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A comparison of Online, In-Person Mindfulness Based Stress Reduction (MBSR) Programs, and First-Line Medication (Escitalopram) Therapy and their impact on Sleep Quality among persons with Anxiety

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Abstract

A comparison of Online, In-Person Mindfulness Based Stress Reduction (MBSR) Programs, and First-Line Medication (Escitalopram) Therapy and their impact on Sleep Quality among persons with Anxiety

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Rationale: There is a need to identify the effectiveness of interventions for anxiety and the impact on sleep. This study sought to examine MBSR and Escitalopram treatments in a clinical trial of anxiety diagnosed patients. This analysis compares treatment effectiveness exploring changes in sleep outcomes between the in-person and online phases.

Methods: Between June 2018 and February 2022, anxiety-diagnosed patients participated in a randomized clinical trial, Treatments for Anxiety: Meditation and Escitalopram (TAME), comparing Mindfulness Based Stress Reduction (MBSR) interventions to Escitalopram. The first half, conducted in-person, demonstrated both treatments as equally effective to reduce anxiety symptoms. Evaluations were conducted in-person or online, per study phase. Due to the COVID-19 pandemic, the interventions transitioned online. The 275 in-person cohort and 202 online cohort participants were randomized 1:1 with a respective 208 and 150 total participants completing the protocol. The 8-week exposures to each treatment were compared in a single blind, randomized clinical trial at baseline and weeks 4, 8, 12, and 24. Participants were examined with CGI-S, PROMIS-T Sleep Disturbance, and PSQI questionnaires.

Results: The mean CGI-S score reductions after 8-weeks of exposure were 1.35 for in-person MBSR, 1.43 for in-person Escitalopram, 1.18 for online MBSR, and 1.63 for online Escitalopram. The mean difference between online treatment groups was 0.45 ($p=0.01$) with greater reductions from the Escitalopram group. Although the online score difference was significant compared to the in-person equivalent ($p=0.03$), the change from baseline was insignificant ($p=0.22$). The two MBSR cohorts had no significant score difference effects over the measured periods.

All treatments and cohorts significantly decreased PROMIS-T Sleep Disturbance and PSQI at the conclusion of the study ($p=<0.01$). Using PROMIS-T, the sleep score differences between the MBSR groups were significantly different ($p=0.03$) at the week 8 study endpoint with a mean difference of 2.09. However, no other score differences between treatment type or exposure method during the duration of the study were significant.

The model development of PROMIS-T Sleep Disturbance and PSQI score changes during the study determined CGI-S difference was significantly associated with sleep improvement outcomes.

Conclusion: Although CGI-S differences were noted between the online exposed Escitalopram group with lower reductions compared to other treatment exposures, sleep disturbance changes remained similar for each exposure group. CGI-S reductions significantly lowered sleep disturbance across all exposures and models though treatment and in-person exposures were not significant.

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Introduction

Anxiety is an increasingly common mental illness in the United States (*Household Pulse Survey*, 2020-2023). The study of effective symptom management through various treatments and platforms is of greater necessity. The Treatments for Anxiety: Meditation and Escitalopram (TAME) study is a randomized clinical trial conducted between June 2018 and February 2020 compared Escitalopram (Lexapro) with in-person Mindfulness Based Stress Reduction (MBSR) treatment to manage anxiety symptoms measured by the Clinical Global Impressions-Severity scale (CGI-S) based on a randomized sample of 208 patients across three (New York, Boston, and Washington DC) medical centers in the US and showed that MBSR was comparable to first-line anxiety medication Escitalopram (Hoge et al., 2023).

An additional cohort of 150 total participants was added during the COVID-19 pandemic with a remote delivery of the same interventions to further study whether the in-person or online presentation formats moderates the differences in the two treatment methods. The goal of this current study is to analyze the anxiety and sleep-related outcomes of participants from the online phase of the clinical trial using the CGI-S score, the Patient-Reported Outcomes Measurement Information System (PROMIS-T) Sleep Disturbance and Pittsburgh Sleep Quality Index (PSQI) scores. Treatment groups will subsequently be compared between the online and in-person cohorts to compare outcome differences from presentation and implementation formats. Data analysis for this study includes demographic comparisons between the medication and mediation groups. Variables such as race, gender, and age will be evaluated for significance in models for PSQI and PROMIS-T Sleep Disturbance score both in the online cohort and amongst all observations. Based on this information, the ideal background demographics and methodologies

for implementing medication and meditation treatment can optimize future anxiety symptom management.

From previous studies associated with this data and the treatments involved, the hypothesis is that MBSR and Escitalopram will continue to be equally effective in lessening anxiety symptoms in an online format, similar to the in-person cohort. Because of the strong association between sleep and anxiety symptoms, both the PROMIS-T Sleep Disturbance and PSQI scores are hypothesized to decrease from baseline to more normal levels at the conclusion of the treatment protocol. This effect will be mirrored by the CGI-S score as a significant variable to predicting PROMIS-T Sleep Disturbance and PSQI reduction. Due to the strength of the relationship between anxiety and sleep disturbance, primary anxiety diagnosis may be a significant variable associated with sleep outcome improvement.

Literature Review

As anxiety becomes a more common mental illness within the United States and more treatments are discovered, the subsequent impact of treatments on different anxiety disorders, resulting side effects, and demographic outcome differences continue to be investigated.

The purpose of this study is to assess medication (Escitalopram) and mediation methodologies (MBSR) for anxiety management and sleep quality in patients from New York, Boston, and Washington DC. This will be conducted through comparing the in-person and online course formats and demographic characteristics of patients, effective implementation strategies will be determined for both MBSR and Escitalopram treatments within the context of race, age, sex, and gender as well as mental health comorbidities.

Sleep disturbance is commonly associated with Generalized Anxiety Disorder, Panic Disorder, and Post-Traumatic Stress Disorder (Mellman, 2006). There is often overlap of anxiety

disorders with certain sleep related phenomena including panic attacks and nightmares (Mellman, 2006). Loss of sleep can exacerbate anxiety symptoms and keep treatments ineffective (Mellman, 2006). Responses to stress create nervous system alterations resulting in hormonal, behavioral, and autonomic responses inciting insomnia episodes and limiting Rapid Eye Movement (REM) cycles by increasing arousal (Staner, 2003).

Although numerous anxiety related treatment studies have been conducted, this study uniquely compares in-person to online educational formats for improvements in symptom management, most notably insomnia, assessing meditation and medicative treatments. Given the timing of the study during the COVID-19 pandemic, heightened anxiety levels presented a greater challenge for treatment success, further complicated by switching from in-person to online trainings.

Anxiety Background & Overview

Prior to the COVID-19 pandemic, approximately 15.6% percent of the United States population experienced General Anxiety Disorder symptoms within the past two weeks (Villarroel, 2020). As of 2020, anxiety caused 44.5 million Disability-Adjusted Life Years globally (Collaborators, 2021). Pre-pandemic, anxiety prevalence was relatively stable, though underreporting is frequent (Bandelow & Michaelis, 2015). In subsequent years, these rates have spiked overall with symptoms experienced in the past seven days ranging from 24.5% to 37.2% of the population between April 2020 to July 2023 (*Household Pulse Survey*, 2020-2023). As a direct result of COVID-19 pandemic, worldwide anxiety and depression rates are attributed to a 25% increase (Organization, 2022).

Anxiety in general evolves beyond occasional fear or worry stemming from discomforting situations (Association, 2022). Anxiety goes unrelieved without treatment and

often worsens with time (Health, 2023). Anxiety risk factors include shyness, distress, or nervousness in childhood with unfamiliar situations, stressful, negative life or environmental events, and a family history of mental disorders (Health, 2023). Symptoms can be aggravated by physical health conditions such as heart arrythmia or thyroid issues and intake of caffeine or other substances and medications (Health, 2023). However, the prevalence of anxiety varies amongst different age groups, races, genders, and socioeconomic status along with other biological and environmental indicators. Adolescents are particularly vulnerable to anxiety disorders, though risk tends to decrease with age with a median age of 11 years old (Bandelow & Michaelis, 2015). A New York based study measured anxiety levels in adolescents aged 12 to 22, determining an increase in prevalence from 25% to 40% of the study population in spring 2020 (Hawes et al., 2022). Anxiety, across both a 12-month period and a lifetime period, disproportionately impact women with a 1:1.79 and 1:1.70 ratio of men to women diagnosis, respectively (McLean et al., 2011). Race is an influential determinant for anxiety development, as studies have shown that Native American, White, and Hispanic American populations have the highest rates of anxiety (Esala, 2019). More specifically, White Americans have a greater likelihood of developing Social Anxiety Disorder (SAD) and General Anxiety Disorder (GAD) while Black Americans have a higher propensity for Post-Traumatic Stress Disorder (PTSD) (Asnaani et al., 2010). As an environmental factor, low socioeconomic status tends toward a positive correlation with anxiety symptoms (Catherine DeCarlo Santiago, 2011). A 2011 longitudinal study of family members living in poverty revealed a positive correlation between low Socioeconomic status and negative mental health outcomes including social disorders, anxiety, and depression (Catherine DeCarlo Santiago, 2011). However, women are more

susceptible to socioeconomic related stress than men, resulting in greater rates of anxiety due to economic inequality (Mwinyi et al., 2017).

Other mental health disorders, most notably depression, are highly linked to anxiety (Prevention, 2022). Additionally, COVID-19 has emerged as a recent stressor, promoting anxiety for both patients and those around them. According to the World Health Organization, those with a mental health disorder are more likely to suffer severe complications from COVID-19 including hospitalizations and death (Organization, 2022). Mental health services were disrupted as a result of the shift to e-service mental care, widening the overall mental health gap within populations around the world (Organization, 2022). In a study of 402 screened COVID-19 survivors, 56% scored on the pathological range for mental disorders including PTSD, depression, anxiety, Obsessive Compulsive symptoms, and insomnia (Mazza et al., 2020). Around the world, locations affected by the pandemic have a positive correlation to increased mental health disorders with an estimated prevalence of 4 cases per 100,000. This is exacerbated given the lack of resources available due to greatly impacted areas (Collaborators, 2021).

Anxiety disorders involve emotional and physical symptoms. Emotional symptoms include fear, tension and stress, and irritability while physical symptoms are difficulty breathing, sweating, insomnia headaches and upset stomach (NAMI, 2017). The most common types of anxiety disorders are General Anxiety Disorder, Social Anxiety Disorder, Panic Disorder, and Phobias (NAMI, 2017). The majority of the patients in the TAME study are diagnosed with GAD and SAD, though PD and Agoraphobia patients were included as well.

Generalized Anxiety Disorder (GAD) is a common and disabling illness that is often underdiagnosed and undertreated (DeMartini et al., 2019). The symptoms of GAD include restlessness, fatigue, difficulty concentrating, irritation, and achiness including headache and

muscle tension (Service, 2022). The lifetime morbidity risk over all mental disorders (LMR) is 9.0% with a 12-month prevalence of 2.0% (Kessler et al., 2012). Social Anxiety Disorder (SAD) is characterized by difficulty engaging in social situations. Physical symptoms include blushing, sweating, trembling, heart racing, ridged posture, difficulty making eye contact, and speaking softly (SAMHSA, 2023). Emotionally, patients feel self-conscious about judgement from others (SAMHSA, 2023). SAD LMR is 13.0% and 12-month prevalence is 7.4% (Kessler et al., 2012). Panic Disorder (PD) patients experience similar symptoms as SAD and GAD but have thoughts of impending doom and feeling out of control (SAMHSA, 2023). LMR for PD is 6.8% and 12-month prevalence is 2.4% (Kessler et al., 2012). Phobias are directed at a specific feared object or situation, which result in a patient taking active steps to avoid encountering the fear (SAMHSA, 2023). Phobia-related Anxiety has an LMR of 18.4% and a 12-month prevalence of 12.1% (Kessler et al., 2012). Other common anxiety disorders include: Post-Traumatic Stress Disorder (PTSD), attributed to frightening or distressing events (LMR 10.1%, 12-month prevalence 3.7%), Obsessive-Compulsive Disorder (OCD), marked by repetitive behaviors specifically due to a need for order or to avoid germs (LMR 2.7%, 12-month prevalence 1.2%), and Agoraphobia which is a fear of leaving home and being alone in crowds (LMR 3.7%, 12-month prevalence 1.7%) (Kessler et al., 2012; SAMHSA, 2023).

Anxiety can often be misdiagnosed or underrepresented by medical professionals (DeMartini et al., 2019). GAD can be screened using either the GAD-7 or the simpler GAD-2 test. Both have great sensitivity (68% for GAD-7, 65% for GAD-2) and specificity (88% for both GAD-7 and GAD-2) to diagnose any anxiety in patients (Sapra et al., 2020). The seven-item GAD-7 has the highest correlation to the originally developed 13-item scale (Ebell, 2008). In addition to GAD diagnosis, GAD-7 is accurate detecting PD, SAD, and PTSD (Ebell, 2008). For

the GAD-7 test, the seven following feelings and symptoms are ranked on a scale of 0 to 3 with a higher score ranking as a more frequent occurrence: Feeling nervous, anxious, or on edge; Not being able to stop or control worrying; Worrying too much about different things; Trouble relaxing; Being so restless that it is hard to sit still; Becoming easily annoyed or irritable; Feeling afraid as if something awful might happen (Robert L. Spitzer). However, diagnosing anxiety has a variety of complications, with overlapping symptoms indicating multiple mental health diagnoses and comorbidities. The comorbidity of anxiety with Major Depressive Disorder (MDD) in 50-60% of patients results in difficult isolating anxiety symptoms from depression symptoms to give an accurate diagnosis (Kaufman & Charney, 2000). With different anxiety disorders being able to overlap and emerge at different points during a patient's lifetime, inclusion of neuroimaging and genetic research can provide a further, more comprehensive diagnosis compared to questionnaires (Bystritsky et al., 2013). The most accurate anxiety diagnoses reflect a spectrum of symptoms and potential disorders. Since numerous anxiety disorder expressions may interrelate, a more dimensional overview of anxiety symptoms will help to better manage treatment outcomes (Brown et al., 1998).

In this study, the Clinical Global Impression-Severity (CGI-S) scale is used to measure the degree of anxiety experienced by the patients (Guy, 1976). The CGI-S is a 7-point scale with a score of 1 as normal or not at all ill and 7 as the most severely ill. The rating is clinician based and often used in clinical trials, determined by evaluations of the subject's behavior and in response to the question "Considering your total clinical experience with this population, how mentally ill is the patient at this time?" (Busner & Targum, 2007). Rather than examining symptoms, behavior, and function in the moment of the screening as these can fluctuate, the CGI-S is an overall average of the evaluation over the past week. This scale has proven effective

as a primary outcome treatment measure against many anxiety disorders, including SAD (Zaider et al., 2003). Studies using a self-reported diagnosis have resulted in poor accuracy due to the wide variety of symptoms and limitations of diagnosis (Rose & Devine, 2014). Symptom-based diagnosis helps to differentiate types of anxiety disorders beyond GAD more effectively than self-reporting (Davies et al., 2022). Thus, having the clinician as the evaluator is essential to keep the study blinded and eliminate recall bias from study patients. A review of studies comparing the CGI-S to other popular rating scales evaluating anxiety and depression after use of Escitalopram found a strong correlation between these "standard scales" (Montgomery-Asberg Depression Rating Scale, Panic and Agoraphobia Scale, Hamilton Rating Scale for Anxiety, and the Liebowitz Social Anxiety Scale) and the CGI-S (Borwin Bandelow, 2006). The simplicity of this single-question evaluation by clinicians allows for reliable, accurate assessment of treatment improvement.

Anxiety Treatment

Treatments for anxiety disorders are divided into three major categories: psychotherapy, medication, and complementary health approaches (NAMI, 2017). Though Antidepressants are usually first-line medical treatments, Psychotherapy and Psychosocial treatments can be just as effective (Hoge et al., 2012).

Psychotherapy involves talking with a licensed therapist about stressors and learning ways to manage symptoms effectively (NAMI). Cognitive Behavioral Therapy which explores the connection between thoughts, feelings, and actions is commonly used for anxiety treatment (NAMI). In addition to meditative, self-care practices, the Cognitive Behavior Theory is commonly used to help mentally break down anxiety challenges. Fear confrontation can assist in managing anxiety triggers (Howard, 2023). A pooled analysis of psychotherapy treatment

revealed an 84% improvement in anxiety and a 71% improvement in depression symptom management compared to the control group (Cuijpers et al., 2014). However, in this study self-reports scored lower than clinician provided reports (Cuijpers et al., 2014). CBT treatment with booster sessions show a 64% improvement in managing anxiety symptoms. Compared to CBT without booster sessions with a 48% improvement, continuous and repetitive treatment for anxiety is necessary to mitigate symptom reappearance, particularly in adolescents (Gearing et al., 2013). CBT is easily transferrable to an online format, producing similar improvements in treatment outcomes (Craske et al., 2009). With understanding of modules ranging from 85.4% to 91.6%, online CBT trainings are effective at providing ways to manage symptoms for anxiety patients (Craske et al., 2009).

Medication treatment typically includes Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) (NAMI). Use of anti-anxiety medications rose 10.2% from March 2019 to March 2020 with 9.7 million Americans utilizing these treatments (Petersen, 2020). SSRIs and SNRIs are the first preference for anxiety pharmacotherapy. Due to their addictive properties, Benzodiazepines are not recommended for routine use (Gomez et al., 2018). Additional pharmacotherapy treatments include pregabalin, tricyclic antidepressants, buspirone, and moclobemide (Bandelow et al., 2017). Typically, treatments should continue for 6 to 12 months after symptoms subside (Bandelow et al., 2017). Escitalopram is an antidepressant used for the treatment of Major Depressive Disorder and Generalized Anxiety Disorder. Doses are typically taken in pill or liquid form once a day and range from 10 to 20 mg, depending on what a patient's healthcare provider prescribes (NAMI, 2022).

