of anxiety disorders found that MBSR was noninferior to escitalopram.

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Visual Abstract

Supplemental content

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Anxiety disorders are the most common type of mental disorder, currently affecting an estimated 301 million people globally.[1] Generalized anxiety disorder, social anxiety disorder, panic disorder, and agoraphobia are anxiety disorders associated with considerable distress, impairment in functioning, and increased risk for suicide.[2,3]

Effective treatments for anxiety disorders exist and include medications and cognitive behavioral therapy, but not all patients have access to them, respond to them, or are comfortable seeking care in a psychiatric setting. For example, nearly one-third of people surveyed in 1 study[4] believed that psychiatric medication would interfere with daily activities, and about one-fourth believed it is harmful to the body. Further, roughly two-thirds of patients who do start taking an antidepressant discontinue it.[5] While cognitive behavioral therapy is also effective, it can be difficult for patients to access due to a lack of health care professionals trained in this technique.[6] These challenges support a need for additional evidence-based treatment options for patients with anxiety disorders with broad acceptability.

Mindfulness-based interventions (MBIs) may be seen as a more acceptable option given that mindfulness meditation has recently become more popular. For example, in the US, approximately 15% of the population has tried meditation.[7] Mindfulness meditation has been found to help reduce anxiety; a recent meta-analysis[8] of trials with anxiety disorders found a significant benefit with mindfulness meditation compared with treatment as usual. While MBIs have been shown to decrease anxiety,[9,10] the need to assess the relative effectiveness of MBIs compared with standard therapies for anxiety disorders has been emphasized.[11] Mindfulness-based stress reduction (MBSR) is the most widely researched MBI (over 1000 citations in PubMed) and is available internationally.[12]

To our knowledge, no clinical trial comparing an evidence-based MBI, such as MBSR, with a first-line pharmacological treatment for anxiety disorders has been published. To clarify whether MBSR should be considered an alternative first-line intervention comparable to a gold-standard pharmacotherapy used in primary care, our aim was to compare MBSR with escitalopram, an European Medicines Agency- and US Food and Drug Administration-approved pharmacotherapy for the treatment of anxiety and hypothesized that MBSR would be noninferior to escitalopram.

Key Points

Question Is mindfulness-based stress reduction noninferior to escitalopram for the treatment of anxiety disorders?

Findings In this randomized clinical trial of 276 adults with anxiety disorders, 8-week treatment with mindfulness-based stress reduction was noninferior to escitalopram.

Meaning In this study, mindfulness-based stress reduction was a well-tolerated treatment option with comparable effectiveness to a first-line medication for patients with anxiety disorders.

Methods

Study Design

Our study protocol and analysis plan are published in full elsewhere and in Supplement 1.[13] Treatments for Anxiety: Meditation and Escitalopram (TAME) is a prospective randomized 2-arm parallel-group controlled single-blinded (blinded raters, with unblinded providers and participants) trial to evaluate the relative effectiveness of 8 weeks of MBSR vs escitalopram. Recruitment and enrollment occurred at 3 US hospital sites in Boston, Massachusetts, New York, New York, and Washington, DC. The study was approved by each institution's institutional review board and overseen by an independent data and safety monitoring board. All participants provided written informed consent. The study followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.

Participants

Eligible participants were aged 18 to 75 years with a current primary diagnosis of generalized anxiety disorder, social anxiety disorder, panic disorder, or agoraphobia, as determined by structured psychiatric diagnostic interviews performed by trained clinicians.[14] A diagnosis was determined primary (using clinical judgment with participant input) as the condition with the most severe symptoms and that caused the greatest amount of interference and distress for the patient in their daily life. Eligibility criteria have been described elsewhere[13] and were selected to include a generalizable population of adults with anxiety disorders. Briefly, major exclusion criteria included lifetime bipolar disorder, psychotic disorders, or obsessive compulsive disorder as well as current anorexia or bulimia nervosa, posttraumatic stress disorder, substance use disorders, or significant active suicidal ideation or behaviors. Participants must not have completed MBSR or equivalent training in the past year or had an ongoing daily meditation practice. Patients taking psychiatric medications were excluded except for trazodone (if 100 mg or less), sleep medications (zolpidem and eszopiclone), and benzodiazepines, if at stable dose 4 weeks prior to baseline. Recruitment included online, print, and radio advertisements.

