THE ROLE OF MOBILE TECHNOLOGY FOR FALL RISK ASSESSMENT FOR INDIVIDUALS WITH MULTIPLE SCLEROSIS

BY

KATHERINE L. HSIEH

DISSERTATION

Submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy in Kinesiology
in the Graduate College of the
University of Illinois at Urbana-Champaign, 2020

Urbana, Illinois

Doctoral Committee:

Professor Jacob J. Sosnoff, Chair
Assistant Professor Jason T. Fanning
Assistant Professor Laura A. Rice
Professor Wendy A. Rogers

ABSTRACT

Multiple Sclerosis (MS) is a chronic, progressive neurogenerative disease that affects one million people in the United States (Wallin et al., 2019). Common MS symptoms include impaired coordination, poor walking and balance, and fatigue, and these symptoms put people with MS (pwMS) at a higher risk for falls (Cameron & Nilsagard, 2018). Falls are highly prevalent among pwMS and can result in detrimental consequences including bone fractures and even death (Matsuda et al., 2011). To prevent falls and fall related injuries, it is important to first assess for multiple risk factors and then intervene through targeted treatments (Palumbo et al., 2015).

Fall risk can be assessed through self-report measures, clinical performance tests, or with technology such as force plates and motion capture systems (Kanekar & Aruin, 2013). However, clinicians have time constraints, technology is expensive, and trained personnel is needed. Moreover, due to the COVID-19 pandemic, access to in-person clinical visits is limited. As a result, pwMS may not receive fall risk screening and remain vulnerable to fall related injuries. Mobile technology offers a solution to increase access to fall risk screening using an affordable, ubiquitous, and portable tool (Guise et al., 2014; Marrie et al., 2019). Therefore, the overarching goal of this study was to develop a usable fall risk health application (app) for pwMS to self-assess their fall risk in the home setting. Four studies were performed: 1) smartphone accelerometry was tested to measure postural control in pwMS; 2) a fall risk algorithm was developed for a mobile health app; 3) a fall risk app, Steady-MS, was developed and its usability was tested; and 4) the feasibility of home-based procedures for using Steady-MS was determined. Results suggest that smartphone accelerometry can assess postural control in pwMS. This information was used to develop an algorithm to measure overall fall risk in pwMS and was then incorporated into Steady-MS. Steady-MS was found to be usable among MS users and feasible to use in the home setting. The results from this project demonstrate that pwMS can independently assess their fall risk with Steady-MS in their homes. For the first time, pwMS are equipped to self-assess their fall risk and can monitor and manage their risk. Home-based assessments also opens the potential to offer individualized and targeted treatments to prevent falls. Ultimately, Steady-MS increases access to home-based assessments to reduce falls and improve functional independence for those with MS.

ACKNOWLEDGEMENTS

They say it takes a village to raise a child, but it also takes a village to raise a doctoral student. I would like to acknowledge members of this village who have supported me to reach this stage of my career.

I would like to thank my dissertation committee, Dr. Jacob Sosnoff, Dr. Wendy Rogers, Dr. Jason Fanning, and Dr. Laura Rice for their support and invaluable feedback, not only during my dissertation but during my entire graduate studies. I am particularly grateful for my advisor, Dr. Sosnoff. Not only do I appreciate Dr. Sosnoff for the countless hours spent mentoring me, but I also thank him for all of his advice and support to make me the best scientist and person I can be.

I want to thank the lab members of the Motor Control Research Lab, both past and present. This team is a role model representing who I strive to become, and they are one of my strongest support systems. I am grateful to have such a supportive team that has helped carried me through my graduate studies.

I want to thank my previous mentors from the University of Georgia, the first research lab I was a part of. I want to thank Dr. Cathleen Brown Crowell, Dr. Adam Rosen, Dr. Rumit Singh, Dr. Jupil Ko, and Dr. Christine Samson for their patience mentoring a wide-eyed undergraduate student and guiding me through my first research projects. Working alongside the graduate students at the time gave me insight to the lifestyle of graduate school and opportunities it provides. They provided me a strong research foundation.

I want to thank my mentors at the Center for the Intrepid, especially Dr. Jason Wilken and Dr. Riley Sheehan, for hiring me to work as a research assistant and giving me the opportunity to work in a new lab. During this time, I not only learned more about biomechanics research, but also how to live on my own in the ‘real world’.

I want to thank my family, especially my parents, for all their support and trust. They have supported me in each stage of my career and trust my ‘major life’ decisions.

It takes a village to raise a doctoral student, and this list does not include everyone in this rather large village. I am extremely grateful to be part of this village, and I am forever appreciative of everyone’s support, trust, and kindness.

TABLE OF CONTENTS

CHAPTER 1. BACKGROUND

Multiple Sclerosis

Multiple Sclerosis (MS) is a chronic, neurodegenerative disease of the central nervous system (CNS) that affects approximately one million individuals in the United States.[1] MS is characterized by the breakdown of the blood-brain barrier, resulting in migration of T cells, B cells, and macrophages into the CNS that cause inflammation and demyelination.[2] Lesions form in both white and gray matter, and can be found in the brain, optic nerve, and/or spinal cord.[3] The location and total volume of lesions, however, vary among individuals, making MS a heterogenous disease that is difficult to treat and manage.

There are three forms of MS: relapse-remitting, primary progressive, and secondary progressive (Figure 1.1).[4] Relapse-remitting is characterized by relapses that last from a day to approximately two months, followed by periods of remissions lasting months to years.[4] Relapses result from inflammation and cause an onset of new symptoms or worsening of current symptoms. Remissions, on the other hand, are periods of stability without new symptoms developing. Relapse-remitting is the most common form of MS. In secondary progressive form, relapses stop occurring, and there is a gradual progression of symptoms and increased disability. In primary progressive MS, there are no relapses, but instead a steady increase in disability and symptoms.[4] Depending on the type of MS, symptoms fluctuate frequently over time, making MS a difficult disease to treat and manage.

