Physical Activity during Pregnancy Among People with Multiple Sclerosis

by

Miranda Kimber

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Faculty of Kinesiology, Sport and Recreation
University of Alberta

Abstract:

It is well established that physical activity confers numerous health benefits for both mother and fetus in the vast majority of pregnant individuals. Yet, significant knowledge gaps remain. Of the 12 systematic reviews which informed the Society of Obstetricians and Gynecologists of Canada/Canadian Society for Exercise Physiology 2019 Canadian Guideline for Physical Activity during Pregnancy, not a single study included pregnant people with impairments. As a result, the Steering Committee put out an urgent call to action to initiate research in this area. In response, we conducted a study examining the physiological responses to a single bout of moderate intensity physical activity within pregnant people with Multiple Sclerosis (MS).

We recruited six pregnant people with MS, and six pregnant people without MS >12 weeks gestation to participate in our research study. Participants completed a 20-minute submaximal exercise test instrumented with a Polar H6 heart rate monitor and Freestyle Libre Pro continuous glucose monitor. Acute measurements of fatigue and energy were recorded prior-to, immediately following, 30-minutes and 60-minutes following exercise using the Visual Analog Scale to Evaluated Fatigue Severity (VAS-F). Following exercise, participants wore Actigraph and ActivPAL accelerometers for seven full days. They also completed the International Physical Activity Questionnaire (IPAQ) and Barriers to Physical Activity for Individuals with Mobility Impairments (BPAQ-MI) questionnaire.

Although rating of perceived exertion was not different between groups, mean heart rate during exercise was lower in participants with MS (p = 0.005) as all participants with MS spent less time in the 60-70% heart rate reserve (HRR) zone throughout exercise (p = 0.008). Participants with MS reported lower levels of acute energy immediately following exercise (p =

0.04), but no differences in acute fatigue or glucose prior-to, 30 minutes and 60 minutes following exercise were observed. Spearman correlational analyses demonstrated a significant moderate positive correlation between acute fatigue scores and glucose across exercise among participants with MS (r = 0.63, $p = 0.03$), but no correlation was found among participants without MS (r = -0.22, $p = 0.35$). Chronic physical activity and sedentary measures were not different between groups and individuals with MS listed a greater number of barriers to physical activity compared to individuals without MS. Daily glucose patterns (fasting, 24 hour, peak, nadir, time spent in hyper- and hypoglycemia) were not different between groups, and we observed no correlation between day-to-day fatigue scores via the Modified Fatigue Impact Scale (MFIS), and fasting (r = -0.37) or 24 hour glucose values (r = -0.33).

These data suggest the physiological responses to an acute bout of exercise with the same subjective perception of exertion differ between pregnant individuals with and without MS. Further, our results demonstrate pregnant people with MS engage in smaller amounts of weekly MVPA that may be related to increased barriers to physical activity and fatigue.

Preface:

This thesis is an original work by Miranda Kimber. No part of this thesis has been published previously. This research project received research ethics approval from the University of Alberta Research Ethics Board on June 24, 2020, under the project name: "Exercise and pregnancy in people with multiple sclerosis" (Pro00095678).

Dr. Margie Davenport, Dr. Nancy Spencer and I contributed to the design, acquisition, analysis, and interpretation.

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List of Abbreviations:

MS	Multiple Sclerosis
MRI	Magnetic Resonance Imaging
Th	T-helper
NK	Natural Killer
RPE	Rating of Perceived Exertion
HHQ	Health History Questionnaire
VAS-F	Visual Analog Scale to Evaluate Fatigue Severity
BPAQ-MI	Barriers to Physical Activity for Individuals with Mobility Impairment
MSWS-12	12 item Multiple Sclerosis Walking Severity Scale
MFIS	Modified Fatigue Impact Scale
IPAQ	International Physical Activity Questionnaire
MET	Metabolic Equivalent
LPA	Light Physical Activity
MVPA	Moderate to Vigorous Physical Activity

Chapter 1: INTRODUCTION

Over the last 50 years, a growing body of literature has established the safety and benefits of prenatal exercise for both mother and fetus for most individuals. Recent meta-analyses of randomized controlled trials (RCTs)[1-3] demonstrate that engaging in physical activity throughout pregnancy can reduce the odds of developing gestational diabetes, gestational hypertension and preeclampsia by ~40%,[4] as well as prenatal depression by 67%.[5] Recently, the Society of Obstetricians and Gynecologists of Canada (SOGC) and Canadian Society of Exercise Physiology (CSEP) *2019 Canadian Guideline for physical activity throughout pregnancy* (referred to as the *Guideline*) was released. This *Guideline* was based on an extensive literature culminating in 12 systematic reviews and meta-analyses examining the impact of prenatal physical activity on 37 outcomes related to maternal, fetal and neonatal health. As part of this process, key research gaps were identified including no existing literature on prenatal physical activity in people with impairments. Currently, individuals with impairments are encouraged to discuss the benefits and risks of engagement in physical activity with their obstetric care providers.[1-3]

Rates of pregnancy are rising among people with impairments; however, research surrounding maternal and fetal health within this population remains sparse and there is an urgent call for additional studies. Recent publications have examined the impact of impairments on pregnancy rates, [6] birth outcomes[7] and prenatal care experiences;[8] however, the effects of acute and chronic physical activity during pregnancy have not been investigated.

MS is a condition which preferentially affects females at a 3:1 female: male ratio, and is most often diagnosed in young adults.[9] Despite its high prevalence in individuals during the reproductive years, there remain significant knowledge gaps surrounding maternal health throughout pregnancy. MS is a progressive immune-mediated condition of the central nervous system which results in the disruption or loss of axonal myelin.[10] It is characterized by varying symptoms which most often appear during exacerbations, or relapses, and reduce in severity during periods of remission.[10] Pregnancy has a unique protective effect against MS symptoms where rates of relapse reduce throughout gestation, most significantly in the third trimester.[11] The presence (or absence) of MS symptoms may impact an individual's physiological response to exercise or activity patterns during pregnancy.

To date, physical activity during pregnancy in people with MS, or with any type of impairment, have yet to be investigated. Simply including pregnant people with MS in ongoing prenatal research studies is not sufficient to understand the unique relationship between MS and maternal physiology. In order to broaden the possibilities for more inclusive physical activity research, this thesis concludes with a reflection on the process and considerations of conducting prenatal physical activity research in a population who experiences impairment and examines the non-disabled researcher role and assumptions of disability and pregnancy.

Objective:

The aim of this study was to investigate the physiological responses to acute submaximal exercise, as well as chronic physical activity patterns during pregnancy between people with and without MS. Heart rate and level of fatigue were measured during and in the hour following an acute bout of submaximal exercise. Physical activity patterns were measured using two accelerometry devices (Actigraph and ActivPAL; one week) as well as the International Physical Activity Questionnaire (IPAQ). Additionally, barriers to physical activity were measured using the Barriers to Physical Activity for Individuals with Mobility Impairments (BPAQ-MI). Additionally, this thesis examined the considerations of study methodology and result interpretation when conducting research with participants with MS, particularly as a non-disabled researcher.

Hypotheses:

I hypothesized that the heart rate response to acute submaximal exercise would not be different between participants with and without MS. Further, I hypothesized participants with MS would have reduced physical activity time and increased sedentary time compared to participants without MS during pregnancy.

Limitations:

There are several limitations to the present study, primarily due to COVID-19 restrictions to meet physical distancing requirements to ensure the safety of both participants and researchers. Participants did not perform the exercise bout in person with the researcher, rather the researcher monitored participant safety and intensity via video conferencing. Whenever possible, the participant was be encouraged to have an individual within their social bubble in the room with them. There are numerous measures which would have enriched the physiological data retrieved, such as vascular, electrocardiogram, respiration, thermoregulatory measures, however, they were not available outside of the laboratory environment or without in-person assessment. Additionally, a participatory research design, such as community consultation to determine research priorities, would have confirmed the relevance of the overall project to pregnant persons with MS, however, this was not possible due to the constraints of a Master's thesis such as training required and time.

Language:

It is important to note the disability language choice for this proposal, and subsequent publications that result of this work as this is inherently connected to the values and ideas being shared by the author(s).[12] In explicitly commenting on my language choice, I aim to be transparent in the model of disability utilized in this proposal. A blend of the International Classification of Functioning, Disability and Health (biopsychosocial) model of disability and social model of disability are utilized throughout this proposal. Within the biopsychosocial model of disability, impairment refers to biological manifestations or differences within the body, whereas disability refers to the exclusion, marginalization and discrimination of individuals with impairments experience.[13] In the social model of disability impairment and disability are distinguished, similar to the biopsychosocial model, however, the social model focuses mostly on social structures, oppression and attitudes as factors which limit individuals as opposed to biological manifestations.[14] Together, these models highlight the relevance of physiological and societal impacts on people with MS, which aligns well with my intention of this thesis. Personally, I align largely with an understanding of disability through a social model lens, however, the influence of the body is often minimized within this model[15] and the language model does not explicitly distinguish between impairment and disability (i.e. disabled individual). It was important that this project identify the influence of the body and society since I measured physiological response and barriers to physical activity and reflect on their interrelatedness on the outcomes. Most importantly, I aimed to avoid depicting MS through the lens of the medical model of disability which conceptualizes disability as an individual tragedy which is not influenced by social, economical or political factors.[16] The language choices in this thesis align with both of these models of disability. The language used distinguishes impairment as a diagnosis that an individual is assigned (i.e. individual with/without MS), and disability as something an individual experiences (i.e. individual who does/does not experience disability). Further, I also utilized the term “non-disabled” when speaking about myself which aligns with the social model of disability, where the oppression and difficulties associated with disability are considered socially constructed and occur since impairments are not adapted for, valued or accepted in larger society. This was appropriate when speaking about myself, as I do not have an impairment nor do I experience disability in society, and person-first language does not capture this sentiment appropriately. Peers (2018) described the numerous assumptions of disability among adapted physical activity research, such as disability as personal tragedy and the naturalized desire to contain, manage or cure impairment, which are assumed to be the reality of all individuals who experience disability.[17] As someone who does not experience disability, I aimed to appropriately represent participants in this study and their experiences through engaging in a reflexive practice of questioning my assumptions of disability which arose during this project. Processes I employed included not using value-ridden descriptors of disability experience or impairment (i.e. "suffer with…", "abnormal", "healthy" vs "unhealthy") and seeking and listening to insight from participants or other individuals who experience disability on the knowledge derived from this project when completed. Lastly, gender neutral language was used throughout this thesis in understanding that pregnancy is experienced by a multitude of genders.

Chapter 2: LITERATURE REVIEW

Pregnancy and Disability:

People with impairments have increased opportunities for childbearing as patient advocacy, recognition of reproductive rights and medical advancement increases.[8] Reproduction among individuals with impairments has been policed for centuries through eugenic practices such as forced sterilization.[18] Eugenics was born out of desire to remove poverty, alcoholism, sexual deviance and criminal behavior from society, and was highly supported by Canada, Europe and the United States.[19] Understood as a societal remedy of 'feeblemindedness', sterilization occurred internationally to remove reproduction among individuals with impairments. Alberta's infamous alignment with this movement began with the government mandated Sexual Sterilization Act in 1928.[20] This act continued until 1972, when a change in government occurred, and under the former's authority over 2800 individuals were sterilized.[20] Government mandated sterilization practices no longer occur, however, the ideologies which birthed this movement, still persist today. The sexual and reproductive health of people with impairments is often overlooked and people often report numerous barriers to reproductive care including inaccessible equipment, health care provider insensitivity and a lack of knowledge surrounding disability.[21, 22] A juxtaposition of sexual health and disability has been created by the eugenics movement which has labelled people with impairments as asexual and incapable of parenting children.[23] This ideology persists across health research as well, with prominent knowledge gaps surrounding pregnancy and disability. Recent evidence indicates pregnancy among people with impairments is increasing, however, there remains large gaps in knowledge surrounding the maternal health of this population. Brown et al., (2020) analyzed pregnancy rates in Ontario, Canada among people with physical, sensory and/or developmental impairments between 2003/2004 and 2017/2018. Across this period, the proportion of pregnancies in people with impairments increased from 8.5% in 2003/2004 to 18.5% in 2017/2018, while rates among people without impairments decreased. These findings combat assumptions that pregnancy rarely occurs in people with impairments and advocates for greater attention to the prenatal care needs of this population.[6] Other recent data indicates that people with physical, intellectual/developmental and sensory impairments have increased odds of developing hypertensive disorders of pregnancy (OR 1.45, 95% CI, 1.16-1.82) and caesarian delivery (OR 1.31, 95% CI, 1.02-1.68).[7] This systematic review and meta-analysis was the first of its kind to analyze risk for perinatal complications among people with impairments, and called for more high-quality evidence to examine reasons for increased risk of adverse pregnancy outcomes, as well as potential interventions to support people with impairments throughout their pregnancies. In people without impairments, evidence demonstrates physical activity throughout pregnancy provides ample benefit to the mother and is proposed as a preventative intervention to reduce pregnancy complications.[1-3] At this time, it is unknown if similar results may occur among pregnant individuals with impairments.

Multiple Sclerosis:

Multiple Sclerosis (MS) is an inflammatory autoimmune condition which leads to demyelination of axons within the CNS.[24] Roughly 2.5 million individuals worldwide are diagnosed with MS and the prevalence in Canada is among the highest in the world. In Alberta, 1 in 400 individuals are diagnosed with MS.[25] MS preferentially affects females at a 3:1 female: male ratio and is most often diagnosed in people aged 20 to 40 years, with the mean age of onset at 30 years.[9] This condition has a variable course and severity between individuals, however, common symptoms include fatigue, pain, ambulatory impairment and depression.[26]

Types of MS:

MS is categorized into four types, each characterized by condition progression (**Figure 1**). Relapsing-remitting MS is the most common type and is diagnosed in 90% of individuals with MS.[26] It is characterized by periods of relapse where current symptoms are exacerbated or new symptoms develop, followed by remission, a period where no new symptoms are developing and current symptoms are stable.[27] Relapse periods occur for a minimum of 24-48 hours and typically last for eight weeks, however, this is variable between individuals. This period is triggered by an autoimmune response from autoreactive T cells within the CNS, which attack the myelin sheath's surrounding axons. The migration of T cells across the blood brain barrier is considered the first trigger of MS symptoms,[10] and relapse periods occur due to release of cytokines from autoreactive T cells which damage the myelin sheaths surrounding axons in the CNS.[28] If symptoms subside for a minimum of one month, an individual is considered to be in a remission or recovery period where symptoms are stable and there is no disease progression.[29] Relapsing-remitting MS progresses as myelin is increasingly damaged and irreversible axonal loss occurs,[30] and most individuals eventually progress to secondary-progressive MS.[27] The progressive forms of MS do not cycle through periods of relapse and remission. Primary progressive MS is a steady progression of MS symptoms without cycles of relapse and remission. While relapse periods occur in progressive-relapsing MS, between relapses, there is a steady progression of MS symptoms as opposed to remission periods.[27]

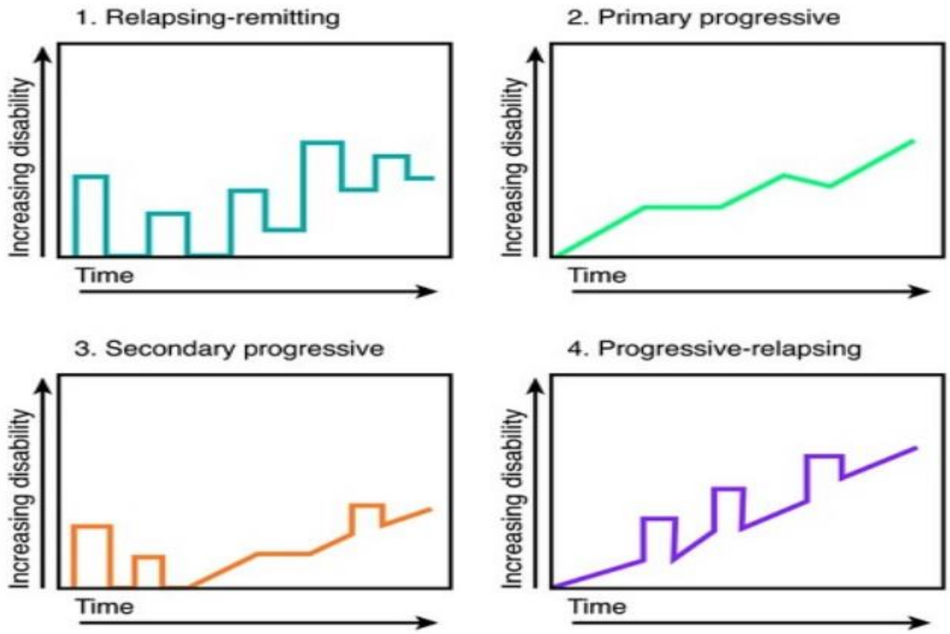


Figure 1. Types and courses of multiple sclerosis (MS). From Lublin FD & Reingold SC. Defining the clinical course of multiple sclerosis: Results of an international survey. Neurology 1996: 46(64); 907–911.

Symptoms of MS:

MS prognosis varies largely between individuals due to environmental factors, locations of lesions, myelin damage, extent of axonal loss and type of MS.[31] As such, function of the CNS is variable between individuals and symptom presentation is diverse. Typically, initial symptoms include sensory impairments, optic neuritis, limb weakness, gait ataxia, clumsiness, and bowel and bladder symptoms.[30] MS is diagnosed based on medical history, symptom presentation and neurological examination using magnetic resonance imaging (MRI), lumbar puncture for cerebrospinal fluid and blood sample analysis.[32] Often symptoms such as speech impairment, vertigo, sensory loss, tremors, pain, spasticity, depression and heat intolerance occur later in MS progression.[33] Individuals with MS report experiencing a number of "invisible symptoms" such as pain, fatigue and depression.[27] Fatigue is a multidimensional symptom with numerous origins and is one of the most common and debilitating symptoms of MS.[34] The etiology of this symptom remains unclear, however, there are central, peripheral and psychological mechanisms involved. Individuals may experience fatigue, which is directly related to the pathophysiology of MS, termed central fatigue, where there is inability to sustain central drive to motoneurons.[35, 36] Additionally, fatigue may be the result of factors not specific to MS, such as sleep problems, pain, deconditioning or depression, and may be peripheral (loss of force generation within a muscle) or cognitive in origin.[36] There are often discrepancies between self-reported fatigue and measure of impairment (via the Expanded Disability Status Score), suggesting motor and cognitive fatigue do not correlate, and are experienced in a variety of ways among individuals with MS.[37] Depression may amplify fatigue and individuals with MS are two times more likely to report depression than those without MS.[38] It is unknown if depression is due to a psychological response to the condition itself, or if the neuroendocrine alterations associated with MS impact brain centres responsible for emotion.[35]

Multiple Sclerosis and Pregnancy:

Multiple sclerosis is most often diagnosed in people during their childbearing years.[9] Historically, people with MS were told to avoid pregnancy out of fear that disease progression would accelerate.[39] The Pregnancy In Multiple Sclerosis (PRIMS) study altered perceptions of pregnancy among people with MS.[40] In a prospective examination of relapse rate in 269 pregnant people with MS, it was found that rates of relapse declined slightly during the first and second trimesters, with substantial decreases in the third trimester. Following delivery, the risk of relapse increased in the first 3-4 months postpartum. After this initial rebound, rates of relapse in the postpartum period are similar to pre-pregnancy. This pattern has been supported by other studies,[41-46] although recent data proposes that these historical findings do not reflect the experiences of the majority of people with MS who are pregnant today. The PRIMS study was published in 1998. Subsequently the diagnostic criteria for MS have been updated allowing for earlier diagnosis. As a result, people diagnosed today typically have milder conditions during pregnancy.[47] Further, the heightened relapse risk postpartum identified in the PRIMS study was identified in people with highly active MS prior to pregnancy. Recently, among 466 pregnancies in people with MS it was observed that annual relapse rates declined from 0.37 prior to pregnancy to 0.14-0.07 during pregnancy, however, a relapse rebound was not observed (0.27 in the first 3 months postpartum).[47] It is hypothesized these results are due to improved MS diagnostic criteria, as well as the high rates (87.3%) of exclusive breastfeeding amongst the cohort. People who exclusively breastfed had a significantly reduced risk of postpartum relapse compared to those who did not breastfeed ($p = 0.0032$), even among people with more active MS prior to pregnancy.[48] Collectively, pregnancy appears to be protective against MS symptomology, and people with milder MS may expect a similar postpartum relapse rate to that experienced prior to pregnancy. Further population-based research is needed to develop a comprehensive understanding of relapse rate during pregnancy and postpartum.

