MINDFULNESS-BASED COGNITIVE THERAPY INTERVENTION FOR THE TREATMENT OF LATE-LIFE DEPRESSION AND ANXIETY SYMTOMS IN PRIMARY CARE: A RANDOMIZED-CONTROLLED TRIAL

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"Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less" (Marie Curie)

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Abstract

Depression and anxiety are disabling psychiatric conditions worldwide. Approximately 10-20% of older adults treated in primary care settings suffer from late-life depression (LLD) and/or latelife anxiety (LLA). Older adults are often undertreated and/or do not receive the appropriate treatment for LLD and/or LLA in primary care, due to the lack of available resources and high demands on the health care system. Evidence has shown that antidepressants are the first line of treatment for LLD and LLA in older adults, in primary care settings. Typically, the geriatric population does not respond well to psychotropic medication due to comorbidities with other illnesses and polypharmacy, leading to high readmission rates. As the population ages, the number of older adults treated in primary care increases; therefore, there is an urgent need to find effective, scalable, and potentially cost-effective alternative therapies. This study examined the potential benefit that Mindfulness-Based Cognitive Therapy (MBCT) may have on the symptoms of LLD and/or LLA in older adults compared to treatment as usual (TAU). A sample of 61 older adults (age = 67.8 ± 6.2 years) with symptoms of depression and/or anxiety were randomized to MBCT or TAU in a primary care setting. Primary outcomes measured a post-pre change in depression symptoms (PHQ-9). The secondary outcome examined a post-pre changes in anxiety symptoms (GAD7) anxiety scores. Exploratory outcomes included a post-pre changes in health-related quality of life and quality of sleep. The study also aimed to assess feasibility, acceptability and tolerability of the MBCT intervention with the geriatric population. Results from this study showed that participants in the MBCT group, compared to TAU, significantly improved in depressive and anxiety symptoms scores as well in the health-related quality of life scores. The MBCT intervention was feasible with an enrollment rate of 80.3% and an intervention completion rate of 78%. The MBCT intervention was acceptable with a study retention rate of 87%. Most of the participants found the MBCT intervention tolerable, enjoying the mindfulness meditation intervention; especially the guided meditations. In conclusion, the MBCT intervention may potentially benefit and give an alternative treatment for older adults in primary care suffering from depression and/or anxiety symptoms. Implementing these types of evidence-based therapies could target more people at once and reduce the amount of staff required which may potentially lead to less costs overall. To our knowledge, this is the first well-controlled RCT study in the field using MBCT for older adults with symptoms of depression and/or anxiety in primary care. Future studies are needed to replicate and to evaluate the effects of MBCT while using an active control group. The long term-effects of MBCT must also be studied as well as studies implementing more formal systematic diagnostic when assessing depression and/or anxiety in this population.

Résumé

La dépression et l'anxiété sont des troubles psychiatriques invalidants dans le monde entier. Environ 10-20% des personnes âgées traitées dans des établissements de soins de première ligne souffrent de dépression gériatrique (DG) et/ou d'anxiété gériatrique (AG). Les adultes âgés sont souvent sous-traités et/ou ne reçoivent pas le traitement approprié pour DG et/ou AG dans les soins primaires, en raison du manque de ressources disponibles et des fortes exigences du système de santé. Les antidépresseurs constituent le traitement de première ligne pour la DG et/ou la AG dans les établissements de soins de santé primaires. En général, la population gériatrique ne répond pas bien aux médicaments psychotropes en raison d'une comorbidité avec d'autres maladies et de la polypharmacie, ce qui entraîne des taux de réadmission élevés. À mesure que la population vieillit, le nombre d'adultes âgés traités en soins primaires augmente, il est donc urgent de trouver des thérapies alternatives efficaces, extensibles et potentiellement rentables. Cette étude a examiné le bénéfice potentiel que la Thérapie Cognitive Basée sur la Pleine Conscience (TCBPC) pourrait avoir sur les symptômes de la DG et/ou la AG par rapport au traitement usuel (TAU). Un échantillon de 61 adultes plus âgés (âge = 67.8 à 6.2 ans) présentant des symptômes de la DG et/ou la AG a été randomisés pour passer au test TCBPC ou TAU dans un contexte de soins primaires. Les critères d'évaluation principaux mesuraient un changement post-pré de symptômes de dépression (PHQ-9). Le résultat secondaire a examiné les scores d'anxiété post-pré-changements dans les symptômes d'anxiété (GAD7). Les résultats exploratoires incluaient des changements postérieurs à la modification de la qualité de vie et de la qualité du sommeil liés à la santé. L'étude visait également à évaluer la faisabilité, l'acceptabilité et la tolérabilité de l'intervention TCBPC auprès de la population gériatrique. Les résultats de cette étude ont montré que les participants du

groupe TCBPC, comparés aux groupes TAU, avaient considérablement amélioré leurs scores de symptômes de dépression et d'anxiété, ainsi que leurs scores de qualité de vie liés à la santé. L'intervention TCBPC était faisable avec un taux d'inscription de 80,3% et un taux d'achèvement de l'intervention de 78%. L'intervention TCBPC était acceptable avec un taux de rétention de l'étude de 87%. La majorité des participants ont jugé l'intervention TCBPC tolérable, appréciant l'intervention de méditation de pleine conscience; en particulier les méditations guidées. En conclusion, l'intervention TCBPC peut potentiellement bénéficier et offrir un traitement alternatif aux personnes âgées souffrant de dépression et/ou de symptômes d'anxiété en soins primaires. De plus, la mise en œuvre de ces types de thérapies fondées sur des preuves pourrait cibler plus de personnes âgées à la fois et réduire le personnel clinique requis, ce qui pourrait potentiellement réduire les coûts globaux. À notre connaissance, il s'agit de la première étude randomisée bien contrôlée (RCT) sur le terrain utilisant la TCBPC pour les personnes âgées présentant des symptômes de dépression et/ou d'anxiété en soins primaires. Futures études sont nécessaires pour répliquer et évaluer les effets de la TCBPC en utilisant un groupe de contrôle actif. Les effets à long terme de la TCBPC doivent également être étudiés, de même que les études mettant en œuvre un diagnostic systématique plus formel lors de l'évaluation de la dépression et/ou de l'anxiété dans cette population.

Author Contributions

This thesis contained one manuscript following general guidelines of manuscript submission with an introduction, followed by the methods, results, discussion, conclusion, and future directions pertaining to research. The manuscript entitled "Mindfulness-Based Cognitive Therapy Intervention for the Treatment of Late-Life Depression and Anxiety Symptoms in Primary Care: A Randomized Controlled Trial" was co-authored by myself, Dr. Gabriela Torres-Platas, Claudia Belliveau, Joyce Wu, Neeti Sasi, Jocelyn Fotso, Angela Potes, Dr. Zoë Thomas, Allana Goodman, Dr. Karl Looper, Dr. Marilyn Segal, Dr. Marcelo Berlim, Dr. Akshya Vasudev, Nona Moscovitz, and Dr. Soham Rej.

My supervisor, Dr Soham Rej, and research associate Dr Gabriela Torres-Platas contributed to the conception of the research questions for this study, wrote the protocol, REB approval, and revisions for the initial phases of the study. Both revised and edited the manuscript extensively. Dr Torres-Platas supervised data collection and entry for the first two phases and she also provided guidance for the data analysis. Dr Rej and my Committee Members, Dr Marcelo Berlim and Akshya Vasudev provided a lot of feedback and considerations that helped to facilitate critical thinking and reflection, as well as sharpening my thoughts and writing abilities. The remaining authors contributed to the study design and/or data collection. Also, all reviewed manuscript drafts for content and approved the final version of the manuscript.

My contribution to this study involved the study design, writing the REB approval and amendments for the third phase of the study, to evaluate assess participants, collecting and entering data, and training volunteers. I was also responsible for cleaning, analyzing, and interpreting the data collected. I drafted the manuscripts and all the sections from this thesis. I also revised, edited, and modified the thesis according to the feedback obtained from the co-authors.

Abbreviations

AIS: Athens Insomnia Scale
EQ-5D: EuroQol, (Health-related Quality of life)
GAD-7: Generalized Anxiety Disorder-7
LLA: Late-life Anxiety
LLD: Late-life Depression
MBCT: Mindfulness-Based Cognitive Therapy
MBSR: Mindfulness-Based Stress Reduction
PHQ-9: Patient Health Questionnaire-9
TAU: Treatment as Usual
WHO: World Health Organization

Chapter 1: Introduction

This thesis aimed to investigate the adaptation of an 8-week Mindfulness-Based Cognitive Therapy (MBCT) as an alternative treatment for older adults suffering from symptoms of depression and anxiety in Montreal primary care settings. MBCT is a well-known alternative approach that was developed as a treatment for relapse prevention in depression (Segal, Williams, & Teasdale, 2002). Recently, the efficacy of MBCT has also been proven as an effective treatment for depression and/or anxiety in younger adults (Sado et al., 2018; Strauss, Cavanagh, Oliver, & Pettman, 2014). However, research is lacking when exploring the effects of MBCT in late-life depression (LLD) and/or late-life anxiety (LLA).