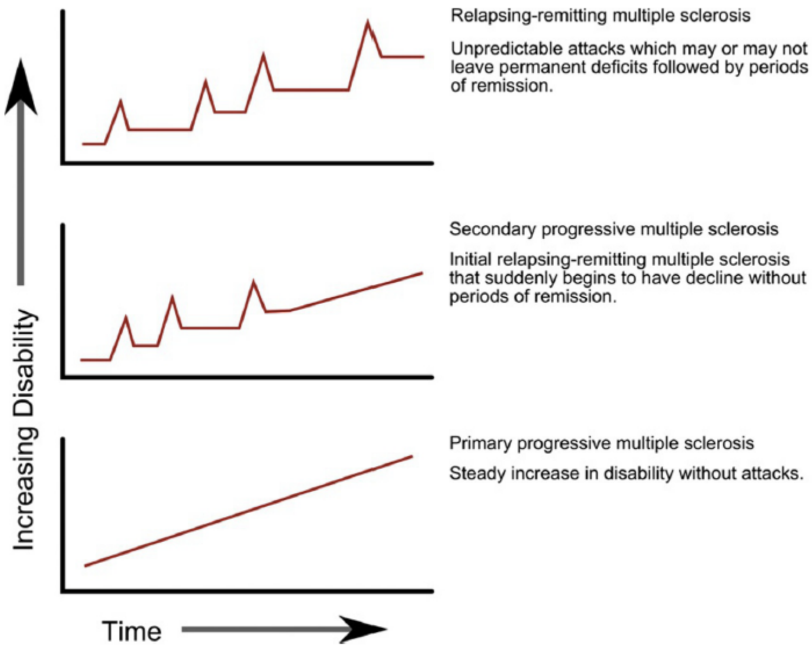


Figure 1.1. The three different types of multiple sclerosis: relapse-remitting, secondary progressive, and primary progressive.

Source: Cameron, M. H., & Nilsagard, Y. (2018).

MS affects areas of the brain, brainstem, spinal cord, and optic nerves, and resulting in a range of symptoms from sensory (i.e., pain, reduced proprioception), motor (i.e., spasticity, mobility impairment), to cognitive (i.e., slowed processing speed) symptoms.[2,5] Symptoms differ from one individual to the other, and depending on the type of MS, new symptoms may develop throughout the course of the disease. Motor, cognitive, and sensory MS symptoms put those with MS at a higher risk for falls. For instance, symptoms such as spasticity, loss of coordination, decline in sensation, and cognitive impairment can largely affect an individual's ability to walk and maintain balance.[4] People with MS (pwMS), therefore, are at a significant risk for falls.

Falls in Individuals with Multiple Sclerosis

Falls are a significant health concern for pwMS. One in two pwMS fall in any six-month period.[6] Falls can also result in detrimental consequences. For instance, up to 50% of falls result in an injury such as contusions or fractures, and 23% of those falls require medical care.[7] Falls can also result in fear of falling, which can lead to activity restriction and social isolation.[8] Therefore, preventing falls in pwMS is critical to improve overall quality of life.

A widely adopted paradigm for falls prevention is to screen for fall risk by assessing multiple risk factors and then to intervene with tailored treatment strategies.[9] Indeed, a systematic review from Sosnoff et al.[10] and a meta-analysis from Gunn et al.[11] demonstrated that exercise interventions can improve mobility and reduce fall risk in pwMS. Paired with fall risk screening by assessing multiple fall risk factors, targeted treatments can maximize functional independence for pwMS (Figure 1.2).

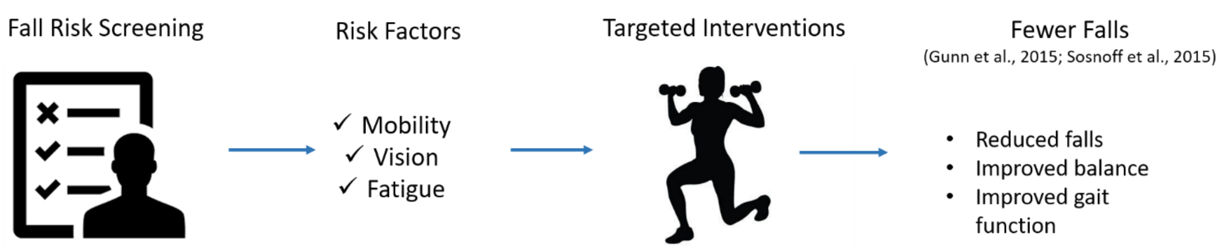


Figure 1.2. Fall risk screening identifies modifiable risk factors for each individuals. Individuals can then be treated through interventions targeting specific risk factors to reduce falls.

Assessing fall risk factors is a critical component of screening. Falls in MS stem from a complex interplay of pathological, psychosocial, and environmental factors.[12] Therefore, when screening for falls, it is important to assess for multiple risk factors. For instance, MS can impair vision, walking function, and/or balance confidence which may result in a fall. MS symptoms also vary from one individual to another depending on lesion location and volume, and MS symptoms fluctuate within an individual over time. Screening is critical to identify multiple risk factors unique to each individual.

There are multiple factors that contribute to falls in pwMS. One of the most significant contributing factor for falls that affects 50-80% of pwMS is impaired postural control.[4] Maintaining control of the body in response to perturbations is imperative to prevent falls. Postural control involves processing input from the visual, vestibular, and somatosensory systems and executing movement through the musculoskeletal system to maintain upright posture.[13] However, due to its disease pathology, pwMS display postural control deficits. MS can impair proprioception and vision which alters the body's internal orientation in relationship to the environment.[14] Moreover, MS may also cause in delays in motor output, resulting in difficulty re-establishing upright posture. Several studies have shown impaired postural control in pwMS. PwMS have performed worse on the Berg Balance Scale,[15-17] functional reach,[18,19] and time on tandem stance[18,20] compared to healthy individuals. Moreover, when measuring Center of Pressure (COP), pwMS have a greater COP path length, COP velocity, and 95% confidence ellipse during quiet stance, indicating impaired postural stability.[21] Over 16 studies also examined postural stability during quiet stance with eyes closed in pwMS and found greater COP displacement and COP velocity compared to age-matched controls, suggesting worse somatosensory and/or vestibular function in pwMS.[21] Overall, scientific evidence over the last decade has demonstrated reduced postural control in pwMS due to mechanisms from MS pathology.