Randomization and Blinding

Potential participants deemed eligible on phone screening were scheduled for an in-person consent and structured interview with a study clinician. The study statistician (M.M.) made a computer-generated concealed block randomization schedule that was stratified by site and baseline anxiety severity (low = Clinical Global Impression of Severity [CGI-S][15] score ≤4; high = CGI-S >4). The randomization schedule was programmed into the study electronic data capture software (Research Electronic Data Capture [REDCap] version 12.4.12). The baseline CGI-S score for each participant was entered into REDCap, which then assigned the treatment group. In this single-blinded trial, the computer-generated randomization assignment was revealed through REDCap to the research assistant, who then relayed the assignment to the site study clinician, but all symptom severity ratings for the primary outcome were performed by independent evaluators who were blinded to treatment allocation.

Procedures

The CGI-S is a widely used treatment-sensitive instrument that assesses overall severity of symptoms on a scale from 1 (not at all ill) to 7 (among the most extremely ill).[15] Independent evaluator ratings were performed at baseline (week 0), midtreatment (week 4), end point (posttreatment week 8), and follow-up (weeks 12 and 24). Study participants were instructed and reminded not to disclose their treatment group to the independent evaluator. A random 5% of independent evaluator sessions were corated, yielding a CGI-S interrater reliability of κ = 0.80. Participants also met at weeks 1, 2, 4, 6, and 8 (end point) and follow-up visits (weeks 12 and 24) with an unblinded study clinician for safety monitoring, including assessment of adverse events, clinical worsening, and emerging suicidality, with referral if needed to the most appropriate level of medical care based on clinician judgment.

Interventions

MBSR

MBSR is a manualized 8-week protocol with weekly 2.5-hour long classes, a day-long retreat weekend class during the fifth or sixth week, and 45-minute daily home practice exercises.[16] Study participants received MBSR classes at clinic and community sites. Qualified instructors taught the theory and practice of several forms of mindfulness meditation, such as breath awareness (focusing attention on the breath and other physical sensations), a body scan (directing attention to one body part at a time and observing how that body part feels), and mindful movement (stretching and movements designed to bring awareness to the body and increase interoceptive awareness). A qualified MBSR instructor (M.A.D.) reviewed audio recordings from a representative session from every MBSR teacher to ensure treatment fidelity. Participants' class attendance was recorded by the MBSR teacher or through self-report to the unblinded study clinician.

Escitalopram

Escitalopram was initiated at 10 mg daily orally and increased to 20 mg daily at week 2 if well tolerated or delayed if not. Adherence was measured by pill count and patient report. Medication management visits with a study clinician (M.D. or N.P.) occurred at weeks 1, 2, 4, 6, and 8 (end point). After end point, patients wishing to continue taking escitalopram were assisted in doing so.

Outcomes

The primary outcome measure was the CGI-S[15] scale for anxiety, assessed by trained clinicians. Our primary patient-reported outcome was the Overall Anxiety Severity and Impairment Scale (OASIS).[17]

Sample Size and Statistical Analysis Plan

The sample size was determined using a noninferiority margin based on previous similar studies.[13] Following published guidelines and taking into account the minimal clinically important difference change score for the CGI-S, we adopted a noninferiority margin of −0.495 as the largest clinically acceptable margin.[13] To be more conservative for the sample size estimation, we reduced the margin to −0.33, which generated a target randomized sample size of 368 providing 80% power with a 1-sided type I error of 0.025 (or equivalently with 95% CI) for a noninferiority test. However, due to the SARS-Cov-2 pandemic, we had to stop enrollment at 276. After discussion with the data and safety monitoring board and trial sponsor, it was determined that since 276 randomized participants (with 208 participants who completed the trial) still provided 80% power to determine noninferiority with our clinically acceptable a priori margin of −0.495, we thus confirmed this margin, clarified the sample size and margin on ClinicalTrials.gov, agreed not to attempt to reopen enrollment after the pandemic, and moved forward with data analysis.