In long term care facilities, LLD and LLA disorders are among the most frequent disorders treated in the geriatric population (Cassem, 1995). With the population aging, the severity of chronic conditions has augmented, causing increasing demands for health care services (Cassem, 1995). LLD and LLA contribute to the highest readmission rates in outpatient and primary care services (Heeren, Dixon, Gavirneni, & Regenold, 2002). Depression is an important factor associated with increased length of stay (Koenig, Bhalla, & Butters, 2014) and increased risk of adverse events post-discharge (Preyde & Brassard, 2011). Studies have also shown that LLD and LLA have a high impact on mortality rates (Schulz et al., 2000; Schulz, Drayer, & Rollman, 2002). Interestingly, suicide in older adults is more common than at any other age group, and depression is one of the major risk factors (Suresh Kumar, Anish, & George, 2015). An appropriate treatment for depression could reduce the risk of further deteriorating mental and physical health as well as prevent premature mortality (von Ammon Cavanaugh, Furlanetto, Creech, & Powell, 2001).

The geriatric population is therefore in need of alternative treatments for LLD and LLA. Many studies have shown that psychotherapy and antidepressants are the first-line treatments in LLD and LLA, however, very few older adults in primary care receive access to these treatments (Lin et al., 1995; Unutzer, Katon, Sullivan, & Miranda, 1999). Furthermore, there is also mounting evidence that the geriatric population do not respond well to antidepressants. This is due to polypharmacy, greater side effects, and/or multiple medical comorbidities (Kok & Reynolds, 2017; Small, 1997). More importantly, when given the option, many older adults in primary care prefer a form of psychotherapy treatment for LLD when compared to antidepressant medication treatment (Dwight-Johnson, Sherbourne, Liao, & Wells, 2000; Rokke & Scogin, 1995). However, psychotherapy treatment is not always available or is underused in primary care settings (Gum et al., 2006). Therefore, we urgently need to adopt alternative approaches not only to help relieve misdiagnosis and mistreatment of older adults but also to find efficacious and effective treatments for the prevention/relapse of LLD and LLA in primary care settings (Unutzer et al., 1999).

MCBT, a non-pharmacological intervention, may be beneficial to improve acute depression and/or anxiety symptoms in adults later in life. This study aimed to explore the effects of a randomized controlled trial (RCT) of MBCT compared to treatment as usual (TAU) in older adults with symptoms of depression and/or anxiety in primary care. We hypothesized that participants in the MBCT group, compared to TAU, would have a significant reduction in depression and/or anxiety symptoms, as well as improvement in health-related quality of life and sleep. In addition, we also investigated the feasibility, acceptability and tolerability of MBCT intervention in older adults suffering from depression and/or anxiety symptoms in primary care settings. This study aimed to find a feasible and scalable alternative treatment to improve the health care delivery to older adults living with LLD and/or LLA symptoms. References for Chapter 1: Introduction

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Chapter 2: Literature Review

Overview

This literature review first provides background information to understand at a deeper level the epidemiology of LLD and LLA, and their impact on an older adults' quality of life. Then, we will discuss the existing treatments for LLD and LLA. We will also acknowledge the available treatment and barriers encountered by older adults in primary care settings when receiving this treatment. In addition, we will lightly explore the background of Mindfulnessbased Interventions (MBIs), their beneficial effects with different health-related conditions (such as depression and anxiety in the general population and in older adults), as well as their methodological flaws and unwanted effects in certain populations. Next, we will discuss the evidence of the effectiveness of well-structured MBIs: Mindfulness-based stress reduction (MBSR) and Mindfulness-based cognitive therapy (MBCT) in the treatment of physical and mental health illness. To conclude, we will review in depth MBCT effectiveness in the treatment of depression and/or anxiety for young adults and the recent emergent literature in geriatric populations. This section will also include certain limitations and literature gaps.

Late-Life Depression (LLD) and Late-Life Anxiety (LLA): Depression and Anxiety in Older Adults

Depression and anxiety are major contributors of global illness burden. These conditions affect individuals from different backgrounds and countries, and the rate of older adults diagnosed is increasing annually (WHO, 2018). Anxiety disorders are the most prevalent disorder in most countries with a range between 2.4% to 18.2%, followed by mood disorders 0.98% to 9.6% (WHO, 2018). Interestingly, depression is ranked as the number one cause of global disability, and anxiety as number six. They account for 7.5% and 3.6% of total years

lived with disability in 2015, respectively (WHO, 2017). In 2016, the global estimation of the number of people living with depression and anxiety exceeded 322 million and 275 million, respectively (IHME, 2017). Although, these worldwide figures may be an underestimate (Demyttenaere et al., 2004; Kessler et al., 2005).

Approximately 15-20% of older adults aged ≥ 60 suffer from chronic or recurrent mental disorders (Alexopoulos & Chester, 1992; Beekman, Copeland, & Prince, 1999; WHO, 2017). Among them, late-life depression (LLD), dementia and late-life anxiety (LLA) are the three most common, affecting around 7%, 5% and 3.8% world's older population. Depression is more common among older females between the ages of 55-74 years, estimating at 7.5%, compared to 5.5% total found in older males (WHO, 2018).

LLD and LLA have tremendous negative impacts on older adults. These include effects on their health, functioning, well-being (Beekman et al., 2002; Smalbrugge et al., 2006) and overall quality of life (Blazer, 2003; Brenes, 2007). Symptoms of depression have strong effects on physical and emotional well-being, vitality, mental health and social functioning. In addition, adults with anxiety have been shown to have a stronger association with increased symptoms of pain (Brenes, 2007). Individuals with chronic illness are more prone to have depression than general population (Cassem, 1995).

LLD and LLA are also highly associated with cognitive impairment (DeLuca et al., 2005). Symptoms of LLD and LLA can be precursors to cognitive decline and the cognitive dysfunction can often remain even after depression is treated (DeLuca et al., 2005). This can lead to worsening global functioning and reduce the patients' quality of life (A. M. Koenig et al., 2014). A systematic review and a meta-analysis conducted by Devi Bastida et al. (2016), found that individuals with a history of depression are at higher risk of developing dementia compared to

those without depression (odd ratio and hazard ratio values ranging from 1.72 to 3.59 and 1.72 to 5.44, respectively. Among non-demented individuals with LLD, 40-60% of them are detected to suffer from cognitive impairment (C. A. Hall & Reynolds-Iii, 2014). In addition, some studies have found LLD may contribute to 1.5-2 times increased risk of developing several types of dementia, including Alzheimer's disease and vascular dementia (Diniz et al., 2013; Jorm, 2001; Ownby et al., 2006). These numbers are staggering and the cases of dementia and cognitive impairment continue to increase as our population ages; with 9.9 million new cases estimated each year worldwide, or in other words one new case every 3.2 seconds (Alzheimer's Association, 2019).

LLD and LLA not only have negative consequences on an individual's health but also, they are a major burden to the health care system; particularly in primary care. This increased burden is often due to the high demands of service utilization, high incidence in patients with multiple comorbidities, high levels of impaired functioning, more work days lost, and higher rates of mortality (Lecrubier, 2001; Lepine, 2001). The World Health Organization conducted a large study with 25916 adults from 15 countries, investigating different perspectives of psychological problems in primary care settings. The most frequent psychological problems found in this study were depression, anxiety, alcohol misuse, somatoform disorders and neurasthenia (Sartorius et al., 1993). More than 50% of patients in primary care who are diagnose with depression, also meet criteria for anxiety symptoms (Hirschfeld, 2001). This comorbidity can provide a significant challenge for patients to receive the appropriate diagnosis and treatment, increasing the predisposition of further developing illness, and may rise the utilization of primary care services. Treatments that effectively address both the LLD and LLA can potentially reduce a significant amount of overall burden on primary care services.

As the world's population ages, the number of people living with LLD and LLA symptoms will also grow substantially. The world's population will be expected to more than double between 2015 and 2050, from 900 million to 2 billion of people above 60 years (WHO, 2018). In addition, LLD and LLA are important contributors to suicide mortality in older adults (J.L. Pearson, 2002). Every year, around 1 million people die by suicide (Lepine, 2001). In the United States, higher rates of successfully attempt suicide are observed among older adults compared to any other age group (Pearson, 2002). Even if the global economy spent large amounts of money every year (around 1 trillion USD) on the prevention and treatment of depression and anxiety (WHO, 2017), there remains much to be done, especially in primary care settings, where most older adults prefer to seek treatment (Alexopoulos & Chester, 1992; Klap, Unroe, & Unutzer, 2003).

