MODIFYING DIET AND EXERCISE IN MULTIPLE SCLEROSIS: A PILOT STUDY

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MODIFYING DIET AND EXERCISE IN MULTIPLE SCLEROSIS: A PILOT STUDY

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ABSTRACT

Background: Modest weight loss can have significant health benefits and reduce the risk of developing chronic health comorbidities (Van Gaal et al., 1997). It remains unclear whether weight loss in individuals with multiple sclerosis (MS) can aid in reducing disease burden.

Purpose: The three aims of this single arm non-randomized study include, (1) Develop and assess the feasibility and acceptability of a six-month telehealth, behavioral weight loss program for people with MS; (2) Examine the primary outcome variable, percent weight loss, from baseline to six-month follow-up; and (3) Assess minutes of physical activity and servings of fruits and vegetables eaten daily in people with MS.

Methods: Participants were provided with a Fitbit device, Fitbit Aria Scale, and a premium subscription to the Lose It! application. Program recommendations included eating 1200 – 1500 calories a day and working up to 150 minutes of moderate intensity physical activity per week over six months. Group members met weekly to discuss topics related to healthy living in MS and attended two individual calls with the group leader. Qualitative and quantitative data were used to examine facilitators and barriers to behavior
change, perceived benefits of weight loss and healthy lifestyle practices, and patient satisfaction with the program. Changes in diet and physical activity routines were monitored via questionnaires at baseline and follow-up. Percent weight loss was calculated at follow-up.

Results: Eight people were consented and enrolled in the program. On average, participants attended 17 of the 24 weekly sessions ($SD = 7.15$). Average percent weight loss was $10.57\%$ ($SD = 7.20$). Nearly all participants strongly agreed the program helped them live a healthier lifestyle ($3.87 \pm 0.35$ on 0 to 4 Likert scale). Activity scores increased from \textit{insufficiently active} ($M = 13.0$, $SD = 14.98$) to \textit{active} at follow-up ($M = 43.50$, $SD = 21.31$; $t(7) = -3.33$, $p = 0.013$). Self-reported fruit and vegetable servings increased overall but fruit consumption was the only variable that was significantly increased ($M = -0.54$, $SD = 0.59$; $t(7) = -2.61$, $p = 0.035$).

Discussion: Taken together, results from this pilot trial will be used to inform future study directions. Weight loss interventions tailored to people with MS could potentially improve the health and quality of life for hundreds of thousands of patients.
The faculty listed below, appointed by the Dean of the College of Arts and Sciences have examined the thesis titled “Modifying Diet and Exercise in Multiple Sclerosis: A Pilot Study,” presented by Julia S. Cozart, a student candidate for the Master of Arts degree, and certify that in their opinion it is worthy of acceptance.

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OVERVIEW

Aims

1) Develop and assess the feasibility and acceptability of a 6-month telephone administered behavioral weight loss intervention tailored to individuals with MS. We collected qualitative and quantitative feedback data that will be used to inform future study directions.

2) Examine percent weight loss from baseline to follow-up as the primary outcome variable. We expected patients to demonstrate statistically and clinically significant weight loss at the 6-month follow-up.

3) Assess minutes of physical activity and amount of fruits and vegetables eaten daily in people with MS. We expected that participants would report increased engagement in physical activity, and increased fruit and vegetable consumption at the 6-month time point.
CHAPTER 1
INTRODUCTION

Review of Literature

Multiple Sclerosis

Multiple Sclerosis (MS) is a chronic disease that is characterized by the body’s immune system attacking the central nervous system (CNS). Inflammatory attacks on myelin lead to damaged areas in the brain and spinal cord called ‘lesions.’ Magnetic resonance imaging (MRI) is often used to confirm the presence of lesions in the brain, and a subsequent diagnosis of MS. Patients commonly present with symptoms such as numbness, gait disturbance, fatigue, vision loss, pain, and bladder and bowel dysfunction. MS is a growing concern because it can be debilitating and negatively affect quality of life.

Prevalence. MS affects nearly 2.3 million people worldwide, including over 400,000 Americans - for every 100,000 Americans, 150 will be diagnosed (Dilokthornsakul et al., 2016). MS can occur at any age, although most individuals are diagnosed between the ages of 20 and 50, and the diagnosis is more common in women. Most ethnic groups are affected by MS, including Caucasians, African Americans, Asians, and Hispanics/Latinos. MS was thought to be more common among Caucasians of northern European ancestry (Kingwell et al., 2013), but recent findings have shown it is increasingly common in African American women. In a study of 496 recently diagnosed patients with MS, the incidence rate per 100,000 was higher in African Americans (10.2%) than in Caucasians (6.9%), Hispanics (2.9%), or Asian Americans (1.4%) (Langer-Gould, Brara, Beaber, & Zhang, 2013). Conflicting findings have been reported, but some studies have shown that African Americans are more likely to be older when diagnosed and have greater disease severity compared to Caucasians (Cree et al., 2009). These findings could be due to disparities in
healthcare, or genetic and environmental factors (Rivas-Rodriguez et al., 2018). Overall, MS occurs in nearly all ethnicities, but various elements may influence the prevalence and severity of the disease. One aspect that may contribute to discrepancies in MS prevalence is geographical location. MS is more prevalent in areas that are further away from the equator. Genetic and environmental causes of MS may help explain why the prevalence of MS is not uniform on a global scale.

**Causes.** The cause of MS is unknown, but a combination of genetic and environmental factors is thought to play a role. Evidence for genetic factors includes identical twin concordance rates, familial aggregation of MS (although this could also be due to similar environments), and specific genes associated with MS susceptibility.

In monozygotic twins, when one twin has MS, the other has a 25-30% chance of being diagnosed as well (Cree, 2014) Dizygotic twins have a 3-5% increased risk of MS and individuals that have an immediate relative with MS also have a slightly increased risk (Cree, 2014). Twin studies and familial aggregation demonstrate the role of genetics in MS, while simultaneously illustrating that environmental exposures must also contribute to the etiology of the disease. It is possible that similar environments for families could explain familial aggregation. Nearly 15-20% of patients with MS report a family history (Cree, 2014). Familial aggregation of MS has been studied but with varying outcomes (Ebers, 2005; O'Gorman et al., 2011; O'Gorman et al., 2013; Westerlind et al., 2014). The extent to which various genetic and environmental factors contribute to developing MS is unclear, and more work is needed to determine whether estimates can be generalized to various patient demographics.
Specific genes associated with MS have been identified. Changes in the HLA-DRB1 gene and the interleukin 7 receptor (IL-7R) gene have been identified as genetic risk factors for developing MS. The HLA-DRB1 and IL-7R genes play a role in immune system development and may contribute to the autoimmune process that damages myelin. Considering the concordance rates among identical twins and the identified genes in MS, genetic factors play a significant role in determining who is diagnosed with the disease.

Environmental factors including infectious agents, geographic patterns, Vitamin D status, and lifestyle factors (i.e., smoking and obesity) have been linked to developing MS. Infectious agents are environmental factors such as viruses and bacteria that may affect MS susceptibility. Two herpesviruses – Epstein Barr virus (EBV) and Human Herpesvirus 6 (HHV-6 also called Roseola) have been associated with MS (Virtanen et al., 2012). Haahr and colleagues found that late infection (i.e., around puberty or after) with EBV and a history of mononucleosis are notably associated with an increased MS risk (Haahr et al., 2004). Similarly, some evidence suggests that HHV-6 is related to MS pathogenesis, but research findings have provided mixed results and its exact relationship with MS remains unknown (Leibovitch et al., 2014). It is hypothesized that HHV-6 impacts MS risk because it is known to attack the nervous system and has immunomodulating properties (Voumvourakis et al., 2010). In a recent systematic review examining the relationship between HHV-6 and MS, of the 61 studies evaluated, 41% reached statistically significant results (Voumvourakis et al., 2010). Overall, there is evidence that infectious agents such as EBV and HHV-6 may contribute to MS susceptibility.

Low levels of vitamin D, among other environmental influences, may increase the risk of developing MS. Vitamin D status may partly explain why MS is more prevalent at higher
latitudes, but various geographic, demographic, genetic, and infectious factors are likely involved. Along with the heightened risk of MS, there is a relationship between vitamin D status and disease severity. Vitamin D deficiency is associated with greater disease severity, and the relationship is likely bidirectional such that patients with more aggressive disease courses have lower vitamin D levels due to heat sensitivity and mobility challenges (Runia et al., 2012; Shahbeigi et al., 2013; Thouvenot et al., 2015). From this perspective, low vitamin D may contribute to disease severity, but increased disease severity likely maintains or lowers vitamin D levels because of the challenges patients with progressive MS face.

Smoking and obesity are environmental factors that affect the incidence and progression of MS. Smoking increases the risk of developing MS and has been shown to accelerate disease progression (Healy et al., 2009). In a large North American Research Committee on MS (NARCOMS) cohort, more than 50% of people with MS reported they currently smoked or had smoked in the past (R. Marrie et al., 2009). Reports have shown that people with MS who smoke have more active inflammation and greater brain atrophy, both of which are linked to greater disability in MS (Healy et al., 2009; O'Gorman et al., 2012; Zivadinov et al., 2009). Smoking is a behavior that can be reduced and yield significant health benefits. A research study by Ramanujam and colleagues (2015) found that patients who quit smoking may be able to delay disease progression from RRMS to SPMS (Ramanujam et al., 2015). Individuals in the study were classified as quitters or continuers based on their smoking status after disease diagnosis. The median conversion time from RRMS to SPMS in individuals who quit smoking following their MS diagnosis was 8 years after those who continued smoking.
Obesity affects over 650 million adults worldwide. Obesity in childhood and adolescence is also an environmental risk factor for developing MS and may contribute to more disease activity in patients who are already diagnosed (Guerrero-Garcia et al., 2016; Hedstrom et al., 2012; Munger et al., 2013; Xia et al., 2016). Modern lifestyles have increased sedentary habits and introduced diets that are full of processed, high-calorie foods. Additionally, busy schedules and lack of free time make it more difficult for individuals to prioritize eating well and exercising often.

Cardiovascular risk factors and health comorbidities (e.g., obesity and type 2 diabetes) have been correlated with disease onset and progression in MS (Tettey, Simson, Taylor, & van der Mei, 2014). Obesity is considered a chronic low-grade inflammatory state (Novo et al., 2017). Adipose tissue or fat tissue (AT) stores energy in the body and is involved in various physiological processes. AT is composed of cells called adipocytes (fat cells) which are involved in activities that may regulate inflammatory states. Under conditions of obesity, adipocytes secrete excessive amounts of pro-inflammatory substances (Ouchi et al., 2011). Therefore, obesity may contribute to the increased neuroinflammation observed in people with MS, however more research is needed to determine the function of AT in various diseases, like MS.

**Subtypes.** MS is categorized into different subtypes: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), and primary progressive MS (PPMS) (Lublin et al., 2014). Around 85% of patients are first diagnosed with RRMS. In RRMS, patients experience relapses of old or new symptoms followed remission. RRMS consists of intermittent relapses or exacerbations, which differ in frequency and severity, but patients maintain a stable baseline between relapses.
The subtype of MS a person is diagnosed with may change over the course of the disease. Up to 90% of RRMS patients advance to SPMS after 25 years (Ebers, 2001). Patients with SPMS may still have relapses and times of remission, but a gradual worsening of the disease occurs over time. The progressive disability in people with SPMS accounts for most of the disability seen in the illness. Individuals with this subtype have more severe relapses with less complete remissions that are shorter and eventually non-existent.

Individuals with PPMS progress relentlessly and only about 15% of the MS population are diagnosed with the subtype. Problems appear and gradually worsen over time. There is progressive disability from the start without distinct relapses or remissions. The progressive worsening of symptoms is caused by nerve damage or loss rather than inflammation.

**Symptoms.** MS symptoms can vary from patient to patient and change throughout the disease course. Each patient is different but common MS symptoms include fatigue, gait difficulties, numbness or tingling, spasticity, muscle weakness, vision problems (vision loss, blurred or double vision), depression and other emotional changes, dizziness, sexual dysfunction, bowel and bladder problems, pain, and cognitive changes (Brownlee et al., 2017; de Sa et al., 2011). MS symptoms are unpredictable and can occur at any time.

**Treatments.** Although there is no cure for MS, several medications can modify disease progression in people with RRMS. Disease-modifying therapies (DMTs) are prescribed to patients with MS to prevent future damage from occurring. Over a two-year period, DMTs may decrease MS relapses by 18 – 68% (Gajofatto et al., 2015; Mitsikostas et al., 2017). Additionally, patients using DMTs may have fewer, smaller lesions on MRI scans. Bandari and colleagues (2012) summarized efficacy data of disease-modifying
therapies for RRMS and found that there was a 29 - 92% reduction in Gd-enhancing (gadolinium) lesions and a 31 - 83% reduction in new or enlarging T2 lesions over a two-year period (Bandari et al., 2012).

DMTs limit disease activity and modify disease course, while other medications are used to manage MS symptoms like fatigue, depression, spasticity, pain, and bladder and bowel dysfunction. Not every relapse requires treatment, but steroids (high dose intravenous methylprednisolone) are the primary method of treatment for disabling relapses that may impair vision or cause motor disability (Pandit et al., 2011). Symptoms such as fatigue, spasticity, pain, depression, bladder dysfunction, and sexual dysfunction are also commonly treated with pharmacological interventions (Henze et al., 2006; Pandit et al., 2011).