The per-protocol analysis was prespecified as primary, and the intent-to-treat (ITT) sample as secondary, as is typical for noninferiority trials, to account for the increased chance of evidence in favor of noninferiority in ITT analyses.[18] Participants completing at least 6 of the 9 MBSR sessions[19] or at least 6 weeks of escitalopram use with nonmissing end point CGI-S data were considered to have completed the trial.

Baseline characteristics of the participants were summarized using descriptive statistics for all randomized participants as well as for those who completed the trial by treatment groups and are presented in **Table 1**. We collected data on race and ethnicity as required by our trial sponsor; these data were collected using a multiple-choice self-report form based on the National Institutes of Health standard enrollment table. Treatment group differences at baseline were tested using 2-sample *t* tests, χ^2, and Fisher exact tests as appropriate. Baseline characteristics were also compared between those who completed the trial and those who did not using similar bivariate statistical tests (eTable 1 in Supplement 2) to evaluate whether characteristics of those who did not complete the trial were significantly different at baseline compared with those of participants who did complete the trial.

Primary outcome assessment at end point was first conducted for the sample of participants who completed the trial consistent with the primary preplanned analysis and then as planned for all randomized participants (ITT sample) by imputing end point scores for those who did not complete the trial and were without week-8 data. The change in the outcome indicating the amount of improvement was computed by subtracting the end point score from the baseline score. Endpoint CGI-S data were imputed using multiple imputation with multivariate normal regression methods combining 50 imputed samples after establishing that missingness was at random. The multivariate normal regression model for imputation included age, employment status, race, sex, site, use of benzodiazepines, primary diagnosis, total number of secondary diagnoses, baseline CGI-S score, and high vs low severity used in stratification. Secondary analyses of the primary outcome were conducted using linear mixed models to further examine the trends in CGI-S in the ITT sample, including data for baseline and weeks 4, 8, 12, and 24. The mixed models with random effects at participant level were adjusted by age, race, sex, site, baseline severity variable used for stratification, and the number of secondary diagnoses and included interactions between treatment group and time indicators entered as

Table 1. Baseline Characteristics for All Randomized Participants and Those Who Completed Protocol at 8 Weeks

Variable[a]	Randomized			Completed protocol		
	No (%)			No. (%)		
	MBSR	Escitalopram	*P* value	MBSR	Escitalopram	*P* value
No.	136	140	NA	102	106	NA
Site						
Georgetown University Medical Center	61 (45)	63 (45)	NA	50 (49)	50 (47)	.38
New York University Langone	32 (24)	35 (25)		18 (18)	27 (25)	
Massachusetts General Hospital	43 (32)	42 (30)		34 (33)	30 (28)	
Disorder severity						
Low	68 (50)	70 (50)	NA	54 (53)	55 (51)	.82
High	68 (50)	70 (50)		48 (47)	52 (49)	
Sex			.78			.40
Female	101(74)	106 (76)		74 (73)	83 (78)	
Male	35 (26)	34 (24)		28 (28)	24 (22)	
Age, mean (SD), y	33 (12)	33 (13)	.67	33 (12)	34 (14)	.92
Race[b]						
Asian	27 (20)	24 (17)	.67	23 (23)	18 (17)	.68
Black	19 (14)	21 (15)		15 (15)	17 (16)	
White	83 (61)	83 (59)		59 (58)	64 (60)	
Other[c]	7 (5)	12 (9)		5 (5)	8 (8)	
Ethnicity[b]						
Hispanic/Latino	7 (5)	18 (13)	.02	4 (4)	14 (13)	.02
Education						
≤High school	5 (4)	4 (3)	.32	4(4)	3 (3)	.23
Some college	25 (18)	26 (19)		18 (18)	22 (21)	
College degree	43 (32)	59 (42)		30 (29)	44 (41)	
Graduate school degree	63 (46)	51 (36)		50 (49)	38 (36)	
Marital status						
Single	82 (60)	86 (61)	.58	63 (62)	64 (60)	.95
Living with partner/married	47 (35)	43 (31)		34 (33)	37 (35)	
Divorced/widowed/separated	7 (5)	11 (8)		5 (5)	6 (6)	
Employment status						
Not applicable	17 (13)	11 (8)	.20	13 (13)	8 (8)	.43
Full-time	73 (54)	88 (63)		56 (55)	63 (59)	
Part-time	16 (12)	20 (14)		10 (10)	15 (14)	
Student/dependent on spouse	30 (22)	21 (15)		23 (23)	20 (19)	
Primary diagnosis						
Panic disorder	2 (1.5)	9 (6)	.20	0	9 (8)	.01
Agoraphobia	2 (1.5)	2 (1.4)		2 (2)	1 (1)	
Social anxiety disorder	48 (35)	44 (31)		35 (34)	37 (35)	
Generalized anxiety disorder	84 (62)	85 (61)		65 (64)	59 (56)	
Comorbid conditions						
Major depressive disorder	12 (9)	17 (12)	.24	8 (8)	12 (11)	.41
Panic disorder	22 (16)	27 (19)	.30	17 (17)	23 (22)	.38
Agoraphobia	12 (9)	16 (11.4)	.30	7 (7)	11 (10)	.38
Social anxiety disorder	29 (21)	45 (32)	.03	24 (24)	34 (32)	.18
Generalized anxiety disorder	16 (12)	27 (19.3)	.06	12 (12)	26 (24)	.02
Comorbid conditions, No.						
0	46 (35)	40 (29)	.15	30 (29)	32 (30)	.08
1	49 (36)	44 (31)		40 (39)	28 (26)	
2	27 (20)	35 (25)		24 (24)	28 (26)	
3	14 (10)	16 (11)		8 (8)	15 (14)	
4	0	5 (4)		0	4 (4)	