Treatment of Late-Life Depression and Late-Life Anxiety

Several treatments have been traditionally recognized to be efficacious and effective treatments for LLD and LLA. Cognitive Behavioral Therapy (CBT) has been a well-known treatment for depression and anxiety in older adults (Cuijpers et al., 2013; Gould, Coulson, & Howard, 2012a; Hall, Kellett, Berrios, Bains, & Scott, 2016; Tompson, Kemp, Langer, & Asarnow, 2015) and it has been shown to be more effective than a wait list control group or TAU. However, the efficacy of this treatment when compared to an active control group is not yet well established in the literature (Gould et al., 2012a). Recent meta-analyses found that different psychotherapies may be effective for treating LLD: interpersonal therapy (IPT; De Mello, de Jesus Mari, Bacaltchuk, Verdeli, & Neugebauer, 2005), problem solving treatment (PST) (Bell & D'Zurilla, 2009) as well as Behavioral Activation (BA) and activity scheduling (Cuijpers, van Straten, & Smit, 2006; Cuijpers, van Straten, & Warmerdam, 2007).

Pharmacological treatments are also commonly used among older adults, such as: benzodiazepines, anxiolytics, sedative-hypnotics and antidepressants (e.g. selective serotonin reuptake inhibitors [SSRIs], serotonin/norepinephrine reuptake inhibitors [SNRIs], and tricyclic antidepressants [TCAs]) (Small, 1997; Unutzer & Park, 2012; WHO, 2017). However, geriatric patients do not always respond well to antidepressant treatments. It has been shown in randomized controlled trials, that the rates of treatment resistant cases for patients with LLD using SSRIs rise up to 77% and range between 55% to 81% using SNRIs (Lenze et al., 2008).

Treatment of Late-Life Depression and Late-Life Anxiety in Primary Care

The geriatric population who suffer from depression and anxiety disorders are frequent users of health care services (Koenig & Kuchibhatla, 1999). Older adults with LLD compared to non-depressed geriatric patients almost double the number of doctor's appointments. These patients also spent more time than expected in hospital units and are more likely to receive a greater number of pharmacological medications (Alexopoulos et al., 2002; Luber et al., 2000). In fact, approximately 10-20% of patients with LLD and LLA choose to rely on primary care physicians and other primary care clinicians/services when seeking psychiatric treatment (Beekman et al., 1999; Klap et al., 2003; Park & Unutzer, 2011; Wetherell et al., 2004). In the United States, the rates of geriatric patients with depression who are treated in primary care can reach up to 80% (Regier et al., 1993).

However, there are several challenges to these patients when being treated in primary care institutions. For example, physicians face difficulties when diagnosing geriatric patients in primary care (Katz, 1998). This can be due to overlapping symptoms from multiple medical comorbidities, cognitive changes, decreased physical and mental functioning, and the presence of other psychiatric disorders. In consequence, the multiple symptomatology in geriatric patients can prevent the ability to differentiate LLD/LLA with other physical and/or cognitive and/or mental disorders.

In addition, older adults are more reluctant to seek for help for emotional problems compared to younger adults (Lenze, Mulsant, Shear, Houck, & Reynolds, 2002; Small, 1997; Wetherell et al., 2004). In one study, it was shown that older adults (n = 77) were less likely to engage in primary care programs associated with mental health (e.g. counseling, stress management), when compared to younger adults (n = 312). However, younger and older adults were both willing to engage in programs promoting physical health (such as healthy living class, fitness program; Wetherell et al., 2004). Interestingly, when older adults are compared to younger adults, studies show that they tend to avoid reporting their mental health treatment history (29% vs. 51%) or current treatment (11% and 23%), due to fear of stigma related to mental health treatment (Diefenbach & Goethe, 2006; Klap et al., 2003; Lenze et al., 2002).

In primary care, there is a gap between the efficacy versus effectiveness when treating depressed geriatric populations. Under research conditions, there are efficacious treatments that are found to be significant for LLD. However, when these treatments are applied to the real world of primary care, they are found to be less effective. Additionally, LLD is often under-detected and undertreated in geriatric patients (Reynolds, Alexopoulos, Katz, & Lebowitz, 2001; Unutzer, Katon, Sullivan, & Miranda, 1999). For example, antidepressants are an important treatment modality for LLD, but patients do not always receive the appropriate dosage and/or duration of treatment (Lin et al., 1995). Also, geriatric patients often receive multiple medication to treat several illnesses, and consequently they are susceptible to drug-drug interaction due to polypharmacy. Older adults are also more vulnerable to increased side effects, poor tolerance, and a decreased response to psychotropic medications (up to 60% treatment non-

response; Jin, Kim, & Rhie, 2016; Lenze et al., 2008; Mittmann, 1997; Small, 1997). In addition, geriatric patients in primary care prefer active treatments for LLD, such as counseling (57%) compared to psychotropic medication (43%; Gum et al., 2006). The proportion of older primary care patients receiving their preferred treatment is much lower for those who would choose counseling (33%) compared to those that choose medication (70%). This can have significant impact on clinical outcomes and service usage (Gum et al., 2006; Pinquart, Duberstein, & Lyness, 2006; Wetherell et al., 2004). Furthermore, wait lists for physician and other clinician appointments is another systemic barrier that can prevent successful assessment and/or treatment of LLD and LLA in primary care settings (Katz, 1998; Unutzer & Park, 2012).

Mindfulness-Based Interventions

Recent emerging group-based therapies such as Mindfulness-Based interventions (MBI) could be cost-effective and scalable to assist many patients at once (Kabat-Zinn, 2013). Mindfulness meditations in the East were conceived as part of traditions to religions such as Hinduism, Judaism, and especially Buddhism (Kirmayer, 2015; Trousselard, Steiler, Claverie, & Canini, 2014). Buddhism traditions embrace and nurture a variety of mindfulness meditation practices. Common ethical and moral principles are rooted in those meditations, such as *samatha* (concentration, calmness, and stability), *jhana* (absorption), and *vipassana* (insight). Different meditation practices are used to promote diverse aspects (Kirmayer, 2015).

Mindfulness meditation is the west comprises different techniques tradition that promote concentration and/or contemplation; some of them include: sitting/walking meditation, repeating a mantra, breathing exercises, tai-chi, qigong, and some yoga features (Vasudev et al., 2018). These techniques were popularized in the West by secular institutions and non-religions individuals usually trained in Buddhist practices (Kabat-Zinn, 2013).

Mindfulness meditation cultivates the art of being rather than doing, promoting 'momentto-moment non-judgmental awareness', and engaging participants in self-caring and selfregulation of the body and mind to achieve balance and positive mental health (Kabat-Zinn, 2013). Nowadays, mindfulness-based psychotherapies in the West have been effective and affordable approaches to treat physical and mental disorders (Vasudev et al., 2018). Therefore, they have gained popularity over the last 20 years as key forms of psychotherapeutic interventions (Hofmann, Sawyer, Witt, & Oh, 2010; Khoury et al., 2013; Schmidt et al., 2011).

Different mindfulness mediations styles have been associated with neural activation, as well as psychological and neurophysiological change (Tomasino, Chiesa, & Fabbro, 2014). A meta-analysis of MRI studies conducted by Boccia, Piccardi, and Guariglia (2015) found that mind-body relaxation meditation increases activation in cortical areas related to processing self-relevant information, self-regulation and awareness, focused problem solving, adaptive behavior and interception. Meta-analyses by Geiger et al. (2016) and Hofmann et al. (2010) have shown that mindfulness interventions are effective to treat mood disorders, anxiety disorders, stress-related illnesses; as well as improve quality of life and social functioning. A recent systematic review suggests that MBIs may reduce emotional distress and increase empathy, compassion and prosocial behaviors (Luberto et al., 2018). There is also evidence that MBIs are potentially beneficial for older adults with mental illness and cognitive disorders (Reynolds et al., 2001).

Nevertheless, despite the evidence-based efficacy of MBIs in the treatment or prevention of mental health disorders, there are mixed findings due to methodological flaws, uncontrolled studies, small sample sizes, heterogeneous populations studied, and less rigorous approaches leading to diverse clinical outcomes (Geiger et al., 2016; Vasudev et al., 2018). Additionally, averse/unwanted effects are not systematically reported in studies with MBIs, making it harder to assess their prevalence (Cebolla, Demarzo, Martins, Soler, & Garcia-Campayo, 2017; Davis & Hayes, 2011; Dobkin, irving, & Amar, 2012; Shapiro, 1992). There is some evidence that intensive meditation practice that includes long retreats can be harmful to individuals suffering from acute psychiatric disorders, or to individuals with a severe history of mental illness (e.g. schizophrenia; Alsubaie et al., 2017; Davis & Hayes, 2011; Dyga & Stupak, 2015; Linden, 2013; Manocha, 2000; Shapiro, 1992). However, findings from a meta-analysis and several other studies have suggested that mindfulness-based interventions and meditation with yoga are beneficial for improving negative psychotic symptoms (Davis & Hayes, 2011; Khoury et al., 2013). It is still unclear whether the unwanted symptoms/adverse treatment reactions are directly linked to the mindfulness meditation practices or if those practices facilitate the emergence of symptoms (Dyga & Stupak, 2015; Linden, 2013).