The mechanisms underlying of the protective effect of pregnancy have not been determined. Evidence suggests that hormonal and immune responses to pregnancy may play a role in the reduction of relapses throughout pregnancy. During pregnancy, there is an increase in reproductive hormones such as estradiol, progesterone, prolactin and glucocorticoids which are essential for suppressing immune function during pregnancy[49] in order to protect the fetal cells against immune rejection.[50] It has been suggested, that heightened levels of circulating estrogens throughout pregnancy and reduced levels during postpartum may contribute to patterns of relapse rates noted throughout pregnancy and postpartum.[51] Further, there is evidence that estrogens have a potential neuroprotective effect such as reduction of CNS inflammation, protection against demyelination and protection against axonal loss.[51] However, this conflicts with recent findings suggesting postpartum relapse rate is not significantly elevated and a potential protective effect of breastfeeding[48] when estrogen levels are further reduced.[52] It is thought the hormonal adaptations to pregnancy alter the T-helper (Th) cell profile from predominantly Th1 (proinflammatory cytokines) to Th2 (anti-inflammatory cytokines).[53] This results in reduced inflammation during pregnancy for people with MS, which is a Th-1 driven disorder.[54] Natural killer (NK) cells are important for developing placental vasculature, promoting placental growth and providing immunomodulation at the fetal-maternal interface;[55] however, their role during pregnancy is not established. Pregnant people with MS have significantly increased activation of CD3+, CD56+ and CD8+ cells compared to non-pregnant people with MS ($p < 0.001$) and pregnant people without MS ($p < 0.001$).[56] As CD8+ NK cells have been reported to improve production of Th2 cytokines in a several mouse models,[57, 58] it is speculated that CD8+ NK cells play an important role in modulating the T-cell response during pregnancy in people with MS.[56] Airas et al (2007) observed a significant increase in $CD56^{bright}$ NK immune cells in 42 pregnant individuals with relapsing-remitting MS.[41] Following delivery, the cell rates decreased, accompanied by increased rates of relapses post-partum.[41] $CD56^{bright}$ NK cells display promising results in the regulation of autoimmune disease by limiting the survival of activated T cells.[41] The immune adaptations to pregnancy may largely contribute to the decreased relapses throughout gestation and an increased relapse risk postpartum.

Maternal, fetal and birth outcomes associated with MS during pregnancy are inconclusive due to diverse findings in the literature. Studies have suggested an increased risk of preterm birth, low birth weight,[59] and assisted delivery;[60] however, these results are not consistently demonstrated. In a cohort of 1185 deliveries, people with MS did not have increased risk of gestational diabetes (OR 0.9, 95% CI, 0.7-1.1, $p = .28$), preeclampsia (OR 1.1, 95% CI, 0.8-1.6, $p = .38$), preterm delivery (OR 1.2, 95% CI, 0.9-1.5, $p = .10$) and fetal growth restriction (OR 1.2, 95% CI, 0.7-1.8, $p = .53$).[61] A significant risk of caesarean section was determined (OR 1.4, 95% CI, 1.3-1.6, $p < 0.001$), however, a range of 9.6-41.1% of caesarean delivery rates has been observed across studies and appears greatly influenced by geographical location.[44] Overall, data indicates people with MS are not at a higher risk for pregnancy and neonatal complications than people without MS.[62] Despite heterogenous results, it is generally accepted that MS does not render a pregnancy as high-risk and should not limit birthing options among people with MS.[63] It is important to note, however, that exposures to certain disease modifying therapies, such as teriflunomide or fingolimod, in the first trimester increase risk of adverse fetal outcomes.[47] Adverse birth outcomes due to disease modifying therapies are not commonly reported as more than 40% of people with MS are not on pharmacological therapies in the year before conception and physicians typically do not prescribe therapies with high risk of teratogenicity to people of child-bearing age.[47]

Multiple Sclerosis and Physical Activity:

There is a large body of research on the outcomes of exercise among people with MS, which largely investigates its effects on function, symptom management and participation in activities of daily living. Physical activity is mostly used for the management of MS symptoms, however, more research is starting to examine how it may impact condition pathology. The following section of this literature review summarizes the acute physiological responses to exercise, the chronic adaptations to exercise, and the barriers to physical activity experienced by individuals with MS.

Acute physiological responses:

Historically individuals with MS were instructed to avoid physical exertion out of fear that it would make individuals feel worse or negatively affect condition progression.[64] The acute symptom response to physical activity likely led to this recommendation, however, the benefits of physical activity are well-established (discussed in Chronic Physiological Response). The formation of scar tissue and loss of axonal myelin within the gray matter areas of the brain such as the hypothalamus, medulla and brain stem result in autonomic and endocrine dysfunction in individuals with MS.[65, 66] Further, there are transient symptomatic responses to exercise. This has influence on the exercise tolerance of individuals with MS and the acute cardiovascular and thermoregulatory responses to exercise.[67]

Cardiovascular

Evidence indicates individuals with MS experience both central and peripheral cardiovascular dysfunction. Peripherally, individuals with MS have diminished forearm blood flow response following forearm occlusion than individuals without MS.[68] Further, lower resting muscle sympathetic nerve activity and levels of norepinephrine[69] suggest individuals with MS have reduced sympathetic control of peripheral vasculature. Blunted arterial pressure response to isometric handgrip[70] and graded arm ergometry exercise[71] have been recorded, potentially due to reduced sympathetic outflow and impaired peripheral mechano- and chemoreceptors.[67] Central command of heart rate is also blunted during isometric handgrip[72] and dynamic arm and leg cycling exercise,[71] potentially due to lesions within higher brain centres.[72] Hansen et al. (2003) reported individuals with MS had significantly slower heart rate increase at initiation of endurance exercise (within 20 seconds) (14±7 bpm) than those without MS (20±8 bpm, $p < .05$), suggesting a specific impairment of central command as metabolic response is not present in this short time-frame.[73] Collectively, this suggests there are both central and peripheral limitations to the cardiovascular system of individuals with MS. As lesions may appear anywhere along the CNS, the acute cardiovascular response to exercise may be diverse in individuals with MS. It is suggested that adaptations be made in consideration of cardiovascular limitations when prescribing an intensity of exercise for an individual with MS;[67] however, there are no cardiovascular contraindications specific to this population.

Thermoregulatory

Often individuals with conditions characterized by autonomic dysfunction, such as MS, experience thermoregulatory impairment due to unmatched heat production and heat dissipation in response to increasing body temperature.[74] A heightened core temperature response to passive heating and aerobic exercise has been extensively reported in individuals with MS as the autonomic sweat response to increasing heat is attenuated.[75-82] This results in reduced heat dissipation while heat production increases, and therefore core temperature is higher for a given external temperature or exercise intensity compared to individuals without MS.[78] Although heat acclimation and training status can improve heat dissipation in individuals without MS,[83] it was determined that aerobic exercise training for 15 weeks did not improve sweat rate nor sweat gland output despite progressions in aerobic capacity.[75]

Symptom response:

Individuals with MS report a temporary worsening of symptoms following physical exertion from individuals with MS,[84] termed symptom instability. The most reported symptom exacerbations include sensory symptoms (pins and needles, tingling, pain), reduced vision and fatigue.[85] Temporary symptom exacerbation may be caused, in part, by Uhthoff's phenomenon where an increase in core temperature disrupts conduction along demyelinated axons.[74] The heightened core temperature response of individuals with MS to exercise may trigger Uhthoff's phenomenon temporarily causing blurred or reduced vision, however, any current symptom may temporarily worsen.[86] This response is reversible through cooling methods such as cold shower or drinking ice cold water, however, individuals with MS are advised to avoid situations which trigger the response. Uhthoff's phenomenon also exacerbates central fatigue symptoms due to disruption of action potentials along demyelinated axons resulting in reduced recruitment of spinal motor units in the CNS.[74] Central and peripheral fatigue also reduce the ability to activate muscle mass and therefore individuals with MS typically exert less force even when matched for age, body mass and fat free mass.[87] People with MS demonstrate earlier onset of muscle fatigue during isometric contraction of the ankle dorsiflexors (8 min) compared to those without MS (12 min), with a more rapid decline in maximal voluntary force.[88] The level of leg fatigue response to exercise is positively correlated to exercise intensity and tympanic temperature during exercise,[89] suggesting severity of fatigue is dependent on exercise intensity. Lastly, sensory impairments following exercise, such as pins and needles or pain, may be exacerbated following exercise. Smith et al., (2006) determined that 44% of participants with MS experienced an increase in the number of sensory symptoms immediately following low-intensity exercise.

Chronic physiological response:

While there are some transient symptom exacerbations immediately following a bout of physical activity, engaging in consistent exercise has multiple benefits for individuals with MS. Currently, it remains unclear if the effects of exercise attenuate the natural consequences of inactivity, or if there is reversing of pathophysiology of MS. Research has largely focused on the effect of exercise on the mental, physical, sensory and participation outcomes of people with MS. This review will cover the impact on fatigue symptoms in people with MS.

Fatigue:

Exercise is one of the leading strategies for management of fatigue among people with MS[90] as this symptom is poorly managed using pharmacological treatment alone.[91] When compared to pharmacological trials, exercise interventions had stronger and more significant effects on reducing levels of patient-reported fatigue.[91] Among 26 randomized control trials exercise therapy significantly improved fatigue compared to no-exercise conditions (SMD -0.53, 95% CI -0.73 to -0.33, Z = 5.19, $p < 0.01$).[92] Trials described above used self-report questionnaires to measure fatigue, which cannot distinguish between central, peripheral or psychological fatigue. It is difficult to distinguish the origin of fatigue from these questionnaires, or whether the reduction in fatigue is due to direct improvements in muscle performance or indirectly by impacting other influencing factors such as depression or sleep disorders.[37] Exercise may benefit both the motor and cognitive components of fatigue, however, certain methodologies may be used to specify which component of fatigue is being ameliorated. Chang et al., (2011) determined 8-weeks of functional electrical stimulation exercise significantly improved central fatigue index (p = .02) and general fatigue index (measured via Modified Fatigue Impact Scale) (p = .02), and that improvement in central fatigue contributed significantly to improvements in general fatigue (p < .01). Changes in peripheral fatigue were not observed, suggesting a greater contribution of central fatigue to the overall perception of fatigue.[93] It is likely that the cardiovascular, immunologic, neuroendocrine and neurotrophic changes associated with exercise may improve central fatigue, while psychological and peripheral fatigue benefit via alterations in deconditioning, sleep disorders and depression.[36] Collectively, evidence indicates exercise therapies are effective at reducing fatigue in individuals with MS, however, these studies are limited by small sample size, lack of control group and lack of participants currently experiencing clinically significant fatigue.

Barriers to physical activity:

Despite the numerous benefits of physical activity, approximately 80% of individuals with relapsing-remitting MS do not meet physical activity guidelines.[94] Inactive individuals with MS have higher risk of developing conditions related to inactivity, such as coronary heart disease, which increase the risk of condition progression.[95] As such, it is important to understand the barriers to physical activity and exercise opportunities in this population. Kayes et al., (2011) determined that greater self-efficacy and a lower number of perceived barriers to physical activity were significantly associated with greater participation in physical activity.[96] Individuals with MS have identified environmental, economic, psychological and physical barriers to physical activity.[97] In a review of all qualitative studies that have identified barriers and facilitators to physical activity and exercise in people with MS, environmental (physical and social accessibility) and personal (fatigue, fear and self-efficacy) were most commonly reported.[98] Commonly cited environmental barriers include exercise prescription not suited to one's abilities, lack of accessible parking and warm ambient temperatures within indoor fitness environments.[98] Many individuals with MS cite their symptoms, most notably fatigue, are barriers to physical activity participation. While evidence suggests consistent exercise improves fatigue, individuals with MS report feeling overwhelmingly fatigued following acute bouts of physical exertion. Thus, this is a significant barrier to physical activity participation. In an analysis of associations among objective measures of physical activity (via accelerometry) and symptoms, there was a moderate inverse correlation between symptoms and physical activity ($p = -.42$).[99] Further, a 1-SD increase in symptoms was associated with a .24-SD reduction in physical activity. Collectively, individuals with MS perceive their symptoms as a barrier to physical activity in addition to physical and social environments. It is integral to note that while the symptoms themselves may be an identified barrier, there are numerous environmental factors which may mediate the effect of one's symptom. For example, individuals with MS report the use of a mobility device reduced their participation in physical activity.[100] which may be the result of a lack of accessible equipment or insufficient space between equipment for mobility devices.[101]

Cardiovascular adaptations to pregnancy:

The cardiovascular system undergoes extensive changes during pregnancy in order to optimize oxygen and nutrient delivery to the developing fetus. Plasma and red blood cell volumes expand throughout gestation, leading to an increase in blood volume by 50%.[102] Additionally, heart rate (HR) increases progressively throughout pregnancy by 10-20 beats per minute, reaching peak rates in the third trimester[103] due, in part, to reduced parasympathetic control of HR during pregnancy.[104] Consequently, heart rate variability (HRV), the variation in time intervals between heartbeats, is reduced during pregnancy indicating dominance of sympathetic control of resting HR.[105] Stroke volume (SV) increases throughout gestation as well, reaching a peak of 20-30% by term.[106] As a result, cardiac output (Q) increases in order to pump the elevated blood volume throughout the body and to the placenta.[107] Further, maternal vascular adaptation occurs with a 20% drop in systemic vascular resistance (SVR) and increased filling capacity of venous circulation to accommodate the increased blood volume.[108] This vasodilation during healthy pregnancy results in a decrease or no change in arterial blood pressure throughout gestation.[103] The peak drop in blood pressure occurs during the second trimester, reaching a nadir of 10 mm Hg below pre-pregnancy values. This adaptation is due, in part, to a blunted sympathetic vasoconstrictor response observed during pregnancy.[109] causing altered regulation of blood pressure demonstrated by reduced baroreflex response at rest.[110, 111] Pressure then begins to rise close to preconception values during the third trimester[103] as blood volume and cardiac output increase.[112] The extensive adaptation to the cardiovascular system during healthy singleton pregnancy has been reported extensively, however, these changes have not been characterized among people with MS.

Physiological response to exercise during pregnancy:

The profound adaptations to pregnancy alter the physiological response to exercise. It is known that engaging in regular exercise throughout pregnancy has numerous benefits such as a 39% reduction in the odds of having a macrosomic baby (>4000 g)[113] and 67% reduced odds of developing prenatal depression.[5] As well, the acute maternal cardiovascular responses to exercise are altered during pregnancy. At initiation of exercise, parasympathetic withdrawal occurs along with sympathetic activation, leading to a rise in HR and lower HRV.[114] During pregnancy, the magnitude of parasympathetic withdrawal is reduced at exercise onset due to decreased vagal control at rest. Therefore, despite elevated HR at rest during pregnancy, HR increases similarly during submaximal exercise between pregnant and non-pregnant people.[112, 115] Additionally, reduced parasympathetic withdrawal during exercise contributes to similar reductions in HRV during exercise compared to non-pregnant people.[104, 116] Despite diminished baroreflex control at rest, normotensive pregnant people maintain blood pressure regulation during exercise.[104] It is known that pregnant people have an increased dilatory response to vascular shear stress[117] and blunted sympathetic control of vasculature;[105] however, less is known concerning the peripheral hemodynamic responses to exercise. While blood flow to working muscles increases substantially during exercise, evidence indicates submaximal exercise does not impair uteroplacental blood flow[118], however, further research is needed to investigate peripheral blood distribution during maximal exercise, particularly within the third trimester.[119] The physiological responses to exercise are altered during pregnancy due, in part, to adaptations to the cardioautonomic system. As autonomic dysfunction is commonly reported in MS, it is very possible these observed cardiovascular responses to exercise may be altered in pregnant people with MS.

Fatigue is a very common symptom of pregnancy[120], however, the effect of prenatal exercise on this symptom has received little research attention. It has been observed that a 4-week moderate-vigorous exercise intervention resulted in significant decreases in fatigue ($p = .01$).[121] As well, only one study has investigated acute fatigue following exercise during pregnancy which revealed non-significant reductions in mental and physical fatigue following acute resistance exercise.[122] Currently, the understanding of exercise and fatigue during pregnancy is unknown in both people with and without MS.

Summary:

The physiological responses to exercise and activity patterns during pregnancy in people with MS have not been determined. I aim to assess the acute heart rate and fatigue response to exercise and characterize chronic physical activity patterns of people with MS during pregnancy.

It is known that autonomic dysfunction commonly occurs in individuals with MS and may influence cardiovascular response to exercise. As pregnancy is a unique period of immunosuppression and reduced relapse rate, as well as profound physiological adaptation,[112] it cannot be assumed pregnant people with MS will exhibit similar responses to exercise as people without MS. It is important to understand associations between adaptations to pregnancy and exercise tolerance to reduce adverse pregnancy outcomes among people with MS. Additionally, individuals with MS report reduced activity and higher amounts of sedentary time than individuals without MS, which is of consequence to overall health and may be detrimental to maternal and fetal health. I propose to measure differences in physiological response (heart rate and fatigue) to submaximal exercise, activity patterns and barriers to physical activity between people with MS and without MS during pregnancy.