In addition to pharmacological treatments, healthy lifestyle changes may help patients with MS manage their symptoms. Although some diets have been proposed to help treat MS, these diets have not been rigorously tested to determine how they affect disease activity. Instead, most MS specialists recommend following the same dietary guidelines that are recommended by the American Heart Association and the American Cancer Society. In a study assessing the relationship between diet quality and MS disease severity in MS, over 2000 patients completed the Diet Habits Questionnaire (DHQ), which has an overall score ranging from 0-50 with higher scores indicating a better diet quality (Hadgkiss et al., 2015). Every 10-point increase on the DHQ was associated with 30% decreased likelihood of having greater disability, and higher scores were also linked to better health-related quality of life (Hadgkiss et al., 2015; Katz Sand, 2018). Overall,
several studies have shown that diet quality likely has a significant impact in patients with MS.

In addition to a high-quality diet, exercise may help patients with MS enhance mobility, increase strength, reduce fatigue, and improve mood (Motl et al., 2017). The effects of exercise offer many health benefits and help improve quality of life in people with MS. In a meta-analysis by Paltamaa and colleagues (2012), aerobic exercise helped patients with mild and moderate disability improve their balance. Similarly, in a review done by Asano and Finlayson (2014), they concluded that aerobic exercise had a greater impact on reducing self-reported fatigue than education and pharmacotherapies. Another study by Leavitt and colleagues (2014), found that patients who participated in an aerobic exercise therapy program had improved memory by 53.7% measured with the CVLT, though another study found only a small relationship between cognition and exercise in MS (Oken et al., 2004; Romberg et al., 2005). Overall, several studies have examined the effects of various exercises on fatigue, depression, memory, quality of life, pain, and disability status in MS with promising results. A behavioral weight loss intervention for patients with MS that incorporates a high-quality diet and moderate exercise may help individuals achieve significant improvements in their overall functioning.

**Obesity in the U.S.**

The terms overweight and obese are used by the Centers for Disease Control and Prevention (2016) to describe weight that is higher than what is advised and considered healthy for a specific height. Obesity status can be assessed using a screening tool known as Body Mass Index (BMI). Adult are considered overweight if their BMI ranges from 25.0 – 29.9, and a BMI of 30 or greater is considered obese.
Modern lifestyles have contributed to obesity due to the growing imbalance between caloric intake and expenditure (Palavra et al., 2016). In 2015-2016, the prevalence of obesity in the U.S. as reported by the Centers for Disease Control and Prevention (CDC), was 39.8%, affecting nearly 93.3 million U.S. adults. As for global statistics on obesity, in 2016, at least 1.9 billion adults worldwide were considered overweight and 650 million of these were considered obese Organization (2018).

**Health Burden of Obesity.** Obesity increases the risk of developing chronic health conditions including hypertension, diabetes, cardiovascular diseases, osteoarthritis, sleep apnea, cancer, and depression (Pi-Sunyer, 2009). Obesity places a serious risk on public health and can be a costly economic burden. In 2008, the costs of obesity in the US were estimated to be around $147 billion (Finkelstein et al., 2009). Obesity is not only costly for healthcare systems but also in terms of lost productivity. Kudel and colleagues (2018) confirmed that work productivity declines with elevated BMI. Similarly, as they expected, they found that comorbidity increased as BMI increased. In general, obesity is a preventable condition that can be eliminated by making lifestyle changes such as, eating a well-balanced diet and regularly engaging in physical activity (Ofei, 2005). The economic burden associated with obesity further supports the need for a weight loss intervention for individuals with MS. A behavioral weight loss program may help patients with MS lose weight and reduce healthcare costs associated with obesity.

**Obesity and MS**

Obesity is prevalent in patients already diagnosed with MS. According to the results from a study involving the NARCOMS patient registry in 2006, nearly 50% of the 8,983 participants with MS were overweight (26.4 %) or obese (23.8 %) (R. A. Marrie et al., 2009). These statistics may underestimate rates of overweight and obesity in MS since
individuals are likely to under-report their weight and over report their height in self-report questionnaires. Obesity is a risk factor for many chronic health conditions, like MS (Munger et al., 2009; Wesnes et al., 2015). Hedstrom and colleagues (2012) found that individuals with a BMI greater than or equal to 30 had a two-fold increased risk of MS, and this association was significant in men and women.

Several research studies have shown that obesity in adolescence is a risk factor for developing MS (Gianfrancesco et al., 2014; Gianfrancesco et al., 2016; R. A. Marrie et al., 2009; Munger et al., 2013; Munger et al., 2009). Results from Langer-Gould found that obesity was significantly associated with an increased risk of pediatric-onset MS (Langer-Gould, Brara, Beaber, & Koebnick, 2013). Another study by Munger and colleagues (2009) identified associations between obesity and MS in young females; specifically, obesity at age 18 was associated with a two-fold increased risk of MS. This finding persisted even when researchers controlled for smoking, latitude of residence at age 15, and ethnicity (Munger et al., 2009). Hedstrom and colleagues (2012) also identified an association between elevated BMI before age 20 and increased risk of MS in both men and women. They concluded that individuals who had a BMI greater than 27 at age 20 had a two-fold increased risk of developing MS compared to individuals with normal BMI values (Hedstrom et al., 2012). Overall, there is evidence that obesity in young adulthood, may be associated with MS susceptibility, and this finding seems to be more pronounced in women than men.

Although obesity is a risk factor for MS, the interaction between obesity and MS disease activity is not entirely understood. So far, studies indicate that obesity is likely to harm MS disease severity and progression. Obesity in patients that already have MS may
negatively affect the response to treatment. In a study by Kvistad and colleagues (2015), 80% of overweight or obese patients with RRMS (BMI ≥ 25) had MRI disease activity compared to only 48% of the normal-weight patients (BMI < 25) during interferon-beta treatment. In this study, no evidence of disease activity (NEDA status) was defined as no relapses, maintained disability status, and no MRI activity. In patients with normal weight, 26% obtained NEDA status compared to 13% of patients with a BMI greater than 25 (Kvistad et al., 2015). The study concluded that BMI may affect interferon-beta treatment response.

Obesity may also have a significant impact on mood and quality of life in patients with MS. Cambil-Martin and colleagues (2016) found that patients with MS who were overweight reported higher levels of depression, lower functioning, and worse self-reported health status than patients who had a normal weight. Overall, maintaining a healthy weight may help reduce relapses and prevent disability progression in MS (Cambil-Martin et al., 2016; Oliveira et al., 2014; Pilutti et al., 2019). Obesity increases MS susceptibility, makes MS symptoms more difficult to manage, may interfere with treatment, and accelerates the progression of MS. A behavioral weight loss study for patients with MS may help individuals modify their lifestyle and decrease the risk of complications due to obesity.

**BMI and the Brain.** In a recent study, MS patients with a higher BMI had decreased normalized gray matter volume (Mowry et al., 2018). Normalized gray matter loss is typically associated with greater disability in patients with MS (Honce, 2013), although Mowry and colleagues (2018) were not able to demonstrate an association between the two. Another study identified an increased T1 lesion burden in overweight and obese
people with MS (Kappus et al., 2016). Additionally, they found that patients with MS who had one or more cardiovascular risks present (e.g., hypertension, heart disease, smoking, overweight/obesity defined as BMI greater than 25, and type 1 diabetes) had increased lesion burden and more advanced brain atrophy (Kappus et al., 2016). These findings were not present in the MRIs of the age and sex-matched healthy control group. These results indicate that cardiovascular comorbidities may play a role in MS disease progression.

Interestingly, in adults who do not have MS, several studies have shown that obesity also appears to be associated with lower brain volume (Debette et al., 2010; Enzinger et al., 2005; Gustafson et al., 2004; Ward et al., 2005). Other studies in healthy adults have shown that BMI is associated with a risk of dementia (Kivimaki et al., 2018). In individuals with existing Alzheimer’s disease or mild cognitive impairment, studies have shown that obese individuals had greater reductions in brain volume than those with normal BMIs (Bobb et al., 2014; Ho et al., 2010; Janowitz et al., 2015; Kharabian Masouleh et al., 2016; Raji et al., 2010). Considering the findings between obesity and neurodegeneration in adults without MS, it is unclear whether this association in people with MS is due to an MS-specific process or if the impact of obesity on the brain is more generalized. Nevertheless, obesity may accelerate the rate of gray matter and overall brain volume loss that is already at play in those with MS. In a small study of morbidly obese people undergoing bariatric surgery, weight loss was accompanied by increases in white matter and gray matter density compared to pre-operative MRI scans (Tuulari et al., 2016). It is unknown how weight loss might affect brain volume in patients with MS.

Lifestyle factors such as obesity can be modified. It is possible that weight loss may reduce MS-related disability. More research is needed to fully understand this relationship
in MS, but educating patients about obesity, the benefits of living a healthy lifestyle, and maintaining a healthy weight may aid in delaying disease progression.

**Shared Symptoms in MS and Obesity**

There are many shared symptoms between MS and obesity such as impaired mobility, bodily pain, and depression. Obesity may also aggravate MS symptoms and increase the risk of developing other conditions unrelated to MS. Being overweight is associated with more pain in patients with MS (Marck et al., 2017), and can negatively affect mood and emotions (Cambil-Martin et al., 2016). People with MS who are overweight are likely to have higher scores on the EDSS, which implies greater disability (Ben-Zacharia, 2015). Fitzgerald and colleagues (Fitzgerald, Tyry, Salter, et al., 2018) found that patients who reported living a healthy lifestyle and eating a healthy diet had less disability and MS symptom burden.

**Mobility.** Mobility limitations frequently affect individuals living with MS and are usually a major concern for patients and clinicians. Studies indicate that within 15 years of disease onset, approximately 50% of people with MS require at least some assistance walking, such as a cane (Larocca, 2011; Myhr et al., 2001; Weinshenker et al., 1989). Mobility related issues are concerning and can be a source of frustration due to the unpredictable and progressive nature of MS (Bethoux et al., 2011b). Therefore, gait and walking difficulties are routinely assessed. Patients with reduced mobility may have trouble working and maintaining their independence (Halper et al., 2010).

Individuals who are overweight or obese are more likely to have mobility-related disability than patients who do not have excess body fat (Ettinger et al., 1994). In a large study with MS patients recruited using the NARCOMS registry, researchers found that if
a patient-reported having one risk factor associated with cardiovascular diseases like obesity, the individual had a 51% heightened chance of experiencing mobility challenges. Patients with two or more risk factors for cardiovascular diseases, like hypertension and obesity, had increased chances of experiencing mobility challenges by more than 200% (Marrie et al., 2010).

**Fatigue.** Fatigue is the most common symptom that up to 80% of patients with MS report. In addition, fatigue can affect quality of life, ability to work, and overall productivity. Most research on obesity and fatigue focuses on sleep disorders, like sleep apnea. The effect of obesity on physical and mental fatigue is not well understood, although Weiland and colleagues (Weiland et al., 2015) reported that obesity worsens fatigue.

**Mood.** Depression is associated with symptoms of fatigue and anxiety, which are strong predictors of quality of life in MS (Salehpour et al., 2014). Suicidal ideation is also a concern in patients with MS. In one study, 20% of people with MS reported suicidal ideation at least once during 6 months (Viner et al., 2014). Lifetime prevalence rates of depression in patients with MS have been reported around 50% (Patten et al., 2017; Sadovnick et al., 1996), which is roughly two to three times higher than the general population (Patten et al., 2017). Although minor depressive symptoms are more commonly reported, prevalence rates of significant depression in MS range from 27% - 54% (Minden et al., 1987; Zorzon et al., 2001). Patients with both MS and obesity report worse depression, quality of life, and slower ambulation (Fisher et al., 2018). The relationship between mood and BMI is complex and likely bi-directional. Depression levels measured using the Beck Depression Inventory have demonstrated significantly higher rates of depression in overweight versus normal weight patients with MS (Cambil-Martín et al.,
Additionally, patients had worse depression, lower functioning, and worse self-reported health status compared to normal weight people with MS. In another study, individuals MS were assessed for depression before and after bariatric surgery and following the surgery patients had reduced depressive symptoms (Fisher et al., 2018). Obesity is associated with higher levels of depression in the general population and in MS specifically. A behavioral weight loss intervention for patients with MS may help reduce levels of depression and improve overall mood.

**Weight Loss Interventions in MS**

Exploring weight loss interventions for modifiable risk factors in MS, such as obesity, may help alleviate patient disease burden. Few studies have examined behavioral weight loss programs tailored to people with MS. Fitzgerald and colleagues (Fitzgerald, Vizthum, Henry-Barron et al., 2018) examined the effect of calorie restriction (CR) on changes in weight and functional outcomes in MS. Patients were assigned to either the control diet (patients consumed 100% of their calorie needs), the daily CR diet (patients consumed 78% of their calorie needs), or the intermittent CR diet (patients consumed 25% of their calorie needs for 2 consecutive days, then consumed 100% of their calorie needs for 5 days). Body composition, functional status, fatigue, mood, and sleep quality were assessed at baseline and 8-weeks. Overall, their study helped patients with MS lose weight and concluded that the CR diet was safe and feasible, at least in the short-term, for patients with MS. Patients in the CR groups lost a median of 3.4kg, however, changes in weight did not significantly differ by the type of CR diet. Additionally, they found potentially meaningful improvements in emotional health using CR diets. Neither CR group was associated with improvement in FAMS score (Functional Assessment of MS) in comparison to the control
group, and no significant changes in fatigue or sleep quality were observed. This study had two major limitations which were (1) enrolling only patients with RRMS on injectable therapies and (2) the short duration of the study (8 weeks). It is not known if these results are generalizable to all patients with MS patients or if patients could adhere to this sort of diet for a time period longer than 8 weeks. Given these study findings, CR and weight loss represent a promising means of managing clinically relevant MS symptoms, particularly mood symptoms, without imposing significant additional risks.