Overall, MBIs have been found to be relatively safe and well-tolerated in clinical settings with younger adults with depression, anxiety and other mental health and physical symptoms (e.g. sleep, pain; Alsubaie et al., 2017; Reiner, Tibi, & Lipsitz, 2013). Specifically, MBIs that integrate short meditation practices, cognitive behavioral therapy aspects and mindful movement components, such as MBSR or MBCT, can be positive for improving symptoms from psychiatric and physical health conditions (Day et al., 2019; Khoury et al., 2013).

Mindfulness-Based Stress Reduction (MBSR)

One of the most popular 8-week mindfulness-based interventions to reduce stress and pain is Mindfulness-Base Stress reduction (MBSR). MBSR was developed in 1979 by Jon Kabat-Zinn, a scientist and a professor emeritus of medicine, at the Center for Mindfulness in Medicine, Health Care and Society, University of Massachusetts Medical School (Kabat-Zinn, 2013). Jon Kabat-Zinn integrated mindfulness meditation teaching and practices from Buddhist traditions, and scientific, medicinal and psychological approaches from the West into the MBSR program. Mindfulness-Base Stress reduction was originally designed to assist patients with a wide range of medical illness who were not responding well to traditional treatments (Kabat-Zinn, 2013). Over the past 35 years, research and clinical findings have demonstrated the beneficial effects of MBSR in reducing physical and psychological symptoms as well as improve symptoms of a broad range of medical diagnosis and conditions. These conditions include chronic pain, anxiety (Hoge et al., 2013), asthma (Pbert et al., 2012), cancer (Carlson et al., 2013), high blood pressure (Reiner et al., 2013), chronic illness (Zernicke et al., 2013), fibromyalgia (Schmidt et al., 2011) and sleep disturbances (Andersen et al., 2013). Reliable and consistent findings have also shown that the benefits observed of MBSR are maintained up to three years of follow-up (Kabat-Zinn, 2017). MBSR is often delivered to heterogeneous populations of patients with a diversity of medical and psychiatry illnesses, aiming to reduce stress and suffering. Despite these findings, other mindfulness-based interventions such as Mindfulness-Base Cognitive Therapy (MBCT) were created to target specific psychiatry populations.

Mindfulness-Based Cognitive Therapy for Depression and/or Anxiety

MBCT was initially conceived as a non-pharmacological intervention that was highly effective in preventing depression relapse in patients with three or more recurrent episodes of depression (Kuyken et al., 2008; Piet & Hougaard, 2011; Segal et al., 2010). Inspired by the MBSR's significant findings in reducing stress and promoting well-being, MBCT was developed in 2002, by Segal, Williams and Teasdale. Similarly, to MBSR, the 8-week group MBCT intervention offers tools for patients to better manage their thoughts, feelings and perceptions by promoting awareness, focusing on the present moment in a non-judgmental way and accepting a situation as they are (Fjorback, Arendt, Ornbol, Fink, & Walach, 2011; Piet & Hougaard, 2011;

Segal, 2002). Unique to MBCT, Segal et al. (2002) modified MBSR by adding components of cognitive behavioral therapy; a reliable psychological treatment for depression. Some of the CBT components include psychoeducation approaches to learn from depression and anxiety symptoms, thought process, and problem-solving to let go of negative emotions (Cuijpers et al., 2013; Segal, 2002). In MBCT, participants are encouraged to apply the teachings on a daily bases using mindfulness exercises and homework. In addition, it is recommended that patients are careful screened before course entry to appropriately assess diagnosis and functionality (Crane & Williams, 2010; Gotink et al., 2015; Rycroft-Malone et al., 2014).

In the past two decades, MBCT has been shown to be an acceptable, effective and beneficial treatment for individuals in remission, or recovery from major depression in younger adults. Segal et al. (2002) found that in patients with three or more previous depressive episodes, MBCT was associated with a lower rate of longer-term relapse/recurrence (40%) compared to those in the TAU group (66%) over a 12-month follow-up (Galante, Iribarren, & Pearce, 2013; MacKenzie, Abbott, & Kocovski, 2018; Segal Z. V., 2002). In addition, several studies provided evidence that individuals in remission/recovery in the MBCT group combined with medication, had lower relapse rates than those with only medication treatments (Kuyken et al., 2008; Segal et al., 2010). However, there are mixed results of meta-analysis and reviews regarding the number of episodes of prior major depressive disorders required to observe significant depression relapse prevention with MBCT (Galante et al., 2013; Piet & Hougaard, 2011).

Recent evidence in younger adults suggests that MBCT may also be a favorable treatment for current episodes of depression and/or anxiety disorders. Although there was a high heterogeneity of participants in the samples (Galante et al., 2013), emerging evidence has shown MBCT effectiveness as a treatment for current/acute depression, anxiety, insomnia, mood disorders, and emotional regulation, among other psychological and physical conditions (Britton, Shahar, Szepsenwol, & Jacobs, 2012; Gotink et al., 2015; Zernicke et al., 2013). In a meta-analysis of RCTs performed by Strauss and colleagues (2014) with different MBIs - among them MBCT intervention – it was suggested MBCT may be beneficial for younger adults with an acute episode of depression. The study was underpowered to find significant effects of MBIs for current episodes of anxiety (Strauss et al., 2014).

Although there is some evidence for the efficacy of MBCT in acute symptoms of depression and/or anxiety with younger adults, the potential benefits of MBCT for late-life depression and/or late-life anxiety symptoms have been less explored (Kuyken et al., 2016). A qualitative study by Smith, Graham, & Senthinathan (2007) was done to determine whether MBCT was suitable for older adults with subsyndromal depressive symptoms. MBCT was found to be helpful for older adults with recurrent depression; they also suggested some modifications required for this population due to physical limitations. Another pre-post study with qualitative data suggested that older adults with recurrent or chronic depression perceived an MBCT intervention as acceptable. Participants were able to complete the homework practices and maintained them after six months of the MBCT course (Williams, Meeten, & Whiting, 2018). Foulk, Ingersoll-Dayton, Kavanagh, Robinson, and Kales (2014) performed an exploratory pre-post analysis of 5 MBCT groups targeting older adults with depression and/or anxiety. Their findings suggest that significant improvements associated with positive changes, in reported depression, anxiety, ruminative thoughts and sleep disturbances, were observed after using MBCT with older adults (Foulk et al., 2014). In addition, previous findings from a retrospective case series in our lab found that MBCT was a well tolerable and effective alternative treatment in adjunction to TAU for geriatric outpatients with major depression and/or anxiety disorders (Labbe et al., 2016). As of yet, Helmes and Ward (2017) completed the only RCT of MBCT with older adults in the literature. Findings from this study demonstrated that MBCT was efficacious in reducing symptoms of anxiety in older adults from residential care (Helmes & Ward, 2017). However, there has not yet been an RCT assessing the efficacy of MBCT in older adults with both depression and anxiety symptoms in primary care.

The following manuscript is based on the present master research project and supports the evidence that MBCT may be effective in reducing acute depression and anxiety symptoms in older adults in primary care settings.

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Chapter 3: Manuscript

Mindfulness-Based Cognitive Therapy Intervention for the Treatment of Late-Life Depression and Anxiety Symptoms in Primary Care: A Randomized Controlled Trial

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Abstract

Background

By 2030, 50% of patients with mental disorders will be aged 60+ and will receive treatment mostly in primary care. Approximately 10-20% of older adults treated in primary care suffer from depression and/or anxiety symptoms, but access to efficacious, scalable, well-tolerated and potentially cost-effective therapies remains challenging. Mindfulness-based Cognitive Therapy (MBCT) may be potentially beneficial but has not yet been rigorously investigated for depression and/or anxiety in older adults.

Methods

In this randomized controlled trial, 61 older adults from primary care settings with symptoms of depression and/or anxiety were randomized to MBCT or treatment as usual (TAU) from September 2016 to December 2017. The primary outcome was a change in Patient Health Questionnaire (PHQ-9) depression scores between baseline and 8-week follow-up. The secondary outcome was a change in General Anxiety Disorder questionnaire (GAD7) anxiety scores, while exploratory outcomes included changes in the quality of life and sleep.

Results

The MBCT group had significantly reduced depression scores compared to TAU (-7.9 ± 4.4 vs. - 4.0 ± 4.7; <u>U</u>=179.5, p = .002) and anxiety scores (-6.4 ±5.0 vs. -2.0 ±3.8; t(51)=-3.58, p = .001), as well increases in health-related quality of life (-0.6±3.5 vs.0.4±2; U = 241, p = .048).