Chapter 3 METHODS AND PROCEDURES:

Ethics Approval:

Approval for this study was received by the University of Alberta Biomedical Human Research Ethics Board (Pro00095678). Prior to testing, written informed consent was obtained from all participants.

Participants:

Participants were recruited through flyers or advertisements in websites, social media, and relevant health and recreation settings. Participants with MS were recruited through the MS Society of Canada research portal and health care staff at the Edmonton MS Clinic.

Inclusion Criteria:

Pregnant people with and without MS were recruited, pregnant people without MS were recruited as controls to examine the differences in physiological responses to exercise and physical activity patterns during pregnancy between groups. All participants were above the age of 18 years, resided in Canada and were >12 weeks of gestation. There were no restrictions on parity, mode of conception via assistive reproductive therapies or type of MS.

Exclusion Criteria:

Participants could not be current smokers (non-smoker for at least one year) or have an absolute contraindication to prenatal exercise (per the 2019 Canadian Guideline for Physical Activity throughout Pregnancy)[1-3]. Absolute contraindications to exercise during pregnancy include ruptured membranes or premature labour, persistent second or third trimester bleeding or placenta praevia, gestational hypertension or preeclampsia, incompetent cervix, evidence of intrauterine growth restriction, high-order pregnancies, uncontrolled type 1 diabetes, hypertension, thyroid disease or any other serious cardiovascular, respiratory or systemic disorder.

All participants completed pre-participation screening questionnaires to determine eligibility to participate in the exercise protocol. To participate in the exercise portion of this study, pregnant people were asked to complete the PARMed-X for Pregnancy. Pregnant people were not eligible to participate in the exercise portion of study if they answered 'yes' to any of the questions regarding absolute contraindications to exercise in pregnancy (Section C of the PARMed-X form). Any participants who answered 'yes' to any of the relative contraindications to exercise in pregnancy (also Section C of the PARMed-X form), were referred to their medical professional for further advice regarding participation. Relative contraindications to exercise included history of spontaneous abortion or premature labour in previous pregnancies, mild/moderate cardiovascular or respiratory disease, anemia, or iron deficiency (Hemoglobin ≤ 100 g/L), malnutrition or eating disorder, or other significant medical conditions.

Experimental Design:

This study was conducted while COVID-19 restrictions were in place and in-person research assessments were not possible. As such, participants completed the exercise test and physical activity tracking from their homes. All required equipment and tracking materials were delivered to participants and questionnaires were completed online. Participants were asked to refrain from caffeine, alcohol, and strenuous exercise 12 hours prior to their exercise test.

Equipment:

Participants were sent the Polar H6 heart rate monitor (Polar Electro Oy, Kempele, Finland) worn around the chest with the sensor placed just inferior to the sternum. The monitor wirelessly connected to the Polar A370 watch (Polar Electro Oy, Kempele, Finland) which displayed continuous heart rate in beats per minute and recorded heart rate to download offline. Participants were also sent the FreeStyle Libre Pro Flash Glucose Monitoring System (Abbott, Chicago, IL, USA) to wear during the exercise test and remaining study period. This device adhered to the skin on the back of the upper arm and recorded interstitial fluid glucose at 15-minute intervals. The device was adhered to the skin the night prior-to the exercise test to ensure the flash system was calibrated properly at the time of exercise.

Experimental Protocol:

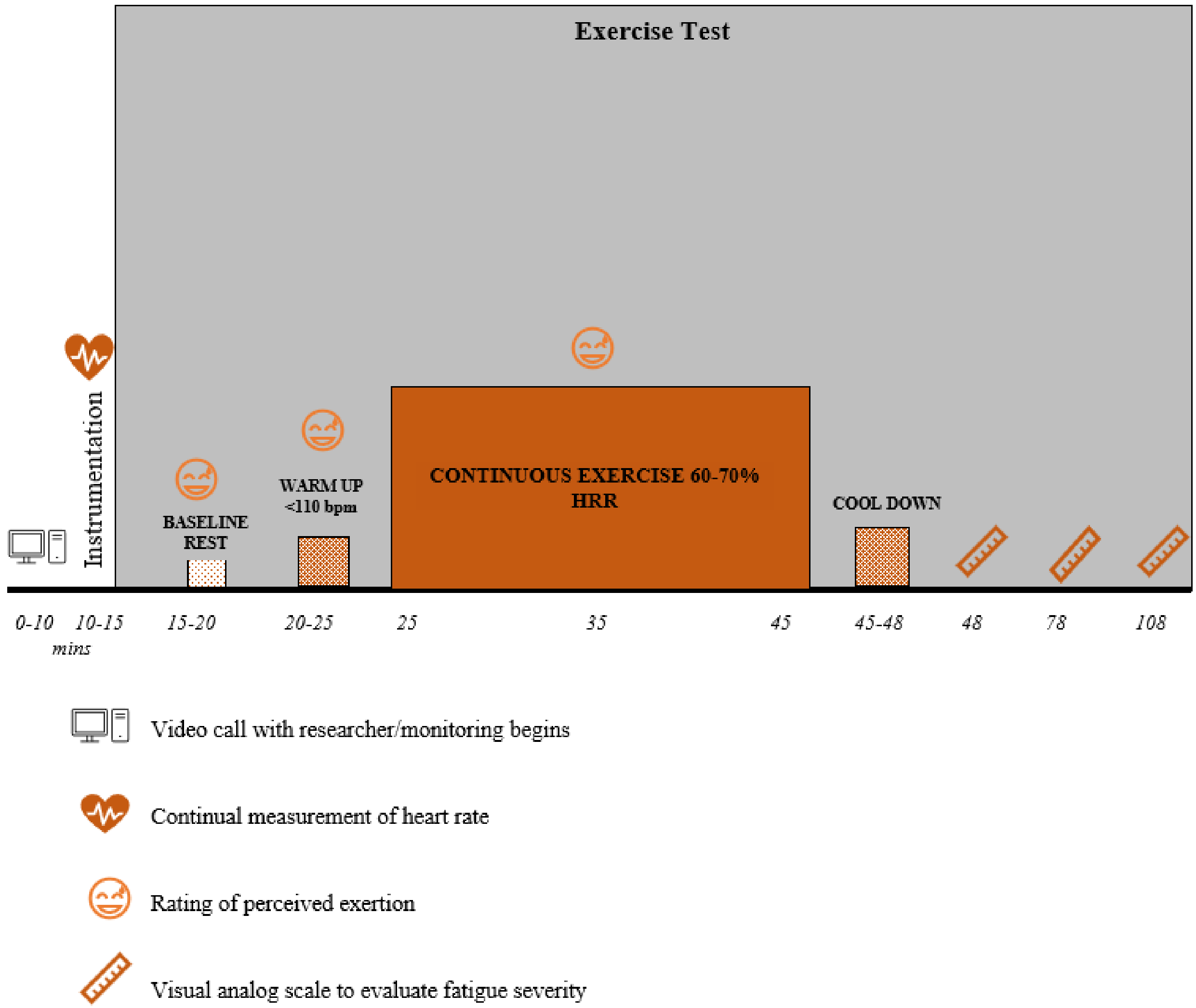
Baseline:

Participants rested quietly for 10 minutes prior to testing. The heart rate at the final minute of baseline ($HR_{resting}$) and calculated maximal heart rate ($HR_{max} = 220 - age$) was used to calculate heart rate reserve (HRR) using the following formula: $HRR = HR_{max} - HR_{resting}$. To calculate the target heart rate for exercise intensity the HRR formula was used: $Target\ HRR = ([HR_{max} - HR_{resting}] * desired\ intensity) + HR_{resting}$. The participant completed the Visual Analogue Scale to Evaluate Fatigue Severity (VAS-F) (Appendix A) following a minimum of 5-minutes of rest.

Submaximal Exercise Protocol:

Participants were instructed to begin with a 3-minute warm up at a HR <110 bpm. Following the warmup, participants completed the exercise test at an intensity of 60-70% HRR for 20-minutes. Participants selected an exercise modality which was accessible to them for their at-home participation (cycling, jogging, incline walking), and monitored their heart rate using the Polar A370 watch to ensure they remained in the prescribed 60-70% HRR intensity throughout exercise. Participants were asked to provide their Rating of Perceived Exertion (RPE) using the Borg 0-10 scale (Appendix B) during the warmup, and at 10 minutes of exercise. Following 20 minutes of exercise, the participant then completed a 3-minute cool down. Immediately following the cool down, the participant completed the VAS-F, and completed it every 30 minutes for one hour following exercise. Figure 2 demonstrates a full overview of the exercise test session.

Figure 2. Schematic and timeline of exercise test.



Questionnaires:

Participants completed questionnaires and tracked their physical activity and MS symptoms for 7 days following the exercise protocol. Participants completed the Health History Questionnaire (HHQ), Barriers to Physical Activity for Individuals with Mobility Impairments

(BPAQ-MI), and Modified Fatigue Impact Scale (MFIS). Participants with MS also completed the SymptoMScreen to characterize symptoms amongst the group.

Participants were also contacted following delivery and asked to complete a questionnaire which requested basic descriptive information of delivery and postpartum outcomes such as gestational age at delivery, mode of delivery (e.g. vaginal, instrumental or Caesarean, emergency, etc.), development of complications (e.g. gestational hypertension, preeclampsia, gestational diabetes mellitus, etc.) breastfeeding status, and fetal outcomes (e.g. infant birth weight and length, preterm birth, complications). All questionnaires are found in Appendices C-F.

Physical Activity and Sedentary Measures:

Participants wore an actigraph (Actigraph wGT3X-BT Monitor, Actigraph LLC, Pensacola, Florida, USA) and activPAL (PAL Technologies Ltd, Glasgow, UK) for seven consecutive days and nights to record 24-hour physical activity and sleep/wake measurements. The actigraph was worn around the waist during waking hours and moved to the wrist during sleeping hours. The activPAL was adhered to the midline of the anterior surface of the thigh using a waterproof, transparent dressing (3M Tegaderm, London, ON, Canada). Individuals also tracked their activity and sleep behaviours on an accelerometer log (Appendix G). Activity data was then downloaded onto specific software and analyzed for activity levels and sleep/wake measurements.

The use of accelerometry in populations with MS has been widely investigated.[123-125] It has been suggested that accelerometry may not validly estimate energy expenditure and instead indicates walking mobility.[126] As such, participants also completed the International Physical Activity Questionnaire (Appendix H), which is validated for use in populations with MS.[123, 125]

Glucose Monitor

Participants were provided with the FreeStyle Libre Pro Flash Glucose Monitoring System (Abbott, Chicago, IL, USA) to wear for the entirety of the study period. This device adheres to the skin and records interstitial fluid glucose levels at 15-minute intervals for a maximum of 14 days. The glucose sensor was applied on the back of the upper arm following cleaning with an alcohol wipe. A needle is contained within the applicator, which was placed over the insertion site and firmly pushed into the skin to insert the sensor device. Glucose values were recorded internally and can be viewed on the handheld reader by scanning the sensor. Following 7-days of wear, participants removed the sensor and returned the used sensor and reader for offline download through the Freestyle Libre Pro software for desktop (Abbott, Chicago, IL, USA).

The Freestyle Libre Flash Glucose Monitoring system has been previously used with pregnant individuals with type 1, type 2 and gestational diabetes, and is a valid, reliable and safe measurement of glucose values.[127] This device has not been investigated in individuals with MS, however, the only factor of concern was that the glucose sensor could not be worn during an MRI, which was communicated prior-to participation.

Symptom Tracking:

Participants with MS tracked their symptoms using the MS one-to-one symptom tracker (Appendix I). This product is intended for individuals with MS to maintain a record of their symptoms to report to their healthcare provider. Participants recorded; 1) the symptom they experienced, 2) the time of day it was experienced, 3) the duration of the symptom, 4) if the symptom is novel, 5) the severity of the symptom, 6) and the effect on daily life. The severity and effect on daily life were rated on Likert scales.

Reflexive Journaling

I maintained a reflexive journal throughout data collection, analysis, and writing/result presentation. Reflexive journaling throughout the research process is an important self-reflective analysis of the interplay between researcher and the researched,[128], including imbalances of power between researcher and research participants, as well as non-disabled and disabled. The maintenance of a reflexive journal served to continuously examine my social and political positionality as a non-disabled researcher, with quantitative and medical model training, conducting disability health research. Individuals who experience disability have voiced that research can reproduce the systems which maintain oppression and limit individuals with impairments, as opposed to empowering them.[129, 130] Therefore, this practice was integral to the goal of presenting a methodology, findings and interpretations that did not reinforce the social and political power indifferences that exist between myself and the participants.[131] Employment of this practice communicates that results of research, quantitative or not, are influenced by relational sociopolitical constructs and that are capable of transmitting powerful messages about health and disability.

CHAPTER 4: ANALYSIS

Data Analysis

Heart Rate

Polar H6 heart rate monitors were used to measure heart rate during submaximal exercise, and the Polar A370 watch was used to record heart rate data. Heart rate data was downloaded from the Polar A370 watch onto Polar Flow Web Service (Polar® Flow). Polar H6 heart rate monitors report heart rate (bpm) once per second. The following outcomes were calculated: 1) Resting heart rate; 2) Mean heart rate during exercise; 3) Change in heart rate during exercise; 4) Time spent in prescribed 60-70% HRR; 5) Heart rate recovery following exercise.

Resting heart rate was determined by averaging heart rate during the last minute of the 10-minte baseline. Mean heart rate during exercise was calculated by averaging heart rate across the 20-minute period, and maximum change in heart rate was determined by calculating the difference between resting and maximum heart rate achieved during exercise. Average heart rate intensity (60-70% HRR) across participants was determined, as well as time spent in prescribed heart rate intensity. Heart rate recovery is an indicator of cardioautonomic function, and a predictor of all cause mortality.[132] We calculated this metric through recording change in heart rate during the first 2 minutes of cool-down immediately following exercise. Change in heart rate at 15 second variables were compared between groups. Values for each outcome were averaged and contributed to each group's means.

Fatigue

Chronic fatigue was assessed using the MFIS which measures physical, cognitive, and psychosocial fatigue. Participants responded to 21-items consisting of 9 physical items, 10 cognitive items and 2 psychosocial items and could complete the questionnaire at any point during the 7-day study period. The maximum score is 84 for total score, 28 for physical subscale, 40 for the cognitive subscale and 8 for the psychosocial subscale. Participant responses for each subscale were averaged and contributed to each group's means.

Acute fatigue was assessed using the VAS-F, which contains 18-items consisting of 13 fatigue items and 5 energy items and asks participants to record how they currently feel on a scale from 0-10. Participant responses for each subscale were averaged and contributed to the group's mean. Participants were also asked to record level of exertion using the Borg RPE 1-10 scale prior-to, during (at 10-minutes), and immediately following exercise.

Glucose

Data from the glucose sensor devices were downloaded to Microsoft Excel files using the FreeStyle Libre Software Version 1.0 software and analyzed offline. Interstitial fluid glucose was measured and used as a proxy for blood glucose levels. Daily glucose outcomes were mean 24-hour (midnight to midnight), peak and nadir glucose, time in target (3.3-7.8 mmol/L), time spent < 3.3 mmol/L, and time spent > 7.8 mmol/L. The glucose outcomes were calculated using days 1 to 3 of the study period. Acute glucose values were immediately prior-to exercise, immediately following, 30 minutes and 60 minutes following exercise.

Physical Activity and Sedentary Behaviour

Actigraphs and activPALs were used to measure physical activity and sedentary behaviour throughout the study period. Non-wear and sleep times were confirmed using participant activity and sleep logs. Values for each outcome were averaged and contributed to the group means. Only days with > 600 mins of wear time were included for analysis and at least 2 valid days were required.

Actigraph data were downloaded then analyzed using ActiLife 6.13 software and Microsoft Excel. Actigraph accelerometers recorded triaxial data at 30 Hertz, and data were downloaded in 60-second epochs. Number of and time spent in Freedson counts were used to determine time spent in sedentary (< 100 counts per minute [cpm]), time spent in light physical activity (LPA) (199 – 1951 cpm), and time spent in moderate to vigorous physical activity (MVPA). The following outcomes were calculated: 1) Average wear time per day; 2) Time spent in sedentary; 3) Time spent in LPA; 4) Time spent in MVPA.

ActivPAL data were downloaded and processed in PALanalysis v8 and Microsoft Excel. The acitvPAL is an inclinometer which uses information from static acceleration and the angle of the thigh to determine posture (lying/sitting, upright) and dynamic acceleration to determine stepping.[133] The following outcomes were calculated: 1) Total sedentary time (sitting/lying time in minutes); 2) Number of prolonged sedentary bouts (≥ 30 minutes); 3) Number of breaks in sedentary time (transition from sitting or lying behaviour to upright posture); 4) Time spent in LPA and MVPA. Time spent in LPA and MVPA were determined by summing standing and stepping event durations under 3 metabolic equivalents (METs) and greater than or equal to 3 METs, respectively. Time in sedentary behaviour and number of prolonged sedentary bouts were retrieved and summed from Event data files.[134]

Physical activity and sitting time were also measured using the IPAQ, which records the frequency and duration of vigorous, moderate, and walking physical activity. The frequencies and durations were multiplied, and the resulting volumes were then multiplied by 8, 4, and 3.3 METs, respectively. The IPAQ produces individual scores for intensity of physical activity and sitting time, as well as an overall score of physical activity. Additionally, the IPAQ assigns a categorical value according to the following scoring protocol:

Highly active: Vigorous-intensity activity on at least 3 days and accumulating a minimum of 1500 MET-min/week; or 7 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of 3000 MET-min/week. *Moderately active*: 3 or more days of vigorous activity of at least 20 minutes per day; or 5 or more days of moderate-intensity activity or walking of at least 30 minutes per day; or 5 or more days of any combination of walking, moderate-intensity or vigorous intensity activities achieving a minimum of 600 MET-min/week. *Low active*: No activity is reported or some activity is reported but not enough to meet moderate or high categories.

Measures of sedentary behaviour, LPA, and MVPA across the actigraph, activPAL and IPAQ were compared using two-way ANOVA's to assess an effect of device measurement and group.

Barriers to Physical Activity

The BPAQ-MI questionnaire was used to assess barriers to physical activity between groups. This questionnaire assessed the number of barriers experienced, as well as the severity of the indicated barriers. Sixty-three distinct barriers were presented, and participants indicated "yes" if they experienced a specific barrier. If a barrier was indicated, the severity was rated on a Likert scale from 1 -5 (1 = very small; 5 = very high). The number of barriers indicated were summed and the severity values from multiple Likert-scales are averaged and contributed to group means. Barriers are assessed according to eight domains (Health, Beliefs/Attitudes towards Physical Activity, Friends, Family, Fitness Built Environment, Staff/Programming/Policy, Community Built Environment, and Safety).