(continued)

Table 1. Baseline Characteristics for All Randomized Participants and Those Who Completed Protocol at 8 Weeks (continued)

	Randomized			Completed protocol		
	No (%)			No. (%)		
Variable[a]	MBSR	Escitalopram	*P* value	MBSR	Escitalopram	*P* value
Comorbid conditions, mean (SD)	1.1 (1.0)	1.3 (1.1)	.06	1.1 (0.9)	1.4 (1.2)	.08
Baseline CGI-S score, mean (SD)	4.49 (0.77)	4.54 (0.83)	.60	4.44 (0.79)	4.51 (0.78)	.53
Concurrent benzodiazepine use	4 (3)	7 (5)	.29	2 (2)	6 (6)	.17
Sleep medication	2 (2)	6 (4)	.28	2 (2)	3 (3)	>.99

Abbreviations: CGI-S, Clinical Global Impression of Severity scale; MBSR, mindfulness-based stress reduction; NA, not applicable.

[a] Group means were compared using 2-sample *t* tests. Percentages for categorical variables were compared using χ^2 test or Fisher exact test.

[b] We collected data on race and ethnicity as required by our trial sponsor; these data were collected using a multiple-choice self-report form based on the National Institutes of Health standard enrollment table.

[c] Other included Native American or Alaska Native, more than one race, or other, consolidated because of low numbers in these groups and because test results based on percentages become misleading when the distribution of observations across categories is highly disproportionate.

dummy variables with baseline as the reference category. Predicted margins were computed at each time point for both treatment groups. The patient-reported outcome measure OASIS was described and analyzed using similar methods. Safety outcomes were assessed for all randomized participants. All analyses were conducted in Stata version 15 (StataCorp; commands: *mi impute*, *mi estimate*, *xtmixed*, *margins*, *contrasts*, *marginsplot*) by coinvestigator statistician M.M.

Results

Of 430 adults who consented and were assessed by study clinicians, 276 met study criteria (mean [SD] age, 33 [13] years; 156 [75%] female; 32 (15%) African American, 41 (20%) Asian, 18 (9%) Hispanic/Latino, 122 (59%) White, and 13 (6%) of another race or ethnicity, including Native American or Alaska Native, more than one race, or other, consolidated because of low numbers in these groups and because test results based on percentages become misleading when the distribution of observations across categories is highly disproportionate). Participants were randomized to MBSR (n = 136) or escitalopram (n = 140). In the escitalopram group, 33 participants either did not begin or only partially received treatment, and 1 missed the end point study visit, and in the MBSR group, 34 participants either did not begin or only partially received treatment, resulting in a final sample of 208 participants. See Table 1 for participant characteristics and **Figure 1** for the CONSORT diagram. Participants were enrolled between June 6, 2018, and February 11, 2020.