Unlike many novel technologies such as serotonergic agents, neuropeptides, and glutamates, Escitalopram is FDA-approved to treat GAD and is widely used to treat both SAD and PD (Garakani et al., 2020). Against other SSRIs and SNRIs amongst numerous randomized controlled trials, Duloxetine and Escitalopram had the highest efficacy during and after the study time period (He et al., 2019). Considering most of the clinical trial study population has GAD or SAD as their primary diagnosis, using a proven treatment against these disorders is crucial to this comparative analysis. In an 850-person double-blind, placebo-controlled trial, Escitalopram significantly improved the Hamilton Anxiety Scale score over the 8-week exposure period compared to both the baseline values and placebo controls (Goodman et al., 2005). Since General Anxiety Disorder (GAD) is more common in older adults, a 12-week blinded study comparing Escitalopram to a placebo proved effective and safe with fatigue, urinary challenges, and sleep disturbance as common symptoms for those patients over 60 years old (Lenze et al., 2009). Genetics influence the efficacy of these medications. A randomized, placebo-controlled, double-blind study of adolescents proved that Escitalopram and with the addition of the CYP2C19 phenotype improves the magnitude and trajectory of improvement for adolescents between 12 to 17 years old within an 8-week period (Strawn et al., 2020).

Complementary health approaches are typically a supplement in conjunction with medication treatment (NAMI). These include supplementary medications (for example, vitamins and food products), mind and body treatments (yoga, meditation, tai chi), and animal assisted therapy with horses or dogs (NAMI). From establishment in 1979 by Jon Kabat-Zinn, MBSR is a leading treatment used to treat a variety of emotional, psychological, and physical conditions. MBSR as a treatment has expanded to over 720 medical centers worldwide. At the center of MBSR is the interaction of mind and body to ease pain and improve health outcomes (*History of*

MBSR, 2021). MBSR encourages practice for 8 weeks for 45 to 60 minutes at least 6 days a week to achieve maximum effectiveness for the program (Bitterauf, 2016). The practice involves a whole-body experience from eating habits, meditation skills, yoga, and mantras that allow for self-awareness and relaxation within overwhelming environments (Bitterauf, 2016). The ultimate goal is to connect with the feelings within one's body and mind and learn to contend with adversities throughout the practice in a meaningful, healthy way (Bitterauf, 2016). Across multiple studies of younger populations, Mindfulness-Bases Stress Reduction (MBSR) significantly reduced anxiety symptoms, with a duration of longer than 8 weeks for treatment being an influential contributor to positive treatment outcomes (Zhou et al., 2020). Many trails comparing the impact of MBSR on adolescents' mental health, including the Vliet et al. study have limited participation and do not connect MBSR to sleep improvements through direct measurement (Van Vliet et al., 2017, Urvashi Anand, 2011 #119). MBSR is an effective strategy for anxiety treatment in older adults, significantly reducing geriatric anxiety symptoms by 54% and depression by 14% over the span of the program and maintaining effectiveness over the span of a month after completion (Kabatas Yildiz & Orak, 2023). Compared to an attention control, Stress Management Education, in an 8-week treatment of GAD patients, MBSR is more effective in reducing stress attributed to anxiety, even with similar reductions in overall anxiety during and after treatment (Hoge et al., 2013). MBSR has proven to be effective, not just with mental health issues, but also with chronic illnesses such as cancer, hypertension, diabetes, HIV/AIDS, and other chronic pain (Niazi & Niazi, 2011).

The American Psychological Association recognizes the benefits of mindfulness as a everyday practice which aids in reducing stress and rumination, boosting memory and focus, easing emotional reactions, and improving cognitive flexibility (Association, A. P., 2022). This in

turn improves relationships, lessening physical and mental disease burden and improving outcomes (Association, A. P., 2022). Rather than mitigating mental disease symptoms like a medication would do, the main objective of MBSR is to confront feelings and learn to challenge stressors in healthy ways, finding the source of the anxiety (Hayes, 2012). MBSR is translatable through many cultures and life events, most notably the COVID-19 pandemic (Accoto et al., 2021). A small-scale study of 26 Italian females amidst the 2020 COVID-19 lockdown proved those trained with MBSR education during this adverse event were psychologically flexible and able to contend with traumatic events compared to the unexposed control (Accoto et al., 2021). When learned, MBSR techniques can be utilized repeatedly beyond the 8-week training to help transition patients through different stages of life (*Why Mindfulness-Based Stress Reduction (MBSR)?*). MBSR is a standardized practice, which is well researched, affordable, and supportive to many lifestyles and burdens (*Why Mindfulness-Based Stress Reduction (MBSR)?*).

Anxiety and Sleep

According to a study conducted by Breslau et al., the odds of having insomnia with any anxiety disorder are 2.4 times greater (Breslau et al., 1996). The relationship between insomnia and anxiety is much stronger in those with General Anxiety Disorder (GAD) at 7 times greater risk (Chellappa & Aeschbach, 2022). Due to this high rate of association, insomnia is a symptom used to diagnose GAD (Chellappa & Aeschbach, 2022). Narcolepsy, excessive drowsiness, and cataplexy can be common sleep-related disorders found with anxiety, particularly, PD (Uhde et al., 2009). GAD patients are often unable to distinguish sleep and wakeful phases (Uhde et al., 2009). 50% of psychiatrists misdiagnosed sleep paralysis hallucinations as psychiatric disorders (Uhde et al., 2009). There is a lack of reliable psychiatric markers for insomnia for those anxiety patients who may misinterpret sleep cues (Uhde et al., 2009). Though there are no changes in

REM associated with anxiety disorders since panic attacks occur in 18-45% of PD patients outside of the REM stage, increased sleep latency and decreased continuity is reported in 60-70% of patients with GAD (Papadimitriou & Linkowski, 2005). Those with OCD and PTSD report poor sleep, but testing does not support the claims (Papadimitriou & Linkowski, 2005). Social phobia patients show little difference in sleep parameters (Papadimitriou & Linkowski, 2005). In a sample of youth aged 13 to 16, anxiety preceded insomnia 73% of the time, while insomnia occurred first 69% of the time (Johnson et al., 2006). With a hazard ratio of approximately 3.5, anxiety has an increased risk of insomnia (Johnson et al., 2006). Thus, anxiety disorders typically result in insomnia versus the other way around (Johnson et al., 2006).

Dysregulated cortisol is a mediator of the relationship between sleep and anxiety symptoms (Cox & Olatunji, 2016). Repeated sleep disturbance impacts cortisol levels and can result in the development of an anxiety disorder (Cox & Olatunji, 2016). Treatment of insomnia prior to treating the anxiety disorder may be more effective than concurrent treatment (Cox & Olatunji, 2016). Sleep-related issues in youth are associated with age, severity, external problems, functional impairment, and family burden (Caporino et al., 2017). The greatest reductions were by those with multimodal treatment or with sertraline (Caporino et al., 2017). CBT was effective in reducing sleeplessness (Caporino et al., 2017). A study conducted on youth ages 9-14 deemed that with just CBT or Client Centered Treatment alone, small reductions in insomnia were found (McMakin et al., 2019). With the addition of sleeping TIGERS (a sleep enhancement program) in the second phase of the study, significant improvements in insomnia symptoms were found (McMakin et al., 2019). Sleep quality and sleep latency improved modestly during Cognitive Behavioral Treatment with PD and GAD patients (Ramsawh et al., 2016). Additional treatments for sleep disturbance may be effective for anxiety patients with

insomnia (Ramsawh et al., 2016). SSRIs are useful in lessening anxiety-related sleep disorders as a first line pharmacological treatment (Chellappa & Aeschbach, 2022). 497 patients across seven randomized control trials were compared, analyzing the effects of MBSR treatment on insomniac symptoms (Chen et al., 2020). This pooled review determined a standard mean difference between control and test subjects of -0.69 for sleep quality, -1.83 for depression, and -1.74 for anxiety over the course of the 8-week MBSR course (Chen et al., 2020). A systematic review of literature of 31 studies on Chinese COVID-19 patients found the pooled incidence of depression was 45%, anxiety was 47%, and sleep disturbance was 34% (Deng et al., 2021).

When rating insomnia, single-factor models of sleep disturbance had a poor fit of determining insomnia symptoms (Brossoit et al., 2023). Two factor models are more reflective, proving that dissatisfaction of sleep was more positively correlated with sleep duration and health than insomnia symptoms (Brossoit et al., 2023). PROMIS-8b short form is best modeled using the two-factor sleep construct (Brossoit et al., 2023). In a 2021, the Pittsburgh Sleep Quality Index (PSQI), Athens Insomnia Scale (AIS), Insomnia Severity Index (ISI), Mini-Sleep Questionnaire (MSQ), Jenkins Sleep Scale (JSS), Leeds Sleep Evaluation Questionnaire (LSEQ), SLEEP-50 Questionnaire, and Epworth Sleepiness Scale (ESS) were compared to evaluate their ability to rate sleep (Fabbri et al., 2021). PSQI has good validity and reliability, however factorial structures proved to be an issue with the rating abilities (Fabbri et al., 2021). LSEQ and SLEEP-50 were also lengthy and inaccurate to score (Fabbri et al., 2021). AIS and ISI have a variety of models produced (Fabbri et al., 2021). MSQ and JSS are unreliable due to their age and potential inaccuracy although they showed promise with the cost and ease of use (Fabbri et al., 2021). Finally, the ESS had problems with the factorial structure (Fabbri et al., 2021).

In-person and Online Anxiety Treatment and Education Comparison

Global internet usage has surged since 2019 to 63% (4.9 billion people) of the world's population regularly using the internet (Union, 2021).. The largest increase was in 2020, when there was a 10.3% increase, directly attributed to the COVID-19 pandemic (Union, 2021). In Fall 2021, 9.4 million undergraduate students (61%) were enrolled in at least one distance learning course. 75% were enrolled in 2020 (Statistics, 2023). Though the rates of distance learning are lessening, for-profit, private institutions have the greater capacity to support online learning (Statistics, 2023). During the COVID-19 pandemic 93% of households reported using online platforms for teaching school-aged children (McElrath, 2020). There is a discrepancy in usage amongst high-, middle-, and low-income households, with the latter reporting only 65.8% of children using online resources in this period (McElrath, 2020). One can assume this inequity would affect access to online counseling in the same manner, exacerbating the gaps between socioeconomic status and mental health.

Online education can be an effective method of teaching students, as long as the interactions between them, their teachers, contents, other students, and administrators continue engagement (Daniel Moise, 2021). However, attitudes about implementation and effectiveness of these methods amongst therapists have varied across multiple studies (Bekes et al., 2021). A study of 1257 therapists was conducted prior to the start of online therapy and after 3 months to determine attitude changes about online therapy. Of the four main challenges identified, three (emotional connection, privacy, and therapist boundaries) were alleviated, but distraction increased over time. Older and more experienced therapists perceived less challenges with the online format overall (Bekes et al., 2021). Conversely, surveys of 114 counselors revealed tremendous inefficiency of online therapy programs due to high levels of distraction and

disengagement. Certain clientele were more receptive to treatment but not as conducive to diagnosis and treatments goals (Barker, 2021).

Though counseling sessions have not proven to be as effective, structured therapy programs have produced more favorable results in the online format. A randomized study of college students with mild to moderate anxiety compared online to in person solution-focused therapy and found no difference between the two groups (Novella et al., 2022). Another clinical trial of Cognitive Behavioral Therapy patients proved that the online format compared to in-person was noninferior regarding the treatment outcomes (Axelsson et al., 2020). Online treatment could be easily effective as a first line therapy treatment for anxiety (Axelsson et al., 2020). The net societal cost is lower due to less time with patients spent by counselors every week (Axelsson et al., 2020). MBSR online programs specifically have exhibited success in alleviating anxiety symptoms with online-based Mindfulness anxiety interventions proven more effective in reducing symptoms than controls (Reangsing et al., 2023). Across 26 studies, anxiety was reduced on average approximately 35%, however, program moderators were not overly beneficial to positive outcomes (Reangsing et al., 2023). Those participants who took the 8-week long online MBSR course experiences improved mindfulness, decreased anxiety, decreased stress, and bettered emotional regulation (Sanilevici et al., 2021). These improvements, in particular emotional regulation, are key in mitigating stressful times including the COVID-19 pandemic (Sanilevici et al., 2021). Online MBSR programs are helpful for employees within organizational environments (Bossi et al., 2022). With these trainings, employees in workplaces can improve overall affect within job environments as well as help to mitigate interpersonal conflicts and other stressors (Bossi et al., 2022).

Comparative Anxiety Treatment and Sleep Studies

Other recent studies have examined the relationship between anxiety and the three treatment types (psychotherapy, medication, and complementary) on effectiveness in moderating patient symptoms (Crits-Christoph et al., 2011).

Medication and CBT comparative studies for mental health treatment have shown similar improvements in mental health (Crits-Christoph et al., 2011). GAD patients were randomized and treated with Venlafaxine-XR (an SNRI) medication alone or in combination treatment with CBT (Crits-Christoph et al., 2011). Both groups improved over the treatments after 24 weeks. Using the Hamilton Anxiety Rating Scale (HAM-A), 65% of combination and 71% of medication only patients showed improvement (Crits-Christoph et al., 2011). The Penn State Worry Questionnaire (PSWQ) evaluated 73% of combination and 80% of medication only patients achieved statistically significant improvements (Crits-Christoph et al., 2011). Treatment of depression patients with Antidepressant Medication (Administration) compared to Cognitive Therapy was determined initially to produce similar short-term improvements after 8 weeks. and lasted similarly in the longer term after 16 weeks (DeRubeis et al., 2008). Over a 1-year period of exposure compared to the placebo group, both ADM and CT groups exceeded the controls with fewer instances of depressive symptom relapse (DeRubeis et al., 2008). There were also fewer depression symptom relapses in the CT group (17%) in relation to the ADM group (54%) 1 year following medication withdrawal (DeRubeis et al., 2008). A pooled comparison of 115 studies focused on treatment of adolescent anxiety patients with a mean of 9.2 years old determined SSRIs increased remission of anxiety symptoms by 2.04 times (Wang et al., 2017). Though SNRIs also significantly reduced anxiety symptoms by an average of 65% per clinician report, Benzodiazepines and tricyclics did not (Wang et al., 2017). Compared to untreated controls, CBT significantly reduced anxiety symptoms and increased remission and showed

better response than fluoxetine (a SSRI) (Wang et al., 2017). Combinations therapies involving both CBT and sertraline proved more effective than either treatment alone (Wang et al., 2017). CBT had fewer adverse effects and dropouts than medication treated patients, though there is a lack of studies directly comparing CBT and medications (Wang et al., 2017).

Comparative studies to MBSR have proven this as an effective treatment to alleviating anxiety disorder symptoms. 108 patients with SAD were treated with Cognitive Based Group Therapy or MBSR and compared to waitlist controls then analyzed using the Liebowitz Social Anxiety Scale (Goldin et al., 2016). Both treatments groups improved outcomes in relation to the waitlist group (Goldin et al., 2016). A study of 56 adults with SAD were randomized to MBSR or Aerobic exercise (Jazaieri et al., 2012). Clinical symptoms and subjective well-being were analyzed after 3 months postintervention and re-administration of the intervention (Jazaieri et al., 2012). Both MBSR and aerobic exercise had positive impacts on clinical symptoms and well-being (Jazaieri et al., 2012). Female students suffering from SAD were evaluated with CBT and MBSR (Fatemeh Abbasi 2018). Both CBT and MBSR decreased stress 2.4 times (Fatemeh Abbasi 2018). MBSR was more effective than CBT in reducing stress by 4.82 times (Fatemeh Abbasi 2018). A randomized clinical trial of 105 veterans with one or more anxiety disorders were assigned to MBSR or CBT treatment (Arch et al., 2013). Both treatments were effective at a 3-month follow up (Arch et al., 2013). CBT was better at managing anxious arousal outcomes, but MBSR reduced worry and emotional disorders (Arch et al., 2013). Patients with anxiety were randomly assigned to MBSR or an anxiety disorder education program (Lee et al., 2007). Outcomes were measured with the Hamilton Anxiety Rating Scale, Hamilton Depression Scale, State-Trait Anxiety Inventory, Beck Depression Inventory, and Symptom-90 checklist at

baseline, 2, 4, and 8 weeks during the program (Lee et al., 2007). The MBSR program was superior to the education program on all measurement scales (Lee et al., 2007).

Mindfulness-based meditation programs advertise that improvements in sleep quality are common for patients. However, the results of numerous studies have been mixed across different diagnostic stressors and treatment types. A study of Alcohol Use Disorder patients, who frequently report insomnia as a side effect of withdrawal, found short term increases in total sleep time and undisturbed sleep, as well as a decrease in sleep apnea symptoms in the test group undergoing MBSR training (Wang et al., 2023). A similar increase in sleep quality was found with post-menopausal women in a 2022 study, citing the benefits of collaborative group trainings on overall improvements (Darehzereshki et al., 2022). These benefits do not last long, as demonstrated by a 2013 study of breast cancer patients in Denmark (Andersen et al., 2013). At the 12-month follow-up, the treatment outcomes in sleep quality were equivalent between the MBSR and control group (Andersen et al., 2013). A systematic review of insomniac patients in studies with MBSR as the test treatment revealed that only 4 of the 41 studies definitively proved that MBSR improved sleep outcomes compared to the control (Kim et al., 2022). Limitations include small sample sizes and the influence of biases on the data (Kim et al., 2022).

Though the previous studies revolved around in-person interventions, the COVID-19 pandemic has placed a greater emphasis on online MBSR treatment to improve sleep outcomes. Nurses in COVID-19 care units improved sleep latency and quality amidst stressful occupational climates using MBSR (Nourian et al., 2021). A 12-course online biweekly MBSR class conducted on a subset of 56 insomniacs from Italy during COVID-19 revealed improvements in sleep across 6 different sleep measurement scales (Fazia et al., 2023). Benefits of even brief online interventions on sleep quality and stress reduction were measured on college students in

2022 (Pickett et al., 2022). Attrition rates are similar between the online and in-person studies, though subjects are more likely to maintain adherence with an in-person study (Jiang et al., 2021). Though adherence, attendance, and overall satisfaction are greater with an in-person MBSR study cohort, online interventions have proven to be just as effective as necessary, in light of pandemic-related restrictions (Tomás Esteban Sard-Peck, 2018). Overall, there are limitations for these studies involving sample size, gender, and focusing on a singular medical condition unrelated to anxiety.