Statistical Methods

Descriptive statistics were calculated, and unpaired t-tests and Mann-Whitney were used to compare demographic and BPAQ-MI questionnaire data between participants with and without MS. To assess the differences in heart rate responses to exercise, activity and sedentary patterns between participants with and without MS, independent-sample two-tailed t-tests were used. To assess acute fatigue response to exercise, Friedman tests were used to compare change across exercise and Mann-Whitney tests were used to compare scores between groups at each timepoint. A 2-way repeated measures ANOVA was used to determine time course of heart rate recovery between groups, as well as glucose response across exercise and between groups. Spearman correlation analyses were used to assess correlation between acute glucose and fatigue response to exercise, as well as average 24h daily and fasting glucose values and chronic fatigue (measured using MFIS). Repeated 2-way ANOVA's were used to determine differences in physical activity and sedentary measures across objective and subjective physical activity measures and between groups. Statistical significance was set at $P < 0.05$.

CHAPTER 5: RESULTS

Participant demographics

By design, participant characteristics were not different between groups. Participants with MS (MS participants) and participants without MS (NON-MS participants) were matched for age, gestational age, parity, pre-pregnancy body mass, body mass at participation, or height (see Table 1). Six MS participants enrolled in the study, however, only five participants with MS completed the acute exercise thus the matched NON-MS participant was removed for the acute exercise analysis. All participants were Caucasian. Cognitive fatigue levels, measured via the MFIS, were significantly higher among participants with MS, while physical and psychosocial fatigue were not different between groups (see Table 2).

Table 1. Participant demographics.

Participant Demographic	**MS (n=6)**	**NON-MS (n=6)**	***P***
Age (years)	31±4	31±1	0.83
Gestational age	22.3±5.0	21.5±6.0	0.73
Parity	0±0.5	2±2	0.17
Pre-pregnancy BMI (kg/m^2)	24.9±1.3	24.7±2.7	0.86
BMI (kg/m^2)	27.2±3.0	26.8±1.7	0.82
Ethnicity	6 Caucasian	6 Caucasian	

Data presented as mean ± SD unless otherwise indicated. BMI; Body mass index. Independent t-tests were used to determine statistical differences between groups for continuous data. *Missing data point for one MS participant. MS (n = 5)

Table 2. Day-to-day fatigue levels among MS and NON-MS participants measured using the Modified Fatigue Impact Scale.

Fatigue Domain	**MS (n=5)**	**NON-MS (n=5)**	***P***
Physical Fatigue (/28)	17 ± 6 (13 – 25)	11 ± 5 (4 – 17)	0.14
Cognitive Fatigue (/40)	18 ± 4 (14 – 22)	10 ± 6 (3 – 19)	**0.03**
Psychosocial Fatigue (/8)	3 ± 2 (1 – 6)	2 ± 1 (0 – 2)	0.13
Total Fatigue (/84)	39.2 ± 10.7 (25 – 50)	23.2 ± 9.8 (9 – 35)	0.06

Data presented as mean ± SD (range). Mann-Whitney tests were used to determine statistical significance ($p < 0.05$) between groups.

MS Participants Demographics

All MS participants were diagnosed with relapsing-remitting MS for an average of 5.5 years. Three participants were taking a disease modifying therapy (DMT) at the time of participation (see Table 3). The SymptoMScreen indicated symptom severity was comparably low across subjects[135] (see Table 4).

Table 3. Clinical characteristics of MS participants enrolled in the study.

Clinical Characteristic	**MS (n=6)**
MS Type	6 Relapsing-remitting
Years since diagnosis	5.5±0.8
Disease modifying therapy	1 Intravenous Immunoglobulin
	1 Copaxone
	1 Glatect
	3 Not currently taking DMT

Data presented as mean ± SD unless otherwise indicated. DMT, disease modifying therapy.

Table 4. Symptom severity among participants with MS evaluated using the SymptoMScreen tool.

Symptom Domain	**MS (n=5)**
Walking	0.6±0.5 (0 – 1)
Hand function	0.4±0.9 (0 – 2)
Spasticity and stiffness	1±1.2 (0 – 3)
Bodily pain	0.8±0.8 (0 – 2)
Sensory	0.8±0.8 (0 – 2)
Bladder	1.6±1.5 (0 – 2)
Fatigue	1.4±1.1 (0 – 3)
Vision	0.2±0.4 (0 – 1)
Dizziness	0.4±0.9 (0 – 2)
Cognitive function	0.8±0.8 (0 – 2)
Depression	0.8±0.8 (0 – 2)
Anxiety	0.8±0.8 (0 – 2)
Total Symptom Severity Score	**9.6±8.1 (0 – 21) (/72)**

Data presented as mean ± SD (Range) unless otherwise indicated.

Acute Physiological Responses to Submaximal Exercise:

Heart Rate and Rating of Perceived Exertion

Participants completed the submaximal exercise protocol from their homes, using an exercise modality accessible to them. Participants selected jogging (n = 5), cycling (n = 2), or walking (n = 3).

The heart rate and rating of perceived exertion in response to acute exercise is reported in Table 5. The pre-exercise resting heart rate was not different between groups. Rating of perceived exertion was not different between groups, however, the NON-MS group achieved a higher mean heart rate during exercise and spent a greater proportion of the exercise time in the prescribed target heart rate zone.

Table 5. Resting heart rate and acute heart rate responses to submaximal exercise bout, and time spent in prescribed 60-70% HRR range and rating of perceived exertion during exercise between MS and NON-MS participants.

Heart rate and Exertion Measure	**MS (n=5)**	**NON-MS (n=5)**	***P***
Resting HR	89 ± 6	82 ± 11	0.30
Mean HR	129 ± 11	149 ± 4	**0.005**
Delta Max HR	63 ± 12	76 ± 10	0.11
Time spent in 60-70% HRR (minutes)	3.7 ± 5.7	15.5 ± 5.0	**0.008**
Mean RPE	6.8 ± 1.1	6.2 ± 1.3	0.48

Data presented as mean ± SD unless otherwise indicated. Independent t-tests and Mann-Whitney tests were used to determine statistical significance ($p < 0.05$) between MS and NON-MS participants. HR; Heart rate, HRR; Heart rate reserve, RPE; Rating of perceived exertion

Heart Rate Recovery

The time course of heart rate recovery during the 2-minute cool down period immediately following exercise is shown separately for each group in Figure 3. A two-way repeated measures ANOVA found a significant effect of time (p = 0.0007) but did not find a significant effect of group (MS vs NON-MS).

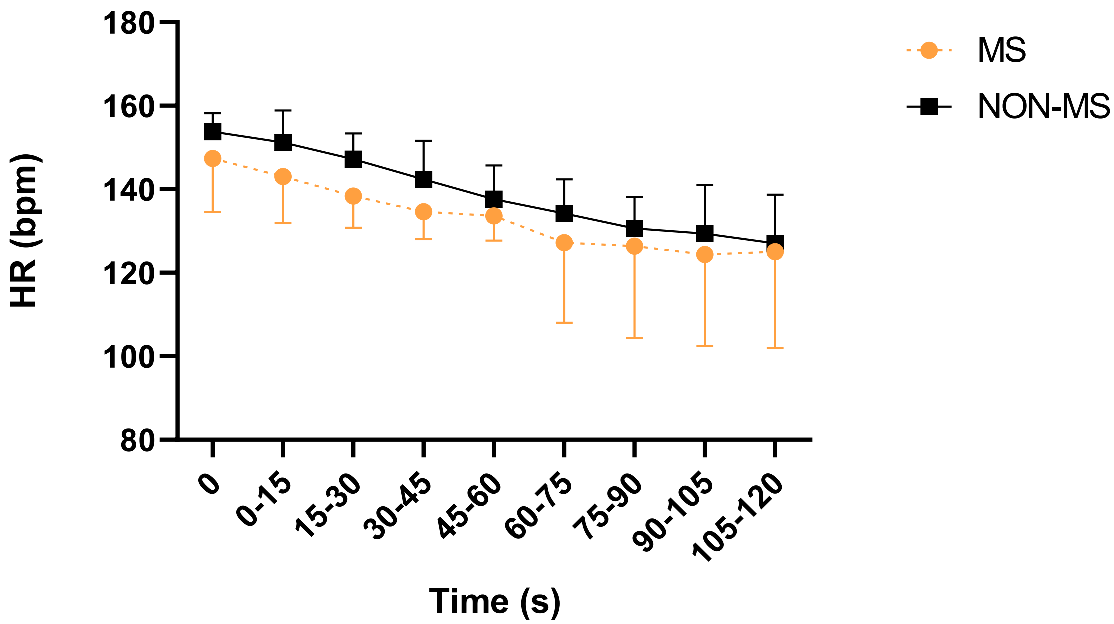
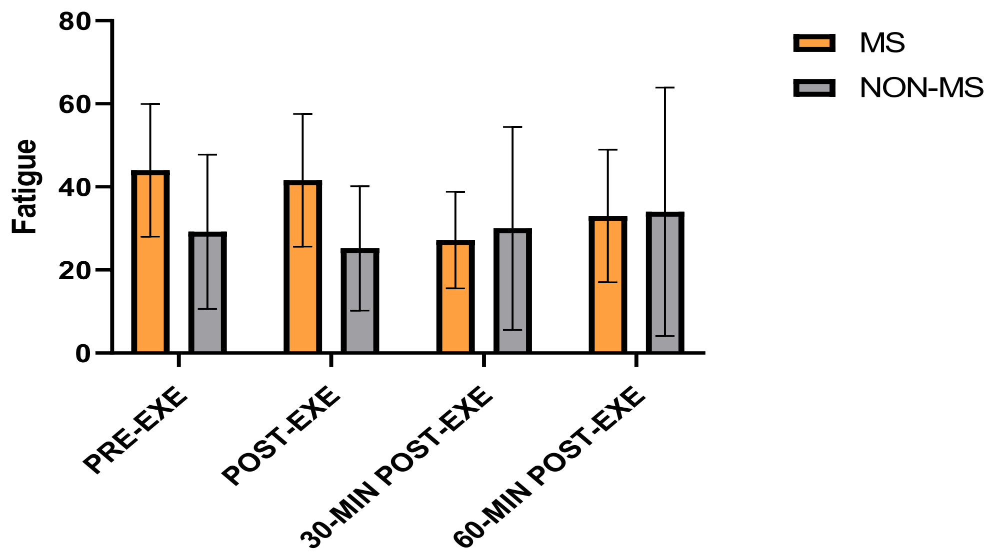


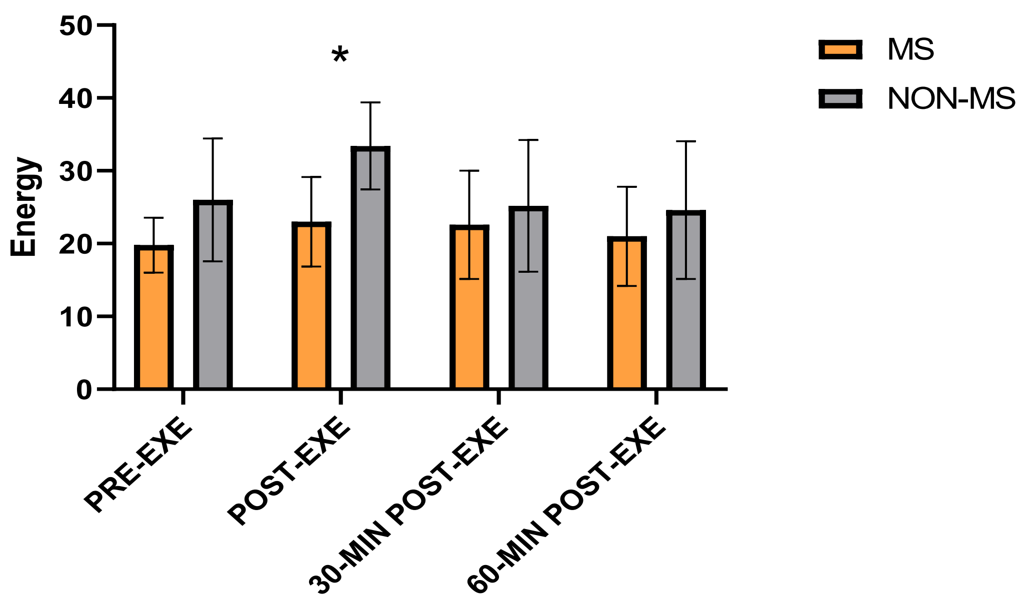
Figure 3. Time course of heart rate immediately following submaximal exercise expressed as 15 second mean (± SD) during the two-minute cool down phase between MS and NON-MS participants. Two-way repeated measures ANOVA were used to determine statistical significance ($p < 0.05$). MS participants: Orange circles and dotted line; NON-MS participants: Black squares and continuous line.

Acute Fatigue

Participants recorded their acute fatigue and energy levels using the VAS-F immediately prior-to and following exercise, and at 30 minutes and 60 minutes following exercise (see Figure 4). A Friedman test revealed fatigue measures did not change across exercise in both groups (MS; $p = 0.16$, NON-MS; $p = 0.69$), as well as energy measures (MS; $p = 0.61$, NON-MS; $p = 0.24$). Mann-Whitney analyses revealed energy values were significantly lower among MS participants compared to NON-MS participants immediately following exercise ($p = 0.04$), while fatigue and energy values were not different between groups across all remaining time points.



A)



B)

Figure 4. A) Acute fatigue response prior-to, immediately following, 30-minutes and 60-minutes following exercise. B) Acute energy response prior-to, immediately following, 30-minutes and 60-minutes following exercise. Both outcomes were measured via the VAS-F. Friedman test and Mann-Whitney test were used to determine statistical significance among groups ($p < 0.05$). PRE-EXE; Immediately prior-to exercise, POST-EXE; Immediately following exercise, 30-MIN POST-EXE; 30 minutes following exercise, 60-MIN POST-EXE; 60 minutes following exercise. *Indicates a significant difference between MS and NON-MS.

Acute Glucose

Acute glucose response to submaximal exercise was not different between MS and NON-MS participants. One MS participant was removed from analysis as the glucose sensor was not properly calibrated at the time of exercise, and one did not wear a continuous glucose monitor during exercise. Two-way repeated measures ANOVA did not find a significant effect of time or group (see Figure 5).

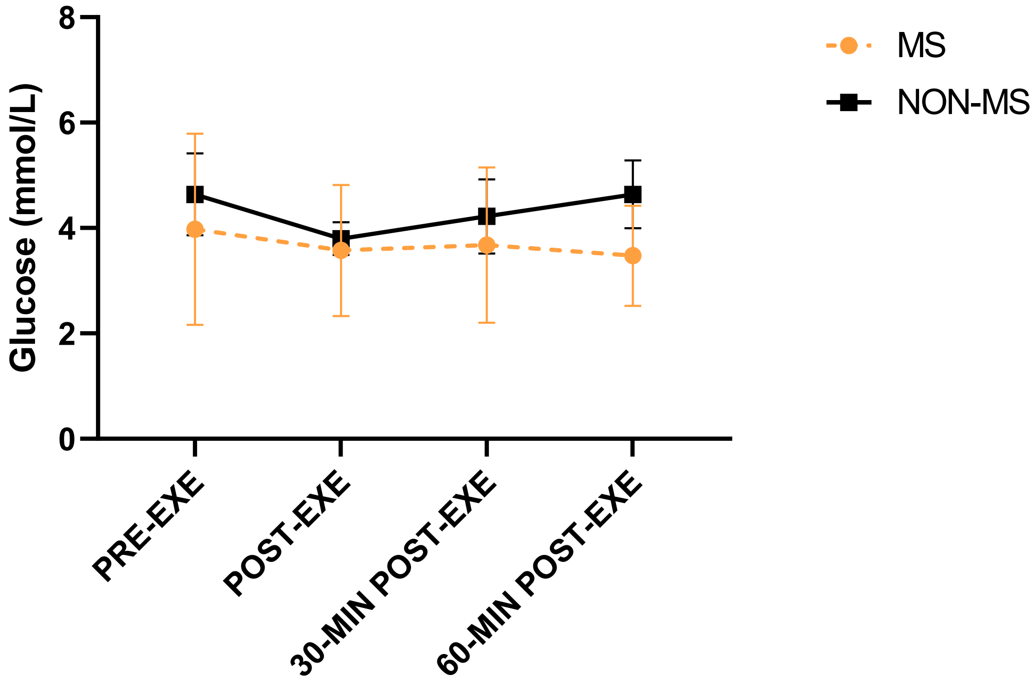
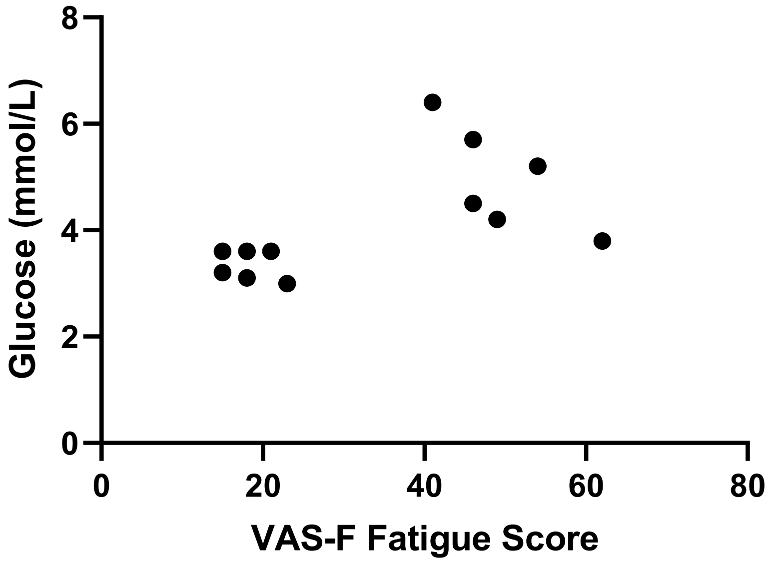


Figure 5. Acute glucose immediately prior-to exercise, immediately following, 30 minutes, and 60-minutes following exercise. MS (n = 3), NON-MS (n = 5). Two-way repeated measures ANOVA were used to determine statistical significance ($p < 0.05$) between groups and across exercise. PRE-EXE; Immediately prior-to exercise, POST-EXE; Immediately following exercise, 30-MIN POST-EXE; 30 minutes following exercise, 60-MIN POST-EXE; 60 minutes following exercise. MS participants: Orange circles and dotted line; NON-MS participants: Black squares and continuous line.