Walking impairments are also common and affect approximately 80% of pwMS.[22] Falls often occur during walking, and improving walking function is important to prevent falls.[23] PwMS walk slower, shorter distances, and less in their daily lives than healthy individuals. This is demonstrated with slower times with the Timed 25 Foot Walk Test and Timed Up and Go (TUG),[19] shorter distances with the 6-minute walk test,[24] and fewer steps as measured with pedometers.[25] PwMS also demonstrate greater gait variability than healthy controls,[26,27] and their gait variability is distinctively different than that of other neurological disorders (i.e., Parkinson's disease, Huntington's disease, Alzheimer's disease).[28] Healthy gait involves a combination of vestibular, proprioceptive, and visual input to activate lower extremity muscle and control center of mass trajectory while walking.[29] Additionally, ankle torque and quadricep strength are needed support the body to initiate and maintain gait.[30] Gait impairments in pwMS may result from MS symptoms. For instance, poor walking endurance may be a result of fatigue,[31] while slowed walking speed may result from impaired muscle coordination or spasticity.[27,32] Elevated gait variability may also result from poor proprioception and reduced muscle strength.[33] Gait impairments are common in those with MS and appear to result from mechanisms underlying MS pathology. Moreover, gait impairments in MS appear to differ than those of other neurological diseases.[28]

While balance and gait impairments are strong predictors for falls in pwMS, there are many other fall risk factors. Psychosocial factors such as poor balance confidence and fear of falling have a 69% and 66% accuracy, respectively, in predicting fallers from non-fallers.[34] Those with moderate disability as measured with the Expanded Disability Status Scale (EDSS) are three times more likely to fall than those of mild disability.[35] Men with MS are 1.2 times more likely to fall in a three-month period than women with MS, and those who use a walking aid are two times more likely to fall than those without a walking aid.[35] Fatigue alone can also predict fallers with a 68% accuracy.[36] Therefore, while balance and gait impairments largely contribute to pwMS's increased fall risk, fall risk is multidimensional. Thus, when assessing for fall risk, it is critical to perform multifactorial screening to identify modifiable risk factors (i.e., factors that can be changed) for each individual.

Smartphone Technology and Fall Risk Assessment

There are multiple methods to assess for fall risk, ranging from self-report measures to clinic-based measures to laboratory-based measures. Self-report measures can assess factors such as fatigue with the Modified Impact Fatigue Scale[37] or walking with the Multiple Sclerosis Walking Scale.[38] While self-report measures are simple to assess, a major limitation is subjective bias.[39] Clinical measures include tests such as the Timed Up and Go or Berg Balance Scale. The advantages of these tests is that they require little instrumentation and can be quick to perform.[40] However, they lack sensitivity and can be prone to ceiling or floor effects, and they may not capture underlying mobility impairments in clinical populations.[17] Laboratory-based measures, such as using force plates, motion capture systems, or wearable sensors, are highly sensitive to minute changes in movement. However, these technologies are expensive and not feasible to have outside of the lab setting.[41,42] Fall risk assessments also require trained personnel to administer the tests, analyze outcomes, and share results.

Smartphone technology offers potential to overcome current limitations to fall risk assessment. Smartphones are affordable, ubiquitous, and portable.[43] Smartphone ownership is also at an all-time high. 77% of all Americans own a smartphone, and approximately 90% of Americans between 18-50 years old own a smartphone.[44] By embedding expert knowledge in a native smartphone application (app), users are able to understand their fall risk with minimal equipment and without the need of trained personnel. Moreover, individuals are able to selfadminister these assessments in their own homes, increasing the likelihood for independent and continued fall risk monitoring.

The evidence for smartphone usage for assessing fall risk has increased over the past several years. Several studies have examined the ability of the accelerometer and gyroscope embedded within smartphones and tablets to measure standing balance and walking.[43,45] Our systematic review found that five studies validated a smartphone or tablet accelerometer with gold standard equipment (i.e., motion capture, force plate) during standing or walking tasks.[46] Fewer studies, however, examined reliability and none examined usability. Our study validating a smartphone accelerometer to a force plate also found root mean square acceleration to discriminate between high and low fall risk older adults.[47] Evidence suggests that not only are smartphone accelerometers and gyroscopes comparable to lab-based technologies, but they are capable of distinguishing between different levels of fall risk. However, most of these studies included healthy young or healthy older adults, and there is less evidence on how smartphone technology is used among clinical populations at risk for falls.

Different groups have also developed and tested mobile applications (app) to measure fall risk. uTUG is an app that measures performance on the Timed Up and Go (TUG).[48] Another fall risk app is based on the Aachen Falls Prevention Scale and determines fall risk based on a set of questionnaires and a single balance task.[49] FallCheck is another app that is a checklist of environmental factors in the home that may be fall hazards.[50] This includes factors such as poor lighting, clutter in rooms, and lack of handrails on staircases. This app does not provide an individualized fall risk score, but rather provides information on how to reduce fall risk through environmental factors. While these studies provide an important foundation for using smartphone apps to assess fall risk, they rely on a single measure or a single questionnaire. They do not provide a comprehensive measure of fall risk, which is critical for pwMS given the multiple fall risk factors. Furthermore, most of the apps developed for fall risk are targeted towards older adults. There are few fall risk apps developed for neurological populations such as MS that measure their unique fall risk factors.

Our lab developed and tested a smartphone app, Steady™ to measure fall risk in older adults. Steady™ consists of two components to compute a fall risk score.[51] The first is a 13-item questionnaire of health history assessing age, gender, number of falls in the last year, and perceived balance confidence. The second component is a progressive postural stability test wherein the device guides participants through five balance tasks of progressive difficulty. These include four 30-second balance tasks (eyes open, eyes closed, tandem, single leg), plus a 30-second sit-to-stand test. The algorithm utilizes information inputted from the health history and completion on the balance tasks to calculate a fall risk score ranging from 0-100. This algorithm was developed based on previous literature of fall risk factors among older adults. We tested the usability of the app through two groups semi-structured interviews with older adults. Older adults reported that the app had high ease of use and found the app to be useful.[51] We also found the algorithm of the app to be comparable to clinical fall risk measures, including the TUG, Physiological Profile Assessment, Berg Balance Scale, and Activities Balance Scale.[52]

While Steady™ is a usable and valid app for older adults, this and other developed apps do not accurately measure fall risk in pwMS because of their unique fall risk factors resulting from MS symptoms. The current algorithm does not include MS factors such as fatigue, disability level, and walking impairment that contribute to fall risk. Additionally, cut-offs for these factors also differ from older adults to pwMS. Therefore, while there is evidence supporting smartphone accelerometry and smartphone apps to assess fall risk in older adults, pwMS do not have an accessible tool to self-asses their risk of falling. Without understanding their fall risk, pwMS remain at risk for fall-related injuries.