Another study by Rimmer and colleagues (Rimmer et al., 2013) examined the effect of a 9-month telehealth weight management program for people with various physical disabilities. Of the 91 participants included in study analyses, 37 (40.7%) of them had MS. All of the participants in the study used some sort of ambulatory assistance (e.g., cane, wheelchair, or walker). Patients in this study were assigned to one of three groups: a physical activity, physical activity and nutrition, and the control. The telehealth intervention had a small but significant effect on reduction in body weight in adults with significant physical disabilities. In addition to reducing BMI, patients reported reduced barriers to exercise and improved physical activity levels and eating behaviors, particularly in the combined physical activity and nutrition group. Obesity is a concerning health issue among people with various disabilities, including MS. Weight loss interventions may help identify successful strategies for weight loss and weight maintenance in the MS population.

**Bariatric interventions.** In one study examining the efficacy of bariatric surgery in patients with MS, patients demonstrated significant weight loss and improved mobility when compared to a non-surgical control group (obese people with MS who did not have surgery) (Bencsath et al., 2017). Over a period of 18 months, patients in the surgical group
lost 77% of their excess weight. Bariatric surgery may be a successful option for patients with MS who are severely obese, which is similar to outcomes found in the general bariatric population. Other bariatric case studies involving patients with MS indicate improvements in patients who lose weight after surgery (Flanagan, 1997; Lutrzykowski, 2008).

**Diet interventions.** Special diets proposed for treating MS symptoms have not been subject to rigorous clinical evaluation. While individuals with MS may experience success or failure with special diets, clinicians typically encourage patients to stay away from specific diets and instead adhere to diet and exercise recommendations from the American Heart Association and the American Cancer Society. Few studies have examined the effects of diet modification in patients with MS (Hempel et al., 2017; James et al., 2013). In a study examining a low-fat, plant-based diet, patients had reduced fatigue, reduced BMI, and improved metabolic markers (Yadav et al., 2016). However, patients with MS at all weights were enrolled in the study because the primary aim was to examine the impact of healthy eating, rather than weight loss. Another study examining an intervention utilizing the paleo diet, relaxation training, exercise, and neuromuscular stimulation found significant changes in fatigue and quality of life in a small sample of non-obese SPMS patients (Bisht et al., 2014). In another large study, Fitzgerald and colleagues found that individuals with MS who regularly eat fruits and vegetables have less disability and less symptom burden (Fitzgerald, Tyry, Salter, et al., 2018). The authors found healthy lifestyle behaviors to be associated with reduced depression, pain, fatigue, cognitive impairment, and disability. Although several studies have investigated diet treatments, many questions remain about the role of nutrition in MS.
**Exercise interventions.** Studies examining exercise and MS have found exercise helpful for reducing pain and fatigue, improving mood, and increasing mobility and strength (Motl et al., 2017). In addition to medical and therapeutic treatments for depression, exercise has been found to be especially useful for managing depression (Mura et al., 2014). In a recent review article regarding exercise interventions in MS, researchers found 99 studies that examined various physical activities in MS including exercise training, progressive-resistance training, balance and gait training, and cardiovascular training (Bisson et al., 2017). Many of the studies in the review had significant positive outcomes, but only 9 of the 99 studies examined listed the comorbidities they used as exclusion criteria. Therefore, the findings in some studies may not be generalizable to people with MS who have other health comorbidities.

**Summary**

Though several studies have found an association between healthy lifestyles and MS symptomology and disease activity, no studies have examined whether a comprehensive weight loss program can lead to weight reduction in patients with MS. In the proposed research study, we will investigate the feasibility and acceptability of a group telehealth behavioral weight loss intervention for patients with MS who are obese. Findings of this pilot study will inform future study directions. In addition, we hope that this intervention helps patients with MS lose weight in a timely, cost-effective, and supportive way.
Goals and Hypotheses

The goals of the present study were:

1) Develop and assess the feasibility and acceptability of a 6-month telephone administered behavioral weight loss intervention tailored to individuals with MS. We collected qualitative and quantitative feedback data that will be used to inform future study directions.

2) Examine percent weight loss from baseline to follow-up as the primary outcome variable. We expected patients to demonstrate statistically and clinically significant weight loss at the 6-month follow-up.

3) Assess minutes of physical activity and amount of fruits and vegetables eaten daily in people with MS. We expected that participants would report increased engagement in physical activity, and increased fruit and vegetable consumption at the 6-month time point.
CHAPTER 2

METHODS

Participants

Eight participants were recruited through the University of Kansas Medical Center MS Specialty Clinic. Participants were encouraged to contact us if they were interested in participating in the study after seeing our flyers in the clinic. Participants who met pre-enrollment criteria over the phone were invited for a baseline evaluation and scheduled for an appointment at UMKC. Subjects were paid a total of $100 as compensation for their participation.

Participants had to meet the following criteria for inclusion in the study: (1) a neurologist confirmed diagnosis of MS (RRMS, SPMS, or PPMS disease course); (2) adults ages 18 – 70; (3) access to a phone; (4) fluent in English; (5) ability to walk twenty-five feet without assistance, a PDDS less than six, and no severe sensory or motor impairment; (6) no medically confirmed MS relapse within the past month; (7) no history of dementia or severe cognitive difficulties; (8) a BMI greater than 29 and less than 50; (9) no history of bariatric surgery or planned bariatric surgery; (10) no history of food allergies or the need for a special diet; (11) no concurrent ongoing behavioral or pharmacological weight loss interventions; (12) no history of insulin dependent diabetes or serious pulmonary/cardiac conditions; (13) weight stability with no history of more than a ten pound weight loss or gain in the three months prior to the study; (14) no planned or recent joint replacement surgeries; (15) no serious psychiatric disorder (e.g., schizophrenia), current suicidal ideation, or current binge eating disorder; (16) no current medical conditions where weight loss is contraindicated as indicated by a physician; (17) no contraindications to exercise (answer ‘no’ to all seven questions on the Physical Activity
Readiness Questionnaire [PAR-Q] or physician approval to exercise if answer is ‘yes’ to one or more questions on the PAR-Q. All MS diagnoses will be confirmed with a board-certified neurologist based on established criteria (Lublin et al., 2014).

**Procedure**

A medical release form was completed by the participant at baseline to confirm the participant’s MS diagnosis, and to confirm they had no contraindications to exercise if any questions on the PAR-Q were marked ‘yes.’ Subjects were then enrolled in the study and assigned an ID number. Those who did not meet eligibility criteria or who had contradictions to exercise were excluded. Participants were assessed in person at baseline and 6-months post-intervention. The clinical assessment began by obtaining written informed consent. Each visit lasted approximately 2 hours. Neuropsychological testing, completion of questionnaires, anthropomorphic measurements, and mobility assessments all took place at the University of Missouri-Kansas City (UMKC) Volker Campus.

**Measures**

**Primary Outcome Measures**

**Demographic and disease characteristics.** Participant demographic information was obtained including age, education level, employment status, gender, and ethnicity. Patients reported disease characteristics such as disease duration, medication use, and MS subtype.

**Anthropomorphic.** BMI was used to determine participant eligibility in the study. Weight and height were measured to calculate BMI (Ogden et al., 2012). Participants were instructed to remove their shoes, hats, layered garments, and items from their pockets so that weight, waist circumference, and height could be recorded. Both waist-to-height ratio
(WHtR) and BMI were used to assess obesity status. For WHtR, waist circumference was measured at the thinnest portion of the waist (i.e., between the iliac crest and the bottom portion of the ribs) with a flat measuring tape (Ashwell et al., 2012; Ashwell et al., 2005; Ashwell et al., 2014; Bosnar-Puretic et al., 2009; Hara et al., 2002; Lee et al., 2008; Rodea-Montero et al., 2014). Participants were instructed to exhale during the measurement to improve reliability of the measurement procedures. Waist measurements were repeated three times and the average circumference was recorded and divided by height in inches to calculate WHtR. Blood pressure was recorded using the OMRON 10 series Plus Blood Pressure Monitor Model BP791IT (Omron, 2012; Overs et al., 2012). During the measurement, participants were seated in a comfortable position, with their back leaning against the back of the chair and both arms supported to maintain the upper arm at the level of the heart. The digital blood pressure monitor displayed blood pressure reading and the measurement was recorded at each clinical visit. Anthropomorphic measurements were used to address aim two of our study, to calculate percent weight loss from baseline to follow-up.

**Fruit and vegetable intake.** The self-report Dietary Screener Questionnaire (DSQ) was administered at each in-person assessment and asked participants to report their food choices over the previous month (Fitzgerald, Tyry, Salter et al., 2018; National Cancer Institute, 2018). Monthly frequencies were converted to daily frequencies using regression scoring algorithms provided by the National Health and Nutrition Examination Survey (NHANES) (CDC 2020). Responses on the DSQ were used to address aim three of our study which was to determine whether daily fruit and vegetable consumption increased at follow-up.
**Physical activity.** The Godin Leisure-time Exercise Questionnaire measured self-reported changes in physical activity (Godin et al., 1985; Sikes et al., 2018). The exercise questionnaire was used to address aim three of our study, which was to examine changes in time spent engaging in physical activity.

**Exploratory Outcome Measures**

**Disease status and comorbidities.** In addition to collecting MS disease-related information (disease duration, medication use, and MS subtype) participants provided a list of medications at both clinical visits. Any health changes or changes in medications were recorded throughout the duration of the study. The Patient Determined Disease Steps (PDDS) (Learmonth et al., 2013) was used to measure patient perceived disability status, and the MS Comorbidity Questionnaire was used to gather information regarding other health comorbidities self-reported by the participant (Horton et al., 2010).

**Mobility and fatigability.** The 25-Foot Walk and 6-Minute Walking Task were used to measure mobility before and after the intervention. The 25-Foot Walk is a mobility test designed to assess gait speed (Bethoux et al., 2011a; Fischer et al., 1999). It included two trials where patients were instructed to walk as quickly and as safely as possible from Point A to Point B (25ft apart). The average score for the two timed trials were calculated. The 25-Foot Walk was used to ensure that patients met the mobility criteria necessary to participate in the study. The 6-Minute Walk is a measure of walking speed and endurance (Goldman et al., 2008). Participants were instructed to walk back and forth along a 30-meter stretch for 6 minutes. Laps were monitored throughout the exercise and distance walked after 6 minutes was recorded.
Fatigability was measured by having participants report their current level of fatigue on the 7-item Profile of Mood States-Fatigue (POMS-F) immediately prior to and following the 6-Minute Walk (McNair, 1971). Fatigability was the difference between pre- and post- 6-Minute Walk POMS-F scores.

**Mood.** The Hospital Anxiety and Depression Scale (HADS) is a 14-item self-report measure of depression and anxiety (Bjelland et al., 2002; Watson et al., 2014; Zigmond et al., 1983). Patients answered questions based on a 1-4 scale, where higher values indicate more mood symptoms.

**Quality of life.** The MSQLI was used to measure additional clinical variables like bodily pain and health status, along with changes in overall quality of life that may be associated with weight loss (Fisk et al., 1994; Halpern et al., 2011a; Halpern et al., 2011b; Rivto, 1997). The MSQLI is a self-report measure that thoroughly assesses 10 broad domains of functioning in people with MS; it includes questionnaires of health status, bodily pain, sexual functioning, bladder control, bowel control, mental health status, perceived cognitive deficits, fatigue, social support, and visual impairment.

**Sleep quality.** Sleep quality was measured using the Pittsburg Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI is composed of nine questions on a zero to three Likert scale, that together, analyze seven domains of sleep (Buysse et al., 1989). Component scores were summed to create the PSQI global score (a global score of five or more indicated poor sleep).

**Cognition.** The Brief International Cognitive Assessment for MS (BICAMS) is a neuropsychological battery validated for examining cognitive impairment in MS (Benedict et al., 2012; Langdon et al., 2012). The battery consists of the Symbol Digit Modalities
Test (SDMT), the California Verbal Learning Test 2nd Edition (CVLT-II), and the Brief Visuospatial Memory Test (BVMT). The SDMT (Smith, 1982) is a screening measure that assesses changes in processing speed. Participants were asked to match numbers to geometric shapes according to a key as quickly as they could. Total score after 90 seconds was calculated, and higher values indicate greater information processing speed. The CVLT-II is a comprehensive assessment of verbal learning and memory (Delis, 1987). Participants were asked to freely recall verbal information immediately and after a short and long delay. Higher scores indicate fewer deficits in verbal learning, memory, and recall. Lastly, the BVMT is a test of visuospatial memory that requires participants to draw geometric figures from memory after a brief learning period (Benedict, 1997). The task is repeated three times and a long delay is administered 20 minutes later. Total score after three trials was recorded along with long delay total, learning score, and percent retention. Higher values indicate greater visuospatial memory and learning abilities.

**Delay discounting.** The 27-item Monetary Choice Questionnaire (MCQ) (Kirby, 2000) is a delay discounting task that presents participants with a series of binary questions like, “Would you rather have $10 today, or $20 in 2 days?” Based on responses, a discounting rate \(k\) was computed for each participant. High \(k\) values indicate greater discounting and a preference for small immediate rewards, whereas low \(k\) values demonstrate a lack of discounting and preference for large, delayed rewards. This measure was included because it is related to our previous work (Bruce et al., 2018) and the way participants attribute rewards has been associated with obesity and other decision-making behaviors (impulsivity and self-control) (Amlung et al., 2016).
Study satisfaction. In addition to the measures above, we created a study satisfaction questionnaire to collect qualitative and quantitative feedback from participants about their experience with the behavioral weight loss program. The satisfaction survey was adapted from a survey used in our previous study aimed at improving treatment adherence in patients with MS (Bruce et al, 2016). Questions in this survey asked participants to rate their satisfaction with specific parts of the study such as using the Lose It! app, attending group meetings, and following the diet and exercise guidelines. The survey was used to address aim one of our study, which was to examine the feasibility and acceptability of the intervention.