Acute Fatigue and Glucose Correlation

Spearman correlational analyses demonstrated a significant moderate positive correlation between acute fatigue scores and glucose across exercise among MS participants (n = 3, r = 0.63, $p = 0.03$), but no correlation was found for NON-MS participants (n = 5, r = -0.22, $p = 0.35$) (see Figure 6). Both data sets analyzed together demonstrated no correlation between acute fatigue and glucose values across exercise (r = 0.17, $p = 0.35$)



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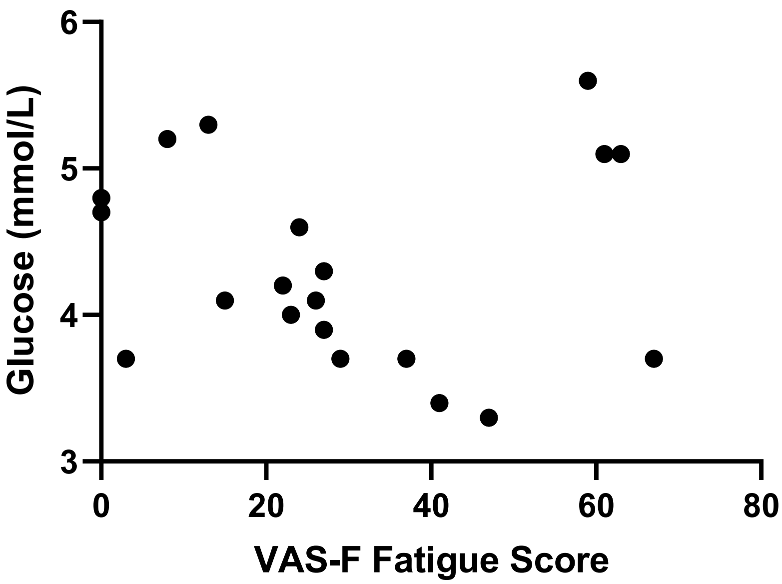
A)



B)

Figure 6. A) Significant positive correlation between VAS-F fatigue scores and glucose values across exercise among MS participants (n = 3). B) No correlation between VAS-F fatigue scores and glucose values across exercise among NON-MS participants (n = 5). Spearman correlation analysis was used to determine correlation coefficient and statistical significance among groups ($p < 0.05$). VAS-F; Visual Analog Scale to Evaluate Fatigue Severity.

Daily Physical activity and Sedentary Behaviour

We did not observe a difference between groups using objective (actigraph or activPAL) or subjective (IPAQ) assessments of physical activity or sedentary behaviour (see Tables 6, 7, and 8). A two-way ANOVA of sedentary, LPA and MVPA behaviour did not determine a significant effect of physical activity measure or group, however, effect of physical activity measure neared significance for sedentary (p = 0.07) and MVPA (p = 0.07) (see Figure 7).

Table 6. Actigraph measured physical activity and sedentary outcomes in MS and NON-MS participants.

Activity Type	**MS (n=5)**	**NON-MS (n=5)**	***P***
Wear time (minutes)	827 ± 46	834 ± 69	0.87
Sedentary (minutes)	571 ± 39	541 ± 39	0.25
LPA (minutes)	234 ± 22	239 ± 105	0.91
MVPA (minutes)	22 ± 13	54 ± 31	0.07
Sedentary (%)	69 ± 3	65 ± 10	0.45
LPA (%)	28 ± 2	28 ± 10	0.96
MVPA (%)	3 ± 2	6 ± 4	0.06

Data presented as mean ± SD unless otherwise indicated. Independent t-tests were used to determine statistical significance ($p < 0.05$) between MS and NON-MS participants. LPA; Light Physical Activity. MVPA; Moderate-Vigorous Physical Activity

Table 7. ActivPAL measured physical activity and sedentary outcomes in MS and NON-MS participants.

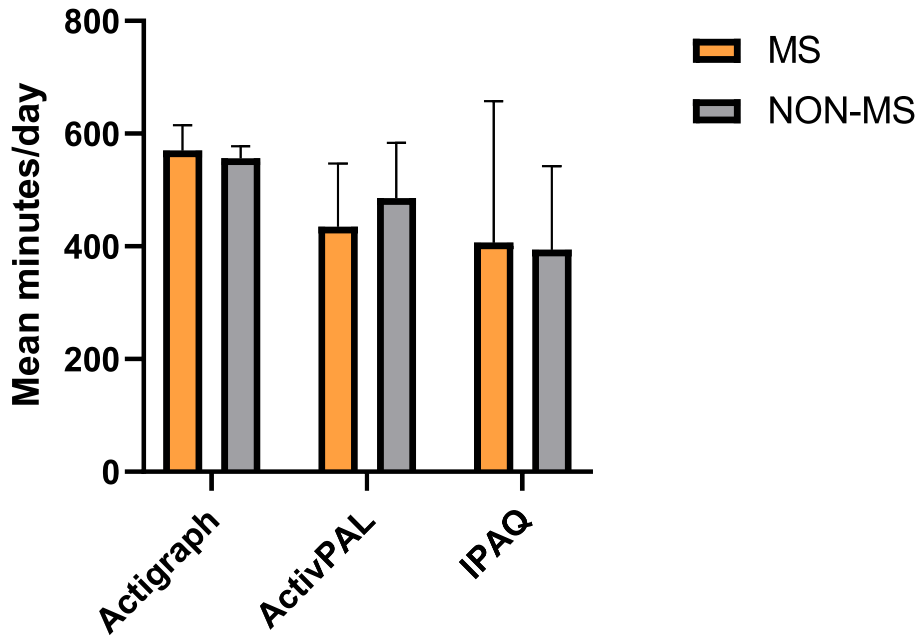
Activity Type	MS (n=5)	NON-MS (n=5)	*P*
Sedentary (minutes)	446 ± 101	444 ± 125	0.97
LPA (minutes)	252 ± 74	252 ± 114	0.99
MVPA (minutes)	52 ± 17	80 ± 30	0.10
Sedentary (% of day)	50 ± 11	51 ± 14	0.95
LPA (% of day)	28 ± 8	29 ± 13	0.94
MVPA (% of day)	6 ± 2	9 ± 4	0.10
# of Prolonged Sedentary Bouts >30 minutes	4.7 ± 1.9	3.9 ± 2.6	0.62
# of Breaks in Sedentary Behavior	53 ± 15	52 ± 10	0.93

Data presented as mean ± SD unless otherwise indicated. Independent t-tests were used to determine statistical significance ($p < 0.05$) between MS and NON-MS participants. LPA; Light Physical Activity. MVPA; Moderate-Vigorous Physical Activity

Table 8. Physical activity and sitting outcomes in participants with and without MS measured using the International Physical Activity Questionnaire.

	MS (n=5)	**NON-MS (n=5)**	***P***
Continuous Variables			
Total MET minutes	3095 ± 2314	4938 ± 5798	0.55
Sitting time (minutes)	405 ± 217	363 ± 145	0.78
VPA (minutes)	12 ± 16	58 ± 87	0.27
MPA (minutes)	92 ± 53	84 ± 56	0.84
Walking (minutes)	184 ± 196	125 ± 149	0.61
Activity Level Categories			
Low active	0	0	-
Moderate active	3	4	-
High active	2	1	-

Continuous data presented as mean ± SD unless otherwise indicated. Independent t-tests were used to determine statistical significance ($p < 0.05$) between MS and NON-MS participants. VPA; Vigorous Physical Activity. MPA; Moderate Physical Activity.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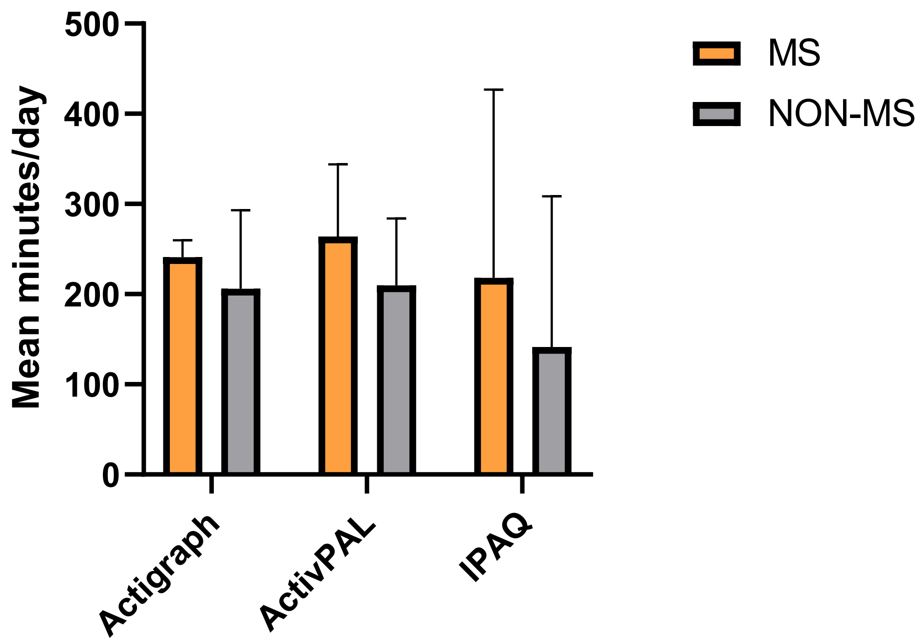
Mean minutes/day
Actigraph
ActivPAL
IPAQ
MS
NON-MS

A)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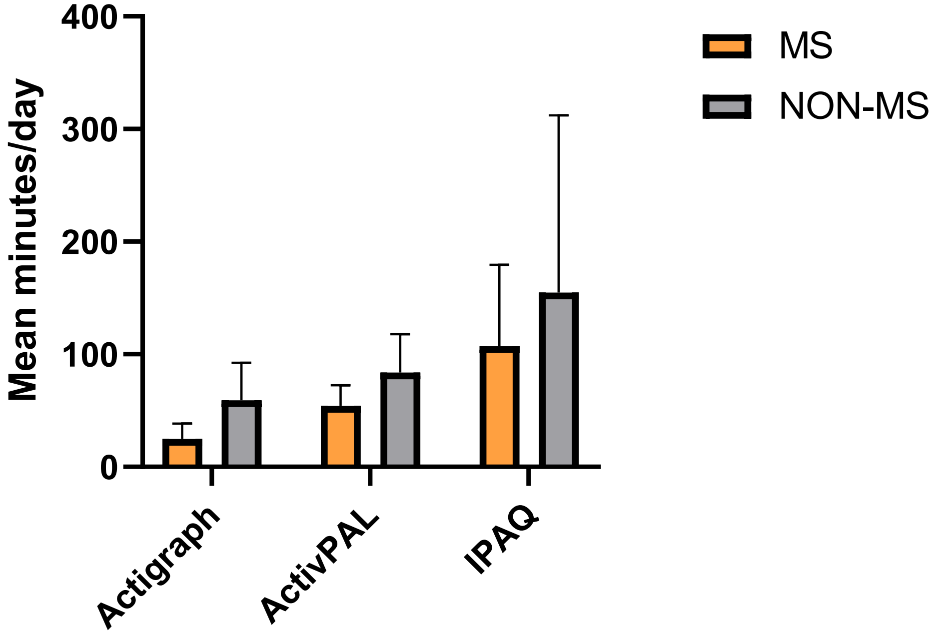

C)

Figure 7. A) Mean minutes per day of sedentary behavior - B) Mean minutes per day of light physical activity - C) Mean minutes per day of moderate-vigorous physical activity across actigraph, activPAL and International Physical Activity Questionnaire measures and between MS and NON-MS participants. Two-way ANOVA were used to determine statistical significance ($p < 0.05$) between each physical activity measurement and across groups. LPA: Light physical activity; MVPA; Moderate to vigorous physical activity; IPAQ: International Physical Activity Questionnaire.

Barriers to Physical Activity

Participants with MS reported a greater number of barriers to physical activity, and mean Likert-scale measures of severity for each barrier domain were not different between groups (see Table 9). Participants with MS identified 38/63 barriers across all domains, while participants without MS identified 17/63 barriers. Both groups identified the most barriers and highest severity scores within the Health domain (MS = 16; NON-MS = 10). Both groups reported they did not experience any barriers relating to Fitness Built Environment or Staff/Program/Policy.

Table 9. Barriers to physical activity reported by MS and NON-MS participants assessed using the Barriers to Physical Activity for Individuals with Mobility Questionnaire. Mean (± SD) severity scores and maximum possible value for each barrier domain are presented.

Barrier Domain	MS (n=5)	NON-MS (n=5)	*P*
Health (/35)	9.4 ± 5.7	5.6 ± 3.8	0.48
Beliefs/Attitudes (/40)	2.0 ± 1.4	1.0 ± 1.4	0.76
Friends (/30)	0 ± 0	0.4 ± 0.9	>0.99
Family (/25)	1.5 ± 1.9	0.2 ± 0.4	0.44
Fitness Centre/Built Environment (/55)	0 ± 0	0 ± 0	NA
Staff /Program/Policy (/50)	0 ± 0	0 ± 0	NA
Community Built Environment (/50)	2.8 ± 3.3	0.2 ± 0.4	0.37
Safety (/30)	0.4 ± 0.9	1.0 ± 1.4	0.72

Data presented as mean ± SD unless otherwise indicated. Multiple Mann-Whitney tests were used to determine statistical significance ($p < 0.05$) between MS and NON-MS participants.

Daily Multiple Sclerosis Symptom Tracking

Participants with MS recorded symptoms, novelty, duration and severity of symptom and effect on daily life for the 7 day period, excluding one participant who tracked MS symptoms for only 3 days. Two participants recorded they felt no symptoms throughout the entire study period (see Table 10). Across the 3 – 7 day tracking period and during or following the exercise protocol, participants who indicated symptom severity, all indicated the symptoms were mild, and predominantly had little effect on their daily activities. Additionally, none of the symptoms reported were novel to the individual. Two participants (0508KC & 0520AT) reported their symptoms arising between 1-2 days following the submaximal exercise protocol. Acutely, one participant (0583KN) reported foot drop arising during the exercise protocol which remained for 30 minutes following exercise.

Table 10. MS symptoms recorded among MS participants across a three to seven day period following a submaximal exercise bout.

Participant 0508KC

Symptom	Novel	Duration (days)	Severity	Effect on Daily Life
Visual Disturbances	No	2.5	Mild	Not too much
Spasticity	No	3	Mild	It is hard to ignore
Fatigue	No	4	Mild	Not too much

Participant 0520AT

Symptom	Novel	Duration (days)	Severity	Effect on Daily Life
Clumsiness	No	0.04	Mild	Not too much

Participant 0567CL

Symptom	Novel	Duration (days)	Severity	Effect on Daily Life
Constipation	No	2	-	-
Dizziness	No	2	-	-
Confusion	No	1	-	-
Memory Loss	No	1	-	-
Overheating	No	1	-	-
Headache	No	1	-	-
Fatigue	No	1	-	-

Participant 0583KN

Symptom	Novel	Duration (days)	Severity	Effect on Daily Life
Right foot drop	No	0.02	Mild	Not too much

Participant 0523NM

Symptom	Novel	Duration (days)	Severity	Effect on Daily Life
No symptoms reported	NA	NA	NA	NA

Participant 0534SVB

Symptom	Novel	Duration (days)	Severity	Effect on Daily Life
No symptoms reported	NA	NA	NA	NA

Daily Glucose Values (fasting, 24 hour, peak, nadir, time < 3.3, time >7.8)

We did not observe a difference in daily glucose values between MS and NON-MS participants. Independent t-tests demonstrated fasting, 24 hour mean, peak, nadir, time in hyperglycemia and hypoglycemia values were not significantly different between MS and NON-MS groups (see Table 11).

Daily Glucose Values and Fatigue Correlation

Spearman correlation analysis determined baseline MFIS fatigue scores were not correlated with 24h mean (MS: r = -0.8, p = 0.33; NON-MS: r = -0.6, p = 0.35) or fasting (MS: r = -0.4, p = 0.75; NON-MS: r = -0.4, p = 0.52) glucose values among each group, and combined (r = -0.37, p = 0.34). One MS participant was removed from analysis as the MFIS was not completed (MS: n = 4; NON-MS: n = 5).

Table 11. Mean daily glucose values (fasting, 24h, peak, and nadir values, and time in target, time below 3.3 mmol/L and above 7.8 mmol/L of MS and NON-MS participants.

	MS (n=5)	**NON-MS (n=5)**	***P***
Fasting (mmol/L)	3.9 ± 0.5	4.0 ± 0.3	0.64
24h mean (mmol/L)	4.4 ± 0.7	4.4 ± 0.2	0.90
Peak (mmol/L)	6.9 ± 1.6	6.6 ± 0.8	0.67
Nadir (mmol/L)	2.9 ± 0.4	2.9 ± 0.4	0.90
Time < 3.3 (mins)	150.7 ± 220.3	85.5 ± 86.5	0.56
Time > 7.8 (mins)	11.1 ± 24.5	0 ± 0	0.34

Data presented as mean ± SD unless otherwise indicated. Independent t-test was used to determine statistical significance (p < 0.05) between MS and NON-MS participants.

CHAPTER 6: DISCUSSION

To our knowledge, this study is the first to examine acute physiological responses to submaximal prenatal exercise and physical activity patterns among pregnant people with MS. Subjective ratings of perceived exertion were similar between both groups during exercise, but MS participants achieved a lower heart rate during the exercise bout. Further, participants with MS reported lower levels of energy immediately following exercise compared to NON-MS participants. Physical activity patterns were not different between groups however, actigraph (p=0.07) and activPAL (p=0.10) trended towards significantly lower MVPA for the MS compared to the NON-MS group. Further, participants with MS reported a greater number, but not severity, of barriers to physical activity compared to NON-MS participants. Acute glucose during and following exercise, heart rate recovery, and daily glucose levels did not differ between participants with and without MS.

Acute Responses to Prenatal Submaximal Exercise

Heart Rate

We observed similar ratings of perceived exertion to an acute bout of exercise between MS and NON-MS participants despite a lower heart rate response for MS participants (MS = 129 ± 11 bpm; NON-MS = 149 ± 4 bpm). These data suggest MS participants subjectively feel they are working at a higher intensity than would be estimated by heart rate during exercise. The reason for this is unclear, however, exercise tolerance is often lower among people with MS compared to controls without MS. This has most often been observed through lower peak aerobic capacity among MS participants,[136] which may be associated with lower daily physical activity levels.[137] Among the current sample, we observed that MS participants participated in lower levels of MVPA during the study period compared to NON-MS (MS; 22 – 52 minutes/day, NON-MS; 54-80 minutes/day). Although this did not reach statistical significance, the number of included participants was small. It has been demonstrated that RPE scores are influenced by level of fitness, where individuals with lower fitness levels perceive themselves under more exertion compared to individuals of higher fitness levels for the same load of activity.[138] Similar results have been replicated in people with MS where participants report a similar level of exertion for smaller workload completed compared to controls without MS.[139, 140] As such, participants with MS may have reduced exercise tolerance compared to controls, and could not achieve as high of an exercise intensity but subjectively felt they were exerting at the same level.