Health Technology in People with Multiple Sclerosis

MS is commonly diagnosed in individuals between 20-40 years of age and is one of the most prevalent neurological diseases among young adults.[53] There is no cure for MS, and instead clinicians focus on managing the disease and its symptoms. PwMS may visit their doctor every six or 12-months for routine check-ups.[54] However, due to the chronic, progressive nature of MS, mild relapses or symptom changes in between this period may go unnoticed and unreported.[54] As a result, electronic health technologies such as computer and mobile apps have become popular to help pwMS track and manage their MS symptoms.[55]

Technology usage is high in pwMS, and electronic health technology has been commonly proposed as a way to monitor their health. It is estimated that 90% of pwMS use a personal computer,[56] and 86% of pwMS use either a smartphone or tablet.[57] Additionally, about 46% of pwMS use a health app, and 98% of users found the app to be beneficial for their health needs.[57] PwMS use electronic health technology for a multiple purposes. 84% of pwMS have exchanged medical information with a health professional and seek interest in sharing vital signs and diagnostic information through eHealth technology.[57] PwMS also use the internet learn more information about MS and search for medical support systems.[58] Mobile apps are also commonly used to for symptom management, such as recording and tracking symptoms of fatigue.[59]

A recent review discussed the available digital health technologies available for pwMS.[54] Most tools focus on treatment, self-management of symptoms, disease monitoring, or rehabilitation.[54] However, there are a lack of tools that focus on screening and assessment, which is the first step in falls prevention. Furthermore, another review of mobile apps identified 30 different health apps for pwMS, and most apps were used for disease management or for treatment information.[60] PwMS reported that health apps are beneficial in that they help them reach a health goal, ask questions to their doctors, and inform how to treat their MS.[57] However, a main criticism reported by pwMS is that most apps were poorly designed which resulted in poor user experience.[60] Therefore, improving usability is critical to improve adoption and engagement of mobile apps. Given the few apps that focus on assessments, along with the adverse consequences of falls, it is critical to develop a usable fall risk app that provides falls screening and fall risk assessment to help pwMS manage their risk for falls.

Mobile apps are commonly used by pwMS to treat and manage their symptoms. However, because there is a dearth of apps that provide screening and assessment, a fall risk app increases access to falls screening and improves self-monitoring and management of fall risk. Furthermore, unlike currently available apps, designing a fall risk app to fit the unique needs of pwMS increases the potential for technology acceptance and adoption. A usable fall risk app brings falls screening to the hands of pwMS, equipping them with a tool to self-assess their fall risk and improve their functional independence.

The overarching goal of this project is to leverage the power of smartphone technology to provide pwMS with usable mobile app to self-assess their risk for falls in the home setting. Smartphone technology can overcome constraints in fall risk screening and bring self-assessments to the hands of the individual. Additionally, a mobile health app offers potential to improve self-management of fall risk and provide targeted treatments to prevent falls and maximize functional independence.

CHAPTER 2. ASSESSING POSTURAL CONTROL WITH SMARTPHONE ACCELEROMETRY IN INDIVIDUALS WITH MULTIPLE SCLEROSIS

Introduction

Falls are a major public health concern for people with Multiple Sclerosis (pwMS). One in two pwMS will fall in a six-month period, and up to 50% of falls result in an injury, ranging from bruises to fractures.[4] Aside from physical injuries, falls may result in a fear of falling which can cause activity curtailment and social isolation.[7] Because of the high prevalence and detrimental consequences of falls in pwMS, it is critical to prevent falls in this population.

Understanding risk factors related to falls is important in developing effective fall prevention treatments. Impaired postural stability is one of the most important risk factors for falls in MS and affects over 50% of pwMS.[61,62] PwMS are often reported to take longer to respond to perturbations, have greater sway, and have a limited boundary of stability compared to their healthy counterparts.[21,63] Postural stability can be assessed with clinical tests, such as the Berg Balance Scale or Timed Up and Go.[17,18] These tests, however, are prone to floor or ceiling effects and do not always capture underlying balance impairments.[17] Lab-based assessments, such as assessing postural sway with a force plate or motion capture system, can capture minute changes in posture but require expensive equipment.[21,62] Wearable sensors are another increasingly popular approach to assess mobility given that they are portable, but they still require trained expertise to operate and analyze.[41]

One alternative solution to measure posture is to leverage the power of smartphone technology. Smartphones are embedded with an accelerometer and gyroscope that can potentially be used to assess postural control.[64] Smartphones are also affordable, ubiquitous, and portable, offering potential for home-based assessments. Previous studies have suggested that smartphone and tablet-based accelerometry can assess postural control in older adults and individuals with Parkinson's disease.[47,65] However, the mechanism underlying postural instability differs for those with MS,[62] and there is limited knowledge of whether smartphone-based accelerometry can accurately assess postural control in pwMS. Understanding the effectiveness of smartphone accelerometry to measure postural control can help inform the development of mobile health applications to improve self-monitoring and self-management of MS and its symptoms.

The purpose of this study was to determine whether smartphone accelerometry can measure postural control in pwMS compared to a research grade accelerometer and force plate measures during standing balance tasks. We also determined whether smartphone accelerometry was capable of discriminating between assisted device users and non-assisted device users, as assisted device usage is a strong predictor of impaired balance and falls in pwMS.[66] We hypothesized that smartphone accelerometry outputs would be comparable to research grade accelerometry and force plate outputs, and that smartphone accelerometry would be capable of discriminating between assisted device users and non-assisted device users.

Methods

Participants

Participants were recruited from the research lab's database. Twenty-seven individuals with MS participated in this study. Participants were included if they were: a) 18 years or older; b) had a physician confirmed diagnosis of MS; b) normal or corrected to normal hearing and vision; c) capable of standing unaided for at least one minute; and d) scored ≤6.5 on the

Expanded Disability Status Scale (EDSS). Participants were excluded if they had any neurological disorder other than MS.