Weight Loss Interventions

Benefits of obesity intervention in non-neurologic populations. The proposed weight loss intervention was adapted from an intervention provided to breast cancer survivors. The study was a NIH-funded trial that helped breast cancer survivors lose weight and maintain their weight loss (Befort, Klemp, Sullivan et al., 2016). After the 6-month intervention, the average percent weight loss was approximately 13% of body weight. Of the participants who completed the 6-month data collection, 90% lost clinically significant weight (>5%). Results from this clinical study show the ability to help patients with medical conditions lose and maintain clinically significant weight. In this feasibility study, we hope to help patients with MS lose statistically significant weight and better understand how weight loss affects MS symptoms.

Use of telehealth interventions in MS. Telephone interventions are convenient for patients who live in rural areas and for patients who have difficulty traveling. Other studies using phone therapies reported reduced depression and insomnia as well as improvement
in quality of life in patients with MS (Baron et al., 2011; Beckner et al., 2010; Cosio et al., 2011). Overall, interventions over the phone reduce cost and increase the availability of individuals who can receive the necessary care.

**Current Weight Loss Intervention**

The primary aim of the intervention is to help patients with MS lose weight over a period of six months. Weight loss will be achieved by encouraging participants to decrease the number of calories eaten each day and increase minutes of physical activity. The goal was to lose weight at approximately 1 to 2 pounds per week for 24 weeks, with the goal of a 10% reduction from their baseline weight. Throughout the program, strategies like self-monitoring, social support, goal setting, and motivational interviewing were used to help participants achieve weight loss.
The program incorporated educational components, like how to read nutrition labels, create a well-balanced meal, and measure proper portion sizes. Weekly modules were customized to the needs of people with MS. Table 1 provides a full list of the modules included in the intervention. MS topics included in the program discussed managing symptoms and relapses, and the benefit of proper nutrition and regular exercise on mood, cognition, and fatigue in MS. In addition, the program informed participants on how to gradually incorporate exercise into their daily routine while considering many MS-related

<table>
<thead>
<tr>
<th>Table 1. Title of modules included in the weight loss intervention.</th>
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<tr>
<td><strong>Example Group Sessions</strong></td>
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<tr>
<td>Getting Started</td>
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<tr>
<td>Self-Monitoring</td>
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<td>Get Moving for Better Health</td>
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<td>Goal Setting for Success</td>
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<tr>
<td>Getting the Social Support You Need</td>
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<tr>
<td>Fruits and Veggies: More Matters</td>
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<td>Physical Activity and MS</td>
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<td>Food Labels</td>
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<td>Eating on the Go</td>
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<td>Take Charge of What’s Around You</td>
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<td>Eating More for Less</td>
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<td>Eating at Social Gatherings</td>
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<td>Overcoming MS Fatigue and Heat Sensitivity</td>
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<td>Physical Activity with MS Symptoms</td>
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<td>How Do You See Yourself?</td>
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<td>Nutrition and MS Part 1</td>
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<td>Nutrition and MS Part 2</td>
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<td>My Plan</td>
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<tr>
<td>My Plate</td>
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<tr>
<td>Picking up the Pace</td>
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<tr>
<td>Smart Shopping and Portion Control</td>
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<tr>
<td>Coping with Negative Self-Talk</td>
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<td>Managing Stress</td>
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<tr>
<td>Preventing Food Relapses</td>
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<tr>
<td>Planning for Weight Maintenance</td>
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The program incorporated educational components, like how to read nutrition labels, create a well-balanced meal, and measure proper portion sizes. Weekly modules were customized to the needs of people with MS. Table 1 provides a full list of the modules included in the intervention. MS topics included in the program discussed managing symptoms and relapses, and the benefit of proper nutrition and regular exercise on mood, cognition, and fatigue in MS. In addition, the program informed participants on how to gradually incorporate exercise into their daily routine while considering many MS-related
symptoms such as fatigue, mobility, vision impairment, pain, balance disturbances, and heat intolerance.

**Telehealth.** Participants attended weekly group-based counseling sessions over the phone. Phone calls were conducted through UMKC’s Zoom conferencing system. Meetings lasted approximately 60 minutes and all sessions were recorded. Participants were expected to attend at least 75% of the meetings. Meetings began with a weekly check-in, and time for participants to discuss and problem solve barriers that occurred throughout the week. The latter part of the meeting was spent discussing a new diet, physical activity, or behavior change topic. The last 10 minutes of the call were reserved for check-out, which involved setting new goals for the week.

**Diet.** The diet portion of the study suggested that participants eat between 1200-1500 calories a day. Participants were asked to eat 5 or more fruit and vegetable servings per day, eat less than 25% of their calories from fat, and consume 20-30 grams of fiber each day. To help participants adhere to the diet program, they were encouraged to eat prepackaged frozen meals from the grocery store. Appropriate frozen meals had less than 350 calories and less than 9g of fat. Participants could also consume canned soup or other quick meals that followed these same guidelines. Adding fresh or frozen fruit and vegetables to each meal, and consuming calorie-free beverages was recommended. In addition, participants were advised to purchase and consume meal replacement shakes to aid weight loss. If participants did not want to consume frozen meals, they were instructed to consume similar homemade meals that followed the same calorie and fat guidelines.
Physical activity. Participants in this program gradually increased time spent engaging in physical activity each week. Table 2 details the progression of physical activity minutes over the six-month period.

Table 2. Scheduled Activity Progression

<table>
<thead>
<tr>
<th>Week of Program</th>
<th>Days per Week</th>
<th>Minutes per Day</th>
<th>Total Minutes per Week</th>
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<tr>
<td>1 - 2</td>
<td>3</td>
<td>15</td>
<td>45</td>
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<td>3 - 4</td>
<td>3</td>
<td>20</td>
<td>60</td>
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<tr>
<td>5 - 6</td>
<td>3</td>
<td>30</td>
<td>90</td>
</tr>
<tr>
<td>7 - 9</td>
<td>4</td>
<td>30</td>
<td>120</td>
</tr>
<tr>
<td>10 - 24</td>
<td>5</td>
<td>30</td>
<td>150</td>
</tr>
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</table>

Physical activity increased from 15 min/day, 3 days/week to 30 min/day, 5 days/week for a total of at least 150 min/week of moderate intensity physical activity (MPA; defined as 11-14 on the Borg Rating of Perceived Exercise scale) by week 12. Participants interested in exercising more worked up to a goal of 225 minutes of physical activity per week. Strategies to monitor and increase exercise intensity were provided, and appropriate types of physical activities (MPA lasting at least 10 minutes) were discussed with participants. Additionally, strategies to plan for weather and other environmental barriers were addressed as well as strategies for increasing the enjoyment of physical activity.

Symptom management. Symptoms related to fatigue, mobility impairment, vision impairment, pain, balance disturbances, and heat intolerance were monitored and addressed throughout the study. The module Physical Activity with MS Symptoms provided information on methods for eliciting safe and beneficial exercise among patients experiencing MS symptoms. When necessary, modifications and MS-specific exercise
resources were provided (e.g., accessible chair exercises, and online videos for walking, biking, weight resistance, and yoga with MS).

**Self-monitoring.** Throughout the program, self-monitoring behaviors were highlighted as the key weight loss strategy. Participants were instructed to use a web-based app for self-monitoring diet (i.e. Lose It!). In addition, participants were given a Fitbit and an Aria scale to monitor their weight and physical activity. Individuals without internet access and/or those who did not wish to use Lose It! could use paper self-monitoring forms and text or email their weight and physical activity minutes each week.

**Statistical Analyses**

To examine the feasibility and acceptability of the telehealth behavioral weight loss intervention among patients with MS, we first calculated percent weight loss for each participant. We expected patients to demonstrate statistically and clinically significant weight loss at 6 months. We used descriptive statistics, and qualitative and quantitative feedback data to gain information on the intervention’s acceptability, perceived efficacy, enrollment and attendance rates, retention and attrition rates, patient feedback, and reported problems. Paired samples t-tests were used to compare differences in baseline and follow-up data on anthropomorphic measures, self-report questionnaires, mobility, and cognitive performance. Effect sizes were calculated to inform future study directions.
CHAPTER 3
RESULTS

A GROUP BASED WEIGHT LOSS AND HEALTHY LIFESTYLE INTERVENTION FOR PEOPLE WITH MULTIPLE SCLEROSIS: A PILOT STUDY

Keywords: Weight Loss, Healthy Lifestyle, Obesity, Multiple Sclerosis

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A GROUP BASED WEIGHT LOSS AND HEALTHY LIFESTYLE INTERVENTION FOR PEOPLE WITH MULTIPLE SCLEROSIS: A PILOT STUDY

Abstract

**Background:** Modest weight loss can have significant health benefits (Van Gaal et al., 1997). The aims of the present study were to: (1) Develop and assess the feasibility and acceptability of a six-month telehealth, behavioral weight loss program for people with MS (pwMS) and (2) Examine preliminary efficacy of the intervention to help patients lose weight (primary outcome), increase exercise, and increase fruit/vegetable intake at 6-months.

**Methods:** Participants (n=8) were provided with Fitbit® technology and a subscription to the Lose It!® application. Program recommendations included eating 1200 – 1500 calories a day and working up to 150 minutes of moderate intensity physical activity per week, over six months. Group members met weekly to discuss healthy living in MS and attended two individual calls with the group leader.

**Results:** Average percent weight loss was 10% (SD = 7.20). Activity increased from *insufficiently active* (M = 13.0, SD = 14.98) to *active* at follow-up (M = 43.50, SD = 21.31). Fruit, but not vegetable consumption increased significantly, \( t(7) = -2.61, p = .035, d = -0.92, 95\% \text{ CI } [-1.04, -0.05] \). Patient satisfaction scores were favorable, and all participants agreed (12.5%) or strongly agreed (87.5%) that the behavioral weight loss program helped them live a healthier lifestyle.

**Discussion:** Weight loss interventions tailored to people with MS can potentially improve the health and quality of life for hundreds of thousands of patients. Results from this pilot trial will be used to inform the development of a larger randomized control trial examining the efficacy of a weight loss intervention designed specifically for pwMS.
Introduction

The etiology of multiple sclerosis (MS) is unknown, but both genetic and environmental factors likely contribute to disease occurrence. Obesity is a modifiable lifestyle factor that is associated with MS onset, severity, and progression (Tettey, Simpson, Taylor, & van der Mei, 2014). Findings have been largely inconsistent regarding the prevalence of obesity in MS (Marck et al., 2016), but many studies have shown that a significant portion of pwMS can be classified as overweight or obese. Overweight and obesity occurrences range from 33.2% - 62.9% in various samples of pwMS (Cambil-Martin et al., 2016; R. Marrie et al., 2009; Pilutti et al., 2012b; Slawta et al., 2003; Tettey, Simpson, Taylor, Blizzard, et al., 2014).

Obesity in childhood and adolescence increases the risk of developing MS (Ascherio, 2013). Obesity also has an independent effect on MS disability status (Tettey, Simpson, Taylor, Blizzard, et al., 2014). Tettey and colleagues (Tettey, Simpson, Taylor, Blizzard, et al., 2014) found that BMI was associated with more severe clinical disability as measured by the EDSS, such that for every 5kg/m² BMI score, patients on average had a 0.38 higher EDSS score (Tettey, Simpson, Taylor, Blizzard, et al., 2014). Even when controlling for age, gender, disease duration, and a number of health comorbidities, another study found obese pwMS were 1.4 times more likely to have moderate or severe disability when compared to people with MS whose BMI was within normal limits (Marck et al., 2016). PwMS and obesity may also have increased lesion burden and reduced gray matter volume when compared to lean pwMS (Kappus et al., 2016; Mowry et al., 2018).

In addition to contributing to disease onset and severity, comorbid conditions associated with elevated BMI worsen MS disease progression (Marrie et al., 2015; R. A. Marrie et al., 2009). Castro and colleagues (Castro et al., 2019) found that pwMS with higher BMI had greater disease activity and clinical disability after two years. Other research highlights how obesity can negatively influence disease progression and potentially interfere with
disease-modifying treatment response (Guerrero-Garcia et al., 2016; Kvistad et al., 2015). The effects of obesity on disease severity, progression, and MRI findings may be especially pronounced among patients with metabolic syndrome (Berrios Morales et al., 2014; Negrotto et al., 2016).

Elevated BMI may further complicate symptoms of MS including fatigue, mobility problems, depression, and reduced overall quality of life (Luppino et al., 2010; Pilutti et al., 2012a; Salem et al., 2014; Weiland et al., 2015). Excess body weight is associated with other health comorbidities like hypertension, diabetes, and cardiovascular disease which may worsen MS disease progression and disability (Marrie et al., 2015; R. A. Marrie et al., 2009). Prevention and management of comorbidities is important for maintaining health-related quality of life. People with MS and obesity report reduced mental and physical health-related quality of life compared to healthy weight pwMS, even when controlling for age, gender, disability status, and number of comorbidities (Marck et al., 2016). They also report increased fatigue, worse mobility, and more depression (Luppino et al., 2010; Pilutti et al., 2012a; Weiland et al., 2015). More studies are needed to understand the complex relationships between obesity and health outcomes in MS. Most research in this area is cross-sectional and few studies have examined the effects of behavioral weight loss on symptom presentation among pwMS and obesity.