Reduced exercise tolerance may also be due to cardiovascular autonomic dysfunction among individuals with MS, which can influence acute physiological response to exercise. Cardioautonomic dysfunction during dynamic exercise, which has been observed among people with MS, is blunted heart rate initiation to graded exercise. Several studies have noted that individuals with MS achieve a significantly lower intensity during exercise testing compared to controls,[141, 142] which could be another effect of cardioautonomic dysfunction. Although it has not been directly tested, some hypothesize that individuals with MS may have a blunted maximal heart rate due to impaired sympathetic cardiac control.[71, 143] Theoretically, this limits the ability to interpret heart rate during exercise, particularly nearing maximal intensities. In the current study, we instructed participants to exercise at 60-70% HRR, however, a maximal heart rate, which is lower than age-predicted, results in a smaller HRR than would be predicted using the traditional formula (HRR = HRmax – HRresting). This would result in participants with MS working at a greater intensity for a given heart rate than would be estimated by the %HRR formula. This, in conjunction with similar levels of exertion reported between groups, may suggest absolute metrics of cardiovascular exertion, such as heart rate, would be higher for a given intensity in pregnant people with MS. Further, a lower sympathoexcitatory response to prenatal exercise may blunt maximal heart rate,[144] producing an aggregated effect in pregnant individuals with MS, limiting HRR even further. These results suggest absolute heart rate during exercise in individuals with MS during pregnancy may not be a valid measure of exercise intensity. Future investigations should conduct graded exercise protocol to examine differences in groups between change in heart rate at each grade, as well as maximal heart rate achieved and reasons for stopping exercise. This investigation could help reveal cardiac sympathetic outflow during increasing exercise intensity, as well as heart rates at volitional exhaustion in this population. Further, establishing resting physiological measures of heart rate and blood pressure, as well as response to a sympathetic challenge, such as a cold pressor test, and resultant physiological response would also provide insight to sympathetic state of pregnant individuals with MS.

Heart Rate Recovery

We observed that heart rate recovery in the two minutes following exercise was not different between MS and NON-MS participants. Specifically, change in heart rate at each 15 second interval and absolute heart rates were not different at each time point. Interestingly, although mean heart rate during exercise was significantly lower in MS participants, heart rate at the end of the exercise period was not significantly different between groups (MS; 145 ± 16, NON-MS;151 ± 8, $p = 0.43$). This suggests participants with MS increased intensity near the end of the 20 minute exercise protocol, however, this value is not representative of the mean heart rate intensity achieved throughout exercise. Heart rate recovery is considered a metric of autonomic cardiac control, and is a strong predictor of cardiovascular mortality.[132] At the end of physical exertion, parasympathetic cardiac control increases while a progressive withdrawal of sympathetic control occurs to reduce heart rate to baseline values.[145] A more rapid recovery (larger reduction in heart rate in the two minutes following exercise) is indicative of higher parasympathetic tone, suggesting a greater level of fitness and overall cardiovascular health.[146] At this point, there are no established criteria for reduction, or lack thereof, of heart rate following exercise that indicate an accelerated or attenuated heart rate recovery. As such, an altered heart rate recovery is determined based on differences between groups within a study. In the current study, we observed change in heart rate was not different between groups at each 15 second period, nor were absolute heart rates at each 15 second period until 2 minutes post-exercise. These results suggest parasympathetic reactivation following exercise is not different between pregnant people with and without MS. Our findings contribute to the contradictory results, which have been observed among people with MS, demonstrating both altered and typical heart rate recovery.[141, 147, 148] Rampichini et al., (2020) observed that short term heart rate recovery (within 30 seconds following exercise) was significantly blunted in participants with MS suggesting that cardiac parasympathetic reactivation is reduced.[147] Our findings of similar heart rate time course immediately following exercise suggest that parasympathetic cardiac control may not be altered in pregnant individuals with MS. Additionally, this corroborates the hypothesis that parasympathetic cardioautonomic dysfunction increases with duration of MS,[149] as time since diagnosis was low amongst our sample. To our knowledge, heart rate recovery has not been investigated among pregnant individuals (without MS) following physical activity. As pregnancy is a state of heightened sympathetic and reduced parasympathetic activity, we hypothesize pregnant individuals may demonstrate an accelerated heart rate recovery following the same relative exercise intensity, compared to non-pregnant individuals. This would likely be a typical adaptation to pregnancy, and not indicative of elevated cardiovascular mortality as is seen in non-pregnant populations.

Although heart rate at the end of exercise was not different, overall intensity achieved was higher among NON-MS participants, which may have influenced results as this is associated with greater increase in sympathetic activity and metabolite response which can cause an attenuated heart rate recovery.[150] Further research is required, with a more tightly controlled exercise protocol, between pregnant individuals with and without MS to determine potential alterations in parasympathetic cardiac control between groups.

Acute Fatigue and Symptomatic Response

Fatigue and energy were not different prior to exercise, however, the MS group experienced lower levels of energy (but not fatigue) immediately following exercise. Values were not different between groups at 30 and 60 minutes of recovery. No change in fatigue or energy levels across exercise suggests the bout of exercise was not fatiguing to either group, but MS participants felt submaximal exercise was more taxing than participants without MS. Exertion during exercise was also assessed through the Borg 10-point RPE scale, which has been validated among people with MS.[151] It has been demonstrated that participants with MS report greater RPE values during repeated submaximal isometric contractions compared to participants with MS, indicating perception of exertion is greater for the same relative intensity among people with MS.[152] However, contradictory results have been observed; Morrison et al., (2008) reported similar RPE between participants with and without MS during submaximal exercise. Further, participants with MS in this study reported higher levels of day-to-day fatigue (measured by MFIS) which suggests MS fatigue symptoms may not effect perception of effort during exercise.[153] While we observed similar levels of acute fatigue immediately prior-to exercise in both groups, cognitive fatigue measured by the MFIS was significantly higher among MS participants. As such, a higher level of cognitive fatigue may have contributed to a similar perceived exertion score for a lower intensity of exercise. An additional consideration includes the temporary onset of symptoms during exercise in people with MS. Anecdotally, 2/5 participants with MS justified an RPE score based on symptoms during exercise (fatigue, overheating, and right foot drop). The sudden onset of symptoms during exercise is an additional physiological response, which might increase perception of exertion during exercise.

Importantly, fatigue did not increase significantly in the hour following submaximal exercise among MS participants. As 83% of individuals with MS indicate fatigue increases substantially following vigorous exercise,[154] this is an important finding which confirms the intensity achieved by MS participants does not induce significant increases in fatigue. Fatigue exacerbations following exercise in people with MS can range from a mild to severe, with a severe exacerbation resulting in an inability to complete activities of daily living following exercise.[155, 156] As such, prenatal exercise intensity, which can induce optimal maternal and fetal benefit, without exacerbating fatigue to a debilitating level, is critical for pregnant people with MS. Symptom exacerbations in the seven days following exercise were not noted either. Two out of five MS participants reported symptoms arising, which ranged from lasting 1 hour – 4 days post-exercise. While we cannot determine if the exercise protocol influenced symptom onset, we report that no adverse or severe symptoms occurred in the seven days following light to moderate exercise among MS participants.

Acute Glucose

Acute glucose response to exercise was not different between participants with and without MS, and glucose values did not change significantly in response to exercise in both groups. No change in glucose across exercise suggests the volume of exercise was not enough to incur a significant reduction in blood glucose. A systematic review observed an inverse dose response relationship between volume of exercise (METs minutes) and glycemic response during pregnancy, as well as a significant influence of duration of exercise.[157] As such, the 20 minutes of light to moderate intensity exercise completed by all participants was likely not a significant stress on the maternal metabolic system. In both groups, data indicated glucose values were trending toward decreasing during exercise and increasing in the hour following exercise. It is possible glucose values began to decrease during exercise, but the 20 minute duration was not long enough to incur a significant reduction in blood glucose. As pregnancy is associated with lower hepatic glycogen stores,[112] these results could indicate glucose would have continued to decrease with longer duration of exercise. Additionally, a properly powered study would reduce between subject variability and it is possible that a significant decrease in blood glucose could be observed in the current protocol.

Acute glucose response to exercise among people with MS has been investigated sparsely. One study investigated the impact of an acute bout of exercise on carbohydrate metabolism in people with MS immediately following an oral glucose test.[158] Plasma glucose was not different between participants with and without MS at rest, and carbohydrate oxidation increased more strongly in participants with MS compared to controls but was not significant. These results are supported by another study, which demonstrated glucose uptake in the leg muscles of participants with MS during walking exercise was not different compared to controls.[159] Together, these results suggest acute glucose response to exercise is not different between people with and without MS (non-pregnant). The present study corroborates these findings in pregnant individuals with MS, observing that acute glucose values prior-to and in the hour following exercise were not different between groups. Although these studies utilized different methodology (venous blood sample[158] and Fluorodeoxyglucose injection prior-to exercise and positron emission tomography/computed tomography following exercise[159]) compared to the current study, this demonstrates that across multiple measures of glucose utilization during exercise, no significant differences were noted. This suggests MS pathology does not directly impact acute glucose response to exercise. Further research is needed to confirm if the maternal adaptations to pregnancy alter acute glucose response during and following exercise in people with MS.

Acute Fatigue and Glucose Correlation

We observed a moderate positive correlation between measurements of acute fatigue and glucose response across exercise in MS participants. A correlation was not found among NON-MS participants, nor when data was grouped together. It is known that MS fatigue can increase substantially following vigorous exercise, however improvements in fatigue have been reported following moderate exercise.[154] As described above, there is minimal research which has investigated acute glucose response to exercise among people with MS, as such the relationship with acute fatigue is unknown. It is likely that this correlation was not observed among NON-MS participants as change in fatigue scores across exercise were not as substantial compared to MS participants. This suggests MS participants may be more sensitive to changes to acute fatigue levels compared to NON-MS participants. This data must be interpreted cautiously as the sample size of MS participants was reduced for this correlational analysis (MS: $n = 3$), whereas NON-MS and grouped analyses containing larger data sets revealed no correlation.

Daily Physical Activity and Sedentary Behaviour

Participants wore objective physical activity and sedentary behaviour monitors (acitgraph and activPAL) and completed subjective assessments of physical activity following the exercise protocol. We observed that physical activity levels and sedentary behaviours were not different between groups, contrary to the hypothesis, although levels of MVPA neared significance in acitgraph and acitvPAL measurements. It has been demonstrated that non-pregnant females and males with MS have greater rates of sedentary behaviour, and individuals with MS achieve less MVPA compared to controls without MS.[137] The reduction in symptom severity typically associated with pregnancy in individuals with MS may contribute to these results as level of symptom severity is positively correlated with sedentary time in individuals with MS.[160] Further, volume of sedentary behaviour is even greater in individuals with MS who experience a mobility impairment,[161] and our sample could all ambulate without the use of assistive devices and did not report significant mobility impairments. An important consideration is a potential sampling bias, which may have influenced physical activity measurements, particularly rates of MVPA among NON-MS participants. While NON-MS participants may be motivated to participate in this study as they are already active during pregnancy, MS participants may instead be more attracted due to the lack of data surrounding MS and pregnancy. As such, NON-MS participants may be reflective of individuals without MS who engage in higher rates of MVPA during pregnancy compared to most pregnant people. Although there are multiple variables which may have contributed to the observed effect, sample size is a considerable limitation of this result and further investigation is required.

Objective and Subjective Measures of Physical Activity and Sedentary Behaviour

The mean minutes per week that MS and NON-MS participants spent in sedentary, LPA and MVPA did not differ significantly between devices, and were not different between groups. An effect of physical activity measure neared significance for sedentary and MVPA behaviour; among both groups, results trended towards participants indicating a greater amount of MVPA through the IPAQ compared to objective measurement devices. However, these differences are not significant at this point, given the influence of a small sample size and high amount of variability among IPAQ data. These results align with previous research among people with MS, which demonstrates only a moderate correlation between physical activity measurements from the actigraph and IPAQ.[123] Further, it was observed that IPAQ and actigraph physical activity measures were not significantly correlated among pregnant people without MS.[162] We also observed near significant effect of physical activity measure across devices for sedentary behaviour ($p = 0.07$). A similar trend was observed among pregnant people (without MS) which demonstrated a weak correlation coefficient ($r < 0.5$) between the activPAL and a subjective sedentary assessment (Sedentary Behavior Two Domain Questionnaire).[163]

A potential influence of our near significant result of an effect of physical activity measure for time spent in MVPA may be the use of subjective descriptors to identify time spent in walking, moderate and vigorous physical activity. The IPAQ describes moderate intensity leisure-time physical activities as doing an activity at a ‘regular pace’, and vigorous intensity at a ‘fast pace’, and provides examples of activities for respondents. As determined earlier, subjective perceptions of exertion were similar between groups, despite a lower intensity of exercise among MS participants. As such, MS participants may indicate they engage in greater amounts of MVPA through the IPAQ due to subjective descriptors, however, objective devices quantify the activity as LPA. While the quantitative value of energy expenditure may not be different between the groups for the same activity, participants may subjectively feel they expend more energy completing the same activity and thus consider it MVPA according to the IPAQ. This effect would be unsurprising, as a common critique of subjective measures of physical activity is misinterpretation of questionnaire wording.[164] It is likely that a combination of objective measurements of physical activity and subjective measures of exertion would help researchers best understand levels of physical activity among pregnant people with MS.

Barriers to Physical Activity

The BPAQ-MI was administered to participants to assess barriers to physical activity between groups and contextualize objective and subjective data from accelerometers and the IPAQ. Participants with MS indicated 33% more barriers to physical activity (n = 38/63) than participants without MS (n = 17/63), but the overall severity of barriers was mild and not different between groups. It has been demonstrated that the BPAQ-MI is negatively correlated with minutes/week of exercise and positively correlated with hours/day of inactivity[165] and as such is an appropriate tool to help further understand objective accelerometry data between groups. The BPAQ-MI results indicate participants with MS experience more barriers relating to health and community-built environment. Specifically, two of five MS participants indicated feeling depressed as a barrier to physical activity, while no NON-MS participants listed this as a barrier. This finding is supported by epidemiological data indicating prevalence of depression is two to five times higher among individuals with MS compared to the general population.[166] Further, a recent study found that individuals diagnosed with MS prior-to pregnancy had an increased risk of developing prenatal depression.[167] Although no MS participants indicated a diagnosis of prenatal or general depression, this finding suggests feelings of depression are a greater barrier to prenatal physical activity compared to pregnant NON-MS participants. A greater number of MS participants also indicated lack of rest areas and access to public washrooms as community-built environment related barriers to physical activity. Higher levels of fatigue among MS participants may contribute to lack of rest area as a barrier to physical activity, but it is unclear why access to public washrooms is a greater barrier compared to NON-MS participants.

While the BPAQ-MI provides important data which enriches our physical activity and sedentary behaviour data, it is difficult to determine if differences in barriers to prenatal physical activity between groups are a greater effect of MS or pregnancy, or potentially an aggregated effect of both. The BPAQ-MI is not validated for use during pregnancy and thus is not designed to detect these changes.

Daily Glucose Outcomes

Overall, we demonstrated that daily glucose outcomes (fasting, 24 hour mean, peak, nadir, time in <3.3, time in >7.8) were not different between pregnant participants with and without MS. Evidence that glucose intolerance is related to MS pathology is conflicting, with evidence both demonstrating[168] and denying[158] glucose intolerance. Despite this, prevalence of glucose intolerance is higher among people with MS compared to those without MS.[168] A proposed hypothesis for observations of altered glucose metabolism in people with MS is mitochondrial dysfunction. It has been demonstrated that the number of mitochondria and their level of activity is heightened within MS lesions,[169] likely due to increased energy needed to survive within the degenerative environment of the CNS.[170] Peripherally, it has been demonstrated that complex 1 activity within mitochondria of the skeletal muscle was significantly reduced in patients with MS.[171] Although not investigated, a lower amount of mitochondrial activity within skeletal muscle may be influenced by reduced physical activity levels typically observed among people with MS.[172, 173] Limited data on glucose regulation during pregnancy in this population suggests prevalence of gestational diabetes is not different than the general population. Conflicting evidence suggests glucose metabolism may be altered in people with MS, and findings suggest this effect occurs later in condition progression.[174] As such, atypical glucose metabolism may not have been observed among participants with MS who were early in condition progression. Overall, our data does not suggest daily glucose patterns differ between people with and without MS during pregnancy, however, greater sample size is required to assess differences.

Daily Glucose and Fatigue Correlation

We observed no correlation between 24 hour and fasting glucose values, and overall fatigue scores measured by the MFIS. Primary contributors to MS fatigue include increased levels of pro-inflammatory cytokines, reduced nerve impulse conduction and mitochondrial dysfunction.[37, 175] Roelcke et al., (1997) observed individuals with MS who experienced fatigue demonstrated reduced cerebral glucose metabolism, suggesting glucose metabolic dysfunction is associated with symptomatic fatigue.[176] However, the relationship between continuous glucose measures and fatigue in people with MS has not been assessed. This has also not been investigated among pregnant people without MS even though fatigue is commonly reported throughout pregnancy. Our study suggests overall MFIS fatigue scores do not correlate with fasting or 24 hour mean glucose values in participants with MS. Thus, other factors likely influenced the heightened cognitive fatigue scores among MS participants.

Strengths

The novelty of this study is an immense strength of this project. We present the first ever data of prenatal physical activity in people with MS which describes unique perceptions of physical exertion in pregnant people with MS. Additionally, we utilized a study design which allowed participants to engage in types of exercise that were accessible to them. This increases the external validity of our data. Further, we have included assessments of barriers to physical activity in aim to contextualize physical activity measures and differences between groups. The purpose of this measure was to better understand contributing factors to physical activity and sedentary behaviour results. Employment of questionnaires regarding barriers to physical activity allows a less presumptive interpretation of accelerometry and physical activity questionnaire data and presents other contributing factors to results apart from condition pathology or symptoms.

Lastly, a strength of this research design was the reflexive journal maintained throughout the project. A reflexive journal invites the examination of personal assumptions at all stages of the research process. Further reflection from the reflexive journal is discussed in Chapter 7.

Limitations

The most notable limitation of this study was the small sample size within each group. A sample size calculation was conducted using data from males and females with MS, which indicated 13 participants per group were required to detect significant differences. As such, unfortunately, this pilot study is underpowered and continued investigation is required to observe differences between groups.

The virtual nature of this study was required due to COVID-19 considerations, which presented a number of limitations to the study design and results. The Polar H6 heart rate monitor utilized in this study was selected as it is a minimally invasive device, which can be sent via mail. The limitation of this instrument is the scope of information it can provide is very small and therefore interpretation is limited. In future investigations, more detailed data can be procured through measurement of acute physiological responses to prenatal exercise such as blood pressure regulation, heart rate rhythm, and thermoregulation. These responses are particularly relevant to maternal and fetal safety throughout exercise and may be meaningful for pregnant people with MS. Additionally, a controlled testing environment could not be achieved thus factors such as ambient temperature, time of day and nutrients consumed prior-to exercise were not controlled and may have influenced acute physiological response to exercise results. Further, as workload could not be objectively calculated, we relied on heart rate as a metric of workload. While we demonstrated heart rate intensity achieved is lower among MS participants, we cannot confirm the workload completed by either group, thus limiting observations of physiological response in relation to work completed. Another limitation of the data, is the lack of racial diversity amongst participants as all participants were Caucasian. This may be due, in part, to recruitment methods largely done through social media including Facebook and Instagram, which may have reached more homogenous populations (young Caucasian females). Unfortunately, this limits the external validity of the data to the larger population of pregnant individuals with MS

Another limitation of the current study is use of medical model tools, which have medical model scoring procedures such as SymptoMScreen and IPAQ. While these questionnaires do provide additional information about each participant, it is integral to note their scoring is largely dichotomous (i.e. active or inactive) which aligns with the medical model. Despite these limitations, what was important to the result interpretations was using the information retrieved from these questionnaires to enrich the results observed, as opposed to label participants.