Escitalopram as an SSRI relieves anxiety symptoms through increasing serotonin levels in the brain (Health). While sleeping, Serotonin promotes non-rapid eye movement sleep (NREM) sleep, though too much serotonin may inhibit rapid eye movement (REM) sleep (Health). Therefore, those on Escitalopram will fall asleep and maintain it easily, though they may have a difficult time recollecting dreams and unbalanced sleep (Health). This effect was proven in a 2014 study conducted on rats (Kostyalik et al., 2014). Though the subjects fell asleep quickly and stayed asleep without disturbance, the transition from NREM to REM sleep was altered, truncating the REM sleep cycle (Kostyalik et al., 2014). In a comparative double-blind study of Amitriptyline, Escitalopram, and a placebo group, those using Amitriptyline had a significant improvement in sleep quality, measured by the PSQI though these were only modest improvements (Herrick et al., 2018). Using data from 22 randomized clinical trials, Escitalopram use in GAD patients was proven to improve sleep better than placebo, but indifferent from paroxetine or venlafaxine even for patients who had insomnia at baseline (Stein & Lopez, 2011). Combining eszopiclone with Escitalopram for GAD patients with insomnia is more effective in improving sleep quality than Escitalopram alone (Pollack et al., 2008). After discontinuation of

eszopiclone, anxiety improvements remained longer in the dual-treated group, as measured at the 10-week mark (Pollack et al., 2008).

Though the aforementioned studies prove the benefits of using MBSR as an anxiety treatment compared to CBT or other education programs, there lacks direct evaluations between MBSR and medicative treatments to determine their relational impacts on alleviation of anxiety symptoms including sleep. Thus, this clinical trial evaluated is first of its kind, relating the effects of MBSR in direct comparison to medicative treatments. Sleep is a direct indicator of anxiety relief and treatment success, thus improvement in sleep quality would translate to mitigation of anxiety symptoms. Therefore, this study comparing online and in-person treatments of the complementary health approach MBSR to Escitalopram, a medication, using sleep quality as an indicator of success is revolutionary to mental health treatment.

Materials & Methods

Study Design

The study was designed in accordance with the Hoge et al. study design Treatment for anxiety: Mindfulness meditation versus escitalopram (TAME). This is a prospective, single blinded (with unblind providers and participants), controlled, randomized trial which focused on evaluating the improvements over an 8-week period of using either MBSR or Escitalopram. Participants were recruited and enrolled at 3 United States-based hospital centers: The Department of Psychiatry for Massachusetts General Hospital in Boston, The Department of Psychiatry Georgetown University Medical Center in Washington, DC, and The Department of Psychiatry for New York University Grossman School of Medicine in New York City. Oversight of the study was conducted by each institution, adhering to their respective systems.

All eligible participants were between 18 to 75 years old with a current primarily diagnosed anxiety disorder (GAD, SAD, PD, or Agoraphobia) verified by interviewing trained clinicians unassociated with the institutions per DSM-5. Other types of anxiety disorders as a primary diagnosis were excluded from participating. They were required to have a full understanding of the procedures and consent process to be included. Medical exclusions included those with serious medical conditions, cognitive impairment, suicidal behavior, and women who were pregnant or planning to become pregnant. Also excluded were those taking sleeping pills or other barbiturates, people with scheduling conflicts, and participants who had currently or previously done MBSR therapies.

Randomization was conducted after the initial in-person (or virtual for the online cohort) interview using block randomization stratified by site and high (CGI-S >4) or low baseline anxiety score. This information was entered into REDCap to assign the treatment group based on these randomization criteria. Independent evaluators for symptom severity ratings remained blind to the treatment groups though the study director, research assistants, and participants were unblind.

Evaluations were conducted at week 0 (baseline), week 4 (midpoint), week 8 (endpoint) and weeks 12 and 24 (follow-up) using the CGI-S scale, which ranks severity of symptoms on a scale from 1 (no symptoms present) to 7 (severe symptom expression). Additional monitoring and potential clinician referral were done to monitor safety, adverse effects, symptom worsening and emergence of suicidality at weeks 1, 2, 4, 6, and 8 as well as follow-up weeks 12 and 24.

Interventions

MBSR treatment design for the meditative cohort involves an 8-week long protocol including weekly 2.5-hour long classes, a day-long retreat at weeks 5 or 6 and daily 45-minute

home-based practices (Santorelli et al. 2017). Practices were taught by qualified instructors and recorded for a subsequent review of fidelity by another qualified instructor (M.A.D.). Teachings incorporate the theory and practice of breath awareness (breathing as a method of calming), body scan (focus to a single body part at a time), and mindful movement (stretching to increase introspective awareness), all forms of mindfulness meditation. Attendance was conducted by the teacher or self-report and in-person classes were held at community sites and clinics.

Escitalopram treatment exposure in the medicative cohort started with daily oral 10 mg doses. This increased to 20 mg doses at week 2 if well-tolerated. Adherence was dually measured by patient report and pill counts. Participants also met with a study clinician (M.D or N.P.) during the trial at 1, 2, 4, 6, and 8 weeks through. Those in this treatment cohort were allowed to continue Escitalopram treatments after the study if they wished.

MBSR online interventions were conducted for the classes, retreat, and practices within these same intervals all via Zoom in the second study phase. The same instructors conducted these interventions allowing consistency between the two phases. For the Escitalopram online phase, the medications were delivered directly to the participant's residence to ensure adherence during quarantine periods rather than being picked up at a local pharmacy or clinic.

Outcomes

For part 1 comparing the in-person and online cohorts as well as treatment exposures, the main outcome was change in CGI-S score, as assessed by trained clinicians. The sleep analysis of these cohorts was measured by self-report using both the Pittsburgh Sleep Quality Index (PSQI) and the 8-item Sleep Disturbance Patient-Reported Outcomes Measurement Information System (PROMIS) T-score as a deviation from the reference population. Part 3 will model these

outcomes using demographic data to interpret success rates with CGI-S, PROMIS-T Sleep Disturbance, and PSQI improvement.

Data analysis

Data analysis for this study was conducted using the SAS 9.4 program. The data was converted into the program from three different Microsoft Excel spreadsheets, one containing the demographics and CGI-S score data, another with the PROMIS-T Sleep Disturbance scores at various timepoints in the study and the third containing PSQI scores for the same timepoints. Within SAS, these tables were merged by study ID to differentiate all variables by individual observation.

Once combined, the Table 1 data was analyzed for the online cohort mirroring the Hoge et al. study of the in-person cohort. The baseline characteristics of all the randomized individuals and all who completed the protocols within the two treatment groups (Escitalopram and MBSR) were compared with chi-square value t-tests to measure any significant difference between the two groups. The mean and standard deviation of CGI-S baseline values for the groups as well as a t-test analysis. CGI-S score analysis compared treatment outcome differences between Escitalopram and MBSR for the online cohort (Table 2) and individual treatments between the online and in-person cohorts to finalize the evaluations for part 1 (Tables 3 and 4). The change from baseline CGI-S measurements to week 8 were calculated as a separate variable by subtracting these values from each other and conducting a t-test with the difference variable.

In part 2, PROMIS-T Sleep Disturbance and PSQI scores were compared at baseline, differentiated by low and high CGI-S anxiety scores for all, online, and in-person observations. Additionally, the online and in-person differences between these groups were determined along with t-tests to flag any significant differences (Tables 5 and 6). Using the same methodologies as

the CGI-S scores, the PROMIS-T Sleep Disturbance and PSQI scores were analyzed in the online cohort to compare treatments (Tables 7 and 10) as well as by treatment, comparing the online and in-person cohorts (Tables 8, 9, 11, and 12). Correlations were assessed between the PROMIS-T Sleep Disturbance and PSQI scores for all observations (Figure 1) and online only observations (Figure 2).

To model the data to determine PROMIS-T Sleep Disturbance or PSQI score in part 3, dummy variables were created for each of the categorical variables present. CGI-S score, treatment, and the following Table 1 variables were included in this analysis: Site, Disorder Severity, Sex, Race, Education, Marital Status, Employment Status, Primary Diagnosis, and Age. For the combined in-person and online cohort analysis, the in-person variable was also included to determine if there was a significant difference based on cohort. Using multiple linear regression, variables were evaluated in the model finding the variable estimate, significance, standard error, and 95% confidence intervals (Tables 13, 14, 15, and 16). Models were built for PROMIS-T Sleep Disturbance and PSQI for the online only cohort (Figures 7 and 9) as well as all observed participants (Figures 8 and 10) based on which variables were significant. This determined which demographic characteristics of the population were most significant to the associated sleep outcome.

Results

Background and Demographic Data

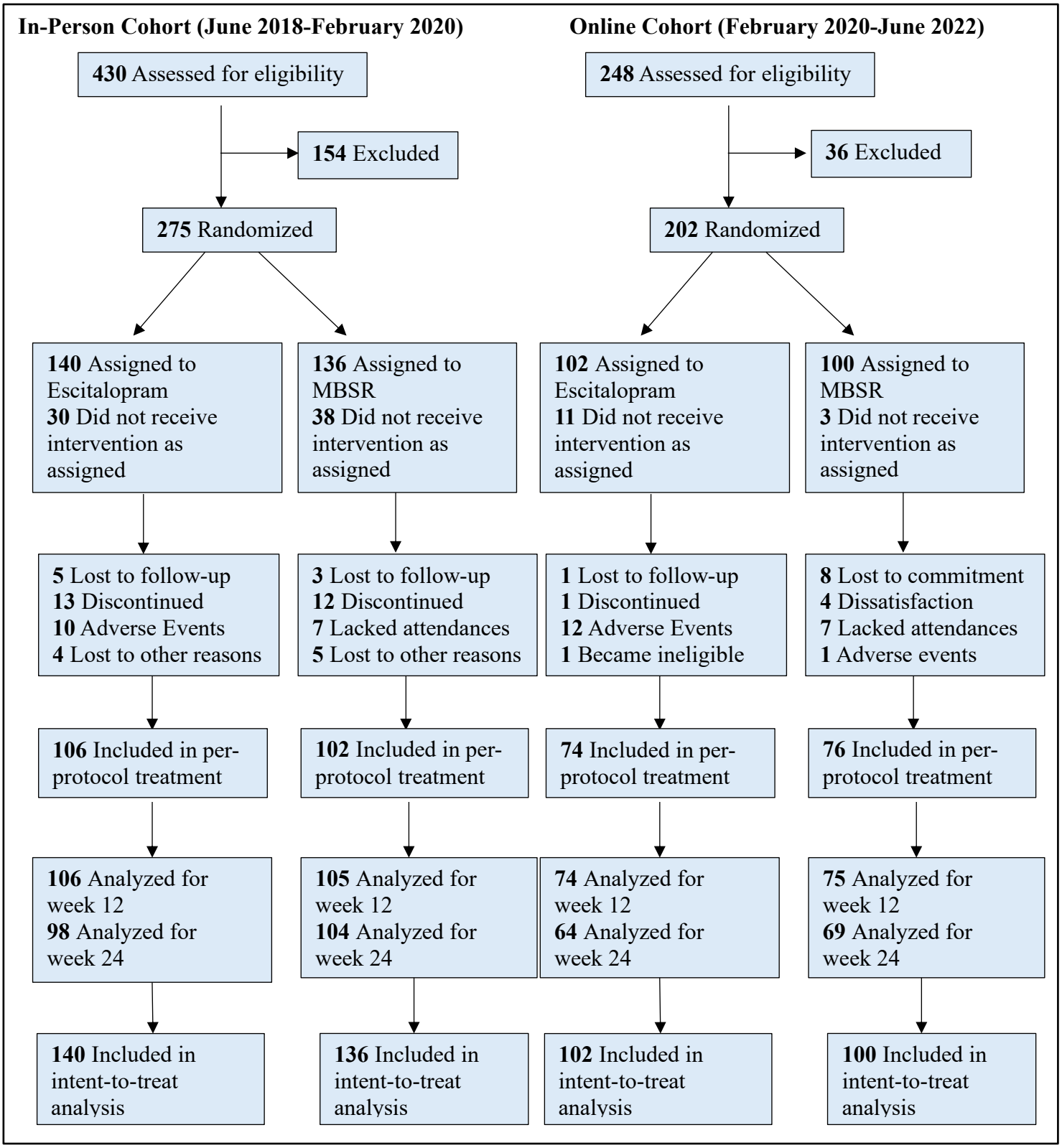
Due to the COVID-19 pandemic, this comparative anxiety treatment study was conducted in two phases. The first group who enrolled between June 2018 and February 2020 received all treatments in-person, as the study was originally designed. The second group received treatments

online for MBSR treatment or via home delivery for Escitalopram after February 2020 to June 2022.

For the in-person cohort, 430 participants were screened and 276 were randomized for inclusion in the study. Of these participants, 136 were assigned to the MBSR treatment group and 140 were to the Escitalopram group. From the start of the study, 33 Escitalopram participants did not complete the trial with an additional missing observation from the end point visit as well as 34 incomplete MBSR patients. This resulted in a sample size of 106 Escitalopram and 102 MBSR participants included in the protocol analysis up to week 8. Week 12 had 106 Escitalopram and 105 MBSR patients while the final measurement at week 24 had 98 and 104 participants, respectively.

The online cohort had 248 patients screened with 36 excluded and 202 ultimately randomized in the study. 102 were assigned to Escitalopram and 100 to MBSR, though 28 Escitalopram and 24 MBSR patients did not complete the full course of the study. This resulted in 74 Escitalopram participants and 76 MBSR participants for the final per-protocol analysis at week 8. The Escitalopram treatment group involved 74 participants at week 12 and 64 at week 24, while the MBSR group had 75 at week 12 and 69 at week 24. Overall, these numbers aligned well for analysis, as exhibited in the CONSORT diagram (Figure 1).

Figure 1.
Consort Diagram for Participant Selection



The baseline and demographic characteristics of the online sample are specified in Table 1, divided by those who are randomized and those who completed the entire study protocol. P-values to compare the MBSR and Escitalopram groups are included for each variable, though none were significantly different. Overall, the demographics align closely with the in-person cohort, analyzed in the Hoge et al. study published in 2023 (Hoge et al., 2023).

For the online cohort, the Georgetown University Medical Center site had the greatest number of participants at around 40% of the study population, though Massachusetts General Hospital had a narrow lead of 39% of the completed Escitalopram group. A larger percentage of the online participant's anxiety was of low severity at around 64% of the randomized patients at baseline, which was higher than that in the in-person sample, around 50%. The mean age remained around 33 years old for all groups and about 70% of the study population were White compared to 60% of the in-person sample. 11% were African-American or Black, 11% were Asian, and 9% of the "Other" race group, which includes Native American/Alaskan Native, those of two or more races, or those identified as "other". Most participants had a College (47%) or Graduate degree (39%), were Single (55%) or Married (40%), and Full-time employees (56%).

General Anxiety Disorder was the most common disorder at around 64%, while Social Anxiety was about 30%. The baseline CGI-S for anxiety in the MBSR group was 4.26 ± 0.74 and 4.34 ± 0.73 in the Escitalopram group. This is a slightly lower baseline than the in-person cohort at 4.44 ± 0.79 and 4.51 ± 0.78 though the difference reflects the higher percentage of high disorder severity present.

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

Variable	Randomized No (%)		*P* Value	Completed Protocol No (%)		*P* Value
	MBSR	Escitalopram		MBSR	Escitalopram	
No.	100	102	NA	76	74	NA
Site			0.29			0.44
GUMC	40 (40)	40 (39)		29 (38)	27 (36)	
MGH	33 (33)	37 (36)		26 (34)	29 (39)	
NYU	27 (27)	25 (25)		21 (28)	18 (24)	
Disorder Severity			0.88			0.64
High	36 (36)	38 (37)		27 (36)	31 (42)	
Low	64 (64)	64 (63)		49 (64)	43 (58)	
Sex						
Female	76 (76)	75 (74)	0.69	60 (79)	55 (74)	0.45
Male	24 (24)	27 (26)		16 (21)	19 (26)	
Age, Mean (SD), y	34.83 ± 14.71	35.44 ± 14.80	0.77	35.75 ± 15.49	33.69 ± 12.90	0.38
Race			1.75			0.34
Asian	9 (9)	9 (9)		8 (11)	6 (8)	
Black	11 (11)	8 (8)		8 (11)	7 (9)	
White	67 (67)	76 (75)		53 (70)	54 (73)	
Other	13 (13)	9 (9)		7 (9)	7 (9)	
Education			0.07			1.21
≤ High School	2 (2)	2 (2)		1 (1)	2 (3)	
Some College	14 (14)	13 (13)		11 (14)	7 (9)	
College Degree	47 (47)	49 (48)		35 (46)	36 (49)	
Graduate School	37 (37)	38 (37)		29 (38)	29 (39)	
Marital Status			0.07			0.49
Single	55 (55)	58 (57)		40 (53)	43 (58)	
Living with Partner/Married	40 (40)	39 (38)		32 (42)	28 (38)	
Divorced/Widowed/Separated	5 (5)	5 (5)		4 (5)	3 (4)	
Employment Status			2.81			3.52
N/A	13 (13)	17 (17)		9 (12)	12 (17)	
Full-time	53 (53)	57 (58)		40 (53)	43 (60)	
Part-time	14 (14)	12 (12)		12 (16)	10 (14)	
Student/Dependent	20 (20)	12 (12)		15 (20)	7 (10)	
Primary Diagnosis			1.57			1.27
GAD	67 (68)	62 (61)		51 (68)	44 (59)	
Social	27 (27)	31 (30)		20 (27)	24 (32)	
Other	5 (5)	9 (9)		4 (5)	6 (8)	
Baseline CGI-S Score Mean (SD)	4.31 ± 0.75	4.26 ± 0.78	0.61	4.26 ± 0.74	4.34 ± 0.73	0.53

Part 1: Online and In-person Anxiety CGI-S Change by Treatment Exposure

The CGI-S scale was used to assess anxiety severity throughout the duration of the protocol and in the follow-up weeks. For the online sample, the differences in measurement between the MBSR and Escitalopram treatments were taken at baseline, week 4 of treatment as the halfway point, week 8 at the conclusion of the treatment protocols, and weeks 12 and 24 as follow-up. The difference from the baseline was measured and compared between the groups as well.