Fitzgerald and colleagues (Fitzgerald, Vizthum, Henry-Barron et al., 2018) examined the effect of caloric restriction on changes in weight and functional outcomes in pwMS. Weight loss and functional outcomes were secondary to examining the safety and feasibility of caloric restriction in a mixed sample of healthy and overweight adults with MS. The authors concluded the diet was safe and feasible, at least in the short-term, and improvements in emotional health were observed but functional outcomes, fatigue levels, and sleep quality were not significantly
changed. Rimmer and colleagues (Rimmer et al., 2013) examined the effect of a 9-month telehealth weight management program for people with various physical disabilities (Rimmer et al., 2013). Of the 91 participants included in the study, 37 (40.7%) had MS. Individuals randomized to the physical activity-only group achieved significant weight loss; however, those in the combined nutrition and physical activity group did not. Despite varied results, participants reported fewer barriers to exercise, and improved physical activity levels. Results from these studies highlight the continued need to examine the impact of weight loss and healthy lifestyle changes in pwMS.

This pilot study is the first to examine a comprehensive telehealth behavioral weight loss program for pwMS. Our protocol was adapted from a study conducted in breast cancer survivors (Befort, VanWormer, DeSouza et al., 2016), where 74% of completers lost 10% of their body weight. The average percent weight loss in the study was 12.8% and participants maintained the weight loss for up to 12-months (Befort, Klemp, Sullivan et al., 2016).

The three aims of the current intervention include: (1) Develop and assess the feasibility and acceptability of the behavioral weight loss program for pwMS; (2) Examine the primary outcome variable, percent weight loss, from baseline to six-month follow-up, and (3) Assess minutes of physical activity and servings of fruits and vegetables eaten daily in pwMS. We expected that patients in the program would demonstrate statistically and clinically significant weight loss at the six-month time point, increase physical activity, and increase consumption of fruits and vegetables.

**Methods**

Participants were recruited into the single-arm, non-randomized pilot study from The University of Kansas Medical Center MS specialty Clinic. The research was approved by the University of Missouri-Kansas City IRB (Project #2016418). Interested participants were screened over the telephone to determine eligibility status. See *Figure 1* for a diagram of
recruitment screening and enrollment. Participants were eligible for the study if they met the following criteria: 18 to 70 years old; a neurologist confirmed diagnosis of MS (Carroll, 2018)

(RRMS, PPMS, SPMS or PRMS but not Clinically Isolated Syndrome); access to a phone and fluent in English; a score ≤ 6 on the Patient Determined Disease Scale (Learmonth et al., 2013) (PDDS) and no severe sensory or motor impairment; no medically confirmed MS relapse in the past month; no history of dementia or severe cognitive difficulties; a BMI > 29 and ≤ 50; no history of bariatric surgery or planned bariatric surgery; no history of food allergies or need for a special diet; no concurrent ongoing behavioral or pharmacological weight loss interventions; no history of insulin dependent diabetes or serious pulmonary or cardiac conditions; weight stability with no history of gaining or losing more than ten pounds in the three months prior to study; no planned or recent joint replacement surgeries; no serious

Figure 1. Flow diagram of pilot trial screening and enrollment.
psychiatric conditions (e.g., schizophrenia), current suicidal ideation, or current eating disorder; no contraindications to exercise (answer to “no” on all seven questions on Physical Activity Readiness Questionnaire [PAR-Q] (Thomas et al., 1992) or physician approval to exercise if one or more questions on the PAR-Q was marked “yes”).

**Measures**

Participants attended two clinical visits (baseline and six-month follow-up) and were compensated a total of $100. At both visits, anthropomorphic measurements were recorded, and participants completed questionnaires about their life, mood, and disease characteristics, as well as surveys regarding their diet, exercise, and sleep habits. At the follow-up, each participant completed an additional study satisfaction questionnaire.

**Demographic and disease characteristics.** Information regarding participant’s age, education level, employment status, sex, and ethnicity were collected. Disease characteristics such as disease duration, medication use, MS subtype, and disability status were also obtained. The PDDS (Learmonth et al., 2013) was used to measure patients’ perceived disability status. Health changes and changes in medications were recorded during individual sessions and at both clinical visits.

**Anthropomorphic measurements.** All measurements were obtained following the strategies outlined in the World Health Organization (WHO) Surveillance Guidelines for Physical Measurements (Organization, 2005). Participants wore no footwear and light clothing to have their weight recorded to the nearest 0.01 pound using a calibrated Health-o-Meter® Model 500KL Eye Level Digital Beam Scale. Height was measured using a Seca® Model 213 Portable Stadiometer. The equation provided by the Center for Disease Control and Prevention (CDC) was used to calculate BMI from participants’ height and weight (lb/in²) (CDC, 2014).

Both waist-to-height ratio (WHtR) and BMI measurements were used to assess changes in obesity status. Staff measured waist circumference at the thinnest portion of the
waist (i.e., between the bottom rib and iliac crest) with a flat measuring tape. Participants were instructed to exhale and relax their arms at their side for each measurement. The process was repeated three times and average waist circumference was recorded for each patient. Waist-to-height ratio was calculated by dividing the average waist circumference by height in inches. To address aim two of our study, percent weight loss was calculated after the six-month assessment.

**Diet quality.** The self-report Dietary Screener Questionnaire (DSQ) was administered at both assessments and asked participants to report their food choices over the previous month (Fitzgerald, Tyry, Salter et al., 2018; National Cancer Institute, 2018). The DSQ addressed aim three of the study by providing daily frequency of fruit and vegetable consumption.

**Physical activity.** The Godin Leisure-time Exercise Questionnaire was administered to assess physical activity status (Godin et al., 1985; Sikes et al., 2018). Responses from the exercise questionnaire provided data regarding time spent engaging in physical activity. Godin scale scores were calculated at baseline and follow-up and classified as *insufficiently active,* *moderately active,* or *active.*

**Exploratory variables.** Additional measures assessing mood and sleep quality were examined as part of the study. The Hospital Anxiety and Depression Scale (HADS) is a self-report scale that assesses levels of depression and anxiety and has been validated in the MS population (Watson et al., 2014). Participants answer 14-items on a scale of one to four, with higher scores indicating greater mood disturbances. Sleep quality was measured using the Pittsburg Sleep Quality Index (PSQI) (Buysse et al., 1989). The PSQI is composed of nine questions (0 to 3 Likert scale), that together, analyze seven domains of sleep (Buysse et al., 1989). Component scores of the PSQI are combined to create a global sleep score (5 or more indicates poor sleep quality).
Table 1. Title of weekly sessions included in the weight loss intervention.

<table>
<thead>
<tr>
<th>Example Group Sessions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Getting Started</td>
</tr>
<tr>
<td>Self-Monitoring</td>
</tr>
<tr>
<td>Get Moving for Better Health</td>
</tr>
<tr>
<td>Goal Setting for Success</td>
</tr>
<tr>
<td>Getting the Social Support You Need</td>
</tr>
<tr>
<td>Fruits and Veggies: More Matters</td>
</tr>
<tr>
<td>Physical Activity and MS</td>
</tr>
<tr>
<td>Food Labels</td>
</tr>
<tr>
<td>Eating on the Go</td>
</tr>
<tr>
<td>Take Charge of What’s Around You</td>
</tr>
<tr>
<td>Eating More for Less</td>
</tr>
<tr>
<td>Eating at Social Gatherings</td>
</tr>
<tr>
<td>Overcoming MS Fatigue and Heat Sensitivity</td>
</tr>
<tr>
<td>Physical Activity with MS Symptoms</td>
</tr>
<tr>
<td>How Do You See Yourself?</td>
</tr>
<tr>
<td>Nutrition and MS Part 1</td>
</tr>
<tr>
<td>Nutrition and MS Part 2</td>
</tr>
<tr>
<td>My Plan</td>
</tr>
<tr>
<td>My Plate</td>
</tr>
<tr>
<td>Picking up the Pace</td>
</tr>
<tr>
<td>Smart Shopping and Portion Control</td>
</tr>
<tr>
<td>Coping with Negative Self-Talk</td>
</tr>
<tr>
<td>Managing Stress</td>
</tr>
<tr>
<td>Preventing Food Relapses</td>
</tr>
<tr>
<td>Planning for Weight Maintenance</td>
</tr>
</tbody>
</table>

Feasibility and acceptability. To measure the feasibility and acceptability of the intervention, a satisfaction questionnaire was adapted from our previous work (Bruce et al., 2016) and administered to collect qualitative and quantitative feedback from participants. Qualitative items asked participants to rate their satisfaction with specific components of the study, such as using the Lose It! app, attending group counseling sessions, and following the diet and exercise guidelines. Other questions asked participants to rate the degree to which different elements of the program influenced their behavior. All questions were based on a zero
to four Likert scale with higher scores indicating greater program satisfaction. Each question provided the opportunity for participants to include qualitative feedback. Additionally, eight items on the survey were open response. These questions inquired about facilitators and barriers to behavior change, perceived benefits, and suggested changes for the intervention.

**Behavioral Weight Loss Program**

The intervention employed several modalities to aid in weight loss, including group and individual counseling via telehealth, technology to aid in self-monitoring, and diet and exercise guidelines to facilitate weight loss. Following the baseline visit, participants were given a premium subscription to the Lose It! phone application, a Fitbit activity tracker, a Fitbit Aria Wi-Fi Scale, and a study binder with materials for each group session.

Participants attended one-hour weekly group calls over the course of six-months. Calls were conducted through UMKC’s Zoom Protected conferencing system and all calls were recorded. The intervention was guided by a motivational and cognitive-behavioral approach. Group leaders worked with participants to promote goal setting, self-monitoring, problem-solving, and relapse prevention. Participants were asked to check in each week during meeting and share progress toward their weekly goals. Each meeting, the focus of discussion involved a new topic (see Table 1), and the final 10-15 minutes of the call was reserved for participants to establish and share new SMART goals for the upcoming week. To encourage accountability, the group leader messaged individuals in the Lose It! application once per week to provide support, feedback, and the opportunity for participants to ask questions, state concerns, and share comments individually. In addition to weekly group calls, participants attended two individual calls during the first and third month (halfway timepoint).
**Diet and physical activity guidelines.** Guidelines for weight loss encouraged participants to log all food and drinks consumed daily in the Lose It! application. Physical activity and weight were monitored using a Fitbit activity tracker and Fitbit Aria scale. A schedule for activity progression was provided to help participants work up to engaging in 150 minutes of moderate intensity physical activity per week (See Table 2). Moderate intensity was defined as an 11 to 14 rating on the Borg Rating of Perceived Exertion Scale (Borg, 1998).

*Table 2. Scheduled activity progression.*

<table>
<thead>
<tr>
<th>Week of Program</th>
<th>Days per Week</th>
<th>Minutes per Day</th>
<th>Total Minutes per Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 - 2</td>
<td>3</td>
<td>15</td>
<td>45</td>
</tr>
<tr>
<td>3 - 4</td>
<td>3</td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>5 - 6</td>
<td>3</td>
<td>30</td>
<td>90</td>
</tr>
<tr>
<td>7 - 9</td>
<td>4</td>
<td>30</td>
<td>120</td>
</tr>
<tr>
<td>10 - 24</td>
<td>5</td>
<td>30</td>
<td>150</td>
</tr>
</tbody>
</table>

Participants were encouraged to eat between 1200 to 1500 calories a day and eat five, one-cup servings of fruit and vegetables per day. Based on previous work (Befort et al., 2016b), additional diet guidelines recommended that participants eat less than 25% of calories from fat, consume 20 to 30 grams of fiber each day, consume entrées with 350 calories or less and less than 9 grams of fat, and drink calorie-free beverages. To make self-monitoring easy and increase initial weight loss, participants were encouraged to eat meals that were easy to track and met the recommended guidelines such as, frozen entrées and meal replacement shakes.

The study team requested that participants weigh in at least one time per week to monitor weight loss progression. We aimed to help participants lose one to two pounds per week over 24 weeks, for a 10% weight reduction from baseline to follow-up.

**Statistical Analyses**
Outcome variables were examined using paired samples t-tests. Average percent weight loss was calculated at follow-up to determine whether participants demonstrated statistically and clinically significant weight loss after engaging in the program. Descriptive statistics along with qualitative and quantitative data were used to examine facilitators and barriers to behavior change, perceived benefits of weight loss and healthy lifestyle practices, and patient satisfaction with the program.

Table 3. Patient demographic and clinical characteristics. Age, disease duration, and education are reported in years. Data averages and standard deviations are reported in mean (SD) format.

<table>
<thead>
<tr>
<th></th>
<th>N = 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>50.00 (9.34)</td>
</tr>
<tr>
<td>Education</td>
<td>17.75 (2.96)</td>
</tr>
<tr>
<td>Ethnicity (Caucasian)</td>
<td>8</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
</tr>
<tr>
<td>Clinical Characteristics</td>
<td></td>
</tr>
<tr>
<td>Relapsing Remitting</td>
<td>8</td>
</tr>
<tr>
<td>Disease Duration</td>
<td>16.71 (12.94)</td>
</tr>
<tr>
<td>PDDS</td>
<td>1.12 (1.55)</td>
</tr>
</tbody>
</table>

Results

Patient characteristics. Eight participants with MS were enrolled and engaged in the 24-week behavioral weight loss program. The final cohort consisted of seven females and one male, with a mean age of 50 (SD = 9.30) years (Table 3). All participants identified themselves as white and averaged 17.75 (SD = 2.96) years of education. Average disease duration for the group was 16.71 (SD = 12.94) years. All participants were diagnosed with a relapsing-remitting disease course, and according to the PDDS, the average participant had mild MS-related disability (M = 1.12, SD = 1.55). Disability status is indicated via
PDDS. A PDDS of 1 corresponds to having some noticeable but minor symptoms from MS with only a minimal effect on lifestyle.