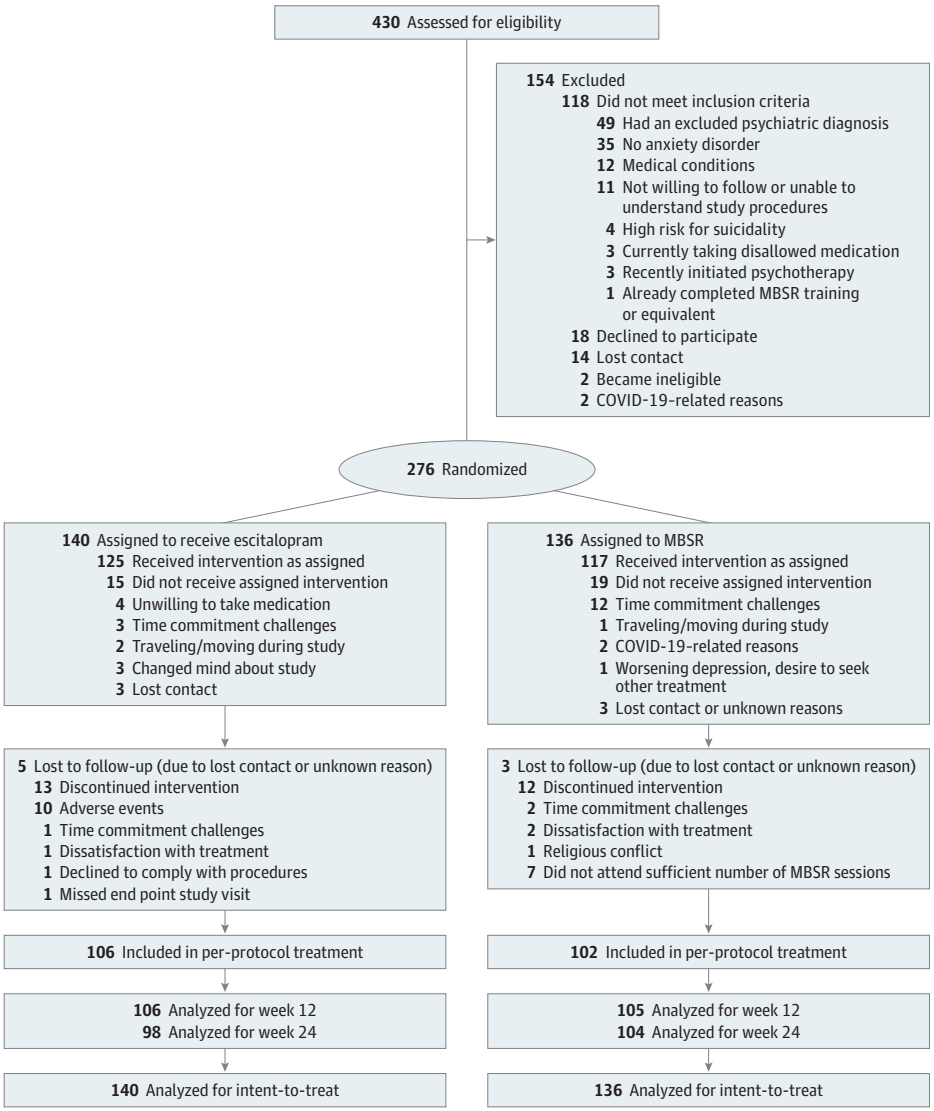
Baseline demographic characteristics were similar between the per-protocol and ITT samples (eTable 1 in Supplement 2) and by treatment group within each sample (Table 1). Clinical severity at baseline was in the moderate to markedly ill range and did not differ by treatment group. Baseline mean (SD) CGI-S score was 4.44 (0.79) for MBSR and 4.51 (0.78) for escitalopram in the per-protocol sample and 4.49 (0.77) vs 4.54 (0.83) in the randomized sample.