Table 2 compiles the differences in measurements between the two groups throughout the duration of the study based on the mean CGI-S score for each treatment. Overall, the Escitalopram group responded better to the treatment with a significant difference 0.35 points in CGI-S ($p=0.05$) compared to the MBSR treatment group at week 8. On average, the change from baseline was 0.45 points greater in the Escitalopram group compared to the MBSR group, also a significant difference ($p=0.01$). The treatment effects did last in both group's follow-up measurements at weeks 12 and 24, though there was still a significantly greater improvement by the Escitalopram cohort at week 24 ($p=0.05$). Thus, in the online cohort Escitalopram proved to be more effective at reducing the severity of anxiety symptoms.

Table 2.
CGI-S Score Treatment Means and Significance (Online Sample)

Online Cohort	**Mean (SD)**		**Mean difference (SE)**	***P* Value**
	MBSR Only	**Escitalopram Only**		
No.	76	74		
Baseline CGI-S Score	4.26 ± 0.74	4.34 ± 0.73	0.07 (0.12)	0.53
No.	76	74		
Week 4 CGI-S Score	3.43 ± 1.11	3.39 ± 0.99	-0.04 (0.17)	0.81
No.	73	70		
Week 8 CGI-S Score	3.10 ± 1.11	2.74 ± 0.97	-0.35 (0.17)	0.05
Change from baseline to end point, mean (SD) [95% CI]	1.18 (0.98) [0.95, 1.41]	1.63 (1.01) [1.39, 1.87]	0.45 (0.17)	0.01
No.	75	74		

Week 12 CGI-S Score	2.83 ± 1.23	2.51 ± 0.97	-0.31 (0.18)	0.09
No.	69	64		
Week 24 CGI-S Score	2.78 ± 1.14	2.42 ± 0.94	-0.36 (0.18)	0.05

Table 3 compares the MBSR treatment's impact on CGI-S score between the online and in-person cohorts. Though the information was presented to the participants in very different formats, there was not significant difference between either of the cohorts throughout the duration of the study and into the follow-up measurements. The change from baseline to week 8 averaged 1.18 for the online cohort and 1.35 for the in-person cohort on the CGI-S scale (p=0.26). Both cohorts followed a similar trend of reduced CGI-S scores into the follow-up, weeks 12 and 24, with the online scores at 2.83 and 2.78 and the in-person at 2.89 and 2.92, respectively.

Table 3.
CGI-S Score MBSR Treatment Means and Significance (Online vs In-person Cohorts)

MBSR Treatment	**Mean (SD)**		**Mean difference (SE)**	***P* Value**
	Online	**In-person**		
No.	76	102		
Baseline CGI-S Score	4.26 ± 0.74	4.44 ± 0.79	-0.18 (0.12)	0.12
No.	76	101		
Week 4 CGI-S Score	3.43 ± 1.11	3.43 ± 1.01	0.01 (0.16)	0.96
No.	73	102		
Week 8 CGI-S Score	3.10 ± 1.11	3.09 ± 1.09	0.01(0.17)	0.96
Change from baseline to end point, mean (SD) [95% CI]	1.18 (0.98) [0.95, 1.41]	1.35 (1.06) [1.15, 1.56]	0.18 (0.16)	0.26
No.	75	96		
Week 12 CGI-S Score	2.83 ± 1.23	2.89 ± 1.09	-0.06 (0.18)	0.75
No.	69	95		
Week 24 CGI-S Score	2.78 ± 1.14	2.92 ± 1.17	-0.13 (0.18)	0.47

On the other hand, Table 4 shows the two Escitalopram cohorts significantly different CGI-S scores beginning at week 8. The online cohort had a significantly lower average CGI-S score at week 8 - 2.74 compared to the in-person cohort's score of 3.08 (p=0.03). However, the change from baseline between the two cohorts was not significantly different, perhaps due to the

online cohort's baseline score being lower than the in-person's (p=0.22). Further deviations persisted in the follow-up weeks with the online cohort scoring significantly lower averaging 2.51 for week 12 and 2.42 for week 24 while the in-person cohort scored 2.95 for week 12 and 2.92 for week 24 (p=0.01, <0.01). This indicates greater adherence to Escitalopram and/or lasting effects long after the treatment ends.

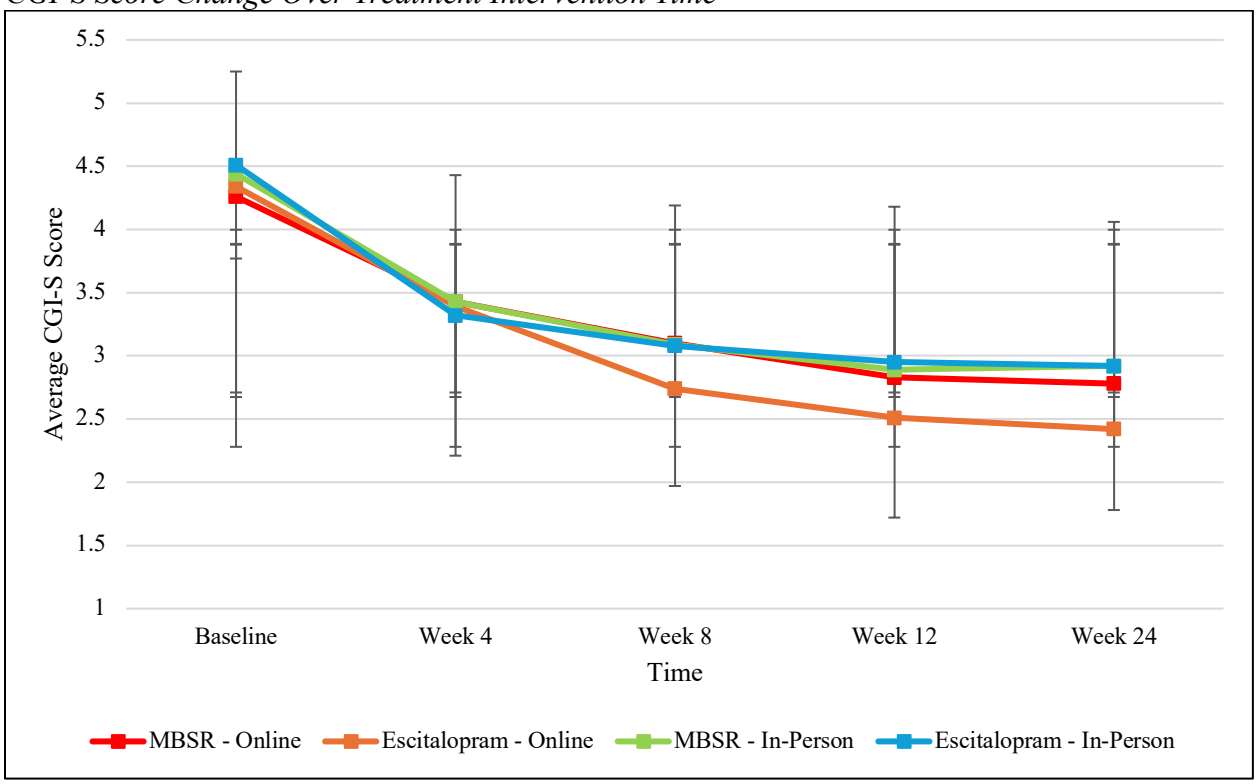
Table 4.

CGI-S Score Escitalopram Treatment Means and Significance (Online vs In-person Cohorts)

Escitalopram Treatment	**Mean (SD)**		**Mean difference (SE)**	***P* Value**
	Online	**In-person**		
No.	74	107		
Baseline CGI-S Score	4.34 ± 0.73	4.51 ± 0.78	-0.18 (0.11)	0.12
No.	74	107		
Week 4 CGI-S Score	3.39 ± 0.99	3.32 ± 1.06	0.07 (0.15)	0.63
No.	70	106		
Week 8 CGI-S Score	2.74 ± 0.97	3.08 ± 1.07	-0.34 (0.16)	0.03
Change from baseline to end point, mean (SD) [95% CI]	1.63 (1.01) [1.39, 1.87]	1.42 (1.17) [1.20, 1.65]	-0.20 (0.17)	0.22
No.	74	102		
Week 12 CGI-S Score	2.51 ± 0.97	2.95 ± 1.07	-0.44 (0.16)	0.01
No.	64	95		
Week 24 CGI-S Score	2.42 ± 0.94	2.92 ± 1.03	-0.49 (0.16)	<0.01

Figure 2 displays the change for each cohort and treatment group during the duration of the study and follow up. The error bars represent the standard deviations. This helps to visualize the overall trends of each treatment group and how closely aligned both MBSR groups are to the in-person Escitalopram group as well as the deviation of the online Escitalopram group with lessening anxiety symptoms from week 8 and beyond.

Figure 2.
CGI-S Score Change Over Treatment Intervention Time



Part 2: Anxiety Treatment Impact on PROMIS-T Sleep Disturbance and PSQI Sleep Scores

Sleep measurements were taken for participants at baseline, week 4, week 8, and week 24, the same points as the CGI-S score measurements. Week 12 was not completed for these measurements in both the online and in-person cohorts, thus this timepoint was not included in the analysis.

The PROMIS-T Sleep Disturbance score is an 8-item test taken to determine the quality, depth, and restoration involving sleep patterns within the past 7 days (, 2021 #121). The self-reported scores are standardized to the general population, with a mean score of 50 and a standard deviation of 10. A higher score in this case would indicate greater overall sleep disturbance. The baseline measurements of the PROMIS-T Sleep Disturbance scores were compared for the online and in-person cohorts, divided based on low or high baseline anxiety

scores. There was a significant difference based on low or high baseline anxiety score for the mean baseline measurement in all observations (p=<0.01), the in-person cohort (p=<0.01), and the online cohort (p=<0.01). The online to in-person average difference for low anxiety was 1.58 (p=0.09) and for high anxiety was 0.85 (p=0.41). Comparing the two groups, this difference was not significant (p=0.40).

Table 5.
PROMIS Sleep Score Baseline Means by Anxiety Severity (Online vs In-person Comparison)

	Anxiety Severity at baseline (CGI-S)		***P* Value**
	Low Anxiety	**High Anxiety**	
Mean PROMIS Sleep Disturbance (8-item) T score at Baseline (Range: 30-73) Available N=329	55.01 (5.64) N = 185	58.23 (6.09) N = 144	<0.01
Mean In-person PROMIS Sleep Disturbance (8-item) T score at Baseline (Range: 30-73) Available N=127	53.92 (5.89) N = 57	57.80 (6.14) N = 70	<0.01
Mean Online PROMIS Sleep Disturbance (8-item) T score at Baseline (Range: 43-70) Available N=202	55.49 (5.49) N = 128	58.64 (6.06) N = 74	<0.01
Online vs In-person Difference (SD)	1.58 (0.92) P = 0.09	0.85 (1.02) P = 0.41	0.40

Over the course of the online treatment, there was a significant overall change from baseline to week 8 (end of treatment) for all observations, in both the MBSR and Escitalopram treatment groups at an average difference of 3.65 (p=<0.01). From the baseline score (p=0.90) to week 4 (p=0.17), week 8 (p=0.39) and week 24 (p=0.36), there was no significant difference between the MBSR and Escitalopram groups. The PROMIS-T Sleep Disturbance score continued to decline in the measurement following treatment completion (week 24), proving the lasting effects of the treatments and mirroring the CGI-S score decline.

Table 6.
PROMIS Score Treatment Means and Significance (Online Cohort)

Online Cohort PROMIS T-Score	Mean (SD) MBSR Only	Escitalopram Only	Mean difference (SE)	*P* Value
No.	76	74		
Baseline PROMIS Score	57.36 ± 5.45	57.24 ± 6.00	-0.12 (0.94)	0.90
No.	72	71		
Week 4 PROMIS Score	55.57 ± 5.06	54.34 ± 5.57	-1.23 (0.89)	0.17
No.	70	74		
Week 8 PROMIS Score	53.93 ± 6.43	53.08 ± 5.29	-0.85 (0.98)	0.39
Change from baseline to end point, mean (SD) [95% CI]	3.10 (6.38) [1.59, 4.63]	4.16 (6.86) [2.57, 5.75]	1.05 (1.10)	0.34
Overall Change		3.65 (6.63)		<0.01
Week 24 PROMIS Score	52.59 ± 5.80	51.65 ± 5.78	0.94 (1.02)	0.36

Comparing the online and in-person MBSR treatment impacts on the PROMIS-T scores, the overall change of all observations from baseline to week 8 was 3.31, a significant difference (p=<0.01). The baseline scores were not significantly different from one another, though the mean difference was much greater than in the online cohort comparison at 1.86 (p=0.07). However, as soon as the week 4 measurement, the differences between the two cohorts became quite evident. At week 4, the difference averaged 2.93 (p=<0.01) and at week 8, the end of the treatment exposure, the difference was 2.09 (p=0.03) with the online cohort having a greater PROMIS-T Sleep Disturbance score at both timepoints. By the follow-up timepoint at week 24, there was no significant difference between the two cohorts, though both groups continued to have a decreased PROMIS-T Sleep Disturbance score (p=0.17).

Table 7.
PROMIS Score MBSR Treatment Means and Significance (Online vs In-person Cohorts)

MBSR Cohort PROMIS T-Score	Mean (SD) Online	In-person	Mean difference (SE)	*P* Value
No.	76	42		
Baseline PROMIS Score	57.36 ± 5.45	55.50 ± 5.08	1.86 (1.00)	0.07
No.	72	51		
Week 4 PROMIS Score	55.57 ± 5.06	52.65 ± 5.18	2.93 (0.94)	<0.01
No.	70	58		

Week 8 PROMIS Score	53.93 ± 6.43	51.84 ± 3.96	2.09 (0.93)	0.03
Change from baseline to end point, mean (SD) [95% CI]	3.10 (6.38) [1.59, 4.63]	3.64 (6.06) [1.75, 5.53]	-0.53 (1.21)	0.66
Combined Overall Change		3.31 (6.24)		<0.01
Week 24 PROMIS Score	52.59 ± 5.80	51.10 ± 5.75	1.49 (1.08)	0.17

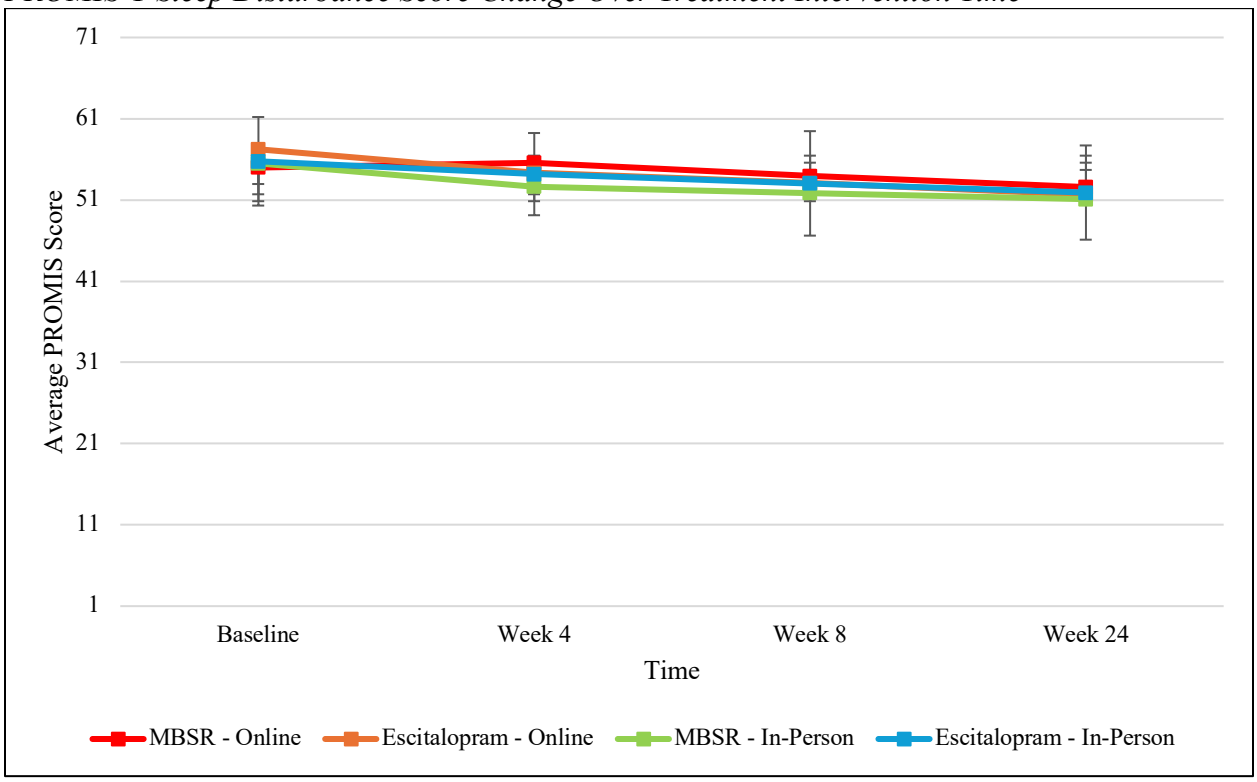
The online and in-person Escitalopram treated cohorts also had a significantly different PROMIS-T Sleep Disturbance score at week 8 compared to the baseline score, averaging 3.73 (p=<0.01). Though these cohort baseline PROMIS-T Sleep Disturbance scores had a larger difference of 1.48 (p=0.15). The gap narrowed as the study started and into the follow-up weeks. Week 4 had a difference of 0.16 (p=0.87), the week 8 difference was 0.04 (p=0.96), and the week 24 difference was 0.26 (p=0.82). With none of these subsequent weeks being significant, this proves both the online and in-person treatments using Escitalopram had a beneficial impact on self-reported sleep. The effects were lasting, as the PROMIS-T Sleep Disturbance score continued to decrease at week 24, 16 weeks after the treatments ended.