Experimental Protocol

All participants underwent static balance assessments while standing on a force plate (Bertec Inc, Columbus, OH) and holding a smartphone (Samsung Galaxy S6, Seoul, South Korea) medially against the chest along the sternum. A research grade accelerometer (Opals, APDM, Portland, OR) was attached to the smartphone (Figure 2.1). Researchers ensured that participants held the phone to the proper orientation aligned to the anteroposterior (AP), mediolateral (ML), and vertical axes for each trial. The force plate was sampled at 1000 Hz, the accelerometer from the smartphone was sampled at an average of 200 Hz, and the Opal was sampled at 128 Hz.

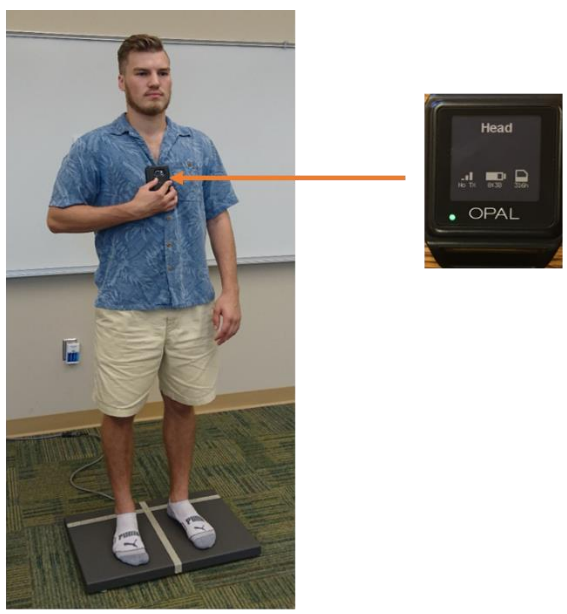


Figure 2.1. Participants stood on a force plate while holding a smartphone against their chest for 5 balance tasks. A research grade accelerometer was attached to the posterior side of the smartphone.

Five standing balance tasks were performed on the following order for 30 seconds each: 1) eyes open, 2) eyes closed, 3) semi-tandem, 4) tandem, and 5) single leg. Two trials of each task were performed. These balance tasks were chosen to challenge participants' sensorimotor systems and base of support and have distinguished fallers and non-fallers with MS in the past.[63] Acceleration from the smartphone and Opal in the mediolateral (ML), anteroposterior (AP), and vertical directions were exported, downsampled to 100 Hz, and processed with a 4th order, low pass Butterworth filter at a cutoff frequency of 5 Hz using a custom MATLAB script (Mathworks Inc., Natick, MA). Root mean square (RMS) acceleration in the ML and AP directions and 95% area ellipse were calculated, as these measures have shown to be valid and reliable in assessing postural control through smartphone accelerometry.[46] Center of Pressure (COP) data from the force plate was exported, downsampled to 100 Hz, and processed with a 4th order, low pass Butterworth filter at a cutoff frequency of 10 Hz using a custom MATLAB script. Parameters included RMS in the ML and AP directions and 95% area ellipse to match those extracted from the smartphone.

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 26 (IBM Corp, Armonk, NY). COP and acceleration measures were averaged for the two trials for each condition. Validity between measures derived from the force plate, smartphone accelerometer, and Opal accelerometer were assessed with Spearman's correlations for all balance conditions. Correlations coefficients of 0.3-0.5 were considered low, 0.5-0.7 were considered moderate, 0.7-0.9 were considered high, and 0.9-1.0 were considered very high.[67] Receiving operating characteristic (ROC) curves were constructed and the area under the curve (AUC) was calculated to determine the level of discrimination between assisted device users and non-assisted device users. Not all participants could complete the more challenging balance tasks, and there was missing data for tandem and single leg conditions. Therefore, ROC curves were only constructed for eyes open, eyes closed, and semi-tandem conditions. Statistical significance was set at $\alpha = 0.05$.

Results

Demographic information of all participants is presented in Table 2.1. Twenty-seven pwMS participated, and 12 were assisted device users and 15 were non-assisted device users. Assisted device users had significantly greater EDSS scores ($p = 0.01$). There were no differences in age between groups ($p = 0.11$).

Table 2.1. Demographic information for all participants.

	Assisted Device Users (n=12)	**Non-Assisted Device Users (n=15)**
Age Mean ± SD	62.1 ± 8.1 years	46.5 ± 12.2 years
Gender	9 females; 3 males	13 females; 2 males
Expanded Disability Status Scale Median (IQR)	6 (5.3-6.4)	2.5 (2.5-3.5)
MS Type	7 Relapse-Remitting 1 Primary Progressive 4 Secondary Progressive	14 Relapse-Remitting 1 Unsure
MS Duration Mean ± SD	18.6 ± 10.1 years	12.9 ± 11.6 years

From the Opal accelerometer, RMS ML acceleration ranged from 0.038 to 0.987 m/s^2, RMS AP acceleration ranged from 0.061 to 0.600 m/s^2, and 95% area ellipse ranged from 0.034E-3 to 0.177 m/s^2. From the smartphone accelerometer, RMS ML acceleration ranged from 0.036 to 0.974 m/s^2, RMS AP acceleration ranged from 0.064 to 0.869 m/s^2, and 95% area ellipse ranged from 0.042E-3 to 0.185 m/s^2. From COP outputs from the force plate, RMS ML ranged from 0.435 to 60.97 mm, RMS AP ranged from 0.174 to 23.98 mm, and 95% area ellipse ranged from 26.72 mm^2 to 5371.55 mm^2.

Table 2.2 depicts Spearman's correlations between smartphone accelerometer outputs and Opal accelerometer outputs, and Table 2.3 depicts Spearman's correlations between smartphone accelerometer outputs and force plate outputs. Scatter plots for correlations for each balance task for the smartphone and Opal outcomes are presented in Appendix A, and scatter plots for correlations for the smartphone and force plate outcomes are presented in Appendix B. There were moderate to strong correlations between the smartphone accelerometer to Opal accelerometer for RMS (ρ = 0.66 – 0.97; p = 0.001 – <0.001) and 95% area ellipse (ρ = 0.72 – 0.94; p = <0.001). There were weak to moderate correlations between the smartphone accelerometer and force plate for RMS (ρ = 0.33 – 0.87; p = 0.02 - <0.001) and 95% area ellipse (ρ = 0.48 – 0.72; p = 0.01 - <0.001).