Conclusion

In our study, MBCT significantly reduced symptoms of depression and anxiety in older adults in primary care. Future research could examine longer-term effects of MBCT in this population, using an active control group, as well as assessments of cognition and neural imaging.

Introduction

Late-Life Depression and Anxiety in Primary Care

Depression and anxiety disorders are common debilitating illnesses, affecting around 300 and 275 million people worldwide, respectively (IHME, 2017; WHO, 2019). Globally, 1 trillion USD is spent on the treatment of depression and anxiety (WHO, 2019). Between 10-20% of older adults experience symptoms of depression and/or anxiety every year in primary care (Beekman, Copeland, & Prince, 1999), and rates of late-life depression (LLD) and late-life anxiety (LLA) are increasing as our population ages (Jeste et al., 1999). Older adults with depression and anxiety symptoms are mostly treated in primary care. In the United States, as many as 80% are treated by their family physician (Kessler et al., 2010).

Depression and anxiety are often under-detected and undertreated in primary care settings (Bland, 2012; Trautmann & Beesdo-Baum, 2017). Moreover, up to 60% of older adults with LLD/LLA demonstrate an inadequate response to traditional antidepressant medication due to poor tolerability, adverse effects, drug-drug interactions, and physical/cognitive comorbidity (Holvast, Massoudi, Oude Voshaar, & Verhaak, 2017; Maust, Langa, Blow, & Kales, 2017). As geriatric patients with LLD/LLA commonly use multiple medications for other medical conditions, polypharmacy remains a concern when prescribing psychopharmacological treatment. Additionally, antidepressants are frequently overprescribed for the management of these conditions (Charlesworth, Smit, Lee, Alramadhan, & Odden, 2015). Although older adults often prefer non-pharmacological interventions over psychotropic (Luck-Sikorski et al., 2017), access to specialist mental health services can be very limited, especially in primary care settings (Klinkman, Schwenk, & Coyne, 1997). Similarly, traditional one-on-one psychotherapy is often costly and inaccessible due to scarce availability of psychiatrists and mental health resources (Wei,

Sambamoorthi, Olfson, Walkup, & Crystal, 2005). Therefore, there is an urgent need for scalable, non-pharmacological interventions that could improve symptoms of depression and anxiety in older adults in primary care.

Mindfulness-Based Cognitive Therapy as a Potential Treatment for Depression and/or Anxiety

Mindfulness-based cognitive therapy (MBCT) is a non-pharmacological intervention primarily designed to prevent depression relapse in adults with a history of recurrent depression (≥3 past episodes; Teasdale et al., 2000) and has gained momentum in the past years given its efficacy. Accumulating evidence shows that MBCT is also effective as a treatment for acute depression and anxiety symptoms in younger adults (Britton, Shahar, Szepsenwol, & Jacobs, 2012; Kuyken et al., 2015). Thus, it may be an alternative intervention to reduce symptoms of depression and/or anxiety in older adults. MBCT includes mindfulness meditation practices in conjunction with cognitive behavioural therapy (CBT) and psycho-education to cultivate non-judgmental present-moment awareness to better manage symptoms of depression or anxiety (Rycroft-Malone et al., 2014; Zindel V. Segal, Williams, & Teasdale, 2002).

There are few uncontrolled and exploratory studies examining MBCT in older adults aged ≥ 60 that have shown that MBCT improved anxiety and depressive symptoms (Foulk, Ingersoll-Dayton, Kavanagh, Robinson, & Kales, 2014; Mathur, Sharma, & Bharath, 2016), as well as decreased ruminative thoughts and sleep problems (Foulk et al., 2014). Additionally, MBCT improved mindfulness skills, and overall quality of life in all patients (Mathur et al., 2016). To the best of our knowledge, there is only one randomized controlled trial (RCT) in the literature that examined MBCT for elderly long-term care residents with anxiety symptoms (Helmes & Ward, 2017). Although small case series have been promising, there has not yet been an RCT of

MBCT for the treatment of both depressive and anxiety symptoms in older aged adults in primary care setting (Labbe et al., 2016; Vasudev et al., 2018).

For these reasons, we performed an 8-week RCT with the aim to assess whether MBCT was more effective compared to treatment as usual (TAU) controls in improving 1) depression; and/or, 2) anxiety symptoms. We also explored feasibility, acceptability, and tolerability of MBCT as well as effects on quality of life and sleep.

Methods

Study Population and Recruitment

In this study, 61 older adults aged 60 years and above suffering from depression and/or anxiety symptoms were recruited between September 1, 2016 and Dec 20, 2017. The recruitment took place from 5 primary care centres from the Integrated University Health and Social Services Centres (CIUSSS-Centre-Ouest de Montréal) Catchment area, which provides health care for approximately 341,700 residents in Montréal, Québec, Canada (Centre-Ouest-de-l'ile-de-Montreal (CIUSSS, 2016-2017). Participants were recruited from the wait list for mental health services, their family doctor at a Local Community Service Centre (CLSC), and/or the CLSC where they received other mental health services. Initial contact with the patients was made through their treating family doctor/psychiatrist, nurse, social worker, psychologists or the clinic's receptionist.

Inclusion/Exclusion Criteria

Participants were included if they had a score of ≥ 10 (moderate depression/anxiety) on the Patient Health Questionnaire (PHQ-9) and/or General Anxiety Disorder-7 (GAD - 7). Participants were excluded if they presented: acute psychotic symptoms, severe personality disorder/ unable to function in a group setting, acute suicidal ideations or intent, being unable to engage with MBCT for physical/ practical reasons, having hearing impairment not improved with hearing aids and/or sound amplification, and/or being unable to communicate in either English or French. Participants were also excluded once they reported changes in psychotropic medication during the 8 weeks of intervention and/or if they started attending weekly active and structured psychotherapy. Informed, written consent was obtained from all patients. Patients who fulfilled selection criteria and filled up a written consent to the study were asked to fill out demographics and clinical self-report questionnaires (20-30 minutes). The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human patients were approved by the Jewish General Hospital ethics committee and was registered with the approval number in ClinicalTrials.gov (NCT02777905).

Randomization and Blinding

Participants were assigned a coded number and randomized 1:1 (using randomizer.org) into two groups MBCT and treatment as usual (TAU). Randomization was performed by a third party not involved in assessment and recruitment. The outcome assessors and investigators were blinded to patients' group allocation, did not assist the MBCT intervention, and were not involved in the randomization. Both groups received regular treatment as usual with a primary care physician/treatment team during the study.

Mindfulness-Based Cognitive Therapy Intervention Group

The MBCT intervention involved weekly 2-hour group sessions for 8 weeks, based on the MBCT manualized protocol (Segal et al., 2002). Participants were encouraged to try different mindfulness techniques during sessions (e.g. silent meditation, body scans, three-minute breathing space, gentle arm movements, chair yoga postures, guided meditations, and compassion meditations). Group discussions focused on reinforcing the guiding principles of mindfulness:

awareness, non-judgment and acceptance. At the end of each weekly session, participants received a sheet with specific instructions on how to complete daily practices, learned during the MBCT group. Home practice consisted of roughly at least 15 minutes of seated meditation and 10 minutes of informal mindfulness (e.g. mindful: walking, brushing their teeth, eating) daily. In addition, participants received electronic reminders about their homework and a summary of home practice, with meditation CDs/online versions as support material. The therapeutic intervention generally followed the manualized protocol (Segal et al., 2002), with some adaptations made to accommodate the needs of older adult participants in the practice (see Appendix 1).

Mindfulness-Based Cognitive Therapy Teachers

In this study, three trained teachers delivered MBCT to 4 groups (6-12 participants in each group). The MBCT teachers comprised of a pool of an occupational therapist, a fifth-year psychiatry resident and a social worker. These teachers had received certification to facilitate MBCT (at the Centre for Mindfulness Studies and/or Sunnybrook Health Science Centre, Toronto, Canada) and had previous experience in running MBCT groups. MBCT Teachers had between 1 to 7 years of meditation experience.

Treatment as Usual Control Group

Participants in the control group received treatment as usual or routine care in the primary care centre, which includes antidepressant medication and/or weekly or biweekly non-structure support counselling with a primary care team member (e.g. social worker, nurse, and/or psychologist). The TAU group was offered the 8-week MBCT intervention after the research intervention was completed and assessed.