Table 8.
PROMIS Score Escitalopram Treatment Means and Significance (Online vs In-person Cohorts)

Escitalopram Cohort PROMIS T-Score	**Mean (SD) Online**	**In-person**	**Mean difference (SE)**	***P* Value**
No.	74	52		
Baseline PROMIS Score	57.24 ± 6.00	55.76 ± 5.30	1.48 (1.01)	0.15
No.	71	58		
Week 4 PROMIS Score	54.34 ± 5.57	54.18 ± 5.48	0.16 (0.98)	0.87
No.	74	63		
Week 8 PROMIS Score	53.08 ± 5.29	53.04 ± 4.20	0.04 (0.81)	0.96
Change from baseline to end point, mean (SD) [95% CI]	4.16 (6.86) [2.57, 5.75]	3.09 (5.08) [1.63, 4.55]	1.07 (1.08)	0.33
Combined Overall Change		3.73 (6.22)		<0.01
Week 24 PROMIS Score	51.65 ± 5.78	51.91 ± 6.73	-0.26 (1.13)	0.82

Figure 3 graphs the reduction over time of all four cohort and treatment combination groups (online MBSR, online Escitalopram, in-person MBSR, and in-person Escitalopram). All groups declined during this span of time, bringing the PROMIS-T Sleep Disturbance scores closer to the general population mean of 50. The effects of all treatments lasted beyond the duration of the protocol, and all were significantly different from the baseline PROMIS-T Sleep Disturbance scores.

Figure 3.
PROMIS-T Sleep Disturbance Score Change Over Treatment Intervention Time



The Pittsburgh Sleep Quality Index (PSQI) is 19 item self-reported questionnaire, generating scores based on the seven components scores including sleep quality, latency, duration, habitual efficiency, disturbance, medication use, and daytime dysfunction (Daniel J Buysse, 1988 #120). Baseline scores PSQI comparing low and high anxiety groups were divided by all observations, the online, and in-person cohorts in Table 9. As in the PROMIS-T Sleep Disturbance Scores, there was a significant difference between the low and high anxiety groups

for all cohorts (p=<0.01). The online versus in-person difference was 0.10 for the low anxiety groups (p=0.34) and -0.71 (p=0.43) for the high anxiety groups. Comparing the two groups, there was no significant difference (p=0.09).

Table 9.
PSQI Sleep Score Baseline Means by Anxiety Severity (Online vs In-person Comparison)

	Anxiety Severity at baseline (CGI-S)		***P* Value**
	Low Anxiety	**High Anxiety**	
Mean Pittsburgh Sleep Quality Index (Range: 1-18) Available N=474	7.32 (2.79) N = 264	9.08 (3.08) N = 210	<0.01
Mean In-person Pittsburgh Sleep Quality Index (Range: 2-18) Available N=272	7.27 (2.84) N = 136	9.33 (3.18) N = 136	<0.01
Mean Online Pittsburgh Sleep Quality Index (Range: 1-18) Available N=474	7.37 (2.73) N = 128	8.62 (2.86) N = 74	<0.01
Online vs In-person Difference (SE)	0.10 (0.34) P = 0.78	-0.71 (0.43) P = 0.10	0.09

For the online cohort comparing the MBSR and Escitalopram treatments, the overall PSQI change for both treatments from baseline to week 8 was 1.77 (p=<0.01). The baseline score difference between treatment groups was 0.55 (p=0.22). No further timepoint measurements had a significant difference. Week 4 had an average difference of 0.03 (p=0.95), the difference at week 8 was 0.58 (p=0.19), and the follow-up at week 24 difference was 0.01 (p=0.98). Though Escitalopram had a greater decrease after the protocol finish, there is no significant association with either MBSR or Escitalopram having a greater effect over the course of the study.

Table 10.
PSQI Score Treatment Means and Significance (Online Cohort)

Online Cohort PSQI Score	**Mean (SD) MBSR Only**	**Escitalopram Only**	**Mean difference (SE)**	***P* Value**
No.	76	74		
Baseline PSQI Score	7.74 ± 2.68	8.28 ± 2.82	0.55 (0.45)	0.22
No.	73	70		
Week 4 PSQI Score	7.00 ± 2.57	7.03 ± 2.60	0.03 (0.43)	0.95
No.	68	74		
Week 8 PSQI Score	5.90 ± 2.46	6.47 ± 2.74	0.58 (0.44)	0.19

Change from baseline to end point, mean (SD) [95% CI]	1.74 (2.56) [1.12, 2.36]	1.81 (3.01) [1.11, 2.51]	0.08 (0.47)	0.87
Combined Overall Change		1.77 (2.79)		<0.01
Week 24 PSQI Score	5.93 ± 2.65	5.94 ± 2.75	0.01 (0.47)	0.98

MBSR treatment PSQI differences between the online and in-person cohorts also remained non-significant at all timepoints. The overall change for all MBSR observations from baseline to week 8 was 2.71 (p=<0.01), a significant change over the protocol completion. The mean difference started at -0.16 (p=0.70) between the two cohorts, increased to a difference of 0.70 (p=0.10) at week 4, then decreased at week 8 to a difference of 0.33 (p=0.40). After the end of the treatments, the online cohort average scores increased slightly at week 24 from 5.90 to 5.93 while the in-person cohort PSQI remained at 5.57. The difference between the two cohorts at this timepoint was insignificant (p=0.41).

Table 11.
PSQI Score MBSR Treatment Means and Significance (Online vs In-person Cohorts)

MBSR Cohort PSQI Score	**Mean (SD) Online**	**In-person**	**Mean difference (SE)**	***P* Value**
No.	76	101		
Baseline PSQI Score	7.74 ± 2.68	7.90 ± 3.03	-0.16 (0.43)	0.70
No.	73	99		
Week 4 PSQI Score	7.00 ± 2.57	6.30 ± 2.86	0.70 (0.42)	0.10
No.	68	99		
Week 8 PSQI Score	5.90 ± 2.46	5.57 ± 2.56	0.33 (0.39)	0.40
Change from baseline to end point, mean (SD) [95% CI]	1.74 (2.56) [1.12, 2.36]	2.32 (2.69) [1.78, 2.85]	-0.58 (0.41)	0.16
Combined Overall Change		2.71 (2.64)		<0.01
Week 24 PSQI Score	5.93 ± 2.65	5.57 ± 2.78	0.36 (0.44)	0.41

The Escitalopram treated cohorts had an overall decrease amongst all observations of 2.05 on the PSQI scale, a significant change at week 8 from the baseline scores (p=<0.01). Like

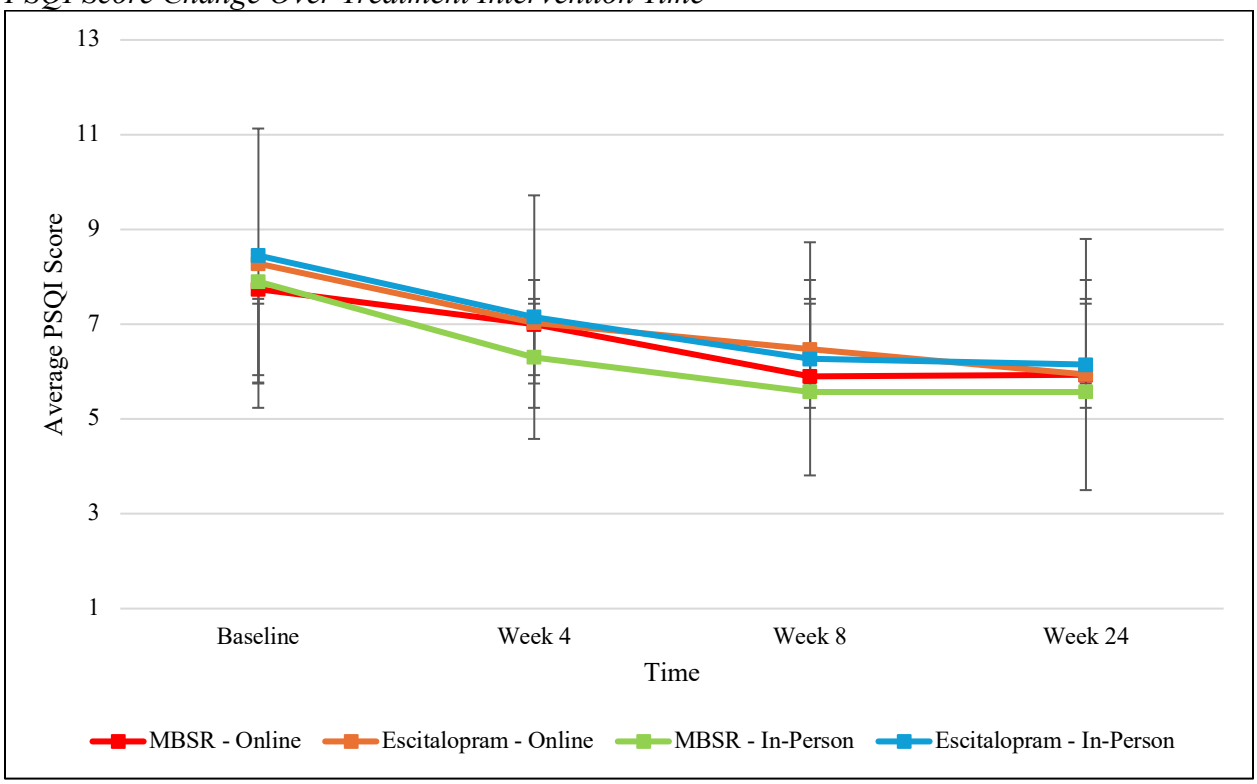
with the MBSR groups, none of the timepoints from baseline to weeks 4, 8, and 24 were significantly different between the two cohorts. The difference at baseline was -0.16 (p=0.71), week 4 had an average difference of -0.12 (p=0.77), and the end of the protocol at week 8 difference was 0.20 (p=0.62). The PSQI measure continued to drop at week 24 with the online cohort having a more of a decrease from week 8. The difference between the two cohorts was -0.22 but was not significant (p=0.62).

Table 12.
PSQI Score Escitalopram Treatment Means and Significance (Online vs In-person Cohorts)

Escitalopram Cohort PSQI Score	**Mean (SD) Online**	**In-person**	**Mean difference (SE)**	***P* Value**
No.	74	107		
Baseline PSQI Score	8.28 ± 2.82	8.45 ± 2.96	-0.16 (0.43)	0.71
No.	70	101		
Week 4 PSQI Score	7.03 ± 2.60	7.15 ± 2.66	-0.12 (0.41)	0.77
No.	74	103		
Week 8 PSQI Score	6.47 ± 2.74	6.27 ± 2.46	0.20 (0.40)	0.62
Change from baseline to end point, mean (SD) [95% CI]	1.81 (3.01) [1.11, 2.51]	2.22 (3.23) [1.59, 2.86]	-0.41 (0.47)	0.38
Overall Change		2.05 (3.14)		<0.01
Week 24 PSQI Score	5.94 ± 2.75	6.15 ± 2.64	-0.22 (0.44)	0.62

Figure 4 plots all timepoints and cohorts (online MBSR, online Escitalopram, in-person MBSR, and in-person Escitalopram) PSQI measurements. There were no significant differences between any of the cohort groups for the PSQI measurements, which differed from the PROMIS-T Sleep Disturbance scores that found a significant difference between the online and in-person MBSR cohorts. This deviation between measurements reflects the need for multiple kinds of scales to capture complex systems such as sleep which are easily impacted by numerous factors.

Figure 4.
PSQI Score Change Over Treatment Intervention Time



Figures 5 and 6 are plots of the correlation between PROMIS-T and PSQI Scores for all completed observations throughout the course of the study and for the online cohort. The R^2 value was 0.64 and 0.65 respectively, with both scores being significantly correlated ($p = <0.0001$).

Figure 5.
Correlation Plot of PROMIS-T and PSQI Scores for All Completed Observations

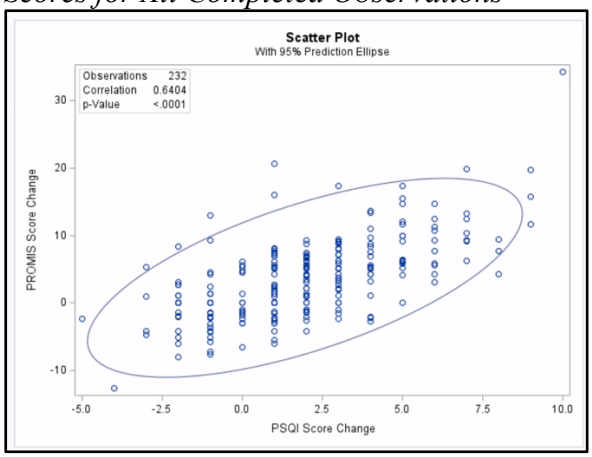
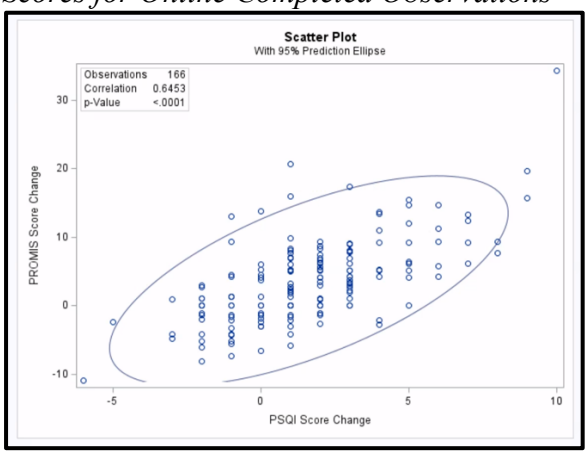


Figure 6.
Correlation Plot of PROMIS-T and PSQI Scores for Online Completed Observations



Part 3: Model Development for Sleep Disturbance PROMIS-T and PSQI Scores with Treatment and CGI-S Change

PROMIS-T Sleep Disturbance modeling included CGI-S score and treatment exposure as potentially significant variables in the model development. Table 13 is the resulting output table for those variables and all Table 1 demographic variables included: Site, Disorder Severity, Sex, Race, Education, Marital Status, Employment Status, Primary Diagnosis, and Age. The intercept change in PROMIS-T Sleep Disturbance score was a positive value at 3.21, which indicates that on average, patients experienced a decreased PROMIS-T Sleep Disturbance score over the course of the 8-week treatment. However, the treatment variable was not significant for these observations (p=0.67), so those with MBSR treatment did not have any decreased effect on PROMIS-T Sleep Disturbance score compared to their Escitalopram-treated counterparts. The model had a significantly associated CGI-S variable at 2.12 (p=<0.01). Therefore, for every one-point increase in CGI-S score, the PROMIS-T Sleep Disturbance variable increased an average of 2.12 points for all online observations. All variables except for site location did not have

significant categories associated with the PROMIS-T Sleep Disturbance score. NYU site patients were significantly different from GUMC patients, since with all online participants there was an average 3.31 score decrease (p=0.03). The MGH site was not significantly different (p=0.75) from GUMC at a decreased value of 0.41.

Table 13.
Online PROMIS-T Linear Regression Variables Estimations

Characteristic	**Estimate**	**Standard Error**	***P* Value**	**95% Confidence Interval**	
				Lower	**Upper**
Intercept	3.21	2.44	0.19	-1.61	8.04
ΔCGI-S Score*	2.12	0.59	<0.01	0.95	3.28
Treatment (ref = Escitalopram)	0.45	1.05	0.67	-1.62	2.52
Site					
GUMC (ref)	0.00	0.00			
MGH	-0.41	1.31	0.75	-3.00	2.18
NYU*	-3.31	1.47	0.03	-6.22	-0.39
Disorder Severity (ref=Low)	2.14	1.30	0.10	-0.43	4.70
Sex (ref = Male)	-1.53	1.19	0.20	-3.89	0.82
Race					
White (ref)	0.00	0.00			
Asian	1.01	1.97	0.61	-2.89	4.91
Black	0.66	1.76	0.71	-2.82	4.14
Other	-0.18	2.15	0.93	-4.44	4.08
Education					
College Degree (ref)	0.00	0.00			
≤ High School	-1.95	3.96	0.62	-9.78	5.88
Some College	2.34	1.84	0.21	-1.29	5.97
Graduate School	0.03	1.16	0.98	-2.26	2.32
Marital Status					
Living with Partner/Married (ref)	0.00	0.00			
Single	-0.09	1.22	0.94	-2.51	2.33
Divorced/Widowed/Separated	2.16	2.84	0.45	-3.45	7.76
Employment Status					
Full-time (ref)	0.00	0.00			
N/A	2.50	1.61	0.12	-0.67	5.68
Part-time	0.48	1.58	0.76	-2.63	3.60
Student/Dependent	-0.21	1.84	0.91	-3.85	3.42

Primary Diagnosis					
GAD (ref)	0.00	0.00			
Social	-0.78	1.19	0.52	-3.13	1.58
Other	-1.16	2.19	0.60	-5.48	3.17
Age	-0.06	0.04	0.19	-0.14	0.03

* Significant variable, included in model

Figure 7 compiles all the significantly associated variables over the course of the 8-week treatment for all online observations (CGI-S and Site) for the PROMIS-T score divided by category if applicable in a single model.

Figure 7.
Multiple Linear Regression Model of PROMIS-T Sleep Disturbance Online Observations Over 8 Week Treatment

$$\Delta\text{PROMIS-T ONLINE} = 3.21 + 2.12\text{CGI-S} - 3.31\text{NYU} - 0.41\text{MGH}$$

Table 14 uses the demographic data to model PROMIS-T Sleep Disturbance amongst all participants involved in the TAME program. The in-person variable was added to this analysis to compare the two cohorts for any significant difference in this sleep score. Analysis of this variable did find it insignificant in the model development (p=0.87), therefore PROMIS-T Sleep Disturbance score was unaffected by online or in-person cohort. The intercept had an average of 3.41 for all participants, slightly higher compared to the online treated group. CGI-S was significant in the PROMIS-T Sleep Disturbance models with a value of 1.40 for all patients (p=<0.01). As a positive value, this demonstrated that the CGI-S change increase in score results in an increased PROMIS-T Sleep Disturbance change. MBSR compared to Escitalopram treatment remained insignificant across all combined observations (p=0.74). Location was a significant variable, as with the online participants, but the overall observations also included employment status. Site location impacted PROMIS-T Sleep Disturbance score, as those at NYU had an average 2.67 decreased score change compared to their GUMC counterparts (p=0.02).