Primary outcome analyses in those who completed the trial at week 8 showed noninferiority for CGI-S score improvement with MBSR compared with escitalopram. Specifically, at week 8, the MBSR group improved by a mean (SD) 1.35 (1.06) and the escitalopram group by 1.43 (1.17) points. The difference between the groups in the primary CGI-S outcome at week 8 (change in MBSR minus change in escitalopram) was −0.07 (95% CI, −0.38 to 0.23; *P* = .65). The confidence interval crossed zero, suggesting that the change was not significantly different between groups. The lower end of this 97.5% (−0.38) was smaller than the prespecified noninferiority margin of −0.495, indicating noninferiority of MBSR compared with escitalopram (**Figure 2**). CGI-S outcomes for each time point by treatment are reported in **Table 2**.

Sensitivity analyses in the ITT sample at week 8 using imputed data also showed a noninferiority of MBSR compared with escitalopram based on the improvement in CGI-S score (eTable 3 in Supplement 2). We had 222 observations for CGI-S at week 8 regardless of participants' completion status. Sensitivity analyses comparing baseline characteristics between participants with and without week 8 data suggested no systematic differences in missingness patterns (eTable 2 in Supplement 2). Multiple imputation was thus performed to impute CGI-S score for participants with no end point assessment. Results summarized over 50 imputed samples generated a mean (SE) of 3.16 (0.11) for MBSR and 3.12 (0.11) for escitalopram at week 8. The difference between groups was estimated using a linear regression model of CGI-S score on treatment group indicator using imputed samples with no other covariates. The CGI-S score was smaller on average by 0.04 points for the ESC group, but the difference was not statistically significant (95% CI, −0.33 to 0.26, *P* = .81). The mean (SE) improvement in the MBSR group was 1.34 (0.10) and 1.43 (0.11) in the escitalopram group. The difference between the groups was estimated to be −0.09 (95% CI, −0.39 to 0.20). The confidence interval crossed zero, indicating no difference between the groups. In addition, the lower end of this 97.5% CI (−0.39) was smaller than the prespecified noninferiority margin of −0.495, showing that MBSR was noninferior to escitalopram.

Next, we examined the primary outcome at follow-up and found that both the MBSR and escitalopram groups continued to improve in the follow-up period (Table 2). The mean (SD) CGI-S score for those who completed treatment was 2.89 (1.09) in MBSR and 2.95 (1.07) in escitalopram (difference = −0.07; *P* = .67) at week 12, and 2.92 (1.17) in MBSR and 2.92 (1.03) in escitalopram (difference = 0.00; *P* > .99) at week 24.

Figure 1. CONSORT Diagram



MBSR indicates mindfulness-based stress reduction.

Longitudinal data were analyzed using a linear mixed model of CGI-S in the ITT sample with random effects at participant level, pooling data across 5 time points: baseline (n = 276), week 4 (n = 226), week 8 (n = 222), week 12 (n = 211), and week 24 (n = 202). The model estimates are presented in eTable 4 in Supplement 2 showing the predicted mean differences with 95% CIs between groups at each time point. Group trajectories over time, based on predicted means, are illustrated in **Figure 3**. Results show that the adjusted mean difference between the groups was −0.07 points (95% CI, −0.31 to 0.17; *P* = .55) at week 8, further confirming the noninferiority of MBSR to escitalopram. Baseline mean (SD) scores for OASIS were 9.2 (2.9) in MBSR and 9.5 (3.0) in escitalopram with no statistically significant difference (*P* = .48). At the primary end point (week 8), treatment groups were not significantly different either (5.8 [3.8] in MBSR vs 5.2 [3.5]; *P* = .21).

The results of the linear mixed models for outcomes are presented in eTable 4 in Supplement 2. The predicted differences between the groups at week 4 show that participants in the escitalopram group experienced larger improvements in the short term by OASIS score (mean, 1.2; 95% CI, −2.02 to −0.35; *P* = .01) in escitalopram. The treatment groups were not significantly different at end point on OASIS score (−0.7; 95% CI, −1.51 to 0.17; *P* = .12).