Outcome Variables

The primary outcome examined changes in depression scores (PHQ-9) between baseline versus 8-week (follow-up) after the MBCT treatment. The PHQ-9 is a brief nine-item self-report scale for screening, diagnosing and measuring the severity of depression based on the DSM-5 criteria for major depressive disorder. PHQ-9 has been validated as an instrument to detect depression in older adults in primary care settings (Phelan et al., 2010). Each of the nine questions is scored from "0" (Not at All) to "3" (Nearly Every Day). PHQ-9 scores of 5, 10, 15, and 20 are interpreted as mild, moderate, moderately severe, and severe depression, respectively (Kroenke, Spitzer, & Williams, 2001). The secondary outcome included a change in anxiety scores (GAD-7). The GAD-7 is a brief seven-item valid self-report scale frequently use to measure the severity of anxiety that uses some of the DSM-IV criteria for generalized anxiety disorder (Jordan, Shedden-Mora, & Lowe, 2017). Each of the seven questions was scored from "0" (Not at All) to "3" (Nearly Every Day). For both questionnaires, summed scores ≥ 10 are considered clinically significant (Kroenke et al., 2001; Spitzer, Kroenke, Williams, & Lowe, 2006).

Feasibility, acceptability and tolerability outcomes were also measured. Feasibility was examined by assessing: 1) the proportion of participants that were eligible who enrolled in the study (enrollment rate); and, 2) the proportion of participants, from the intervention group, who completed at least 6 out of 8 sessions, measured after the 8-week follow-up (intervention completion rate). The acceptability examined the proportion of participants who completed the 8week post assessments (study retention rate/drop-out rate). Lastly, the tolerability of the mindfulness by meditation was measured a 10-point Likert Scale (developed by our research team) after the 8-week intervention. Participants rated their enjoyment for each of the mindfulness practices. Each of the ten questions was scored from 0 (not at all) to

"10" (*very much*). Participants reported the frequency of their own practice at home and if they experienced any negative reactions.

Exploratory outcomes measured changes in scores of the health-related quality of life using the EuroQol 5-D (EQ-5D) questionnaire and quality of sleep assessed with the Athens Insomnia Scale (AIS) after the intervention ended. The EQ-5D is a 5-item self-report that measures the health status of a person in terms of five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each of the five dimensions was scored from 1 (*no problems*) to 5 (*extreme problems*). The AIS is an 8-item self-report used to assess any sleep difficulty a person may have experienced at least three times in the past month. Some questions are related to nocturnal sleep and others to daytime dysfunction. Each of the eight questions was scored from 0 (*no problem*) to 3 (*very delayed* or *did not sleep at all*).

Data Analyses

Baseline demographic and clinical characteristics were compared between groups using chi-squared and two-sided independent t-tests. Primary, secondary and exploratory outcomes measured changes in PHQ-9 depression, GAD-7 anxiety scores, EQ-5D quality of life, and AIS quality of sleep, between baseline and at 8-week follow-up, were analyzed by comparing the median and mean of the intervention versus the control group using the Mann-Whitney U-test and a two-sided independent t-test as appropriate. Feasibility, acceptability, and tolerability outcomes were described using counts, means and percentages. Cohen's *d* was used to measure effect size. We included all available participants' data and made every effort to contact participants for 8-week follow-up assessments, including those participants who were randomized to the intervention group but did not complete the intervention. A *p* value of <.05 was considered significant in all statistical tests. Previous studies of geriatric Mindfulness-Based Cognitive Therapy at McGill

University have demonstrated effects in open-label studies of 0.5 (Labbe et al., 2016). The sample size recruited for this study (n=61) was enough to estimate effect sizes according to Birkett's theory (at least n=10 in each arm) (Birkett & Day, 1994); future sample sizes are needed for confirmatory randomized controlled trials (see *Chapter 4: Extended Discussion*). Normality was assessed using the Shapiro–Wilk test. Statistical analyses were performed using PASW Statistics 18 (Statistical Product and Service Solutions, Chicago, IL, USA).

Results

Feasibility, Acceptability, and Tolerability

A total of 127 patients were approached to assess potential eligibility. Of these patients, 61 were both enrolled and randomized to either intervention (32) or TAU groups (29), resulting in an 80.3% of enrollment rate, from those that met inclusion criteria (76). In the intervention group, 25 out of 32 participants completed at least 6 weeks of the 8-week interventions, resulting in a 78% intervention completion rate. Participants who complete the study (n = 53) filled out baseline and 8-week follow-up assessments, resulting in an 87% study retention rate (13% drop-out rate). The participants who dropped out of the study included 5 assigned to the intervention and 3 to the TAU group. These participants reported that they felt better (n = 1), found a job (n = 3), found the first session "too intense" and "stressful" (n = 1), died (not related to the intervention; n = 1), not able to reach out (n = 1), and data not available (n = 1; see Figure 1). Intervention participants reported, at 8-week follow-up, enjoying the mindfulness meditation intervention (Mean \pm SD; 8.8 ± 1.5 , in the Likert scale). Guided meditation was the most enjoyable meditation (Mean \pm SD; 8.6 ± 1.4 of 10) and the least enjoyable was the body scan (Mean \pm SD; 8.2 ± 1.6 of 10). Additionally, on average participants reported practicing formal mindfulness meditation (e.g. silent meditation) outside the course 0.6 ± 1.7 (*n* =37) days a week for 3.0 ± 10.1 (*n* =42) minutes per day. Three of the twenty-six participants allocated to the intervention arm reported adverse effects such as "pain", "rare and mild dizziness/a headache", and "things come up in thoughts and flashback of traumatic events". The rest of the participants reported positive effects about the intervention and the interventionists (e.g. "It helps me very much. I feel like I am cured" or "Thank you for giving me this opportunity to experience moments of positive time through the day and new tool to use properly").

Clinical and Demographic Characteristics

The mean age of the participants was 67.8 (\pm 6.2; between 60 and 85 years) years and 72.1% (n = 44) were female. There were no statistically significant differences between MBCT and TAU groups at baseline (see *Table 1*).

Primary and Exploratory Outcomes

For our primary outcome, the MBCT group had a significant reduction in depression symptoms (PHQ-9) scores at 8-week follow-up compared to the TAU control group TAU (-7.9 \pm 4.4 vs. -4.0 \pm 4.7; U = 179.5, p = .002; d = .86). Similarly, anxiety symptoms (GAD-7) scores were significant reduced in the MBCT intervention group compared to the control group (-6.4 \pm 5.0 vs. -2.0 \pm 3.8; t(51) = -3.58, p = .001; d = 0.99).

For our exploratory outcomes, the MBCT group had significantly improved quality of life (EQ-5D) compared to TAU (-0.6 ± 3.5 vs. 0.4 ± 2 ; $U_{-}= 241$, p = .048; d = .35). By contrast, there was not significant changes in scores for the quality of sleep (AIS) between groups MBCT compare to TAU (-1.5 ± 5.0 vs. -1.7 ± 4.4; U = 339.5, p = 0.84; d = .04) (see Table 2 and Figure 2).

Discussion

This study was the first RCT to assess the effects of MBCT in older adults displaying depressive and/or anxiety symptoms in primary care. Our results suggest that MBCT is a feasible, acceptable and a tolerable intervention with a large effect sizes for depression (d = .86) and anxiety (d = .99) symptoms in older adults when compared to TAU. Previous RCT studies assessing non-pharmacological interventions on geriatric samples have traditionally shown high attrition rates (20%; Gardette, Coley, Toulza, & Andrieu, 2007; Pinquart & Duberstein, 2007). Our observed attrition rate of only 13%, suggests that this intervention was not only efficacious but also did not cause any significant adverse effects.

Our findings are extending the literature from younger adults (age 18-65) (Finucane & Mercer, 2006; Segal et al., 2010; Strauss, Cavanagh, Oliver, & Pettman, 2014) as well as with other uncontrolled studies in older adults (Labbe et al., 2016; Mathur et al., 2016). Most of the literature in younger adults have found MBCT to be helpful in the maintenance of depression relapse (Segal et al., 2010), usually in patients with a history of multiple episodes. We suggest that MBCT in addition to preventing depression relapse could be efficacious for acute depressive and anxiety symptoms in older adults. This may be because older adults tend to have more spare time, routine lifestyle, and availability to engage in daily practice and thereby could have potentially profited from a regular MBCT practice routine. Additionally, MBCT intervention might have various benefits from the group context, including social support, which can help improve loneliness and isolation, which are common in this age and worsen in depression and anxiety (Landeiro, Barrows, Nuttall Musson, Gray, & Leal, 2017).