**Primary Outcomes**

![Graph showing percent weight loss from baseline to 6-months](image)

*Figure 2. Percent weight loss calculated at 6-months for each participant. N = 8*

**Weight loss.** Two participants were unable to complete physical measurements at follow-up due to concerns about COVID-19. However, both individuals performed a final weigh-in using their Aria Wifi scale and completed all 6-month questionnaires online via Redcap. Percent weight loss was the primary outcome variable for this study, and altogether, participants averaged a 10.57% (SD = 7.20) weight reduction from baseline. Seventy-five percent (6 out of 8) of the cohort lost over 5% of their body weight which is considered clinically significant weight loss (Williamson et al., 2015); sixty-three percent (5 out of 8) lost over 10% of their body weight. Twenty-five percent (2 out of 8) lost very little (< 2%) or no weight. See *Figure 2* for percent weight loss per participant. *Table 4* displays results from paired samples t-tests that compared anthropomorphic measurements,
diet quality, and physical activity status pre- and post-intervention. All analyses involving anthropomorphic changes were significant at the .05 alpha level.

Table 4. Paired samples t-test results comparing baseline and follow-up anthropomorphic measurements, self-reported diet quality and physical activity status, and other exploratory variables. Data averages and standard deviations are reported in mean (SD) format. *missing n=2 for follow-up, b1 cup = 1 serving, p <0.05

<table>
<thead>
<tr>
<th>Anthropomorphic Measurements</th>
<th>Baseline</th>
<th>6-month</th>
<th>M</th>
<th>SD</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BMI (lbs/in²)</strong></td>
<td>37.56 (6.56)</td>
<td>33.35 (6.71)</td>
<td>4.21</td>
<td>2.62</td>
<td>2.02, 6.40</td>
<td>4.55</td>
<td>7</td>
<td>.003*</td>
<td>1.61</td>
</tr>
<tr>
<td><strong>Waist Circumference (in)</strong></td>
<td>43.45 (3.13)</td>
<td>38.45 (4.73)</td>
<td>5.00</td>
<td>3.68</td>
<td>1.14, 8.86</td>
<td>3.33</td>
<td>5</td>
<td>.021*</td>
<td>1.36</td>
</tr>
<tr>
<td><strong>Waist-to-Height Ratio</strong></td>
<td>.67 (0.07)</td>
<td>.59 (0.09)</td>
<td>0.08</td>
<td>0.02</td>
<td>0.02, 0.13</td>
<td>3.50</td>
<td>5</td>
<td>.017*</td>
<td>1.43</td>
</tr>
<tr>
<td><strong>Weight (lbs)</strong></td>
<td>223.20 (33.86)</td>
<td>199.13 (30.70)</td>
<td>24.08</td>
<td>16.24</td>
<td>10.50, 37.65</td>
<td>4.20</td>
<td>7</td>
<td>.004*</td>
<td>1.48</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Physical Activity</th>
<th>Baseline</th>
<th>6-month</th>
<th>M</th>
<th>SD</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Godin Scale Score</strong></td>
<td>13.00 (14.98)</td>
<td>43.50 (21.31)</td>
<td>-30.5</td>
<td>25.89</td>
<td>-52.14, -8.86</td>
<td>-3.33</td>
<td>7</td>
<td>.013*</td>
<td>-1.18</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diet Quality</th>
<th>Baseline</th>
<th>6-month</th>
<th>M</th>
<th>SD</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSQ Fruit</strong></td>
<td>0.78 (0.33)</td>
<td>1.33 (0.28)</td>
<td>-0.54</td>
<td>0.59</td>
<td>-1.04, -0.05</td>
<td>-2.61</td>
<td>7</td>
<td>.035*</td>
<td>-0.92</td>
</tr>
<tr>
<td><strong>DSQ Vegetable</strong></td>
<td>1.46 (0.52)</td>
<td>1.73 (0.09)</td>
<td>-0.26</td>
<td>0.73</td>
<td>-0.87, 0.35</td>
<td>-1.01</td>
<td>7</td>
<td>.346</td>
<td>-0.36</td>
</tr>
<tr>
<td><strong>DSQ Fruit &amp; Vegetable</strong></td>
<td>2.27 (0.72)</td>
<td>3.14 (0.62)</td>
<td>-0.85</td>
<td>1.13</td>
<td>-1.80, 0.09</td>
<td>-2.14</td>
<td>7</td>
<td>.070</td>
<td>-0.76</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Exploratory Variables</th>
<th>Baseline</th>
<th>6-month</th>
<th>M</th>
<th>SD</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HADS Total</strong></td>
<td>8.38 (5.50)</td>
<td>5.75 (4.71)</td>
<td>2.63</td>
<td>3.07</td>
<td>0.06, 5.19</td>
<td>2.42</td>
<td>7</td>
<td>.046*</td>
<td>0.86</td>
</tr>
</tbody>
</table>
Average BMI was significantly decreased by 4.55 lbs/in$^2$ at follow-up $t(7) = 4.55$, $p = .003$, $d = 1.61$, 95% CI [2.02, 6.40], and average waist circumference decreased by 5.00 inches $t(7) = 3.33$, $p = .021$, $d = 1.36$, 95% CI [1.14, 8.86]. Participants’ weight significantly decreased an average of 24.08lbs from baseline to follow-up, $t(7) = 4.20$, $p = .004$, $d = 1.48$, 95% CI [10.50, 37.65].

<table>
<thead>
<tr>
<th>Score type</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>t</th>
<th>df</th>
<th>p</th>
<th>95% CI</th>
<th>d</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>HADS Anxiety</td>
<td>5.25 (2.76)</td>
<td>4.25 (3.12)</td>
<td>1.00</td>
<td>1.53</td>
<td>-0.55, 2.55</td>
<td>1.53</td>
<td>7</td>
<td>0.170</td>
<td>0.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS Depression</td>
<td>3.13 (2.90)</td>
<td>1.50 (1.69)</td>
<td>1.63</td>
<td>1.85</td>
<td>0.08, 3.17</td>
<td>2.49</td>
<td>7</td>
<td>0.042*</td>
<td>0.88</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PDDS</td>
<td>1.13 (1.55)</td>
<td>0.13 (0.35)</td>
<td>1.00</td>
<td>1.60</td>
<td>-0.34, 2.34</td>
<td>1.76</td>
<td>7</td>
<td>0.121</td>
<td>0.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSQI</td>
<td>9.25 (4.83)</td>
<td>8.25 (4.20)</td>
<td>1.00</td>
<td>3.66</td>
<td>-2.06, 4.06</td>
<td>0.77</td>
<td>7</td>
<td>0.465</td>
<td>0.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFIS-5</td>
<td>4.13 (3.76)</td>
<td>5.50 (3.70)</td>
<td>-1.38</td>
<td>2.45</td>
<td>-3.42, 0.67</td>
<td>-1.59</td>
<td>7</td>
<td>0.156</td>
<td>-0.56</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 3. Changes in Godin Scale Scores per participant from baseline to follow-up. Scores are interpreted as < 14 = Sedentary, 14 – 23 = Moderately Active, > 24 Active.
Physical activity. The Godin Leisure-Time Exercise questionnaire has been shown to be a sensitive measure for detecting change in physical activity in MS exercise interventions (Amireault et al., 2015; Godin et al., 1985; Sikes et al., 2018). At baseline, participants’ average Godin Scale score was 13.00 (SD = 14.98), which can be interpreted as insufficiently active or sedentary. Average score at follow-up was categorized in the active range (M = 43.50, SD = 21.31). Figure 3 demonstrates changes in Godin Scale score per participant. Average mean difference was approximately 30 points, or a 70% increase in reported physical activity from baseline to follow-up \( t(7) = -3.33, p = .013, d = -1.18, 95\% \text{ CI} [-52.14, -8.86] \).

Diet quality. Self-reported intake of fruit and vegetables increased at follow-up, but only predicted intake of fruit (1-cup servings) per day was statistically significant. At both time points, average fruit and vegetable intake fell below the recommended 5 servings per day. On average, daily fruit intake at baseline was 0.54 servings (SD = 0.59) lower than values at follow up \( t(7) = -2.61, p = .035, d = -0.92, 95\% \text{ CI} [-1.04, -0.05] \). Predicted intake of vegetables (including legumes) was not significantly different from baseline to follow-up \( (M_{\text{diff}} = -0.26, SD_{\text{diff}} = 0.73) \), but a small to medium effect was found \( t(7) = -1.01, p = .346, d = -0.36, 95\% \text{ CI} [-0.87, 0.35] \). Combined intake of fruits and vegetables (including legumes) were not significantly different \( (M_{\text{diff}} = -0.85, SD_{\text{diff}} = 1.13) \), but there was a large effect size \( (d = -0.76) \).

Exploratory Outcomes

Sleep, mood, disability status, and fatigue. No significant change in sleep quality was observed \( (M_{\text{diff}} = 1.00, SD_{\text{diff}} = 3.66) \) and the effect size was small \( (d = 0.27) \). Mean difference on the PSQI also did not reach the threshold for minimal clinically important
difference (≥3) (McDonnell et al., 2014). Average baseline score on the HADS instrument was within the subclinical range, (Watson et al., 2014) but a significant decrease was still observed at follow-up, $t(7) = 2.42, p = .046$, $d = 0.86$, 95% CI [0.06, 5.19]. Scores on the depression subscale indicated that participants reported significantly fewer depressive symptoms at follow-up, $t(7) = 2.49, p = .042$, $d = 0.88$, 95% CI [0.08, 3.17]. No significant change in reported anxiety symptoms was found, $t(7) = 1.53, p = 0.170$, $d = 0.54$, 95% CI [-0.55 to 2.55], but a medium effect size was observed. Similarly, perceived disability status ratings decreased at follow-up but were not statistically different, $t(7) = 1.76, p = 0.121$, 95% CI [-0.34, 2.34]; however, a medium effect size was found ($d = 0.62$). Scores on the MFIS-5 were not significantly different ($M_{diff} = -1.11$ [95% CI, -8.10, 5.88], $P = 0.718, d = -0.133$) but averages increased suggesting a greater effect of fatigue on patients at follow-up. Effects observed on this measure did not fall within the reliable change indices (Cozart et al., 2021), but it is possible the effects of summer temperatures, stress related to COVID, and other psychosocial factors weighed more heavily on participants at follow-up, as opposed to initial ratings.

**Feasibility and acceptability.** On average, participants attended 72.4% ($SD = 29.8$%) or approximately 17 ($SD = 7.15$) of the 24-weekly sessions. All participants attended both individual calls. No individuals withdrew from the study; however, two participants indicated the time of the group calls (Tuesday evenings) made it difficult for them to regularly participate.
Responses gauging feasibility and acceptability of the study were favorable. All participants agreed (12.5%) or strongly agreed (87.5%) that the behavioral weight loss program helped them live a healthier lifestyle. Most participants indicated the group and individual counseling sessions were very influential (62.5%) or extremely influential (25%) in helping them lose weight.

The majority of participants agreed (37.5%) or strongly agreed (50.0%) that they increased the amount of fruit and vegetables eaten daily due to their participation in the program. Similarly, over 75% of participants agreed (25%) or strongly agreed (62.5%) that they increased time spent engaging in daily physical activity due to the program. 

Figure 4 provides satisfaction ratings that reference various program components. Only one rating averaged below “very satisfied” which was the question asking participants to rate their satisfaction with the frequency of the individual calls. Approximately 63% of the group recommended that individual calls should occur more frequently, with most participants (38%) indicating they preferred monthly individual meetings.

Figure 4. Satisfaction ratings collected from participants at six-month follow up. Rating responses ranged from (0) Not at all satisfied to (4) Extremely satisfied.
Quotes obtained from qualitative responses on the SSQ provided information regarding facilitators and barriers to behavior change. Table 5 contains participant quotes extracted from the survey that are categorized based on themes that appeared. Barriers to behavior change included the effect of the COVID-19 quarantine on work and family schedules (e.g., increased hours and workload and homeschooling children), inconvenient group call time, health problems unrelated to MS, and difficulty prioritizing diet and exercise consistently. Others noted that the COVID-19 quarantine provided them with more time to exercise and helped extinguish habits that attributed to previous weight gain (i.e., eating out regularly). Additional facilitators to behavior change included simple and easy activity tracking, setting weekly SMART goals, accountability of weekly check-ins, self-monitoring, and encouragement from counselors. Overall, individuals who had less success in the program tended to report greater life stressors, mood symptoms, COVID stress, and health problems unrelated to MS.

Table 5. Quotes from the Satisfaction with Study Questionnaire that pertain to program feasibility and acceptability.

<table>
<thead>
<tr>
<th>Quotes Highlighting Acceptability</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Theme</strong></td>
</tr>
<tr>
<td>Efficacy</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Support</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
If I wanted to share something, I did. If not, I was okay to just listen! It was all helpful. I really enjoyed the conversation, the ribbing, the give and take from everyone! It provided mental support knowing there are others out there going through the same things.

| Goal Achievement | For years I had not been that active, so this was a big change for me…I could do the elliptical and worked up in total minutes spent for the weeks pretty well! Better than I expected!

I was able to meet or exceed all expectations.

I was able to redirect myself back to eating healthy and being mindful of what I was eating again. I had been previously and lost sight of it. |
| --- | --- |

| Perceived Improvements | I'm so glad I've been eating a more healthy diet! I feel so much better!

I could even tell when riding my bike; how much easier, in a sense, it seems compared to back before the study.

I just feel better overall. More active, happier, more self-confidence. |
| --- | --- |

| Barriers to Behavior Change | The calls were inconvenient for me with kids at home and during dinnertime. It would've been more helpful for me to have a group chat versus weekly timed phone calls.