No serious adverse events occurred during the study across the 2 arms. At least 1 study-related adverse event occurred for 110 participants randomized to escitalopram (78.6%) and 21 participants randomized to MBSR (15.4%) (*P* < .001). Adverse events (considered possibly or definitely related to study treatment) that occurred in 5% or more of participants in the escitalopram group were insomnia or sleep disturbance (n = 51; 41%), nausea (n = 44; 35%), fatigue (n = 33; 26%), headache (n = 23; 18%), somnolence (n = 18; 14%), anorgasmia or delayed orgasm (n = 14; 11%), abnormal dreaming (n = 11; 9%), decreased appetite (n = 11; 9%), jitteriness (n = 11; 9%), decreased libido (n = 9; 7%), dizziness/lightheaded/faint (n = 8;

6%), increased sweating (n = 8; 6%), and anxiety (n = 7; 5%). The only adverse event (possibly or definitely related to treatment) that occurred in 5% or more of participants in the MBSR group was increased anxiety (n = 13; 11%). A full list of adverse events across treatment arms is reported in eTables 5 and 6 in Supplement 2.

No participants discontinued due to clinical worsening or emerging suicidality. The completion rate (completing at least 6 of the 9 MBSR sessions or at least 6 weeks of escitalopram) for participants was 75% for MBSR (n = 102) and 76.5% (n = 106) for escitalopram. At 12-week follow-up, 75 (78%) of the escitalopram group reported continued treatment, and 48 (49%) in MBSR had continued meditating (defined as at least 4 days a week). By 24-week follow-up, 53 (52%) were still taking escitalopram while 27 (28%) in MBSR were still doing regular mindfulness meditation.

Discussion

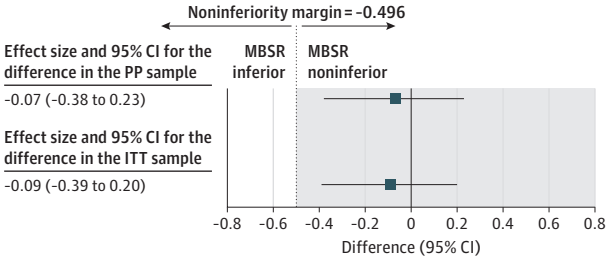
Our prospective randomized clinical trial found that MBSR was noninferior to escitalopram for the treatment of anxiety disorders. In addition, MBSR was safe and well tolerated, with fewer adverse events associated with treatment compared with escitalopram. The magnitude of symptom reduction in the escitalopram group (mean of 1.4 points on the CGI-S) was comparable to published studies that established escitalopram as more effective than placebo. For example, Davidson et al[20] compared escitalopram with placebo for generalized anxiety disorder and found a decrease of 1.4 points on the CGI-S. In another example, Asakura et al[21] reported a decrease of 1.1 points on the CGI-S in a randomized clinical trial using escitalopram for social anxiety disorder.

To our knowledge, this is the first study comparing a standardized evidence-based MBI with a first-line medication for anxiety disorders. Costa et al[22] compared an experimental MBI based on movement exercises rather than the traditional sitting meditation, with fluoxetine in patients with generalized anxiety disorder and failed to show noninferiority. Compared with our MBI, the dropout rate in Costa et al[22] was higher (nearly 40% vs 25%), the sample size was smaller (165 vs 276), the intervention length was shorter (16 hours vs 27 hours), and the intervention structure and content were fundamentall different. We are unaware of other noninferiority studies comparing MBIs with medications in anxiety disorders. Strengths of our study include a carefully diagnosed and well-characterized patient sample, trained clinical raters blinded to treatment allocation doing assessments, and a prespecified clinically meaningful noninferiority margin.