MGH based participants did not have a significantly different PROMIS-T Sleep Disturbance score at 1.49 points fewer than the GUMC located participants, similar to the online-only cohort (p=0.14). Those who specified N/A as a job had a significantly increased PROMIS-T Sleep Disturbance change score compared to full-time employees valued at an average of 3.55 for all participants (p=<0.01). The other employment groups, Part-time and Student, did not have significantly associated outputs compared to the reference Full-time with values of 1.05 (p=0.41) and -0.77 (p=0.58) respectively.

Table 14.
All Observations PROMIS-T Sleep Disturbance Linear Regression Variables Estimations

Characteristic	**Estimate**	**Standard Error**	***P* Value**	**95% Confidence Interval**	
				Lower	**Upper**
Intercept	3.41	2.04	0.10	-0.62	7.44
ΔCGI-S Score*	1.40	0.43	<0.01	0.55	2.26
Treatment (ref = Escitalopram)	0.27	0.84	0.74	-1.38	1.92
Site					
GUMC (ref)	0.00	0.00			
MGH	-1.49	1.00	0.14	-3.46	0.49
NYU*	-2.67	1.16	0.02	-4.97	-0.38
Disorder Severity (ref = Low)	1.53	0.91	0.10	-0.27	3.32
Sex (ref = Male)	0.06	0.95	0.95	-1.82	1.95
Race					
White (ref)	0.00	0.00			
Asian	-0.15	1.36	0.91	-2.83	2.52
Black	0.02	1.26	0.99	-2.51	2.47
Other	-0.05	1.67	0.98	-3.35	3.25
Education					
College Degree (ref)	0.00	0.00			
≤ High School	1.36	2.69	0.61	-3.95	6.66
Some College	1.78	1.35	0.19	-0.89	4.44
Graduate School	0.60	0.95	0.53	-1.27	2.48
Marital Status					
Living with Partner/Married (ref)	0.00	0.00			
Single	-0.29	0.96	0.77	-2.18	1.61
Divorced/Widowed/Separated	-1.36	2.04	0.51	-5.38	2.66

Employment Status					
Full-time (ref)	0.00	0.00			
N/A*	3.55	1.26	<0.01	1.08	6.03
Part-time	1.05	1.27	0.41	-1.46	3.56
Student/Dependent	-0.77	1.39	0.58	-3.51	1.96
Primary Diagnosis					
GAD (ref)	0.00	0.00			
Social	-1.37	0.94	0.15	-3.22	0.49
Other	-2.10	1.71	0.22	-5.46	1.27
Age	-0.04	0.04	0.25	-0.11	0.03
In-Person (ref=Online)	-1.12	0.87	0.19	-2.84	0.58

* Significant variable, included in model

These values are modeled in Figure 8 with the associated variables and averaged values to depict the overall changes in PROMIS-T Sleep Disturbance score for all participants after 8 weeks of treatment.

Figure 8.
Multiple Linear Regression Model of PROMIS-T Sleep Disturbance All Observations Over 8 Week Treatment

$$\Delta\text{PROMIS-T ALL} = 3.41 + 1.40\text{CGI-S} - 2.67\text{NYU} - 1.49\text{MGH} + 3.55\text{NAJOB} + 1.05\text{PARTTIME} - 0.77\text{STUDENT}$$

Analysis for PSQI measurements in all online participants was conducted in the same manner as the PROMIS-T Sleep Disturbance patients. However, with a smaller-range scale from 0 to 21, the scores result in seemingly more menial effects compared to the PROMIS-T though each point holds greater value in the PSQI. Table 15 lists the values of each model for the entire online cohort. The baseline intercept change in PSQI is positive for all observations at a value of 1.10. Like in the PROMIS-T Sleep Disturbance evaluations, there was also no significant difference between treatment types and PSQI outcome. This signifies that both treatments are effective at improving sleep based on this scale. CGI-S score had an average value of 0.92 in all online participants with a significant and positive correlation to the PSQI score change ($p=<0.01$). Unlike with the PROMIS-T Sleep Disturbance assessment, both anxiety disorder

groups had significant relevance to the development of the overall model. Social Anxiety Disorder (SAD) was a significantly associated variable for all online observations with a value of 1.14 decrease compared to the reference GAD (p=0.03). The Other Diagnosis group, when comparing to the same reference group had a decreased change value of 1.98 for the entire cohort (p=0.04). Therefore, this proves that the primary anxiety diagnosis substantially impacts sleep outcome using the PSQI evaluation when undergoing symptom treatment.

Table 15.
Online PSQI Linear Regression Variables Estimations

Characteristic	Estimate	Standard Error	*P* Value	95% Confidence Interval	
				Lower	Upper
Intercept	1.10	1.04	0.29	-0.95	3.15
ΔCGI-S Score*	0.92	0.25	<0.01	0.42	1.42
Treatment (ref = Escitalopram)	0.36	0.45	0.43	-0.53	1.25
Site					
GUMC (ref)	0.00	0.00			
MGH	-0.06	0.56	0.91	-1.17	1.04
NYU	-0.02	0.64	0.98	-1.24	1.28
Disorder Severity (ref=Low)	0.35	0.55	0.53	-0.75	1.44
Sex (ref = Male)	-0.49	0.51	0.34	-1.50	0.52
Race					
White (ref)	0.00	0.00			
Asian	0.38	0.86	0.66	-1.31	2.08
Black	-0.46	0.78	0.56	-1.99	1.08
Other	0.55	0.92	0.55	-1.26	2.37
Education					
College Degree (ref)	0.00	0.00			
≤ High School	-0.15	2.01	0.94	-4.13	3.82
Some College	-0.12	0.78	0.88	-1.67	1.43
Graduate School	0.20	0.49	0.69	-0.78	1.17
Marital Status					
Living with Partner/Married (ref)	0.00	0.00			
Single	0.29	0.52	0.59	-0.74	1.32
Divorced/Widowed/Separated	-0.28	1.20	0.82	-2.66	2.11
Employment Status					

Full-time (ref)	0.00	0.00			
N/A	0.53	0.69	0.44	-0.83	1.88
Part-time	-0.96	0.67	0.15	-2.29	0.36
Student/Dependent	-0.24	0.80	0.76	-1.81	1.34
Primary Diagnosis					
GAD (ref)	0.00	0.00			
Social*	-1.14	0.51	0.03	-2.14	-0.14
Other*	-1.98	0.93	0.04	-3.83	-0.13
Age	-0.01	0.02	0.64	-0.04	0.03

* Significant variable, included in model

The online cohort PSQI multiple linear regression model is represented in Figure 9 through the values and groups which were significant to the model development including the CGI-S and anxiety diagnosis variables.

Figure 9.
Multiple Linear Regression Model of PSQI Online Observations Over 8 Week Treatment

$$\Delta\text{PSQI ONLINE} = 1.10 + 0.92\text{CGI-S} - 1.14\text{SAD} - 1.98\text{OTHERDIAGNOSIS}$$

Table 16 comprises the multiple linear regression model variables for all observations to determine significant association with the PSQI score. The intercept was positive for the model at 0.88. Additionally, as in all other models, there was no treatment difference between the MBSR and Escitalopram groups (p=0.56). Thus, as an overall average, all treatments equally reduced the PSQI score to within more normal ranges. As with all other sleep models, the CGI-S score remained significant. For the whole study, this averaged 0.79 PSQI score reduction for every one-point decrease in CGI-S (p=<0.01). Though the In-person variable was included in this analysis to compare the two cohort, it was not significantly associated with PSQI change (p=0.13). Like the online cohort, SAD was significant for all observations valued at -1.09 revealing that participants diagnosed with SAD were less likely to see improvements in their PSQI compared with GAD patients from the course of the 8-week treatment (p=<0.01). As with all observations using the PROMIS-T Sleep Disturbance score evaluation, Employment status, in

particular the Student category, was significantly associated with a reduced change in PSQI sleep score. Compared to their Full-time employed counterparts, Students/dependents over the 8-week treatment course had on average 1.12 fewer PSQI score points difference from the baseline score. Therefore, sleep issues persisted more in this group (p=0.02). Part-time workers and those who responded N/A had on average a 0.17 reduced change (0.72) and 0.89 increased change (p=0.08) compared to Full-time employed participants, respectively. Unlike the Student category, these are not significant associations.

Table 16.
All Observations PSQI Linear Regression Variables Estimations

Characteristic	**Estimate**	**Standard Error**	***P* Value**	**95% Confidence Interval**	
				Lower	**Upper**
Intercept	0.88	0.79	0.27	-0.68	2.44
ΔCGI-S Score*	0.79	0.16	<0.01	0.49	1.10
Treatment (ref = Escitalopram)	0.19	0.31	0.56	-0.43	0.78
Site					
GUMC (ref)	0.00	0.00			
MGH	-0.24	0.37	0.51	-0.97	0.48
NYU	0.28	0.42	0.50	-0.54	1.10
Disorder Severity (ref=Low)	0.34	0.33	0.30	-0.31	0.99
Sex (ref = Male)	0.64	0.35	0.07	-0.05	1.34
Race					
White (ref)	0.00	0.00			
Asian	0.09	0.45	0.84	-0.80	0.99
Black	0.21	0.47	0.65	-0.71	1.13
Other	0.12	0.62	0.85	-1.10	1.33
Education					
College Degree (ref)	0.00	0.00			
≤ High School	0.44	1.10	0.69	-1.72	2.59
Some College	0.49	0.49	0.32	-0.48	1.45
Graduate School	0.33	0.36	0.36	-0.38	1.03
Marital Status					
Living with Partner/Married (ref)	0.00	0.00			
Single	-0.12	0.35	0.74	-0.81	0.57
Divorced/Widowed/Separated	-0.75	0.75	0.32	-2.23	0.74

Employment Status					
Full-time (ref)	0.00	0.00			
N/A	0.89	0.51	0.08	-0.12	1.90
Part-time	-0.17	0.48	0.72	-1.13	0.78
Student/Dependent*	-1.12	0.47	0.02	-2.05	-0.19
Primary Diagnosis					
GAD (ref)	0.00	0.00			
Social*	-1.09	0.34	<0.01	-1.76	-0.42
Other	-1.17	0.65	0.07	-2.44	0.11
Age	-0.02	0.01	0.26	-0.04	0.01
In-Person (ref=Online)	0.48	0.32	0.13	-0.14	1.11

* Significant variable, included in model

The three significant variables in this model (CGIS-S, Primary Diagnosis, and Employment Status) as well as the intercept are modeled in Figure 10 as a multiple linear regression of the overall PSQI score for the TAME study.

Figure 10.
Multiple Linear Regression Model of PSQI All Observations Over 8 Week Treatment

$$\Delta PSQI\ ALL = 0.88 + 0.79CGI\text{-}S - 1.09SAD - 1.17\ OTHERDIAGNOSIS - 1.12STUDENT - 0.17PARTTIME + 0.89NAJOB$$

Discussion

This study offered insight into the relationship between meditative (MBSR) and medicative (Escitalopram) techniques in reducing anxiety outcomes including symptom management and sleep across in-person and online/remote exposures. With these findings and further studies into the intricacies of anxiety treatment, the goal is to provide anxiety diagnosed patients with optimal treatment options to mitigate symptoms and improve their quality of life. Understanding further demographic or exposure characteristics and the consequential outcomes from anxiety exposure and treatment provides clinicians and patients with the ability to make informed decisions about their health.

Both Escitalopram and MBSR were effective treatments in the virtual and in-person cohorts in this study, reducing the CGI-S score for patients through the 8-week protocol and the post-treatment follow up. The average CGI-S score reduction from baseline to 8 weeks (treatment completion) for the online MBSR group was 1.18 points, online Escitalopram decreased 1.63 points, in-person MBSR reduced 1.35 points, and in-person Escitalopram declined 1.42 points. There was a significant difference between the week 8 scores comparing the online Escitalopram group to the online MBSR treatment group ($p=0.05$) as well as to the in-person Escitalopram group ($p=0.03$). The week 24 follow up CGI-S score comparison was also significant in these evaluations ($p=0.05$ and $p=<0.01$, respectively). However, the change from baseline was only significant for the online treatment comparison groups ($p=0.01$). This proves that the online cohort Escitalopram treatment had a greater and longer lasting effect than any other treatment group.

The implementation of the online treatments could have impacted the outcomes of this study, as CGI-S score improvements in the Escitalopram online cohort differed significantly from the online-treated MBSR group. As noted in the methods section, the Escitalopram was delivered directly to the participant's homes as opposed to receiving the treatments at the clinic. Therefore, the resulting adherence to these protocols could have been affected thus improving the overall outcomes of this cohort. The further decline of CGI-S scores beyond the initial 8-week exposure treatment in both Escitalopram cohorts and further deviation of the online cohort from the in-person could have resulted from continuation of treatment, which was permitted by the researchers. Though the online MBSR cohort missed out on some foundational components of the training including in-person collaboration for group meetings and retreats, this cohort did not exhibit any significant difference from the in-person cohort regarding their CGI-S outcomes

from baseline to weeks 4 and 8 and the follow-up timepoints at weeks 12 and 24. Adherence may have been greater in the online MBSR cohort, but as noted in previous studies, distraction levels are much greater with online programs, detracting from treatment effectiveness (Barker, 2021). Compared to the Hoge et al. analysis of the in-person cohort, the online cohort did not have the same equality of CGI-S score reduction between the MBSR and Escitalopram, revealing that method of presentation affects adherence and subsequent anxiety treatment outcome. Thus, the hypothesis was disproven due to the difference between Escitalopram and MBSR treated patients in the online cohort.

Regarding the PROMIS-T Sleep Disturbance and PSQI scores as measures of sleep improvement, all groups had an average overall significant change from the baseline measurement to week 8 ($p=<0.01$). This demonstrates that all treatments were effective at improving sleep quality when measured using the PROMIS-T Sleep Disturbance and PSQI evaluations. The only significant difference noted between compared groups, either online between treatment methods or by treatment type comparing in-person or online exposure was between the in-person and online MBSR groups using the PROMIS-T Sleep Disturbance score. At week 4, there was a significantly steeper decline in the averaged in-person measure at 52.65 compared to the online cohort at 55.57 ($p=<0.01$). This difference continues at the week 8 evaluation with the in-person cohort having lower average values ($p=0.03$). However, by the week 24 measurement, there was no significant differences between the MBSR treatment exposed cohorts. The PSQI measurement comparisons between the online MBSR and Escitalopram as well as the between treatment comparisons for online and in-person cohorts were all insignificant. Even with a significant overall change value for all treatment and exposure combinations, the PSQI scores of MBSR and Escitalopram treatments with online and in-person

exposure had similar sleep outcomes. There remains a strong correlation linking the PROMIS-T Sleep Disturbance and PSQI scores for the online and in-person cohorts, indicating that the evaluations are reflective of one another.

Due to the high rate of insomnia associated with GAD at 7 times greater risk in diagnosed patients, the overall average reduction in both PSQI and PROMIS-T Sleep Disturbance scores in all groups over the course of the study is expected. Approximately 63% of those who completed the study protocol were diagnosed with GAD as the predominant diagnosis amongst participants in the study. With this strong association and overall change improvements amongst all cohorts involved in the studies, no matter the treatment or methodology of exposure, the hypothesis was proven with both the PROMIS-T Sleep Disturbance and PSQI as scales of measuring sleep outcomes. However, there is a notable difference between the PROMIS-T Sleep Disturbance and PSQI when comparing the online and in-person MBSR groups, as the PROMIS-T Sleep Disturbance indicates a significant difference at 4 and 8 weeks during the protocol treatment. Therefore, the online treated cohort may not have been as receptive to MBSR, affecting sleep improvements. There is no true way of knowing whether outside events, specifically the COVID-19 pandemic, surrounding the online cohort may have affected receptiveness to the MBSR treatment or exacerbated anxiety symptoms over the duration of the treatment. Since we only have results concerning symptom improvements through the CGI-S, PROMIS-T Sleep Disturbance, and PSQI scores we can just conclude that all treatments were effective at mitigating the symptoms of anxiety, specifically insomnia, at the conclusion of the treatment protocol (week 8) compared to baseline measurements.

Overall, there were many patterns presented in the model development for the PROMIS-T Sleep Disturbance and PSQI estimations based on cohort. The PROMIS-T Sleep Disturbance

and PSQI score models all included CGI-S difference as a significant variable, establishing anxiety severity as strongly impactful to both sleep scores. In both the online cohort and all participants, treatment exposure comparing Escitalopram and MBSR had no significant impact on overall sleep outcomes. Comparing the in-person and online cohorts in the overall PSQI and PROMIS-T Sleep Disturbance models, no significant difference was present, meaning the two exposures had similar influence on sleep improvement. Location variation on PROMIS-T Sleep Disturbance scores was seen in overall and online models, with NYU based participants experiencing a significantly lower PROMIS-T Sleep Disturbance change. Primary diagnosis influenced PSQI sleep outcomes, as those with SAD haver a lower score difference in all participants, specifically those in the online treatment cohort. Other diagnosis was significant for PSQI score with the online cohort. In terms of employment status, the all observations with PROMIS-T Sleep Disturbance evaluations had a significant reduction in score compared to full-time working participants for those who responded N/A, while student participants in the TAME study using PSQI evaluation had a reduced change in score over the course of the 8-week program.