Lastly, a collaborative and participatory research design was not utilized within this research project. This may limit the relevance of our results to pregnant people with MS and may not address concerns within the community.

Future Directions

Future investigations with larger sample sizes are needed to understand acute physiological responses to prenatal exercise in people with MS. Research should investigate perceptions of exertion and symptomatic response at multiple exercise intensities throughout pregnancy. Further, long-term studies examining the benefits of, accessibility and barriers to physical activity during pregnancy in people with MS should be conducted. Specifically, prenatal physical activity prescriptions which can induce beneficial maternal and fetal physiological adaptation but do not incur non-favourable fatigue or other symptomatic responses must be determined. Lastly, it is important to understand the meaningfulness and impact of exercise for individuals with MS during pregnancy. While we know that physical activity is highly effective in managing MS symptoms, there are unique factors that may influence willingness to engage in physical activity during pregnancy. Future investigations should be tailored to meet the questions and needs of pregnant individuals with MS.

CHAPTER 7: CONCLUSIONS AND REFLECTION

Based on the current results, pregnant individuals with MS experienced similar perceptions of exertion as individuals without MS for a lower intensity of exercise. Our results suggest fitness levels between groups, and symptomatic response to exercise may have limited participants with MS from achieving comparable exercise intensities. Participants with MS reported significantly lower levels of energy immediately following exercise, but levels of fatigue and energy were not different between groups prior-to, 30 and 60 minutes following exercise. Additionally, we note that during pregnancy, individuals with MS engage in similar levels of sedentary behaviour, LPA and MVPA during pregnancy, as individuals without MS. Participants with MS experienced a higher number of barriers compared to participants without MS, although both groups reported mild barrier severity.

This is the first study to investigate acute physiological responses to prenatal physical activity in individuals with MS, as well as physical activity, fatigue, and glucose patterns. There are significant gaps in our knowledge of prenatal health among people with MS. Notably, it is unknown if current prenatal physical activity recommendations are appropriate for this population. The present study determined individuals with MS did not experience adverse fatigue response to the light to moderate exercise performed but reported similar levels of exertion for a lower exercise intensity. As such, it is unclear if meeting guideline recommendations would induce adverse fatigue outcomes. Further research is required to better understand the ability to, and effect of meeting current physical activity recommendations during pregnancy among people with MS.

Reflections of Disability and Health Research

Throughout the present study, I maintained a reflexive journal to continually examine my role and influence as a non-disabled researcher conducting disability research. This chapter presents a reflection on my attempt to conduct an exercise physiology and disability research study outside of the medical model of disability. It contains critical reflections and key passages from my reflexive journal. Firstly, I examine the reliance on the medical model in MS and physical activity research and my efforts to divert from this model. Secondly, I reflect on my attempt to adopt a post-positivist paradigm, and how positivist physical activity and disability research may utilize post-positivist methodology moving forward.

Medical Model and Multiple Sclerosis Research

As described earlier, there is extensive research that has demonstrated physical activity has numerous benefits for individuals with MS. Specifically, how physical activity can help individuals with MS manage symptoms, or even potentially remediate condition pathology. While it is critical that this research inform healthcare for people with MS, many have advocated that the remediation of impairment is not the only, and not always the most important, aspect of health for people with impairments.[177-181] The concept that improved health of those with impairments revolves around alleviation of impairment aligns with the medical model of disability which positions disability as tragedy and unhealthy, or at least, not healthy.[16] Health is often positioned on a spectrum, where an individual can be more or less healthy.[182] In individuals with impairments, a diagnosis is assumed to be the key limitation to achieving greater health, and therefore sliding on the scale towards healthy requires reduction of impairment.

The medical model of disability considers the treatment of impairment, including management of symptoms, the highest priority of people with impairments which has trickled down into research priorities of exercise physiology.[183] In order to demonstrate that physical activity can improve the health of people with MS, which is solely considered the remediation of impairment, the research must centre around treatment of impairment. The medical model is heavily relied on within this research field, as it still promotes that benefits of physical activity for people with MS are exclusively tied to treatment of impairment. Therefore, investigating effects of physical activity outside of the context of impairment is largely un-investigated because it holds little to no value under the medical model.[184]

As a result, the introduction of a research study that does not uphold the understanding of exercise as a way to cure or manage MS, may be met with misunderstanding of its relevancy for people with MS. My personal experiences of describing this research project to others, is often met with what I term "So what? Moments". Below, the reflexive journal passage was written following a call with a prospective participant where I described the study in detail, including the relevance and purpose of the study. The individual did not participate in the study following the recruitment call but would have participated as an individual without MS:

> An uncomfortable moment occurred today where a potential participant, who did not have MS, questioned to relevance of the project to individuals with MS. After the question was asked, I fell silent and felt awkward since I had already described the novelty of the study and the lack of data in prenatal physical activity prior. So I imagine what was really being asked being asked was 'How does this project fix MS?'. This was not the first time that someone had looked at me as if I hadn't quite finished yet after I describe my research. I call these instances "So what? Moments.". It is unsurprising that the relevance of this project be questioned as the medical model of disability is used most often in healthcare and health research. If the dominant narrative is 'healthy = cured', then of course, disability health research would naturally surround curing or alleviating impairment. These moments are uncomfortable, and even though I feel strongly about the need for this project, they still make me worry the project may not be perceived as well as I hope it will be…

One reason these moments occur is because the medical model of disability clashes with the research objectives of this project, as there is no attempt to remediate MS. The described research project is concerned with understanding if and how pregnant people with MS can obtain benefits of prenatal physical activity that have already been investigated in pregnant people without MS (described in Chapter 2) and hence the utility of the research is often questioned. Unfortunately, these moments mean it can be difficult to justify the need for and objectives of this research project particularly within medical and research arenas. Nevertheless, the need to do this work is urgent. Diverting away from the medical model within exercise physiology and MS research opens up new opportunities to generate knowledge within the field, which will challenge others to understand health as much more than impairment. Further, this also challenges the dominant medical model and requires collaboration with the people who experience the conditions we are researching to determine what needs to be researched and how. If the medical model continues to be to the primary lens through which health, impairment and exercise are understood, then people with impairments will continue to be excluded from health research and clinical gaps in knowledge will remain.

Post-positivist Paradigm and Disability Health Research

Disability research methodology, across numerous fields of research, has been debated and scrutinized for years.[185] Within exercise physiology and disability research, also called the biological area of adapted physical activity,[183] there have been a number of critiques of the positivist paradigm commonly utilized.[131, 183, 185, 186] Positivism seeks for a single objective reality that can be accurately understood and measured and researchers employ a *scientific method* to discover this truth.[131] Often within a positivist design, there is an underlying assumption that the researcher holds academic neutrality, where the researcher and researched do not influence one another.[131, 187] The existence of academic neutrality is largely rejected, particularly in the relationship between a non-disabled researcher and participants with an impairment.[188] The perspectives of the researcher influence all variables involved in the research process, starting with the research question. If we assume all people with impairments *only* desire to remedy their impairment-related health, and we believe exercise can do this, then we will continue to only study how exercise can improve impairment-related health.[189] From the conception of this project, my aim was to conduct research outside of the medical model, but I was acutely aware that my positionality as a non-disabled researcher still influenced the study objectives, chosen measurements and interpretations. Although participatory research approaches have been used to combat these biases,[190] it was not feasible in the timeframe of a Masters program. Therefore, I opted for the employment of a post-positivist paradigm which allowed me to conduct a quantitative research project whilst attempting to measure some subjective influences not typically considered. I also engaged in reflexive journaling as a tool, commonly used in qualitative methodologies and constructivist and participatory paradigms, among others, to examine my role as a non-disabled researcher and hidden assumptions in this study.

Post-positivism was born as a critique of positivist methodology, although it still largely agrees with a single objective reality.[187] Importantly, post-positivism values subjectivity and invites differing perspectives to help arrive at a conclusion.[131] This approach does not differ greatly from positivist design concerning study procedures and methodology, however, the distinction is evident between the evaluation and inference from the resulting data. For example, I used the BPAQ-MI questionnaire as a means to contextualize objective physical activity data. This was important considering access to physical activity opportunities is often not considered when comparing accelerometry data between individuals with and without MS. Only measuring objective physical activity between groups and assuming differences, or no differences, are only due to impairment, does not acknowledge that engagement in physical activity is related to a multitude of barriers external to an individual's physiology. In a reflexive journal passage, I described this process as an opportunity to be in the role of a listener:

> Explicitly avoiding relying on the medical model for this project has provided an opportunity to develop a project which pushes the boundaries of positivist research. The use of a questionnaire to understand how barriers to physical activity are prevalent in a participant's life, for example, isn't done explicitly as a way to control for that variable. But, to see how it interplays with objective accelerometry results. To me, this distinction is critical since it moves away from the idea of objectivity and neutrality to the role of a listener. The aim becomes to listen to experiences of participants instead of pulling small fractions to tell my own story.

Within disability research, the researcher holds the position as the creator of knowledge, while the researched are participants of this research or 'researched on'.[191] This imbalance of power means the researcher will request what is needed from the researched, and opportunities to voice their own experiences are not presented or needed. In other words, there is no requirement for the researcher to hold a position of a listener because they are typically listened to. This echoes the medical model informed relationship described earlier between healthcare professionals determining what the is required to advance the health of people with impairments. Considering my example of accelerometry studies, when data is only informed by objective measures, the story being told by the researcher is one-sided, particularly when data is compared between groups with and without an impairment. We are automatically to assume that differences between groups are due to the presence of impairment, and the influence of social factors is ignored and not told. Presenting even small opportunities to have participants voice their experiences introduces novel aspects which have the potential begin disrupting the narratives and stories, which are often not consented to, told about the population being researched. Although the addition of a questionnaire is small manner to interject life experiences, particularly compared to other methods such as interviews, it is strikingly different compared to the other disability and physical activity research. The current study presents an example of how more meaningful analysis which includes assessment of factors apart from impairment can be used within MS and physical activity research. I believe post-positivist methods invite more instances of subjectivity within MS and physical activity research, which can begin to shift the relationship of the power imbalance of the researcher as the sole creator of knowledge about individuals with MS, or other types of impairment.

Moving Forward

Within quantitative MS and physical activity research, I believe that the employment of tools which measure or can derive meaningfulness of physical activity among people with MS should be utilized. A recent interdisciplinary and interparadigmatic study of a singing and dancing protocol for individuals with muscular dystrophy revealed that participants indicated the fatigue they experienced from the training was meaningful and pleasurable to them.[192] This was surprising for the quantitative research team members since fatigue is often naturally assumed to be negative within disability research. This demonstrates that opinions of participants are powerful and valid and provide important contributions to quantitative data. Lastly, an important direction, which I believe is integral to challenging the medical model within physical activity and disability research, is the inclusion of qualitative, or other non-positivist, researchers and those with impairments within the peer-review process. This will directly disrupt the cycle which continues to exclude the voices of individuals with impairments from research and challenge an exclusively medicalized interpretation of data from mostly non-disabled peers. While preparing this thesis, feedback from a reviewer with a qualitative research background revealed a number of areas where my intentions did not align with what was communicated. For example, there were a number of areas where language choices were heavily medicalized, such as "impaired" when describing physiological responses. Although this term is commonly employed among quantitative exercise physiology research, it still reinforces the narrative of disability as an individual burden in comparison to those without impairment.

I believe disability health researchers have a responsibility to consider the greater societal, economic and political influences at play within research projects. Maintenance of a reflexive journal and including a reflective chapter is an uncommon process of quantitative research, but was an important and valuable tool. It challenged me to acknowledge that I have a position of power to produce knowledge about a community to which I do not belong to, and then to consider what my research was communicating.

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Appendices:

Appendix A. Visual Analog Scale to Evaluate Fatigue Severity

Visual Analogue Scale to Evaluate Fatigue Severity (VAS-F)

ID #_________ Date__________

Time _________a.m. __________p.m.

We are trying to find out about your level of energy before and after your night of sleep. There are 18 items we would like you to respond to. This should take less than 1 minute of your time. Thank you.

DIRECTIONS: You are asked to circle a number on each of the following lines to indicate how you are feeling RIGHT NOW.

For example, suppose you have not eaten since yesterday.
What number would you circle below?

not at all hungry 0 1 2 3 4 5 6 7 8 9 10 extremely hungry

You would probably circle a number closer to the "extremely hungry" end of the line.
This is where I put it:

not at all hungry 0 1 2 3 4 5 6 (8) 9 10 extremely hungry

NOW PLEASE COMPLETE THE FOLLOWING ITEMS:

1.	not at all **tired**	0	1	2	3	4	5	6	7	8	9	10	extremely **tired**
2.	not at all **sleepy**	0	1	2	3	4	5	6	7	8	9	10	extremely **sleepy**
3.	not at all **drowsy**	0	1	2	3	4	5	6	7	8	9	10	extremely **drowsy**
4.	not at all **fatigued**	0	1	2	3	4	5	6	7	8	9	10	extremely **fatigued**
5.	not at all **worn out**	0	1	2	3	4	5	6	7	8	9	10	extremely **worn out**
6.	not at all **energetic**	0	1	2	3	4	5	6	7	8	9	10	extremely **energetic**
7.	not at all **active**	0	1	2	3	4	5	6	7	8	9	10	extremely **active**
8.	not at all **vigorous**	0	1	2	3	4	5	6	7	8	9	10	extremely **vigorous**

9.	not at all **efficient**	0	1	2	3	4	5	6	7	8	9	10	extremely **efficient**
10.	not at all **lively**	0	1	2	3	4	5	6	7	8	9	10	extremely **lively**
11.	not at all **bushed**	0	1	2	3	4	5	6	7	8	9	10	totally **bushed**
12.	not at all **exhausted**	0	1	2	3	4	5	6	7	8	9	10	totally **exhausted**
13.	**keeping my eyes open** is no effort at all	0	1	2	3	4	5	6	7	8	9	10	**keeping my eyes open** is a tremendous chore
14.	**moving my body** is no effort at all	0	1	2	3	4	5	6	7	8	9	10	**moving my body** is a tremendous chore
15.	**concentrating** is no effort at all	0	1	2	3	4	5	6	7	8	9	10	**concentrating** is a tremendous chore
16.	**carrying on a conversation** is no effort at all	0	1	2	3	4	5	6	7	8	9	10	**carrying on a conversation** is a tremendous chore
17.	I have absolutely **no desire to close my eyes**	0	1	2	3	4	5	6	7	8	9	10	I have a tremendous **desire to close my eyes**
18.	I have absolutely **no desire to lie down**	0	1	2	3	4	5	6	7	8	9	10	I have a tremendous **desire to lie down**

Appendix B: Rating of Perceived Exertion

rating	description
0	NOTHING AT ALL
0.5	VERY, VERY LIGHT
1	VERY LIGHT
2	FAIRLY LIGHT
3	MODERATE
4	SOMEWHAT HARD
5	HARD
6	
7	VERY HARD
8	
9	
10	VERY VERY HARD (MAXIMAL)

Appendix C. Health History Questionnaire

Date of Birth: _____/______/_____ Height: ______________ Weight: _____________
Due/Delivery Date: ____________________ Marital Status: _____________________
Section A – Background Information:
1) What is your ethnic background?
□ Caucasian □ Hispanic □ Aboriginal (please circle: First Nations, Métis, Inuit)
□ Asian □ African American □ Other, please specify _________________
2) What education level did you complete? Please check all that apply.
□ Elementary school □ High school □ College
□ University (please circle: certificate, bachelor, master, doctorate)
□ Other, please specify________________
3) Postal Code _______
Section B – Health History:
Personal history is related to your own health. Family history is related to your immediate "Maternal" family (including your Mother and Father, your siblings or your other children) as well as the father of your children and his immediate family.
4) Please check any and all that apply:

	Personal History	Family History
Stroke	□	□
Hypertension	□	□
Heart Attack	□	□
Heart Murmur	□	□
Blood clots	□	□
Other cardiovascular disorders (please specify)	□	□

If you checked for "Family History", please indicate which family member(s) are affected:
____

	Personal History	Family History
Type I Diabetes	□	□
Type II Diabetes	□	□
Pre-diabetes/Impaired Glucose Tolerance	□	□
Polycystic Ovarian Syndrome	□	□
Obesity	□	□
Other metabolic disorders (please specify)	□	□

If you checked for "Family History", please indicate which family member(s) are affected:
____

	Personal History	Family History
Asthma	□	□

Sleep Apnea	◻	◻
COPD	◻	◻
Other respiratory/breathing disorders (please specify)	◻	◻

If you checked for “Family History”, please indicate which family member(s) are affected:

____

	Personal History	Family History
Alzheimer’s	◻	◻
Cognitive impairment	◻	◻
Parkinson’s	◻	◻
ALS (Lou Gehrig’s Disease)	◻	◻
Seizures	◻	◻
Epilepsy	◻	◻
Multiple Sclerosis	◻	◻
Depression	◻	◻
Other neurological disorders (please specify)	◻	◻

If you checked for “Family History”, please indicate which family member(s) are affected:

____

	Yes	No
Any other major surgery, illness or injury not listed above?	◻	◻

(If yes, please Specify)

____

	Yes	No	Unknown
Were you born pre-mature (before 37wks)	◻	◻	◻

If yes, what week were you born? ______________________________

What is the year of birth of your Mother? ______________________________

What is the year of birth of your Father? ______________________________

What is your birth order? 1 = first born, 2 = second born etc.

____

	Yes	No
Do you smoke?	◻	◻

(If yes, how many cigarettes per day?)

____

(If you have quit, how long since your last cigarette?)______________________________

(Are you exposed to second-hand smoke? Please indicate if at home or other):

____

	Yes	No
Do you drink caffeine regularly?	◻	◻

How many cups of caffeinated beverage do you drink: per day?________ per week? ________

Yes No

Are you currently taking any medications? ◻ ◻
(If yes, please list medications)

Do you have any other health concerns you think we should be aware of?

PEOPLE
Please check any and all that apply

	Yes	No
Are you post-menopausal?	◻	◻

(If not, how long since your last period?)

	Yes	No
Are you on hormone replacement therapy?	◻	◻
Are you currently using oral contraceptives?	◻	◻

(If yes, what is the brand?)