Limitations

This study has limitations. Treatments in this study were not matched for time and attention, as participants in the MBSR group spent more time engaged in treatment-related activities than those in the escitalopram group, and this design allowed only for single-blinding procedures. However, this comparative effectiveness trial was designed to inform clinical decision-making in the real world rather than test the theoretical efficacy of 2 time-matched arms, and contact

Figure 2. Noninferiority Diagram



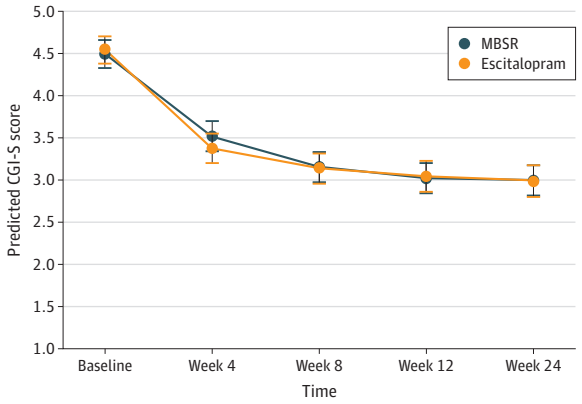
Effect sizes and noninferiority confidence intervals of primary outcome for mindfulness-based stress reduction (MBSR) vs escitalopram (week 8 end point). Difference is the improvement in MBSR minus improvement in escitalopram. Shaded region indicates region of noninferiority. ITT indicates intent-to-treat; PP, per-protocol.

Table 2. Primary Outcome Assessment Clinical Global Impression of Severity for Mindfulness-Based Stress Reduction (MBSR) vs Escitalopram

CGI-S score	Mean (SD)		Mean difference (SE)	*P* value
	MBSR	Escitalopram		
No.	102	106		
Baseline	4.44 (0.79)	4.51 (0.78)	−0.07 (0.11)	.53
No.	136	140		
Week 4	3.42 (1.01)	3.34 (1.04)	0.09 (0.14)	.55
No.	101	106		
Primary end point (week 8)	3.09 (1.09)	3.09 (1.07)	0.00 (0.15)	.98
No.	102	106		
Change from baseline to end point, mean (SD) [95% CI]	1.35 (1.06) [1.15 to 1.56]	1.43 (1.17) [1.20 to 1.65]	−0.07 (0.16) [−0.38 to 0.23]	.65
Follow-up (week 12)	2.89 (1.09)	2.95 (1.07)	−0.07 (0.15)	.67
No.	96	102		
Follow-up (week 24)	2.92 (1.17)	2.92 (1.03)	0.00 (0.16)	1
No.	95	95		

Abbreviation: CGI-S, Clinical Global Impression of Severity.

Figure 3. Longitudinal Data



Predicted Clinical Global Impression Severity scale (CGI-S) score based on a linear mixed model adjusted by age, sex, race, site, and total number of secondary diagnoses. MBSR indicates mindfulness-based stress reduction.

with the research study team was matched between the groups, with the clinical safety and assessment visits using the same procedures and carried out by the same members of the study staff. Sleep medications and benzodiazepines were also allowed if stable for at least 4 weeks prior to entry; however, the rate of use was minimal (<5%) and did not vary by group (Table 1). Other limitations include a sample that was predominantly female with a relatively high education level, the lack of data on disorder chronicity, and recruitment at 3 urban academic medical centers, which may limit the generalizability of the findings.

Conclusions

In this trial, an MBSR was shown to be a well-tolerated treatment option with comparable effectiveness to a first-line medication for patients with anxiety disorders. Problematic habitual thought patterns characterize anxiety disorders, and mindfulness training specifically focuses the mind on the present moment; thus, individuals practice seeing thoughts and sensations as merely transient mental phenomena and not necessarily accurate reflections of reality.[23] This reappraisal process improves emotion regulation, and individuals become less reactive to thoughts and sensations.[24] In addition, mindfulness is practiced with a nonjudgmental, accepting attitude, which over time appears to increase self-acceptance and self-compassion.[25]

Of note, MBSR in this trial was delivered in person, with trained meditation teachers available weekly to answer questions and guide practices, limiting any extrapolation in support of mindfulness apps or programs that are delivered over the internet. Future studies should assess the clinical effectiveness of virtual delivery of MBSR, other MBIs, and of mindfulness apps.

Although replication in different settings is warranted, this study's finding of the noninferiority of MBSR to a first-line pharmacotherapy for treatment of anxiety provides support for mindfulness meditation as an evidence-based treatment option for adults with anxiety disorders.

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Concept and design: Hoge, Bui, Mete, Dutton, Simon.
Acquisition, analysis, or interpretation of data: All authors.
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Statistical analysis: Mete.
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