As hypothesized, CGI-S score reduction had a strong association with lowered PROMIS-T Sleep Disturbance and PSQI scores as it was a significant variable in every multivariable linear regression sleep model generated. This relationship strengthens the connection between anxiety symptoms, particularly those associated with GAD, and sleep deprivation. The PSQI score captured this connection as all participants, specifically those in the online cohort diagnosed with SAD had significantly lower PSQI score changes compared to GAD diagnosed participants. In the online cohort specifically, any other diagnosis besides SAD and GAD was also significantly associated with lessened change in PSQI. Considering the insignificant differences associated

with the two treatment groups, MBSR and Escitalopram, treatment as an insignificant variable to sleep change aligns with the outcomes presented earlier. Though the in-person variable was insignificant in all combined models, including the PROMIS-T Sleep Disturbance, this may be due to the inclusion of all data in the model for analysis, not separated by treatment type. Perhaps if one were to look at the PROMIS-T Sleep Disturbance or PSQI in models divided by treatment exposure, variables such as the in-person within the MBSR cohort for PROMIS-T Sleep Disturbance would flag as significant. A surprising discovery was the impact of location within the PROMIS-T Sleep Disturbance evaluations. The NYU based participants had significantly lowered PROMIS-T Sleep Disturbance changes over the 8-week exposure than the GUMC based equivalents, which could indicate discrepancies in how the materials were presented to the participants and/or adherence differences to these procedures. Additionally, there could be outside variables which have the potential to affect sleep patterns, such as sleep disturbances due to street noise which have not been accounted for in this particular study but could be influential factors in PROMIS-T Sleep Disturbance outcomes. The increase in PROMIS-T Sleep Disturbance change with N/A employed participants as well as reduction in students with PSQI evaluations could be evident of lifestyle differences within these populations compared to full-time employed participants. Fluctuations in student schedules and stress levels could impact sleep outcomes while those who do not have a job or are self-employed have a greater flexibility to lengthen their sleep schedules without disturbance.

Limitations of this study center around population sample size, bias resulting from study design, and participant diversity. The size of this study was effectively reduced by half due to the COVID-19 pandemic and split in two cohorts, separated by the online and in-person exposures. Although this did provide us with an additional comparison variable, it limited the ability to

effectively compare MBSR and Escitalopram treatment over the duration of time which was initially intended. Conducting the study as a single blind study with the participants and study directors unblinded was a necessity for implementation. However, this study was designed to be focused on practical application. Bias was limited in the CGI-S evaluations by having independently associated, blinded evaluators rather than the participants themselves conduct evaluations. However, the PROMIS-T Sleep Disturbance and PSQI evaluations were by self - report of the participants, which is potentially impacted by detection and recall bias. The lack of diversity within the population with most participants being white, educated, women diagnosed with GAD from three distinct urban academic centers limits the ability to make larger population generalizations based on these study outcomes.

Future studies could involve larger populations, perhaps in a nationwide study which could incorporate greater participant diversity and allow further examination of the outcome differences between MBSR and Escitalopram in a wider setting. MBSR could also be compared against different anxiety medications including Benzodiazepines, Azapirones, SNRIs and other SSRIs to determine effectivity across a broader range of treatment. Additionally, MBSR could be compared to other non-medicative treatments including CBT and Cognitive Based Group Therapy to gauge effectiveness of these alternative treatments. Incorporating an online and in-person format comparison within these studies could help researchers to better understand optimal methods of treatment implementation. Having a greater database of participants and a more reliable judgement of medication efficacy compared to MBSR would strengthen this comparison and potentially allow for MBSR to be seen as an effectual alternative to medication treatment.

Conclusion

Comparing the online MBSR treatment to the in-person equivalent and in-person provided Escitalopram treatments, there was no significant difference in CGI-S outcome differences from the baseline measurement to the conclusion of the 8-week study protocol as all reduced anxiety symptom appearance equally. However, the online provided Escitalopram treatment cohort had significantly lowered CGI-S scores compared to the other three groups. Further studies of this comparison could enhance understanding of whether the at-home delivery boosted adherence to the study protocol by this cohort.

As measured by both the PROMIS-T Sleep Disturbance and PSQI scales, sleep disturbance significantly decreased from baseline to week 8 in all exposure groups. There were no significant differences between the in-person and online Escitalopram cohorts as well as between the online MBSR and Escitalopram treatment. There was a significant difference between the online and in-person MBSR cohorts at weeks 4 and 8. Although both treatment and in-person exposure were not significant variables in the model development for PROMIS-T Sleep Disturbance and PSQI, the strength of association between sleep score and CGI-S score decline was evident throughout each of the models as well as between site and PROMIS-T Sleep Disturbance score and primary diagnosis and PSQI score. Lifestyle differences through qualitative assessment could be evaluated further to differentiate how employment status affects sleep disturbances when measuring on the PROMIS-T Sleep Disturbance and PSQI scales.

Further insights and a wider range of demographic differences can assist in evaluating in-person and online CGI-S, PSQI, and PROMIS-T Sleep Disturbance changes comparing MBSR to Escitalopram. This study had demonstrated that both treatments are effective at mitigating anxiety symptoms and enhancing sleep outcomes. This is the first study of its kind, detailing the

change in anxiety outcomes and sleep outcomes with a comparative analysis of MBSR and Escitalopram in an online and in-person exposure settings.

References

Accoto, A., Chiarella, S. G., Raffone, A., Montano, A., de Marco, A., Mainiero, F., Rubbino, R., Valzania, A., & Conversi, D. (2021). Beneficial Effects of Mindfulness-Based Stress Reduction Training on the Well-Being of a Female Sample during the First Total Lockdown Due to COVID-19 Pandemic in Italy. *Int J Environ Res Public Health*, *18*(11). https://doi.org/10.3390/ijerph18115512

Andersen, S. R., Wurtzen, H., Steding-Jessen, M., Christensen, J., Andersen, K. K., Flyger, H., Mitchelmore, C., Johansen, C., & Dalton, S. O. (2013). Effect of mindfulness-based stress reduction on sleep quality: results of a randomized trial among Danish breast cancer patients. *Acta Oncol*, *52*(2), 336-344. https://doi.org/10.3109/0284186X.2012.745948

Arch, J. J., Ayers, C. R., Baker, A., Almklov, E., Dean, D. J., & Craske, M. G. (2013). Randomized clinical trial of adapted mindfulness-based stress reduction versus group cognitive behavioral therapy for heterogeneous anxiety disorders. *Behav Res Ther*, *51*(4-5), 185-196. https://doi.org/10.1016/j.brat.2013.01.003

Asnaani, A., Richey, J. A., Dimaite, R., Hinton, D. E., & Hofmann, S. G. (2010). A cross-ethnic comparison of lifetime prevalence rates of anxiety disorders. *J Nerv Ment Dis*, *198*(8), 551-555. https://doi.org/10.1097/NMD.0b013e3181ea169f

Association, A. P. (2022). Anxiety Disorders. *Diagnostic and Statistical Manual of Mental Disorders*, 215-231. https://www.psychiatry.org/patients-families/anxiety-disorders/what-are-anxiety-disorders (5)

Axelsson, E., Andersson, E., Ljotsson, B., Bjorkander, D., Hedman-Lagerlof, M., & Hedman-Lagerlof, E. (2020). Effect of Internet vs Face-to-Face Cognitive Behavior Therapy for Health Anxiety: A Randomized Noninferiority Clinical Trial. *JAMA Psychiatry*, *77*(9), 915-924. https://doi.org/10.1001/jamapsychiatry.2020.0940

Bandelow, B., & Michaelis, S. (2015). Epidemiology of anxiety disorders in the 21st century. *Dialogues Clin Neurosci*, *17*(3), 327-335. https://doi.org/10.31887/DCNS.2015.17.3/bbandelow

Bandelow, B., Michaelis, S., & Wedekind, D. (2017). Treatment of anxiety disorders. *Dialogues Clin Neurosci*, *19*(2), 93-107. https://doi.org/10.31887/DCNS.2017.19.2/bbandelow

Barker, G. G. (2021). Online therapy: lessons learned from the COVID-19 health crisis. *British Journal of Guidance and Counselling*, *50*(1), 66-81. https://doi.org/10.1080/03069885.2021.1889462

Bekes, V., Aafjes-van Doorn, K., Luo, X., Prout, T. A., & Hoffman, L. (2021). Psychotherapists' Challenges With Online Therapy During COVID-19: Concerns About Connectedness Predict Therapists' Negative View of Online Therapy and Its Perceived Efficacy Over Time. *Front Psychol*, *12*, 705699. https://doi.org/10.3389/fpsyg.2021.705699

Bitterauf, M. (2016). Mindfulness-Based Stress Reduction Program Handbook. https://www.psychopap.com/wp-content/uploads/2021/07/MBSR-Handbook-Single-Page-Final.pdf

Borwin Bandelow, D. S. B., Ornah T. Dolberg, Henning Friis Andersen, and Dan J. Stein. (2006). What Is the Threshold for Symptomatic Response and Remission for Major Depressive Disorder, Panic Disorder, Social Anxiety Disorder, and Generalized Anxiety Disorder? *The Journal of Clinical Psychiatry*.

Bossi, F., Zaninotto, F., D'Arcangelo, S., Lattanzi, N., Malizia, A. P., & Ricciardi, E. (2022). Mindfulness-based online intervention increases well-being and decreases stress after Covid-19 lockdown. *Sci Rep*, *12*(1), 6483. https://doi.org/10.1038/s41598-022-10361-2

Breslau, N., Roth, T., Rosenthal, L., & Andreski, P. (1996). Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry*, *39*(6), 411-418. https://doi.org/10.1016/0006-3223(95)00188-3

Brossoit, R. M., Stark, H. P., Crain, T. L., Bodner, T. E., Hammer, L. B., Mohr, C. D., & Shea, S. A. (2023). Multidimensionality of the PROMIS sleep disturbance 8b short form in working adult populations. *Sleep Health*, *9*(6), 925-932. https://doi.org/10.1016/j.sleh.2023.08.001

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the DSM-IV anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *J Abnorm Psychol*, *107*(2), 179-192. https://doi.org/10.1037//0021-843x.107.2.179

Busner, J., & Targum, S. D. (2007). The clinical global impressions scale: applying a research tool in clinical practice. *Psychiatry (Edgmont)*, *4*(7), 28-37. https://www.ncbi.nlm.nih.gov/pubmed/20526405

Bystritsky, A., Khalsa, S. S., Cameron, M. E., & Schiffman, J. (2013). Current diagnosis and treatment of anxiety disorders. *P T*, *38*(1), 30-57. https://www.ncbi.nlm.nih.gov/pubmed/23599668

Caporino, N. E., Read, K. L., Shiffrin, N., Settipani, C., Kendall, P. C., Compton, S. N., Sherrill, J., Piacentini, J., Walkup, J., Ginsburg, G., Keeton, C., Birmaher, B., Sakolsky, D., Gosch, E., & Albano, A. M. (2017). Sleep-Related Problems and the Effects of Anxiety Treatment in Children and Adolescents. *J Clin Child Adolesc Psychol*, *46*(5), 675-685. https://doi.org/10.1080/15374416.2015.1063429

Catherine DeCarlo Santiago, M. E. W., Jessica Stump. (2011). Socioeconomic status, neighborhood disadvantage, and poverty-related stress: Prospective effects on psychological syndromes among diverse low-income families. *Journal of Economic Psychology*, *32*(2), 218-230. https://doi.org/https://doi.org/10.1016/j.joep.2009.10.008

Chellappa, S. L., & Aeschbach, D. (2022). Sleep and anxiety: From mechanisms to interventions. *Sleep Med Rev*, *61*, 101583. https://doi.org/10.1016/j.smrv.2021.101583

Chen, T. L., Chang, S. C., Hsieh, H. F., Huang, C. Y., Chuang, J. H., & Wang, H. H. (2020). Effects of mindfulness-based stress reduction on sleep quality and mental health for insomnia patients: A meta-analysis. *J Psychosom Res*, *135*, 110144. https://doi.org/10.1016/j.jpsychores.2020.110144

Collaborators, C.-M. D. (2021). Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet*, *398*(10312), 1700-1712. https://doi.org/10.1016/S0140-6736(21)02143-7

Cox, R. C., & Olatunji, B. O. (2016). A systematic review of sleep disturbance in anxiety and related disorders. *J Anxiety Disord*, *37*, 104-129. https://doi.org/10.1016/j.janxdis.2015.12.001

Craske, M. G., Roy-Byrne, P. P., Stein, M. B., Sullivan, G., Sherbourne, C., & Bystritsky, A. (2009). Treatment for anxiety disorders: Efficacy to effectiveness to implementation. *Behav Res Ther*, *47*(11), 931-937. https://doi.org/10.1016/j.brat.2009.07.012

Crits-Christoph, P., Newman, M. G., Rickels, K., Gallop, R., Gibbons, M. B., Hamilton, J. L., Ring-Kurtz, S., & Pastva, A. M. (2011). Combined medication and cognitive therapy for

generalized anxiety disorder. *J Anxiety Disord*, *25*(8), 1087-1094. https://doi.org/10.1016/j.janxdis.2011.07.007

Cuijpers, P., Sijbrandij, M., Koole, S., Huibers, M., Berking, M., & Andersson, G. (2014). Psychological treatment of generalized anxiety disorder: a meta-analysis. *Clin Psychol Rev*, *34*(2), 130-140. https://doi.org/10.1016/j.cpr.2014.01.002

Daniel Moise, A. D., Mihaela Diana Oancea Negescu, Carol Cristina Gombos. (2021). Online Education During Pandemic Times:Advantagesand Disadvantages. *European Journal of Sustainable Development*, *10*(4), 63-71. https://doi.org/10.14207/ejsd.2021.v10n4p63

Darehzereshki, S., Dehghani, F., & Enjezab, B. (2022). Mindfulness-based stress reduction group training improves of sleep quality in postmenopausal women. *BMC Psychiatry*, *22*(1), 254. https://doi.org/10.1186/s12888-022-03869-4

Davies, M. R., Buckman, J. E. J., Adey, B. N., Armour, C., Bradley, J. R., Curzons, S. C. B., Davies, H. L., Davis, K. A. S., Goldsmith, K. A., Hirsch, C. R., Hotopf, M., Hubel, C., Jones, I. R., Kalsi, G., Krebs, G., Lin, Y., Marsh, I., McAtarsney-Kovacs, M., McIntosh, A. M., . . . Eley, T. C. (2022). Comparison of symptom-based versus self-reported diagnostic measures of anxiety and depression disorders in the GLAD and COPING cohorts. *J Anxiety Disord*, *85*, 102491. https://doi.org/10.1016/j.janxdis.2021.102491

DeMartini, J., Patel, G., & Fancher, T. L. (2019). Generalized Anxiety Disorder. *Ann Intern Med*, *170*(7), ITC49-ITC64. https://doi.org/10.7326/AITC201904020

Deng, J., Zhou, F., Hou, W., Silver, Z., Wong, C. Y., Chang, O., Huang, E., & Zuo, Q. K. (2021). The prevalence of depression, anxiety, and sleep disturbances in COVID-19 patients: a meta-analysis. *Ann N Y Acad Sci*, *1486*(1), 90-111. https://doi.org/10.1111/nyas.14506

DeRubeis, R. J., Siegle, G. J., & Hollon, S. D. (2008). Cognitive therapy versus medication for depression: treatment outcomes and neural mechanisms. *Nat Rev Neurosci*, *9*(10), 788-796. https://doi.org/10.1038/nrn2345

Ebell, M. H. (2008). Diagnosis of anxiety disorders in primary care. *Am Fam Physician*, *78*(4), 501-502. https://www.ncbi.nlm.nih.gov/pubmed/18756659

Esala, J. V. a. J. J. (2019). Beyond Symptoms: Race and Gender Predict Anxiety Disorder Diagnosis. *Society and Mental Health*, *9*(1), 111-125. https://doi.org/https://doi.org/10.1177/2156869318811435

Fabbri, M., Beracci, A., Martoni, M., Meneo, D., Tonetti, L., & Natale, V. (2021). Measuring Subjective Sleep Quality: A Review. *Int J Environ Res Public Health*, *18*(3). https://doi.org/10.3390/ijerph18031082

Fatemeh Abbasi , K. S., and Fakhri Tajikzadeh1. (2018). Comparison of the Cognitive Behavioral Therapy (CBT) and Mindfulness-Based Stress Reduction (MBSR): Reducing Anxiety Symptoms. *Womens Health Bulletin*, *5*(4). 10.5812/whb.60585

Fazia, T., Bubbico, F., Nova, A., Bruno, S., Iozzi, D., Calgan, B., Caimi, G., Terzaghi, M., Manni, R., & Bernardinelli, L. (2023). Beneficial Effects of an Online Mindfulness-Based Intervention on Sleep Quality in Italian Poor Sleepers during the COVID-19 Pandemic: A Randomized Trial. *Int J Environ Res Public Health*, *20*(3). https://doi.org/10.3390/ijerph20032724

Garakani, A., Murrough, J. W., Freire, R. C., Thom, R. P., Larkin, K., Buono, F. D., & Iosifescu, D. V. (2020). Pharmacotherapy of Anxiety Disorders: Current and Emerging Treatment Options. *Front Psychiatry*, *11*, 595584. https://doi.org/10.3389/fpsyt.2020.595584

Gearing, R. E., Schwalbe, C. S., Lee, R., & Hoagwood, K. E. (2013). The effectiveness of booster sessions in CBT treatment for child and adolescent mood and anxiety disorders. *Depress Anxiety*, *30*(9), 800-808. https://doi.org/10.1002/da.22118

Goldin, P. R., Morrison, A., Jazaieri, H., Brozovich, F., Heimberg, R., & Gross, J. J. (2016). Group CBT versus MBSR for social anxiety disorder: A randomized controlled trial. *J Consult Clin Psychol*, *84*(5), 427-437. https://doi.org/10.1037/ccp0000092

Gomez, A. F., Barthel, A. L., & Hofmann, S. G. (2018). Comparing the efficacy of benzodiazepines and serotonergic anti-depressants for adults with generalized anxiety disorder: a meta-analytic review. *Expert Opin Pharmacother*, *19*(8), 883-894. https://doi.org/10.1080/14656566.2018.1472767

Goodman, W. K., Bose, A., & Wang, Q. (2005). Treatment of generalized anxiety disorder with escitalopram: pooled results from double-blind, placebo-controlled trials. *J Affect Disord*, *87*(2-3), 161-167. https://doi.org/10.1016/j.jad.2004.11.011

Guy W. *ECDEU Assessment Manual for Psychopharmacology*. U.S. Department of Health, Education, and Welfare, Public Health Service, Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, Psychopharmacology Research Branch, Division of Extramural Research Programs; 1976.