The standard clinical treatment of LLD and LLA in older adults often includes antidepressants and psychotherapies. Although antidepressants can be beneficial to adults suffering from severe and moderate depression (Vohringer & Ghaemi, 2011), up to 60% of adults suffering from severe and moderate depression, are treatment resistance (Fava, 2003). Additionally, 27% of LLD patients discontinue antidepressant treatments due to adverse effects (Fick et al., 2003) and many older adults are reluctant to complete pharmacological treatment due to poor tolerability and medication toxicity (Fick et al., 2003). Other psychological treatments effective for late-life depression and late-life anxiety such as CBT and Problem Solving Therapy (PST) have been used (Arean et al., 2010; Cuijpers, van Straten, & Smit, 2006; Gould, Coulson, & Howard, 2012; Simon, Cordas, & Bottino, 2015). CBT was found to be more efficacious in LLD, compared to TAU (Serfaty et al., 2009), and waitlisted control (medium effect size d = 0.72; Wuthrich & Rapee, 2013). Similarly, for LLA, CBT was more efficacious than TAU (medium effect g = .67) or waiting list controls (large effect g = 1.10; (Hall, Kellett, Berrios, Bains, & Scott, 2016). In summary, psychopharmacology can often be insufficient or ill-tolerated, and psychotherapeutic interventions seem to be effective in LLD/LLA, with MBCT being potentially more scalable than other forms of psychotherapy.

Strengths and Limitations

This study had several strengths. This is the first RCT of late-life depressive and anxiety symptoms in primary care. It also included a larger sample size than previous studies examining MBCT in older adults, a field in which where there has been only one RCT assessing anxiety in residential care (Helmes & Ward, 2017). One of the main limitations of this study was the absence of an active control to evaluate the beneficial effect of social interaction/support and behavioural activation from participating in group therapy. Due to the lack of an active control group, we cannot attribute with certainty the treatment effects observed in this study to the mindfulness component of the MBCT. Future MBCT studies may measure mediating variables

such as change in mindfulness (e.g Five Facet Mindfulness Questionnaire) which may potentially balance and mitigate to some extent the lack of active controls. Lastly, we used selfreport assessments to measure depression and anxiety symptoms which were more feasible and easier to implement in primary care. In future studies, a more formal systematic diagnostic evaluation could be implemented to investigate comorbidity diagnosis, and adherence to home practice (see Chapter 4: Extended discussion).

Conclusion

This RCT was the first one to address the population of older adults with symptoms of depression and/or anxiety at once, measure the effects of MBCT, and target primary care settings. Clinically, the findings of the present study suggest that MBCT may be a useful adjunct to usual primary care, to reduce symptoms of depression and anxiety and to improve health-related quality of life in a geriatric population. Future trials can replicate our findings and incorporate an active control group (e.g. Health Enhancement Program; Eisendrath et al., 2014), effects of group socialization, longer-term follow-up and other assessments (e.g. clinician-rated instruments, number of depressive/anxiety episodes, neuroimaging, and neuropsychological test batteries). It would also be important to assess the cost-effectiveness of MBCT compared to other forms of group therapy/intervention in primary care settings. In addition, we need to further assess the potential benefits and mechanisms of action for MBCT in older adults with depression and anxiety.

Figure 1

Participants Flow Over the Course of the Study.



ALL GROUPS

Table 1

Baseline Characteristics of Patients Randomized to MBCT Versus Treatment as Usual.

Participant Data	Total Sample (n=61) Mean (±SD) %(n)	Intervention Group (n=32) Mean(±SD)	Control Group (n=29) Mean(±SD)
		%(n)	%(n)
Demographic information			
Female	72.1(44)	78.1(25)	65.5% (19)
Age, yr	67.8+6.2	67.9±6.8	67.7±5.6
Ethnicity, Caucasian	60.7% (37)	59.4% (19)	62.1% (18)
Marital Status			
Married	27.9% (17)	28.1% (9)	27.6% (8)
Common law	4.9% (3)	0% (0)	10.3% (3)
Single	50.8% (31)	50% (16)	51.7% (15)
Widow	11.5% (7)	15.6% (5)	6.9% (2)
Divorced	4.9% (3)	6.3% (2)	3.4% (1)
Levels of education			
Elementary school	3.3% (2)	6.3% (2)	0% (0)
High school	37.7% (23)	37.5% (12)	37.9% (11
Bachelor	33.3% (20)	15% (9)	37.9% (11
Masters/PhD	19.7% (12)	21.9% (7)	17 3% (5)
Living arrangement	19.770 (12)	21.976 (7)	17.570 (5)
With family member	34.4% (21)	31.3% (10)	37.9% (11
Living along	62 204 (28)	65 604 (21)	58 60/ (17
Living in long term	4 9% (3)	6 3% (2)	3 40% (1)
care/seniors'residence/	4.9% (3)	0.5% (2)	5.470 (1)
Medical History			
Number of medical problems	2 1+2 0	2 1+2 2	2 1+1 7
Number of surrent mediaations	2.1±2.0	2.1±2.5	2.1±1.7
Autol health information	5.8±3.4	5.9±3.9	3.7±2.9
A prioty diagnosis	57 40/ (25)	56 20/ (18)	59 60/ (17
Alixiety diagnosis	57.4% (55)	56.3% (18)	51.0% (17
Depression diagnosis	54.1% (53)	56.3% (18)	51./% (15
Others diagnosis	11.5% (/)	6.3% (2)	10.4% (3)
Number of years diagnosed	15.3±12.1	15.2±13.9	15.4±10.5
Number of years symptomatic	21.6±18.5	20.8±19.5	22.4±17.7
		(n=26)	
Number of current psychotropics	1.0±0.94	$1.0{\pm}1.0$	0.9±0.9
Psychotropic Medications	55.7% (34)	59.4% (n9)	51.7% (15
Antidepressants (ATD)	45.9% (28)	43.8% (14)	48.5% (14
Hypnotic/sedatives	21.3% (13)	25.0% (8)	17.2% (5)
ATD and hypnotic/sedatives	16.4% (10)	21.8% (7)	10.3% (3)
Antipsychotics	6.6% (4)	3.1% (1)	10.3% (3)
Other	1.6% (1)	3.1% (1)	0% (n=0)
Current mental health follow-up Habits	47.5% (29)	50.0% (16)	44.8% (13
Alcohol consumption Meditation practice	32.8% (20)	31.3% (10)	34.5% (10
Meditated in the past	49.2% (30)	50% (16)	48.3% (14)
Meditate currently	18.0% (11)	15.6% (5)	20.7% (6)
Minutes per day meditated	3.0±10.1	1.0±3.6	5.6±14.6
(baseline)			
Days per week meditated	0 6+1 7	0.3+0.9	1 0+2 4

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(baseline)

Baseline Scores			
PHQ-9	14.8±5.1	14.2±5.3	15.41±4.9
GAD-7	12.0±4.4	11.6±3.9	12.4±5.0
EQ-5D	11.1±10.3	9.8±3.3	12.5±14.5
AIS	11.2±5.0	10.2±4.8	12.3±5.1

Note. Data are displayed either as mean±SD or as n (%). TAU, treatment as usual; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; EQ-5D, EuroQol Five Dimension Scale (Quality of Live); AIS, Athens Insomnia Scale.

Table 2

Effects of MBCT vs. TAU Across Global Scores of Depression (PHQ-9), Anxiety (GAD-7), Quality of Life (EQ-5D) and Sleep Difficulties (AIS; (n = 53).

Measure	MBCT Group (n=27)		TAU Control Group (n=26)					
	Mean±SD Pre-Test	Mean±SD Post-Test	Mean Change±SD	Mean±SD Pre-Test	Mean±SD Post-Test	Mean Change±SD	Statistics	
	n=27	n=27	n=27	n=26	n=26	n=26	t, U P value	d
Primary and S	econdary Ou	tcomes						
PHQ-9 (Depression)	14.8±4.9	6.9±4.4	-7.9±4.4	15.7±5.1	11.7±6.4	-4.0±4.7	U=179.5, p=0.002	d=0.86
GAD7 (Anxiety)	11.4±3.8	5.0±4.1	-6.4±5.0	12.6±5.1	10.6±5.8	-2.0±3.8	t(51)=-3.58, p=0.001	d=0.99
Exploratory O	Exploratory Outcomes							
EQ-5D (Quality of life)	10.3±3.2	9.7±3.6	-0.6±3.5	9.5±3.2	9.9±3.8	0.4±2.0	U=241, p=0.048	d=0.35
AIS (Quality of sleep)	10.5±4.5	9.0±4.7	-1.5±5.0	12.3±5.3	10.5±5.4	-1.7±4.4	U=339.5, p=0.84	d=0.04

Note. PHQ-9 Patient Health Questionnaire; GAD-7 Generalized Anxiety Disorder Scale-7; EQ-5D EuroQol Five Dimension Scale (Quality of Life); AIS Athens Insomnia Scale; d standardized effect size. SD – Standard Deviation, TAU – Treatment as Usual

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Figure 2



Mean Change in PHQ-9 Depression and GAD-7 Anxiety Scores Between MBCT and TAU Groups

Note. Statistically significant difference between groups at 8-week follow, p < 0.05. Error Bars: 95% CI

Appendix A

Adaptations and Modifications of the MBCT Sessions for older adults

Some adaptations were made in this study to facilitate the intervention for older adults. Main adaptations included: 1) Reducing time of body scan meditation to a maximum of 20 minutes, compared to 30 minutes for the general population; 2) Using chairs rather than yoga mats or the floor during meditation practices (although yoga mats were available); 3) Allowing patients to remain seated during yoga practices, rather than standing or lying, and performing a modified version of sun salutation in the chair; 4) Encouraging patients to modify postures to promote wellbeing and safety; 5) Providing pillows to promote comfort while seated in chairs or lying on the yoga mats; 6) Slowing down the pace of walking meditation to avoid falls; 7) Projecting loudly when guiding discussion or meditation practices in order to facilitate hearing or having facilitators sit near those who could not hear/understand well; and, 8) Taking more frequent breaks.