	Yes	No
Are you pregnant?	◻	◻

(If yes, how many weeks?) ______________________________

	Yes	No
Is this your first pregnancy?	◻	◻
Was assisted reproduction technology used this pregnancy?	◻	◻

Have you been diagnosed with any of the following in your current or any previous pregnancy:

	Yes	No
Gestational Diabetes Mellitus	◻	◻
Impaired Glucose Tolerance/Pre-diabetes	◻	◻
Gestational Hypertension	◻	◻
Preeclampsia	◻	◻
Eclampsia	◻	◻
Placenta Previa	◻	◻
Preterm Labour	◻	◻
High-order pregnancy (i.e.. Twin)	◻	◻
Post-partum depression	◻	◻

If yes, please indicate which pregnancy(ies) were affected:

Was your mother diagnosed with any of the following?

	Yes	Yes while pregnant	No

			with you			
Gestational Diabetes Mellitus	□	□			□	
Impaired Glucose Tolerance/Pre-diabetes	□	□			□	
Gestational Hypertension		□	□			□
Preeclampsia	□	□			□	
Eclampsia		□	□			□
Placenta Previa		□	□			□
Preterm Labour		□	□			□
High-order pregnancy (i.e.. Twin)		□	□			□
Post-partum depression		□	□			□

Section C – Nutrition, Physical Activity and Sleep:

6) What have your eating habits been like in the year before this pregnancy? Check all that apply.:

□ One meal per day, specify when ______________________________________
□ Two meals per day, specify when ______________________________________
□ Three meals per day
□ Snack(s) every day, specify when ______________________________________
□ Special diet, please specify name ______________________________________
□ Trying to follow Canada's Food Guide to Healthy Eating
□ Other nutrition plan, please specify ______________________________________

7) What have your eating habits been like during this pregnancy? Check all that apply.:

□ One meal per day, specify when ______________________________________
□ Two meals per day, specify when ______________________________________
□ Three meals per day
□ Snack(s) every day, specify when ______________________________________
□ Special diet, please specify name ______________________________________
□ Trying to follow Canada's Food Guide to Healthy Eating
□ Other nutrition plan, please specify ______________________________________

8) What was your pattern of physical activity in the year before this pregnancy?

Type of
Physical Activity Frequency
Average Duration
of your exercise sessions Intensity
(light, moderate or strenuous) Location
(home, outdoors, gym, etc.)

____
time(s) per week __________minutes
____
time(s) per week _________ minutes
____

time(s) per week ________ minutes
DEFINITIONS: Light Intensity (minimal effort; e.g. yoga, easy walking, golf, bowling, stretching). Moderate Intensity (not exhausting; e.g. fast walking, baseball, tennis, easy bicycling). Strenuous Intensity (heart beats rapidly; e.g. running, jogging, vigorous swimming, vigorous long distance cycling).
9) During a typical 7-Day period (a week) in the year before this pregnancy, in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?
□ often
□ sometimes
□ never/rarely
10) What was/is your pattern of physical activity been like during this pregnancy?
Type of
Physical Activity Frequency
Average duration
of your exercise sessions Intensity
(light, moderate or strenuous) Location
(home, outdoors, gym, etc.)

____
time(s) per week _______ minutes

____
time(s) per week _______ minutes

____
time(s) per week _______ minutes
11) During a typical 7-Day period (a week) during this pregnancy, in your leisure time, how often do you engage in any regular activity long enough to work up a sweat (heart beats rapidly)?
□ often
□ sometimes
□ never/rarely
12) What is/was your level of stress on most days (please check one box for each time point) ?
Timepoint No stress Low Stress level Moderate stress level High stress level
In the year before your current pregnancy.
During your current pregnancy.
Section D – Body weight:
13) What has been your usual adult body weight? __________ pounds, OR __________ kg
14) What was your body weight one year before this pregnancy?______ pounds, OR ______ kg
15) What was your body weight immediately before this pregnancy? ______ pounds, OR ______ kg
16) How much weight do you or did you plan to gain during this pregnancy?
________ pounds, OR ________ kg

17) How much weight did you gain during this pregnancy?
____________ pounds, OR ____________ kg

18) Did your health care provider tell you how much weight you should gain during your pregnancy?
 No If Yes, how much weight were you told? __________ pounds, OR __________ kg

19) Were you actively trying to reduce your body weight in the year before this pregnancy?
 No If Yes, how much weight did you lose? __________ pounds, OR __________ kg

Section E – Previous Pregnancies:

20) Please fill the following chart.

Age you were Body weight you were immediately before pregnancy Weight you gained during pregnancy Weight retained after pregnancy (never really lost)

1st pregnancy _________pounds,
OR _________kg _________pounds,
OR __________kg _________pounds,
OR __________kg
2nd pregnancy _________pounds,
OR __________kg _________pounds,
OR __________kg _________pounds,
OR __________kg
3rd pregnancy _________pounds,
OR __________kg _________pounds,
OR __________kg _________pounds,
OR __________kg
4th pregnancy _________pounds,
OR __________kg _________pounds,
OR __________kg _________pounds,
OR __________kg
5th pregnancy _________pounds,
OR __________kg _________pounds,
OR __________kg _________pounds,
OR __________kg

21) For each pregnancy, what were the gestational age, gender and approximate birth weight and length?

Gestational Age GenderBirth weight Birth Length

1st baby ________weeks ____pounds___ounces,
OR __________kg _________inches,
OR _________cm
2nd baby ________weeks ____pounds___ounces,

OR __________kg _________inches,
OR _________cm
3rd baby ________weeks ____pounds___ounces,
OR __________kg _________inches,
OR _________cm
4th baby ________weeks ____pounds___ounces,
OR __________kg _________inches,
OR _________cm
5th baby ________weeks ____pounds___ounces,
OR __________kg _________inches,
OR _________cm
22) Please indicate how you fed your baby(ies).
Breastfeeding started Duration of breastfeeding only Age breastfeeding was stopped Age at introduction of first solid foods
1st baby ____Yes,____ No _______ months _______ months _______ months
2nd baby ____Yes,____ No _______ months _______ months _______ months
3rd baby ____Yes,____ No _______ months _______ months _______ months
4th baby ____Yes,____ No _______ months _______ months _______ months
5th baby ____Yes,____ No _______ months _______ months _______ months
Section D – Weight History:
23) What was your birth weight? ________ pounds _________ ounces, OR ________ kg
24) What was your birth length? ____________ inches, OR ____________ centimeters
25) What was the birth weight of the father of your child? ____ pounds _____ ounces, OR ____ kg
26) What was the birth length of the father of your child? ______ inches, OR ______ centimeters
27) How has your body weight been since you were 19 years of age?
☐ stable (always about the same weight, only changing by a couple of pounds when I am not pregnant).
☐ unstable and progressively increasing
☐ unstable, because it has been going up and down often
☐ unstable, I feel I have been gaining weight with each pregnancy
☐ Other, please describe

____
28) Have you ever had an eating disorder?

☐ No
☐ Anorexia
☐ Binge eating
☐ Bulimia
☐ Other, please specify ____

Appendix D. Barriers to Physical Activity for Individuals with Mobility Impairment

Barriers to Physical Activity Questionnaire – Mobility Impairment

Physical activity is defined as any activity that is performed with the intent to improve someone's health. Some physical activities might include exercising at a fitness center, walking/rolling in the neighborhood, or playing sports. Sometimes it is difficult to participate in physical activity for different reasons. This is especially true for people with mobility impairments. I am now going to go over some reasons why someone who wants to be physically active but is not able to be.

a. Thinking over the past 3 months, were there any times when you wanted to participate in physically activity but didn't or was more difficult because …

If YES to part a:

b. In general, when you encounter [insert barrier], how much of a barrier is [insert barrier], on a scale from one to five with one being very small and five being very large?

		No	Yes		Very Small				Very Large
(1)	you get tired or fatigued	1	2	→	1	2	3	4	5
(2)	you were in pain	1	2	→	1	2	3	4	5
(3)	you believe physical activity requires too much work/effort/energy	1	2	→	1	2	3	4	5
(4)	you didn't have an appropriate fitness level to be physically active (e.g., lack of aerobic ability)	1	2	→	1	2	3	4	5
(5)	you felt physical discomfort while being physically active	1	2	→	1	2	3	4	5
(6)	you were afraid of getting injured while being physically active	1	2	→	1	2	3	4	5
(7)	you were depressed	1	2	→	1	2	3	4	5

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Barriers to Physical Activity Questionnaire – Mobility Impairment

		No	Yes		Very Small				Very Large
(8)	you lack the motivation to be physically active	1	2	→	1	2	3	4	5
(9)	you don't have confidence in your ability to be physically active	1	2	→	1	2	3	4	5
(10)	you were embarrassed about your appearance while being physically active	1	2	→	1	2	3	4	5
(11)	you have not seen positive results from previous physical activity	1	2	→	1	2	3	4	5
(12)	you feel you are too old to be physically active	1	2	→	1	2	3	4	5
(13)	you didn't think physical activity would help you	1	2	→	1	2	3	4	5
(14)	being physically active is not enjoyable	1	2	→	1	2	3	4	5
(15)	you don't see a reason to be physically fit	1	2	→	1	2	3	4	5
(16)	you did not have another person with a disability who was physically active to look up to	1	2	→	1	2	3	4	5
(17)	your friends didn't assist you to be physically active	1	2	→	1	2	3	4	5
(18)	your friends are not physically active	1	2	→	1	2	3	4	5
(19)	your friends don't talk about being physically active	1	2	→	1	2	3	4	5
(20)	your friends were not encouraging or supportive of your efforts to be physically active	1	2	→	1	2	3	4	5

Barriers to Physical Activity Questionnaire – Mobility Impairment

		No	Yes		Very Small				Very Large
(21)	your friend's priorities take precedence/priority over you being physically active	1	2	→	1	2	3	4	5
(22)	your family's culture, beliefs, or morals did not place physical activity as a priority	1	2	→	1	2	3	4	5
(23)	your family did not assist you to be physically active	1	2	→	1	2	3	4	5
(24)	your family members are not physically active	1	2	→	1	2	3	4	5
(25)	your family members were not encouraging or supportive of your efforts to be physically active	1	2	→	1	2	3	4	5
(26)	your family did not think physical activity would be helpful to improve your health	1	2	→	1	2	3	4	5
(27)	In the last three months, were there any times that you wanted to go to a fitness center or gym (eg. Bally's or YMCA) but couldn't?	1	2	→	**If no, go to 28**				
	(a) lack of accessible exercise equipment at fitness center	1	2	→	1	2	3	4	5
	(b) the walkways/aisles were too narrow or had obstacles	1	2	→	1	2	3	4	5
	(c) lack of accessible door handles	1	2	→	1	2	3	4	5
	(d) lack of accessible curb cuts at fitness center	1	2	→	1	2	3	4	5
	(e) ground that you walk/roll on was not accessible	1	2	→	1	2	3	4	5
	(f) lack of accessible ramps at fitness center	1	2	→	1	2	3	4	5

Barriers to Physical Activity Questionnaire – Mobility Impairment

		No	Yes		Very Small				Very Large
(g)	lack of accessible bathrooms at fitness center	1	2	→	1	2	3	4	5
(h)	lack of accessible showers/locker rooms	1	2	→	1	2	3	4	5
(i)	lack of accessible elevators at fitness center	1	2	→	1	2	3	4	5
(j)	lack of accessible parking at fitness center	1	2	→	1	2	3	4	5
(k)	lack of access to indoor track for walking/wheeling...............	1	2	→	1	2	3	4	5
(l)	fitness center membership fees were too high	1	2	→	1	2	3	4	5
(m)	your health insurance plan do not cover membership fees ..	1	2	→	1	2	3	4	5
(n)	lack of inclusive marketing	1	2	→	1	2	3	4	5
(o)	lack of accessible classes/programs at fitness center...........	1	2	→	1	2	3	4	5
(p)	other fitness center members were mean or rude	1	2	→	1	2	3	4	5
(q)	lack of accessible walking/rolling paths at parks..................	1	2	→	1	2	3	4	5
(r)	lack of assistance from fitness center staff	1	2	→	1	2	3	4	5
(s)	lack of accessible sport opportunities at fitness center	1	2	→	1	2	3	4	5
(t)	signs showing where things are located were not accessible	1	2	→	1	2	3	4	5
(u)	lack of interpretive services (e.g. sign language)	1	2	→	1	2	3	4	5

Barriers to Physical Activity Questionnaire – Mobility Impairment

		No	Yes		Very Small				Very Large
(28)	lack of access to public restrooms	1	2	→	1	2	3	4	5
(29)	uneven or crooked sidewalks	1	2	→	1	2	3	4	5
(30)	the sidewalks have cracks, gaps, or are under construction	1	2	→	1	2	3	4	5
(31)	lack of rest areas (e.g. benches)	1	2	→	1	2	3	4	5
(32)	potholes in the street, driveways, or parking lot	1	2	→	1	2	3	4	5
(33)	sidewalk's cross slope is too steep/slanted	1	2	→	1	2	3	4	5
(34)	the crosswalks lack traffic lights	1	2	→	1	2	3	4	5
(35)	lack of accessible curb cuts in community	1	2	→	1	2	3	4	5
(36)	lack of accessible transportation to fitness center.........................	1	2	→	1	2	3	4	5
(37)	sidewalks were not wide enough	1	2	→	1	2	3	4	5
(38)	excessive crime or fear of crime in neighborhood	1	2	→	1	2	3	4	5
(39)	the cars drive too fast	1	2	→	1	2	3	4	5
(40)	excessive car traffic in my community	1	2	→	1	2	3	4	5
(41)	the traffic lights or crosswalk signals change too quickly	1	2	→	1	2	3	4	5
(42)	lack of adequate street lighting at night	1	2	→	1	2	3	4	5
(43)	loose dogs in community	1	2	→	1	2	3	4	5

Appendix E. SymptoMScreen

SYMPTOM SCREEN

Please circle **one number that best describes how each MS symptom has affected your everyday life activities.** For example, if it takes you longer to type or text, your hand function may have a 'mild limitation' (circle '2'), but if you gave up typing or texting completely, your hand function may have a 'severe limitation' (circle '4').

	0 – not affected at all	1 – very mild limitation/ I make minor adjustments	2 – mild limitation/ I make frequent adjustments	3 – moderate limitation/ I reduced my daily activities	4 – severe limitation/ I gave up some activities	5 – very severe limitation/ I'm unable to do many daily activities	6 – total limitation/ I'm unable to do most daily activities
Walking	0	1	2	3	4	5	6
Hand function/Dexterity Poor hand coordination, tremors	0	1	2	3	4	5	6
Spasticity & Stiffness Muscle cramping or muscle tightness	0	1	2	3	4	5	6
Bodily pain Achiness, tenderness	0	1	2	3	4	5	6
Sensory Numbness, tingling, or burning	0	1	2	3	4	5	6
Bladder control Urinary urgency, urinary frequency	0	1	2	3	4	5	6
Fatigue	0	1	2	3	4	5	6
Vision Blurry vision, double vision	0	1	2	3	4	5	6
Dizziness Feeling off balance, 'spinning'/vertigo	0	1	2	3	4	5	6
Cognitive function Memory, concentration problems	0	1	2	3	4	5	6
Depression Depressed thoughts, low mood	0	1	2	3	4	5	6
Anxiety Feelings of stress, panic attacks	0	1	2	3	4	5	6

Appendix F. Modified Fatigue Impact Scale

		Never	Rarely	Sometimes	Often	Almost Always
1.	I have been less alert.	0	1	2	3	4
2.	I have had difficulty paying attention for long periods of time.	0	1	2	3	4
3.	I have been unable to think clearly.	0	1	2	3	4
4.	I have been clumsy and uncoordinated.	0	1	2	3	4
5.	I have been forgetful.	0	1	2	3	4
6.	I have had to pace myself in my physical activities.	0	1	2	3	4
7.	I have been less motivated to do anything that requires physical effort.	0	1	2	3	4
8.	I have been less motivated to participate in social activities.	0	1	2	3	4
9.	I have been limited in my ability to do things away from home.	0	1	2	3	4
10.	I have trouble maintaining physical effort for long periods.	0	1	2	3	4
11.	I have had difficulty making decisions.	0	1	2	3	4
12.	I have been less motivated to do anything that requires thinking	0	1	2	3	4
13.	My muscles have felt weak	0	1	2	3	4
14.	I have been physically uncomfortable.	0	1	2	3	4
15.	I have had trouble finishing tasks that require thinking.	0	1	2	3	4
16.	I have had difficulty organizing my thoughts when doing things at home or at work.	0	1	2	3	4
17.	I have been less able to complete tasks that require physical effort.	0	1	2	3	4

		Never	Rarely	Sometimes	Often	Almost Always
18.	My thinking has been slowed down.	0	1	2	3	4
19.	I have had trouble concentrating.	0	1	2	3	4
20.	I have limited my physical activities.	0	1	2	3	4
21.	I have needed to rest more often or for longer periods.	0	1	2	3	4

Instructions for Scoring the MFIS

Items on the MFIS can be aggregated into three subscales (physical, cognitive, and psychosocial), as well as into a total MFIS score. All items are scaled so that higher scores indicate a greater impact of fatigue on a person's activities.

Physical Subscale

This scale can range from 0 to 36. It is computed by adding raw scores on the following items: 4+6+7+10+13+14+17+20+21. 0

Cognitive Subscale

This scale can range from 0 to 40. It is computed by adding raw scores on the following items: 1+2+3+5+11+12+15+16+18+19. 0

Psychosocial Subscale

This scale can range from 0 to 8. It is computed by adding raw scores on the following items: 8+9. 0

Total MFIS Score

The total MFIS score can range from 0 to 84. It is computed by adding scores on the physical, cognitive, and psychosocial subscales. 0

Appendix G. Accelerometry Tracking Sheet

PARTICIPANT ID: ____________ ACCELEROMETER: ______________	Day 1 Date: __________	Day 2 Date: __________	Day 3 Date: __________	Day 4 Date: __________	Day 5 Date: __________	Day 6 Date: __________	Day 7 Date: __________
Time you woke up:							
Time device put on hips:							
Time you went to bed:							
Time device put on wrist:							
Time you went to sleep:							
Please record any time the device was off during the day and why EXAMPLE: 1pm-130pm - shower							
Please report any activities you did during the day and times you did them EXAMPLE: 11-1130am - walk 6-7pm - yoga							
Please record any naps you took throughout the day EXAMPLE: 1-130pm							

Appendix H. International Physical Activity Questionnaire

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

Appendix I. MS one-to-one Symptom Tracking

ms onetoone®

Symptom **Tracker**

Name ____________________________

Date & time	Symptom (include location in body)	Is it new?	Duration (hours, days, weeks)	Severity (check one circle)	Effect on daily life (check one circle)
11/1	Numbness in leg	Ø yes	2 days	O very mild O severe Ø mild O very severe	O has no effect Ø it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect
		O yes		O very mild O severe O mild O very severe	O has no effect O it's hard to ignore O not too much O it has a serious effect

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http://www.msonetoone.com/ms-symptom-tracker.pdf