Hawes, M. T., Szenczy, A. K., Klein, D. N., Hajcak, G., & Nelson, B. D. (2022). Increases in depression and anxiety symptoms in adolescents and young adults during the COVID-19 pandemic. *Psychol Med*, *52*(14), 3222-3230. https://doi.org/10.1017/S0033291720005358

Hayes, D. M. D. a. J. A. (2012). What are the benefits of mindfulness. *Monitor on Psychology*, *43*(7), 64. https://www.apa.org/monitor/2012/07-08/ce-corner

He, H., Xiang, Y., Gao, F., Bai, L., Gao, F., Fan, Y., Lyu, J., & Ma, X. (2019). Comparative efficacy and acceptability of first-line drugs for the acute treatment of generalized anxiety disorder in adults: A network meta-analysis. *J Psychiatr Res*, *118*, 21-30. https://doi.org/10.1016/j.jpsychires.2019.08.009

Health, C. Examining Lexapro's Impact On Sleep Quality. *Medicine Information*. https://cabinethealth.com/blogs/journal/examining-lexapros-impact-on-sleep-quality

Health, N. I. o. M. (2023). *Anxiety Disorders*. NIMH. https://www.nimh.nih.gov/health/topics/anxiety-disorders

Herrick, L. M., Camilleri, M., Schleck, C. D., Zinsmeister, A. R., Saito, Y. A., & Talley, N. J. (2018). Effects of Amitriptyline and Escitalopram on Sleep and Mood in Patients With Functional Dyspepsia. *Clin Gastroenterol Hepatol*, *16*(3), 401-406 e402. https://doi.org/10.1016/j.cgh.2017.10.021

History of MBSR. (2021). MBSR Teachers Collaborative of Greater New York. https://mbsrcollaborative.com/history-of-mbsr

Hoge, E. A., Bui, E., Marques, L., Metcalf, C. A., Morris, L. K., Robinaugh, D. J., Worthington, J. J., Pollack, M. H., & Simon, N. M. (2013). Randomized controlled trial of mindfulness meditation for generalized anxiety disorder: effects on anxiety and stress reactivity. *J Clin Psychiatry*, *74*(8), 786-792. https://doi.org/10.4088/JCP.12m08083

Hoge, E. A., Bui, E., Mete, M., Dutton, M. A., Baker, A. W., & Simon, N. M. (2023). Mindfulness-Based Stress Reduction vs Escitalopram for the Treatment of Adults With Anxiety Disorders: A Randomized Clinical Trial. *JAMA Psychiatry*, *80*(1), 13-21. https://doi.org/10.1001/jamapsychiatry.2022.3679

Hoge, E. A., Ivkovic, A., & Fricchione, G. L. (2012). Generalized anxiety disorder: diagnosis and treatment. *BMJ*, *345*, e7500. https://doi.org/10.1136/bmj.e7500

Household Pulse Survey. (2020-2023). U.S. Census Bureau. https://www.cdc.gov/nchs/covid19/pulse/mental-health.htm

Howard, L. (2023, May 10, 2023). Anxiety disorders will affect nearly 1 in 3 adults: Here's what you need to know. *UC Davis Health*. https://health.ucdavis.edu/news/headlines/anxiety-disorders-will-affect-nearly-1-in-3-adults-heres-what-you-need-to-know/2023/05

Jazaieri, H., Goldin, P. R., Werner, K., Ziv, M., & Gross, J. J. (2012). A randomized trial of MBSR versus aerobic exercise for social anxiety disorder. *J Clin Psychol*, *68*(7), 715-731. https://doi.org/10.1002/jclp.21863

Jiang, A., Rosario, M., Stahl, S., Gill, J. M., & Rusch, H. L. (2021). The Effect of Virtual Mindfulness-Based Interventions on Sleep Quality: A Systematic Review of Randomized Controlled Trials. *Curr Psychiatry Rep*, *23*(9), 62. https://doi.org/10.1007/s11920-021-01272-6

Johnson, E. O., Roth, T., & Breslau, N. (2006). The association of insomnia with anxiety disorders and depression: exploration of the direction of risk. *J Psychiatr Res*, *40*(8), 700-708. https://doi.org/10.1016/j.jpsychires.2006.07.008

Kabatas Yildiz, M., & Orak, O. S. (2023). The effect of the Mindfulness-Based Stress Reduction program on the level of perceived stress and geriatric depression in older adults: a randomised controlled study. *Psychogeriatrics*, *23*(2), 261-272. https://doi.org/10.1111/psyg.12929

Kaufman, J., & Charney, D. (2000). Comorbidity of mood and anxiety disorders. *Depress Anxiety*, *12 Suppl 1*, 69-76. https://doi.org/10.1002/1520-6394(2000)12:1+<69::AID-DA9>3.0.CO;2-K

Kessler, R. C., Petukhova, M., Sampson, N. A., Zaslavsky, A. M., & Wittchen, H. U. (2012). Twelve-month and lifetime prevalence and lifetime morbid risk of anxiety and mood disorders in the United States. *Int J Methods Psychiatr Res*, *21*(3), 169-184. https://doi.org/10.1002/mpr.1359

Kim, S. M., Park, J. M., Seo, H. J., Kim, J., Noh, J. W., & Kim, H. L. (2022). Effects of mindfulness-based stress reduction on adults with sleep disturbance: an updated systematic review and meta-analysis. *BMJ Open*, *12*(11), e058032. https://doi.org/10.1136/bmjopen-2021-058032

Kostyalik, D., Vas, S., Katai, Z., Kitka, T., Gyertyan, I., Bagdy, G., & Tothfalusi, L. (2014). Chronic escitalopram treatment attenuated the accelerated rapid eye movement sleep transitions after selective rapid eye movement sleep deprivation: a model-based analysis using Markov chains. *BMC Neurosci*, *15*, 120. https://doi.org/10.1186/s12868-014-0120-8

Lee, S. H., Ahn, S. C., Lee, Y. J., Choi, T. K., Yook, K. H., & Suh, S. Y. (2007). Effectiveness of a meditation-based stress management program as an adjunct to pharmacotherapy in patients with anxiety disorder. *J Psychosom Res*, *62*(2), 189-195. https://doi.org/10.1016/j.jpsychores.2006.09.009

Lenze, E. J., Rollman, B. L., Shear, M. K., Dew, M. A., Pollock, B. G., Ciliberti, C., Costantino, M., Snyder, S., Shi, P., Spitznagel, E., Andreescu, C., Butters, M. A., & Reynolds, C. F., 3rd. (2009). Escitalopram for older adults with generalized anxiety disorder: a randomized controlled trial. *JAMA*, *301*(3), 295-303. https://doi.org/10.1001/jama.2008.977

Mazza, M. G., De Lorenzo, R., Conte, C., Poletti, S., Vai, B., Bollettini, I., Melloni, E. M. T., Furlan, R., Ciceri, F., Rovere-Querini, P., group, C.-B. O. C. S., & Benedetti, F. (2020). Anxiety and depression in COVID-19 survivors: Role of inflammatory and clinical predictors. *Brain Behav Immun*, *89*, 594-600. https://doi.org/10.1016/j.bbi.2020.07.037

McElrath, K. (2020). *Nearly 93% of Households With School-Age Children Report Some Form of Distance Learning During COVID-19*. https://www.census.gov/library/stories/2020/08/schooling-during-the-covid-19-pandemic.html

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *J Psychiatr Res*, *45*(8), 1027-1035. https://doi.org/10.1016/j.jpsychires.2011.03.006

McMakin, D. L., Ricketts, E. J., Forbes, E. E., Silk, J. S., Ladouceur, C. D., Siegle, G. J., Milbert, M., Trubnick, L., Cousins, J. C., Ryan, N. D., Harvey, A. G., & Dahl, R. E. (2019). Anxiety Treatment and Targeted Sleep Enhancement to Address Sleep Disturbance in Pre/Early Adolescents with Anxiety. *J Clin Child Adolesc Psychol*, *48*(sup1), S284-S297. https://doi.org/10.1080/15374416.2018.1463534

Mellman, T. A. (2006). Sleep and anxiety disorders. *Psychiatr Clin North Am*, *29*(4), 1047-1058; abstract x. https://doi.org/10.1016/j.psc.2006.08.005

Mwinyi, J., Pisanu, C., Castelao, E., Stringhini, S., Preisig, M., & Schioth, H. B. (2017). Anxiety Disorders are Associated with Low Socioeconomic Status in Women but Not in Men. *Womens Health Issues*, *27*(3), 302-307. https://doi.org/10.1016/j.whi.2017.01.001

NAMI. *Complementary Health Approaches*.

NAMI. *Mental Health Medications*.

NAMI. *Psychotherapy*.

NAMI. (2017). *Anxiety Disorders*.

NAMI. (2022). Medication Fact Sheet: Escitalopram. In A. A. o. P. Pharmacists (Ed.). aapp.org: NAMI.

Niazi, A. K., & Niazi, S. K. (2011). Mindfulness-based stress reduction: a non-pharmacological approach for chronic illnesses. *N Am J Med Sci*, *3*(1), 20-23. https://doi.org/10.4297/najms.2011.320

Nourian, M., Nikfarid, L., Khavari, A. M., Barati, M., & Allahgholipour, A. R. (2021). The Impact of an Online Mindfulness-Based Stress Reduction Program on Sleep Quality of Nurses Working in COVID-19 Care Units: A Clinical Trial. *Holist Nurs Pract*, *35*(5), 257-263. https://doi.org/10.1097/HNP.0000000000000466

Novella, J. K., Ng, K. M., & Samuolis, J. (2022). A comparison of online and in-person counseling outcomes using solution-focused brief therapy for college students with anxiety. *J Am Coll Health*, *70*(4), 1161-1168. https://doi.org/10.1080/07448481.2020.1786101

Organization, W. H. (2022). *Mental Health and COVID-19: Early evidence of the pandemic's impact* (Scientific brief, Issue. https://iris.who.int/bitstream/handle/10665/352189/WHO-2019-nCoV-Sci-Brief-Mental-health-2022.1-eng.pdf?sequence=1

Papadimitriou, G. N., & Linkowski, P. (2005). Sleep disturbance in anxiety disorders. *Int Rev Psychiatry*, *17*(4), 229-236. https://doi.org/10.1080/09540260500104524

Petersen, A. (2020). More People Are Taking Drugs for Anxiety and Insomnia, and Doctors Are Worried. *The Wall Street Journal*. https://www.wsj.com/articles/more-people-are-taking-drugs-for-anxiety-and-insomnia-and-doctors-are-worried-11590411600

Pickett, S. M., Kozak, A. T., Lanni, D. J., Warnke, A. S., Gaillard, P., & Jarrett, N. L. (2022). The comparison of brief, online mindfulness and relaxation interventions to reduce stress and improve sleep-related outcomes in college students. *J Am Coll Health*, 1-9. https://doi.org/10.1080/07448481.2022.2066979

Pollack, M., Kinrys, G., Krystal, A., McCall, W. V., Roth, T., Schaefer, K., Rubens, R., Roach, J., Huang, H., & Krishnan, R. (2008). Eszopiclone coadministered with escitalopram in patients with insomnia and comorbid generalized anxiety disorder. *Arch Gen Psychiatry*, *65*(5), 551-562. https://doi.org/10.1001/archpsyc.65.5.551

Prevention, C. f. D. C. a. (2022). *Mental Health Conditions: Depression and Anxiety*. CDC. https://www.cdc.gov/tobacco/campaign/tips/diseases/depression-anxiety.html#one

Ramsawh, H. J., Bomyea, J., Stein, M. B., Cissell, S. H., & Lang, A. J. (2016). Sleep Quality Improvement During Cognitive Behavioral Therapy for Anxiety Disorders. *Behav Sleep Med*, *14*(3), 267-278. https://doi.org/10.1080/15402002.2014.981819

Reangsing, C., Trakooltorwong, P., Maneekunwong, K., Thepsaw, J., & Oerther, S. (2023). Effects of online mindfulness-based interventions (MBIs) on anxiety symptoms in adults: a systematic review and meta-analysis. *BMC Complement Med Ther*, *23*(1), 269. https://doi.org/10.1186/s12906-023-04102-9

Robert L. Spitzer, J. B. W. W., Kurt Kroenke et.al. GAD-7. In (2 ed.).

Rose, M., & Devine, J. (2014). Assessment of patient-reported symptoms of anxiety. *Dialogues Clin Neurosci*, *16*(2), 197-211. https://doi.org/10.31887/DCNS.2014.16.2/mrose

SAMHSA. (2023). *Anxiety Disorders*. https://www.samhsa.gov/mental-health/anxiety-disorders

Sanilevici, M., Reuveni, O., Lev-Ari, S., Golland, Y., & Levit-Binnun, N. (2021). Mindfulness-Based Stress Reduction Increases Mental Wellbeing and Emotion Regulation During the First Wave of the COVID-19 Pandemic: A Synchronous Online Intervention Study. *Front* Psychol, 12, 720965. https://doi.org/10.3389/fpsyg.2021.720965

Santorelli SF, Kabat-Zinn J, Blacker M, Meleo-Meyer F, Koerbel L. Mindfulness-Based Stress Reduction (MBSR) Authorized Curriculum Guide. Center for Mindfulness in Medicine, Health Care, and Society at the University of Massachusetts Medical School. Revised 2017. https://www.bangor.ac.uk/mindfulness/documents/mbsr-curriculum-guide-2017.pdf

Sapra, A., Bhandari, P., Sharma, S., Chanpura, T., & Lopp, L. (2020). Using Generalized Anxiety Disorder-2 (GAD-2) and GAD-7 in a Primary Care Setting. *Cureus*, *12*(5), e8224. https://doi.org/10.7759/cureus.8224

Service, N. H. (2022). *Signs of an anxiety disorder*. NHS. https://www.nhs.uk/mental-health/feelings-symptoms-behaviours/feelings-and-symptoms/anxiety-disorder-signs/

Staner, L. (2003). Sleep and anxiety disorders. *Dialogues Clin Neurosci*, *5*(3), 249-258. https://doi.org/10.31887/DCNS.2003.5.3/lstaner

Statistics, N. C. f. E. (2023). *Distance Learning* (Condition of Education, Issue. https://nces.ed.gov/fastfacts/display.asp?id=80

Stein, D. J., & Lopez, A. G. (2011). Effects of escitalopram on sleep problems in patients with major depression or generalized anxiety disorder. *Adv Ther*, *28*(11), 1021-1037. https://doi.org/10.1007/s12325-011-0071-8

Strawn, J. R., Mills, J. A., Schroeder, H., Mossman, S. A., Varney, S. T., Ramsey, L. B., Poweleit, E. A., Desta, Z., Cecil, K., & DelBello, M. P. (2020). Escitalopram in Adolescents With Generalized Anxiety Disorder: A Double-Blind, Randomized, Placebo-Controlled Study. *J Clin Psychiatry*, *81*(5). https://doi.org/10.4088/JCP.20m13396

Tomás Esteban Sard-Peck, A. M.-A., Maria Teresa Oller Guzmán, Olga Santesteban-Echarri. (2018). Face-to-face versus online program: A comparative study of Mindfulness-Based Stress Reduction in a general Spanish population. *International Conference on Mindfulness*. https://doi.org/10.13140/RG.2.2.19327.30885

Uhde, T. W., Cortese, B. M., & Vedeniapin, A. (2009). Anxiety and sleep problems: emerging concepts and theoretical treatment implications. *Curr Psychiatry Rep*, *11*(4), 269-276. https://doi.org/10.1007/s11920-009-0039-4

Union, I. T. (2021). *Internet use* (Facts and Figures 2021, Issue. https://www.itu.int/itu-d/reports/statistics/2021/11/15/internet-use/

Villarroel, E. T. a. M. (2020). *Symptoms of Generalized Anxiety Disorder Among Adults: United States, 2019*. National Center for Health Statistics. https://www.cdc.gov/nchs/products/databriefs/db378.htm

Wang, Y., Chen, C., Gu, L., Zhai, Y., Sun, Y., Gao, G., Xu, Y., Pang, L., & Xu, L. (2023). Effect of short-term mindfulness-based stress reduction on sleep quality in male patients with alcohol use disorder. *Front Psychiatry*, *14*, 928940. https://doi.org/10.3389/fpsyt.2023.928940

Wang, Z., Whiteside, S. P. H., Sim, L., Farah, W., Morrow, A. S., Alsawas, M., Barrionuevo, P., Tello, M., Asi, N., Beuschel, B., Daraz, L., Almasri, J., Zaiem, F., Larrea-Mantilla, L., Ponce, O. J., LeBlanc, A., Prokop, L. J., & Murad, M. H. (2017). Comparative Effectiveness and Safety of Cognitive Behavioral Therapy and Pharmacotherapy for Childhood Anxiety Disorders: A Systematic Review and Meta-analysis. *JAMA Pediatr*, *171*(11), 1049-1056. https://doi.org/10.1001/jamapediatrics.2017.3036

Why Mindfulness-Based Stress Reduction (MBSR)? Mindful Leader. https://www.mindfulleader.org/why-mbsr

Zaider, T. I., Heimberg, R. G., Fresco, D. M., Schneier, F. R., & Liebowitz, M. R. (2003). Evaluation of the clinical global impression scale among individuals with social anxiety disorder. *Psychol Med*, *33*(4), 611-622. https://doi.org/10.1017/s0033291703007414

Zhou, X., Guo, J., Lu, G., Chen, C., Xie, Z., Liu, J., & Zhang, C. (2020). Effects of mindfulness-based stress reduction on anxiety symptoms in young people: A systematic review and meta-analysis. *Psychiatry Res*, *289*, 113002. https://doi.org/10.1016/j.psychres.2020.113002