Table 2.2. Spearman's correlations (rho) between the smartphone and Opal for root mean square (RMS) acceleration and 95% confidence ellipse area.

		Smartphone Outcomes		
	Eyes Open	**RMS Mediolateral**	**RMS Anteroposterior**	**95% ellipse area**
Opal Outcomes	**RMS Mediolateral**	0.86 (p <0.001)		
	RMS Anteroposterior		0.90 (p = 0.001)	
	95% ellipse area			0.83 (p < 0.001)
	Eyes Closed			
	RMS Mediolateral	0.88 (p <0.001)		
	RMS Anteroposterior		0.90 (p < 0.001)	
	95% ellipse area			0.91 (p < 0.001)
	Semi Tandem			
	RMS Mediolateral	0.89 (p < 0.001)		
	RMS Anteroposterior		0.97 (p < 0.02)	
	95% ellipse area			0.94 (p < 0.001)
	Tandem			
	RMS Mediolateral	0.66 (p = 0.001)		
	RMS Anteroposterior		0.77 (p <0.001)	
	95% ellipse area			0.72 (p < 0.001)
	Single Leg			
	RMS Mediolateral	0.96 (p < 0.001)		
	RMS Anteroposterior		0.99 (p < 0.001)	
	95% ellipse area			0.99 (p < 0.001)

Table 2.3. Spearman's correlations (rho) between smartphone outcome measures and force plate outcome measures for Root Mean Square (RMS) and 95% confidence ellipse area.

Smartphone Outcomes				
	Eyes Open	**RMS Mediolateral**	**RMS Anteroposterior**	**95% ellipse area**
Force Plate Outcomes	**RMS Mediolateral**	0.45 (p = 0.015)		
	RMS Anteroposterior		0.47 (p = 0.017)	
	95% ellipse area			0.48 (p = 0.013)
	Eyes Closed			
	RMS Mediolateral	0.65 (p < 0.001)		
	RMS Anteroposterior		0.73 (p < 0.001)	
	95% ellipse area			0.72 (p <0.001)
	Semi Tandem			
	RMS Mediolateral	0.78 (p < 0.001)		
	RMS Anteroposterior		0.33 (p = 0.11)	
	95% ellipse area			0.69 (p < 0.001)
	Tandem			
	RMS Mediolateral	0.67 (p = 0.001)		
	RMS Anteroposterior		0.87 (p < 0.001)	
	95% ellipse area			0.63 (p = 0.002)
	Single Leg			
	RMS Mediolateral	0.83 (p = 0.001)		
	RMS Anteroposterior		0.89 (p <0.001)	
	95% ellipse area			0.89 (p < 0.001)

ROC curves were constructed to determine the classification accuracy between assisted device users and non-assisted device users. The Area Under the Curves (AUC) are depicted in Table 2.4. For RMS ML, AP and 95% confidence ellipse acceleration from the smartphone, the AUC was statistically significant for eyes open, eyes closed, and semi-tandem stance (p <0.001 – 0.02; Figure 2.2). For RMS AP and 95% confidence ellipse acceleration from the Opal accelerometer, the AUC was statically significant for eyes open, eyes closed, and semi-tandem stance (p = 0.002 – 0.03; Figures 2.2 and 2.3). There was no statistical significance for RMS ML from the Opal accelerometer. For COP outputs from the force plate, the AUC was statistically significant for eyes open, eyes closed, and semi-tandem stance (p = 0.004 – 0.05; Figure 2.2 and 2.3).

Table 2.4. Area under the curve for Receiving Operating Characteristics curves for smartphone outputs, Opal outputs, and force plate outputs. ML = mediolateral; AP = anteroposterior

	Opal		**Smartphone**		**Force plate**	
Condition - *Root Mean Square*	**Area**	***p*-value**	**Area**	***p*-value**	**Area**	***p*-value**
Eyes Open ML	0.70	0.08	0.79	0.01	0.77	0.02
Eyes Open AP	0.86	0.002	0.83	0.01	0.84	0.004
Eyes Closed ML	0.71	0.07	0.85	0.003	0.73	0.05
Eyes Closed AP	0.87	0.002	0.91	<0.001	0.84	0.004
Semi-Tandem ML	0.71	0.07	0.76	0.02	0.76	0.03
Semi-Tandem AP	0.76	0.03	0.84	0.003	0.72	0.07
95% Confidence Ellipse						
Eyes Open	0.76	0.02	0.81	0.01	0.81	0.01
Eyes Closed	0.81	0.008	0.88	0.001	0.86	0.002
Semi-Tandem	0.78	0.02	0.81	0.01	0.78	0.02