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Chapter 4: Extended Discussion

Summary Overview

This thesis has one manuscript that describes an RCT comparing the effects of an MBCT intervention to treatment as usual, on depression and/or anxiety symptoms, health-related quality of life and sleep in older adults suffering from symptoms of depression and/or anxiety in a primary care setting. In addition, the feasibility, acceptability and tolerability of the MBCT with this geriatric population was also assessed. Following the first manuscript there is a brief extension of specific points related to the discussion. Then, a description of the sustained clinical impact that this research project had in our hospital's primary care network. Future directions and comments are presented. Lastly, a conclusion and a final summary are mentioned.

Brief Extended Discussion

Power analysis. Previous retrospective case series of geriatric MBCT at McGill have conducted by our research group demonstrating the effects in reducing symptoms of depression and/or anxiety (Labbe et al., 2016). Based on the promising findings from that small study, formal *a priori* power sample calculations were performed in preparation for this study to help generate estimates for larger confirmatory RCTs, if necessary (n = 100 will likely be sufficient if the true effect size is actually 0.5 in an RCT design). In this pilot study, we were not able to randomize 100 participants due to feasibility financial constraints and stopped recruitment at n = 61. Although, the sample size recruited for this study (n = 61) was sufficient to estimate effect sizes, and we were able to find statistically significant and clinically meaningful results in this RCT (see *Table 2*). According to Birkett's theory, a sample of 10 participants in each arm are sufficient power to estimate effect size in pilot studies, future sample sizes are needed for confirmatory randomized controlled trials (Birkett & Day, 1994).

Sleep results. In our study, we did not observe significant differences between MBCT vs. TAU regarding a change in the quality of sleep during study the follow-up (although both groups had non-significant small improvements in sleep quality). However, findings from a systematic review and meta-analysis of RCTs demonstrated that mindfulness meditation may be beneficial for treating certain sleep disturbances (Rusch et al., 2018). Other pre/post studies have also suggested that MBIs are beneficial for adults with persistent insomnia (Heidenreich, Tuin, Pflug, Michal, & Michalak, 2006) and heterogeneous psychiatric outpatients with mood and/or anxiety disorders and insomnia symptoms; benefits maintained for three months (Ree & Craigie, 2007). In addition, an RCT study showed that MBSR may be an effective treatment for older adults suffering from chronic insomnia (Zhang et al., 2015). Interestingly, investigators reported small effect sizes from two RCT using objective measures of sleep (actigraphy or polysomnography) after MBCT and MBSR interventions were given (Britton, Haynes, Fridel, & Bootzin, 2010; Gross et al., 2011). However, MBIs had significant effects on subjective measures reported by patients compared to objective measures of sleep (Britton et al., 2010). We have several hypotheses regarding why we did not observe changes in sleep quality in our study: 1) Mindfulness-based interventions may not necessarily help sleep quality compared to a TAU control in older adults, despite other benefits to depression, anxiety, and quality of life; 2) Some participants were taking sedatives-hypnotics, which could have affected sleep quality; and, 3) Our self-report questionnaires were not sensitive enough to capture actual changes in the quality of sleep. Therefore, more objective sleep measures, such as actiwatch or polysomnography, could be used in future studies with MBCT in older adults.

Clinical impact in our hospital's primary care network. This exciting graduate study project not only contributed to the mindfulness/mind-body research literature but also had a

clinical impact within our health care system of the Jewish General Hospital, Local Community Service Centres (CLSC) from the Integrated University Health and Social Services Centres (CIUSSS-Centre-Ouest de Montréal) Montreal Centre-West Catchment area. Although most of what follows in this paragraph are mostly anecdotal, it raises important points regarding the importance of translating research findings into clinical practice. Before the data pertaining to this project was available, clinicians from the CLSC Benny Farm were already satisfied with the symptom improvement they observed in some of the patients who participated in the MBCT intervention. Clinically, MBCT therapy had a positive impact on patients' behaviors and functioning. Once the participants finished the 8-week follow up questionnaires for our last group, several clinicians from the CLSC Benny Farm reported that those patients who participated in the MBCT interventions were getting much better in terms of functioning and symptoms of depression and/anxiety. They wanted to implement MBCT groups for their CLSC. Based on the report of clinicians and the significant research findings obtained later from this study, the CIUSSS's Centre-West administration acknowledged the positive impact MBCT intervention had on their patients' health and well-being, and in facilitating clinicians' workload. Following the clinical trial's completion, the CIUSSS Centre-West was willing to fund 8 additional groups of MBCT intervention as a clinical service (free for patients) between 2018 and 2020 in our health care system. There are plans to further expand the sustainability of this initiative as our team is facilitating the training of two CLSC clinicians to be able to provide MBCT long term. As further research is done to assess this treatment and similar interventions for LLD/LLA, we hope that there will be other CLSC/hospitals interested in providing alternative treatments for depression and anxiety symptoms for older adults.

Extended limitations and future directions. In this study, participants self-reported their home practice each week and they were responsible to complete the assignments. In future studies measurements of home practice could be useful to quantify the amount of mindfulness practice participants are engaging in the MBCT group. Facilitators may measure engagement in home practices by asking participants to complete an adherence sheet for each practice at home, filling up questionnaires regarding each practice or using technological approaches to track the homework. Even though we were able to assess that MBCT was superior to TAU, future studies can assess the effects of different aspects of the intervention (e.g. the way in which groups are led, adherence to meditation homework) on treatment outcomes. Although the self-report assessments (PHQ-9 and GAD-7) used in this study to measure depression and anxiety symptoms were feasible and easy to implement in primary care, these self-report questionnaires may be prone to social desirability bias. In future studies, a more formal systematic diagnostic evaluation (e.g. Hamilton-D) could be implemented to investigate comorbidity and formal diagnosis. In addition, since unspecific group therapeutic factors may have a curative effect (Yalom & Leszcz, 2005), future studies may take into account those effects (e.g. using the Therapeutic Factor Inventory; Macnair-Semands, Ogrodniczuk, & Joyce, 2010) when assessing the beneficial effects of MBCT for older adults.

Albeit, the emerging literature regarding MBCT and MBIs have found evidence for efficacy and effectiveness for depression/anxiety among other physical and mental conditions, there is a lot of caution needed when using these programs. To advance the quality of the treatment, practitioners and facilitators should be aware and be able to recognize possible unwanted effects that long-meditations may cause in certain populations with psychiatric illness (e.g. schizophrenics; Linden, 2013; Walsh & Roche, 1979). Further investigation is still needed

to provide evidence of the effects of MBCT as an acute treatment for mental health conditions, especially in LLD and LLA. We recommend that future researchers continue implementing studies with MBIs such as MBCT with more systematic and rigorous approaches when assessing for depression and/or anxiety in older adults. In addition to the ones discussed in the manuscript, it is suggested that future researchers: 1) Employ the use of objective sleep recordings (actigraphy or polysomnography) to quantify the possible effects of MBCT in quality of sleep in geriatric populations; 2) Integrate neuropsychological measures to better assess any cognitive changes that may be promoted by the MBCT intervention; and, 3) Take advantages of neuroimaging tools that can be used to further comprehend the effects of MBCT in the human brain morphology, connectivity and function. In summary, future researchers targeting all these areas could potentially disentangle the mechanisms by which MBCT effectively works as a treatment to LLA and LLD.

References for Chapter 4: Extended Discussion

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Chapter 5: Final Conclusion and Summary

This RCT study provides evidence that the MBCT intervention that we have tailored, as an adjunct to usual primary care, is a safe and efficacious treatment to reduce symptoms of depression and anxiety and to improve health-related quality of life for older aged adults in primary care. This study has a significant scientific and a clinical relevance since there are no previous RCTs in the literature assessing the feasibility, acceptability and tolerability of the MBCT with a geriatric population suffering from LLD and LLA in primary care. In addition, this project had a sustained clinical impact on our hospital's primary care network. Furthermore, the results suggest that it will be valuable to design clinical trials to investigate the effect of late-life depression prevention on mitigating the risk of dementia vascular dementia and Alzheimer's disease. More controlled studies are needed to replicate and validate the findings obtained from this study. In addition, future research of MBCT in LLD and LLA is necessary to further understand the neurobiological and psychological mechanisms of the MBCT intervention in geriatric mental health.