I am having a hard time in general with weight loss. It has nothing to do with the success of the program but my own mindset with covid19 and my kids home 24/7 and feeling like I'm in survival mode. I would stick to it for a while and then fall off track. There is just so much going on right now that I'm having a hard time focusing only on my own diet and exercise.

Had difficulty finding certain foods [in the app] sometimes.

I did increase my activity, just not as much as I would have liked to. This was due in part to the nature of my job changing which forced me to sit more hours in a day.

This covid 19 time was extra hard to deal with everything-- At times that made following through with both the eating and physical exercise components a challenge, but worth it!

I think I am fighting some other health problems. |
| --- | --- |

| Facilitators of Behavior Change | Regular weigh in's and simple/easy step tracking were extremely motivational! It was very affirming to see the pounds melt away and the little fireworks display on the Fitbit when I met my step goal each day!

COVID-19 and quarantines helped actually. I was available every week because of it.

Setting weekly goals on the calls and knowing that I would have to report whether or not I had met my goals was motivational for me.

Logging increases accountability.

I would add that in addition to Lose It!, I began the study by purchasing a NutriBullet and perhaps most helpful of all, a small digital food scale. Both of those pieces of hardware made regulating and recording my food intake so much easier! |
Loved the app! It recognized every food I scanned. I have used previous apps that don't.

The time out of time the pandemic provided was so serendipitous! I had abundant time to exercise and a space to break away from old eating and activity habits that were so unhealthy!

Encouragement from counselor that I was doing well when I felt that I was not from time to time.

Participants reported improvements in overall fitness, self-confidence, energy level, and mood. Table 6 provides percent agreement ratings related to perceived benefits of weight loss and healthy lifestyle practices. All participants agreed or strongly agreed the program provided them with adequate resources to be successful. Over 75% of participants agreed that their mood and fatigue were improved due to healthy lifestyle changes made in the program, and all participants agreed or strongly agreed their stamina improved. The majority of participants did not report perceived improvement in pain levels or cognition.
Table 6. Agreement ratings from perceived benefit questions on satisfaction survey. Ratings range from (0) *Strongly disagree* to (4) *Strongly agree*. Percent agree total is the sum of percent agree and percent strongly agree.

<table>
<thead>
<tr>
<th>% Strongly Disagree</th>
<th>% Disagree</th>
<th>% Neither Agree or Disagree</th>
<th>% Agree</th>
<th>% Strongly Agree</th>
<th>% Agree Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>This program provided me with adequate resources to be successful.</td>
<td>-</td>
<td>-</td>
<td>25%</td>
<td>75%</td>
<td>100%</td>
</tr>
<tr>
<td>My pain level has improved due to the healthy lifestyle changes I have made.</td>
<td>-</td>
<td>-</td>
<td>62.5%</td>
<td>25%</td>
<td>12.5%</td>
</tr>
<tr>
<td>My mobility has improved due to the healthy lifestyle changes I have made.</td>
<td>-</td>
<td>-</td>
<td>37.5%</td>
<td>37.5%</td>
<td>25%</td>
</tr>
<tr>
<td>My mood has improved due to the healthy lifestyle changes I have made.</td>
<td>-</td>
<td>-</td>
<td>12.5%</td>
<td>62.5%</td>
<td>25.0%</td>
</tr>
<tr>
<td>My cognition has improved due to the healthy lifestyle changes I have made.</td>
<td>-</td>
<td>12.5%</td>
<td>50.0%</td>
<td>37.5%</td>
<td>-</td>
</tr>
<tr>
<td>My stamina has improved due to the healthy lifestyle changes I have made.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>62.5%</td>
<td>37.5%</td>
</tr>
<tr>
<td>My fatigue has improved due to the healthy lifestyle changes I have made.</td>
<td>-</td>
<td>-</td>
<td>25.0%</td>
<td>37.5%</td>
<td>37.5%</td>
</tr>
<tr>
<td>This behavioral weight loss program helped me live a healthier lifestyle.</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>12.5%</td>
<td>87.5%</td>
</tr>
<tr>
<td>I have increased the amount of physical activity I engage in daily.</td>
<td>-</td>
<td>-</td>
<td>12.5%</td>
<td>25%</td>
<td>62.5%</td>
</tr>
<tr>
<td>I have increased the amount of fruits and vegetables I eat daily.</td>
<td>-</td>
<td>-</td>
<td>12.5%</td>
<td>37.5%</td>
<td>50.0%</td>
</tr>
</tbody>
</table>

**Discussion**

This pilot study is the first comprehensive behavioral weight loss intervention delivered to patients with MS. Favorable results demonstrate the feasibility and
acceptability of the six-month telehealth program. Participants were motivated to participate in the group calls, as demonstrated by an average attendance rate of 72%. Mean percent weight loss was 10.57% and all anthropomorphic measurements were significantly decreased at follow-up. When averaged across the group, physical activity status increased from *insufficiently active* to *active*. Fruit intake was significantly increased from baseline and all fruit and vegetable variables on the DSQ were higher at follow-up. Although we did not observe significant changes in combined fruit and vegetable intake, a large effect size was found (0.76). Anxiety ratings and perceived disability were exploratory variables that were not statistically different from baseline to post-treatment, but both had medium effect sizes (0.54 and 0.62, respectively). It is possible that results may approach statistical significance given larger sample sizes in the future.

It is worth noting that this study took place from late February 2020 to mid-August 2020, in the middle of the COVID-19 pandemic. No participants reported being diagnosed with COVID-19 throughout the duration of the study, but two participants were unable to complete the follow-up assessment due to concerns about COVID-19. All participants completed 6-month questionnaires online via Redcap to reduce time spent in-person at the 6-month visit. COVID-19 affected each participant differently; some participants reported an abundance of time and flexibility in scheduling that had not existed before and that allowed them to focus more energy on their weight loss efforts. Similarly, most participants were not traveling, eating out at restaurants as often, or gathering for social events and meals which may have helped facilitate weight loss. On the other hand, individuals reported a significant increase in life stressors due to the pandemic that made focusing on weight loss more challenging. Increased workload, schedule changes, homeschooling children,
and health concerns were some of the stressors participants noted. Gym closures also made exercise more challenging for some participants.

Qualitative and quantitative data from the SSQ demonstrated that participants felt positively about the group and individual telehealth meetings. Future interventions should continue to employ telehealth options to make weight loss and healthy lifestyle interventions widely accessible to people with MS. Some individuals had difficulty joining the group calls due to work and family schedules. Continued interventions could incorporate online platforms (Beleigoli et al., 2018) in addition to calls to allow participants to share information and progress at their convenience. Most participants commented that the group provided them with a source of social support and accountability. Several participants indicated the program helped them feel better about themselves and feel better physically, without being too restrictive or difficult to adhere to. Most individuals agreed that the program helped improve their fatigue, energy level, stamina, and mood. Participants also agreed that the program helped them eat more fruits and vegetables, engage in more physical activity, and live a healthier lifestyle overall.

Several limitations of this pilot study must be mentioned, including the absence of a control group. This was not a randomized controlled trial and staff was not blind to treatment. Next steps in our research involve conducting a randomized controlled trial to evaluate the effectiveness of this modality for weight loss and creating healthy lifestyle changes in MS. Similarly, this was a small, pilot trial that consisted of eight people who all identified as white and had RRMS. To better understand the generalizability of these findings and increase external validity, larger, and more diverse cohorts should be included. Here we assessed diet and exercise outcomes via patient self-report. Future studies should
incorporate objective outcome measures such as accelerometry to best examine physical activity changes due to the intervention. Lastly, this study did not include a maintenance phase to monitor the participant’s ability to lose weight and keep it off. Long-term outcomes with the addition of a maintenance phase are needed to better understand weight loss progress and whether weight loss is maintained over time.

Obesity is a risk factor for developing serious health conditions, including MS (Guerrero-Garcia et al., 2016). Overweight and obese individuals are at increased risk for developing MS, and the pro-inflammatory state associated with obesity may contribute to increased disease activity in MS. Evidence from this pilot study provides a promising approach for promoting healthy lifestyle behavior changes and weight loss in pwMS. Results from this trial demonstrate good feasibility and mark the first step in establishing that clinically significant weight loss can be achieved through this program. We adapted and developed a program composed of many elements (group and individual counseling via telehealth, self-monitoring, and technology) that were largely acceptable for pwMS. We are currently conducting a randomized controlled trial informed by this pilot study to further evaluate the effectiveness of the intervention. Given the relationship between MS and obesity, future studies may want to explore whether behavioral weight loss can reduce MS symptoms and slow disease progression.
Additional Outcomes

Patient characteristics. Figure 5 displays weight differences from baseline to follow-up for each participant. All but two participants lost clinically significant weight. Number of participant self-reported health comorbidities were recorded at both clinical visits (Table 7). Average number of health comorbidities was 2.50 at baseline ($SD = 1.31$) and 2.75 at follow-up ($SD = 1.58$). Reported number of comorbidities increased at follow-up, but changes were not statistically significant, $t(7) = -0.607, p = .563, d = -0.215$, [95% CI -1.22, 0.72]. Individuals who reported more health comorbidities at baseline loss less weight ($r = -.815, p = .014$). The average number of prescription drugs taken at baseline ($M = 3.38, SD = 1.19$) and follow-up ($M = 3.38, SD = 1.19$) were equal. Six out of eight individuals in the study reported taking a disease-modifying drug. Participants who
reported taking more medications loss less weight ($r = -0.801, p = 0.017$). All participants indicated they did not currently smoke; five individuals disclosed they were never smokers, and three participants reported smoking regularly in the past.

*Table 7. Frequency of self-reported health comorbidities at baseline and follow-up.*

<table>
<thead>
<tr>
<th>Self-Reported Health Comorbidity Frequencies ($N = 8$)</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Cholesterol (Hyperlipidemia)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>High Blood Pressure (Hypertension)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Disease of Arteries in the Legs (Peripheral Vascular Disease)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Lung Trouble (Asthma, Emphysema, Chronic Bronchitis, COPD)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Skin Cancer</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Migraine</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Thyroid Disease (Graves' disease, Hashimoto's, Thyroiditis; not Thyroid Cancer)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Vitamin B12 Deficiency (Pernicious Anemia)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Degenerative Arthritis (Osteoarthritis)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Hip Replacement (s)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anemia or other Blood Disease</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Open Sore or Ulcer in Lining of the Stomach, Esophagus, Duodenum (Peptic Ulcer Disease)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Liver Problems (Cirrhosis)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Anxiety</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

**Anthropomorphic measurements.** Two participants were unable to complete physical measurements at follow-up due to concerns about COVID-19. Therefore, only six participants had blood pressure assessed at follow-up. Average systolic blood pressure at baseline ($M = 122.67$ mmHg, $SD = 5.13$) was higher than measurements recorded at follow-up ($M = 118.00$ mmHg, $SD = 12.08$), but changes were not significantly different, $t(5) = 1.31, p = .247$, 95% CI [-4.50, 13.83]. Similarly, diastolic blood pressure was higher at baseline ($M_{\text{diff}} = 4.67$, $SD_{\text{diff}} = 7.94$) but not significantly different, $t(5) = 1.44, p = 0.210$, 95% CI [-3.67, 13.00]. Effect sizes for systolic and diastolic measurements fell within the medium effect size range ($d = 0.53$ and $d = 0.59$, respectively).
Feasibility and acceptability. Average participant attendance for group calls was 72% (SD = 29.8%). See Figure 6 for weekly attendance totals. Mean number of sessions attended was 17 (SD = 7.15) out of 24 total.

![Pilot Weekly Attendance](image)

Figure 6. Number of participants who attended each weekly group call.

Additional Exploratory Outcomes

Cognition. Table 8 displays paired sample t-test results comparing objective cognitive performance at baseline and follow-up. No significant differences were found between comparisons of neuropsychological test performance. Participants tended to have equal performances at both visits. The only cognitive measure that differed by at least two points from baseline to follow-up was the sum of scores on trials one through three of the BVMT. Values increased by 3.67 points at follow-up, but changes were not significantly different ([95% CI, -9.74, 2.40], \( P = 0.181, \ d = -0.63 \)). Although results were not statistically significant, a medium effect size was found.
Table 8. Paired samples t-test results comparing baseline and follow-up cognitive performance. Data averages and standard deviations are reported in mean (SD) format. $N = 6$, *$p < 0.05$

<table>
<thead>
<tr>
<th>Cognitive Testing</th>
<th>Baseline</th>
<th>6-month</th>
<th>Mean</th>
<th>SD</th>
<th>95% CI</th>
<th>$t$</th>
<th>df</th>
<th>$p$</th>
<th>$d$</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDMT Total</td>
<td>52.33 (10.33)</td>
<td>52.67 (10.84)</td>
<td>-0.33</td>
<td>3.72</td>
<td>-4.24, 3.57</td>
<td>-0.22</td>
<td>5</td>
<td>0.835</td>
<td>-0.09</td>
</tr>
<tr>
<td>CVLT Trials 1-5</td>
<td>55.17 (2.48)</td>
<td>56.50 (4.81)</td>
<td>-1.33</td>
<td>6.74</td>
<td>-8.41, 5.74</td>
<td>-0.48</td>
<td>5</td>
<td>0.649</td>
<td>-0.20</td>
</tr>
<tr>
<td>CVLT Delay</td>
<td>11.67 (2.58)</td>
<td>11.67 (2.80)</td>
<td>0.00</td>
<td>1.26</td>
<td>-1.33, 1.33</td>
<td>0.00</td>
<td>5</td>
<td>1.000</td>
<td>0.00</td>
</tr>
<tr>
<td>BVMT Trials 1-3</td>
<td>25.67 (4.50)</td>
<td>29.33 (4.59)</td>
<td>-3.67</td>
<td>5.79</td>
<td>-9.74, 2.40</td>
<td>-1.55</td>
<td>5</td>
<td>0.181</td>
<td>-0.63</td>
</tr>
<tr>
<td>BVMT Delay</td>
<td>10.33 (1.21)</td>
<td>10.33 (2.73)</td>
<td>0.00</td>
<td>2.00</td>
<td>-2.10, 2.10</td>
<td>0.00</td>
<td>5</td>
<td>1.000</td>
<td>0.00</td>
</tr>
</tbody>
</table>

**Mobility and fatigability.** Mobility, as measured by the 25-foot walk did not change significantly from baseline to follow-up (see Table 9). On average, participants shaved 0.35 seconds off their walk time, but the difference was not statistically significant ([95% CI, -0.27, 0.97], $P = 0.208$, $d = 0.59$); however, a medium effect size was detected. Fatigability was assessed via self-reported fatigue on the POMS-F questionnaire pre- and post- 6-minute walk. On average, fatigability decreased by one point, and the change was not significantly different ([95% CI, -1.10, 3.10], $P = 0.275$, $d = 0.50$), but a medium effect size was found. Six-minute walk distance decreased by 19.69 meters (approximately 26 ¼ steps) from baseline to follow-up ([95% CI, -5.44, 44.83], $P = 0.100$, $d = 0.82$). Results were not significantly different, but a large effect size was detected. Due to COVID-19 protocols, participants were required to wear a mask at the follow-up assessment whereas no mask was required at baseline. Over half of participants reported that wearing a mask while walking made it challenging to breathe and made them feel overheated. It is possible that difficulty breathing, and heat sensitivity contributed to the observed effect.
Quality of life. The MSQoL inventory is composed of several different measures that assess factors associated with quality of life in MS. Overall, scores on the inventory did not significantly differ from baseline and follow-up. Table 10 provides paired samples t-test results for all quality-of-life variables in the questionnaire.