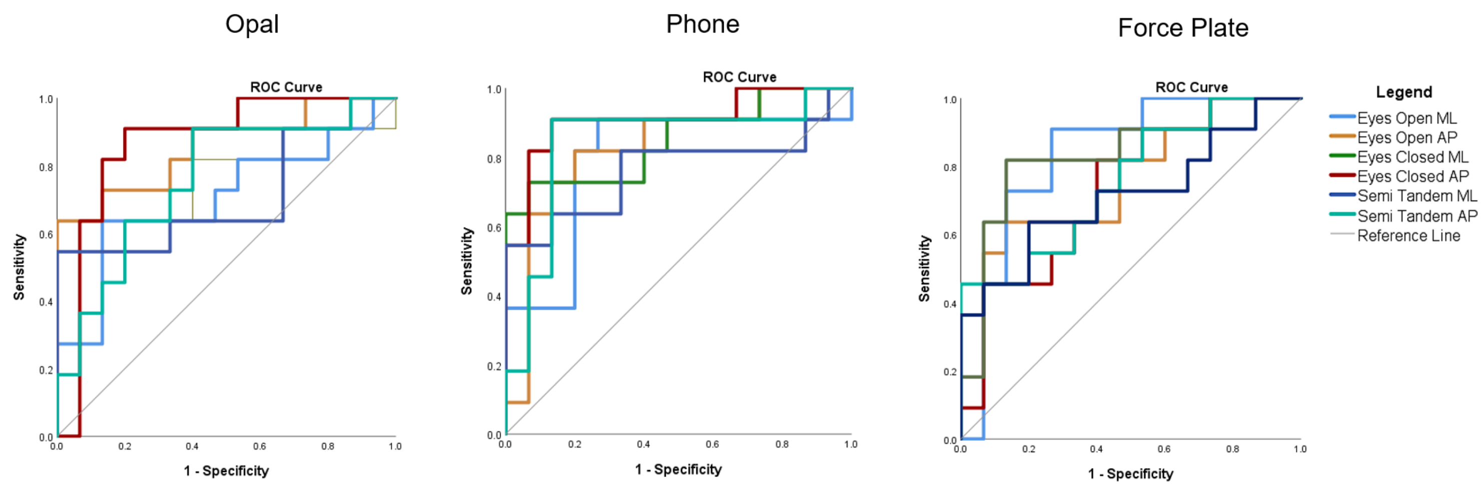


Figure 2.2. Receiving Operating Characteristic (ROC) curves for root mean acceleration derived from the a) Opal, b) phone, and c) force plate to discriminate between assisted device users and non-assisted device users during progressively challenging balance conditions. Curves with a greater area under the curve indicate better ability to discriminate between assisted device and non-assisted device users. ML = mediolateral; AP = anteroposterior

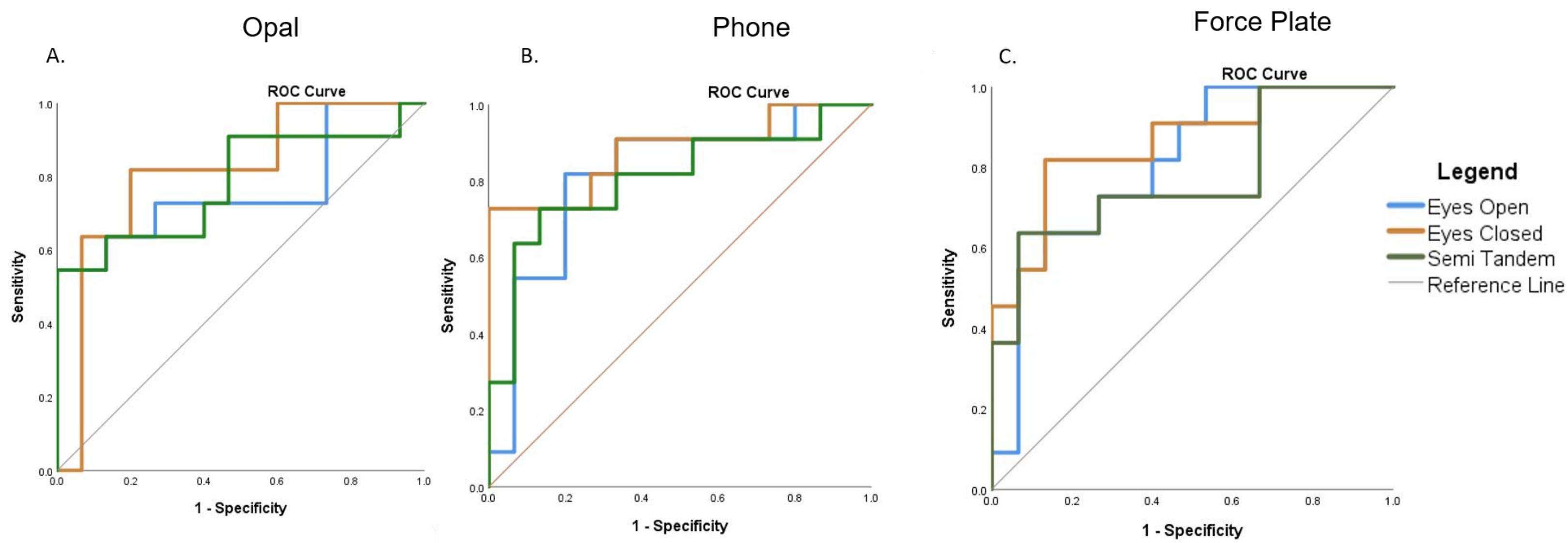


Figure 2.3. Receiving Operating Characteristic curves for 95% confidence ellipse derived from the a) Opal, b) phone, and c) force plate to discriminate between assisted device users and non-assisted device users during progressively challenging balance conditions. Curves with a greater area under the curve indicate better ability to discriminate between assisted device and non-assisted device users.

Discussion

The purpose of this study was to determine if a smartphone accelerometer could measure postural control in pwMS, and if a smartphone accelerometer could discriminate between pwMS who use an assisted device and pwMS who do not use an assisted device. The results support our hypothesis. We found moderate to strong, significant correlations between RMS and 95% area ellipse acceleration from the smartphone and Opal, and we found moderate, significant correlations between RMS and 95% area ellipse acceleration from the smartphone and RMS and 95% area ellipse COP from the force plate. We also found that smartphone accelerometry could discriminate between assisted device users and non-assisted device users, and our results were comparable to those from the Opal and force plate.

We found high correlations ($\rho > 0.7$) for RMS AP and ML and for 95% area ellipse between the smartphone and Opal and moderate correlations between the smartphone and force plate, suggesting that smartphone accelerometry is comparable to measure postural control compared to gold-standard devices in pwMS. As anticipated, we found stronger correlations between smartphone and Opal accelerometry than between smartphone and force plate measures. This is as expected since both accelerometers capture a proxy of center of mass while the force plate captures center of pressure. Force plates are traditionally used to measure posture, [68] but with the growing development of tri-axial accelerometers, our results suggest that smartphone accelerometry may also be used to measure posture. We also found that correlations were stronger as balance conditions became more difficult. This suggests that smartphone accelerometry may be more accurate with greater postural sway.

High AUC (AUC > 0.8) for smartphone accelerometry demonstrate that RMS and 95% confidence ellipse can be used to classify MS assisted deviser users and MS non-assisted device users. PwMS who use assisted devices demonstrate impaired postural control compared to those who do not use assisted devices,[69] and assisted device usage is a strong predictor of falls.[66] Therefore, assessing postural control with smartphone accelerometry may provide insight to understanding those who are at high risk for falls. ROC curves and the AUC for smartphone accelerometry was also comparable to that of the Opal and force plate, indicating similar classification accuracy to gold-standard devices.