Although not statistically significant, average mental health score (as measured by the HSQ) increased from baseline by 5.51 ± 7.50, and a large effect size was detected [95% CI, -11.78, 0.76], \( P = 0.076, d = -0.735 \). Higher scores at follow-up indicate better mental health. Physical health scores remained roughly the same (\( M_{\text{diff}} = -0.58 \) [95% CI, -3.54, 2.39], \( P = 0.660, d = -0.162 \)). The MHI is also used to assess mental health in the MSQoL. Total scores on the MHI increased at follow-up but were not significantly different (\( M_{\text{diff}} = -1.11 \) [95% CI, -8.10, 5.88], \( P = 0.718, d = -0.133 \)). The MHI can be broken down into four subscales - anxiety, depression, behavior control, and positive affect. The depression subscale was the only one that increased at follow up, indicating improvement in depressive symptoms. Scores increased by 5.00 ± 8.02 from baseline and the change was not significant, [95% CI, -11.70, 1.70], \( P = 0.121, d = -0.624 \) however, a large effect size was observed.
Scores on the MFIS-5 were not significantly different ($M_{diff} = -1.11$ [95% CI, -8.10, 5.88], $P = 0.718$, $d = -0.133$) but averages increased suggesting a greater effect of fatigue on patients at follow-up. It is possible the effects of summer temperatures and COVID related psychosocial factors weighed more heavily on participants at follow-up, as opposed to initial ratings.

Pain (PES), sexual satisfaction (SSS), and bladder control (BLCS) were improved at follow-up, but not significantly. See Table 6 for comparisons. Lower scores for sexual satisfaction indicate fewer sexual problems, and likewise, lower scores for the BLCS demonstrate fewer problems associated with bladder control. A medium effect size was observed for both sexual satisfaction ($d = 0.521$) and bladder control ($d = 0.536$). Responses on the bowel control scale (BWCS) remained the same ($M_{diff} = 0.00$ [95% CI, -1.41, 1.41], $P = 1.000$, $d = 0.000$).

A small effect size was detected for changes regarding perceived cognitive impairment (PDQ). Scores on the PDQ decreased at follow up suggesting fewer perceived cognitive difficulties but results were not statistically significant ($M_{diff} = 1.00$ [95% CI, -1.53, 3.53], $P = 0.381$, $d = 0.331$). A small effect size was detected.

Finally, perceived social support ratings increased from baseline to follow-up but did not reach statistical significance ($M_{diff} = -9.38$ [95% CI, -30.03, 11.28], $P = 0.319$, $d = -0.379$). A small effect size was founding indicating participants trended towards greater perceived social support.
Table 10. Paired samples t-test results comparing baseline and follow-up quality of life ratings. Data averages and standard deviations are reported in mean (SD) format. N = 8, MH = Mental Health, HSQ = Health Status Questionnaire.

<table>
<thead>
<tr>
<th>MS Quality of Life</th>
<th>Baseline Mean (SD)</th>
<th>6-month Mean (SD)</th>
<th>Mean Diff</th>
<th>SD</th>
<th>95% CI</th>
<th>t</th>
<th>df</th>
<th>p</th>
<th>d</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSQ Physical</td>
<td>47.07 (9.80)</td>
<td>47.64 (9.14)</td>
<td>-0.58</td>
<td>3.54</td>
<td>-3.54, 2.39</td>
<td>-0.46</td>
<td>7</td>
<td>0.660</td>
<td>-0.162</td>
</tr>
<tr>
<td>HSQ Mental</td>
<td>47.48 (10.83)</td>
<td>52.99 (8.00)</td>
<td>-5.51</td>
<td>7.50</td>
<td>-11.78, 0.76</td>
<td>-2.08</td>
<td>7</td>
<td>0.076</td>
<td>-0.735</td>
</tr>
<tr>
<td>Fatigue (MFIS-5)</td>
<td>4.13 (3.76)</td>
<td>5.50 (3.70)</td>
<td>-1.38</td>
<td>2.45</td>
<td>-3.42, 0.67</td>
<td>-1.59</td>
<td>7</td>
<td>0.156</td>
<td>-0.562</td>
</tr>
<tr>
<td>Pain (PES)</td>
<td>10.88 (4.49)</td>
<td>9.38 (1.92)</td>
<td>1.50</td>
<td>3.74</td>
<td>-1.63, 4.63</td>
<td>1.13</td>
<td>7</td>
<td>0.294</td>
<td>0.401</td>
</tr>
<tr>
<td>Sexual Satisfaction (SSS)</td>
<td>12.14 (8.21)</td>
<td>8.43 (4.69)</td>
<td>3.71</td>
<td>7.13</td>
<td>-2.88, 10.31</td>
<td>1.38</td>
<td>6</td>
<td>0.218</td>
<td>0.521</td>
</tr>
<tr>
<td>Bladder Control (BLCS)</td>
<td>2.00 (3.89)</td>
<td>0.88 (1.81)</td>
<td>1.13</td>
<td>2.10</td>
<td>-0.63, 2.88</td>
<td>1.52</td>
<td>7</td>
<td>0.174</td>
<td>0.536</td>
</tr>
<tr>
<td>Bowel Control (BWCS)</td>
<td>2.13 (2.90)</td>
<td>2.13 (1.89)</td>
<td>0.00</td>
<td>1.69</td>
<td>-1.41, 1.41</td>
<td>0.00</td>
<td>7</td>
<td>1.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Visual Impairment (IVIS)</td>
<td>0.38 (1.06)</td>
<td>1.13 (1.25)</td>
<td>1.38</td>
<td>1.39</td>
<td>-1.91, 0.41</td>
<td>-1.53</td>
<td>7</td>
<td>0.170</td>
<td>-0.540</td>
</tr>
<tr>
<td>Perceived Deficits (PDQ-5)</td>
<td>6.25 (4.83)</td>
<td>5.25 (4.62)</td>
<td>1.00</td>
<td>3.02</td>
<td>-1.53, 3.53</td>
<td>0.94</td>
<td>7</td>
<td>0.381</td>
<td>0.331</td>
</tr>
<tr>
<td>Mental Health Inventory (MHI)</td>
<td>78.47 (14.04)</td>
<td>79.58 (13.09)</td>
<td>-1.11</td>
<td>8.36</td>
<td>-8.10, 5.88</td>
<td>-0.38</td>
<td>7</td>
<td>0.718</td>
<td>-0.133</td>
</tr>
<tr>
<td>Anxiety (MHI)</td>
<td>76.50 (14.88)</td>
<td>73.50 (15.11)</td>
<td>3.00</td>
<td>14.77</td>
<td>-9.35, 15.35</td>
<td>0.57</td>
<td>7</td>
<td>0.584</td>
<td>0.203</td>
</tr>
<tr>
<td>Depression (MHI)</td>
<td>79.38 (15.45)</td>
<td>84.38 (10.50)</td>
<td>-5.00</td>
<td>8.02</td>
<td>-11.70, 1.70</td>
<td>-1.76</td>
<td>7</td>
<td>0.121</td>
<td>-0.624</td>
</tr>
<tr>
<td>Behavior Control (MHI)</td>
<td>88.75 (10.61)</td>
<td>88.75 (12.75)</td>
<td>0.00</td>
<td>6.55</td>
<td>-5.47, 5.47</td>
<td>0.00</td>
<td>7</td>
<td>1.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Positive Affect (MHI)</td>
<td>51.25 (3.54)</td>
<td>45.63 (4.96)</td>
<td>5.63</td>
<td>6.78</td>
<td>-0.04, 11.29</td>
<td>2.35</td>
<td>7</td>
<td>0.051</td>
<td>0.830</td>
</tr>
<tr>
<td>Social Support (MSSS-5)</td>
<td>73.13 (33.59)</td>
<td>82.50 (21.38)</td>
<td>-9.38</td>
<td>24.70</td>
<td>-30.03, 11.28</td>
<td>-1.07</td>
<td>7</td>
<td>0.319</td>
<td>-0.379</td>
</tr>
</tbody>
</table>

Monetary Choice Questionnaire. Delay discounting rates were derived from responses on the MCQ. The delay discounting constant (k) represents behavior response
patterns when choosing between monetary rewards that are either small immediate or large delayed rewards. The automated scoring spreadsheet (Kaplan et al., 2016) considers participant preferences from each item to estimate overall $k$. A larger $k$ value indicates a greater preference for immediate rewards. Smaller $k$ values demonstrate preference for delayed rewards. Overall consistency evaluates the stability of participant response patterns. Values less than 75% typically need further evaluation as they may indicate random responding. In our sample, no consistency scores fell below 75% at either time point. Overall consistency at baseline was 96.30% ($SD = 3.43\%$) and 93.06% ($SD = 4.62\%$) at follow-up. Therefore, no response patterns warranted further evaluation.

Rate of discounting ($k$) was not related to percent weight loss after 6-months, and average $k$ did not significantly differ from baseline ($M = 0.0154$, $SD = 0.0142$) to follow-up ($M = 0.0181$, $SD = 0.0152$).

**Discussion**

In this pilot trial, we found that participants who reported a greater number of health comorbidities lost less weight; similarly, we observed that individuals who reported taking more prescription medications lost less weight. Future studies should continue to investigate the relationship between medication and weight loss to better understand the factors that may interfere with weight loss in MS. An increase in the number of health comorbidities reported at follow-up was found, although the relationship was not statistically significant. One possible explanation for this is that participants engaged in self-monitoring over a 6-month period and were perhaps more attentive to health changes at follow-up compared to baseline.
Participants endorsed several physical and mental changes, but perceptions of cognition remained unchanged. Likewise, no significant changes in objective cognition were observed. More work is needed to understand the relationship between weight loss and cognition in MS.

We expected that distance accounted for during the 6-minute walking task would increase at follow-up. Instead, 6-minute walk distance decreased, and a medium effect size was found. Many participants reported that wearing a mask while walking made it challenging to breathe and made them feel overheated. It is possible that difficulty breathing, and heat sensitivity contributed to the observed effect. Future work should implement identical procedures for mask-wearing to rule out potential confounding variables.

No significant changes on the MSQoL occurred from baseline to follow-up. However, large effect sizes were observed for the HSQ mental, MHI positive affect, and MHI depression scale. Increased scores on these measures indicated greater improvement. Self-reported fatigue increased at follow-up. It is possible the effects of summer temperatures and COVID related psychosocial factors contributed to increased ratings of fatigue at follow-up. Future studies should incorporate larger sample sizes to better understand the relationship between healthy lifestyle changes and health-related quality of life in MS.

Conclusions

Overall, findings from this study establish that clinically significant weight loss can be achieved through this behavioral weight loss program in people with MS. We adapted and developed a program for people with MS composed of many elements (group and
individual telehealth, self-monitoring, and technology) that were both feasible and acceptable to patients. Consequently, this program provides a promising approach for weight loss and promoting healthy lifestyle changes in people with MS.
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VITA

Julia Smith Cozart was born in November of 1992, and is originally from Fayetteville, Arkansas. She graduated from Fayetteville High School in 2011. She received her Bachelor of Arts in Biology, Psychology, and Applied Critical Thought and Inquiry from William Jewell College in 2015.

In 2016, Mrs. Cozart accepted a position as a full-time research assistant at the University of Missouri-Kansas City, in the Clinical Neuropsychology Research Lab under Dr. Jared Bruce. Mrs. Cozart has worked on several research projects funded by the National Multiple Sclerosis Society in her time at the lab, including studies examining medication decision-making, an internet-based cognitive-behavioral intervention for depression in MS, and now a behavioral weight loss and healthy lifestyle program for people with MS.

Mrs. Cozart began working toward her PhD in 2018 at the University of Missouri-Kansas City. Upon completion of her degree requirements, Mrs. Cozart plans to continue her career in clinical psychology and pursue her research interests.