Our results are comparable to previous studies that examined the use of smartphone accelerometry to assess postural control. Past studies have demonstrated that smartphone accelerometers are comparable to force plate and motion capture outputs in clinical populations with impaired postural control including older adults and individuals with Parkinson's disease.[52,65] Another study found that smartphone accelerometer and gyroscope outputs were comparable to clinical assessments (Berg Balance Scale) in stroke survivors.[70] Despite the differing pathological mechanism that contributes to postural instability in pwMS,[4] our results suggest that smartphone accelerometers can be used to quantify postural control in this population. Because postural instability is a key predictor of falls in pwMS,[71,72] smartphone accelerometry offers potential to assess fall risk outside of a lab-based setting.

These results suggest that there is potential to leverage smartphone accelerometry to provide an objective assessment of standing balance in pwMS. Because of the affordable, ubiquitous, and portable nature of smartphones, there is potential to utilize smartphone accelerometers to increase balance assessments in pwMS.[57] Smartphone accelerometry can capture underlying characteristics of balance impairment in pwMS without the expense of force plates or subjective bias of clinical tests. Due to the nature of MS, new symptoms can develop or current symptoms can worsen over time.[2] Smartphones offer potential for pwMS to track and manage their balance that may change as a result of their symptoms. Over 80% of pwMS own smartphones, and approximately 45% of pwMS have used a health application.[57] With the dynamic nature of MS, a smartphone application may allow pwMS to assess their postural control as they notice their symptoms changing and initiate early treatment strategies. Indeed, there is one health application (Floodlight Open) developed to monitor MS symptoms, including mood, manual dexterity, and balance and walking.[73] However, there is limited research on the validity and reliability the mobility measures. Future research should integrate smartphone accelerometry into health apps to improve self-management of MS symptoms.

The results of this study also suggest that there is potential to provide objective postural assessments outside of the research setting. Previous studies have found that even pwMS without clinical disability have balance impairments as measured with force plates or motion capture systems.[19] Therefore, early assessment of postural control paired with targeted treatment can prevent falls before balance impairment worsens. However, it is difficult to identify balance impairment, especially among those with minimal disability, without force plates or motion capture systems.[74] The results of this study suggest that a smartphone accelerometer can assess postural control, and future studies should determine if smartphone accelerometry can identify balance impairment in pwMS with minimal disability. Using a smartphone to assess balance in a clinical setting can help clinicians identify balance impairment early in the course of the disease.

This study is the first to understand smartphone accelerometry in pwMS, but there are also limitations to this study. The smartphone used for this study was a Samsung Galaxy S6, and it is unclear if results are similar for different types of phones. With the quick advancements in technology, future studies should understand if accelerometers differ between types of smartphones. Participants in this study also held the phone against their chest, and it is unclear if other locations provide similar results. A future step is to determine if pwMS can self-assess their postural control, and using the chest is a location that pwMS can easily identify and use. In addition, this study examined standing postural control in pwMS. For pwMS who are non-ambulatory, it is unclear whether smartphone accelerometry can assess seated postural control. Future studies should examine the use of smartphone accelerometry for pwMS who are non-ambulatory. It also remains unclear if smartphone accelerometry is sensitive to changes in postural stability following treatment interventions. Smartphones may offer potential to track individual progress following treatment, and understanding its sensitivity to these changes is warranted.

In conclusion, this study suggests that RMS and 95% confidence ellipse from a smartphone accelerometer is comparable to that from a research-grade accelerometer and force plate in pwMS. Furthermore, RMS and 95% confidence ellipse from a smartphone can discriminate between pwMS who are assisted device users and non-assisted device users. This evidence suggests that an embedded smartphone accelerometer can be used to measure standing postural control in pwMS. These findings provide preliminary results to support the use of smartphone technology as a tool to assess postural control when technology such as force plates or research grade accelerometers are not available. Levering an affordable and ubiquitous tool may increase access to objective postural control assessments.

CHAPTER 3. A FALL RISK ALGORITHM FOR A MOBILE HEALTH APP FOR INDIVIDUALS WITH MULTIPLE SCLEROSIS

Introduction

Falls are a major health concern for individuals with Multiple Sclerosis (MS). Over half of people with MS (pwMS) will fall in a six month period, and a significant portion of those falls will result in a serious injury.[4,7] Fall-related injuries can range from contusions to fractures and even death.[7] In addition to injuries, falls can result in fear of falling, which may lead to activity restriction and social isolation.[8,75] Therefore, preventing falls is critical to increase functional independence in those with MS.

Falls in those with MS stem from an interplay of physiological and psychological risk factors. For instance, postural instability, assisted device usage, high fatigue levels, and low self-efficacy are all associated with falls in pwMS.[21,31,72,75] With the large number of risk factors related to falls, several studies have aimed to identify the most important risk factors to inform treatment strategies.[34,35,61,76] For instance, results from a meta-analysis of over 1,000 pwMS demonstrated that balance impairments, progressive MS, and use of walking aids were most associated with increased fall risk.[77] These results highlight that fall risk is multifactorial, and that assessing multiple risk factors is critical to reduce fall-related injuries through tailored treatments.

Fall risk factors can be assessed through a variety of methods. Certain factors are assessed through validated self-report questionnaires, such the Modified Impact Fatigue Scale to assess fatigue,[37] the Falls Efficacy Scale to assess fear of falling,[78] and the Multiple Sclerosis Walking Scale to assess perceived walking ability.[38] Mobility is assessed through balance and walking performance measures, and can be measured through clinical scales or through technology. Clinical scales such as the Berg Balance Scale or Timed Up and Go involve little instrumentation, but they are prone to ceiling effects and may not always capture underlying mobility impairments in those with MS.[17] Technology such as force plates or motion capture systems are more robust and can capture minute changes in movement, but they are expensive and require trained personnel.[62] Fall risk is multifactorial, and it is recommended to measure both MS symptoms and objective mobility performance for an accurate measure of fall risk.[4,77] However, assessing multiple risk factors takes time, technology to assess mobility is not always feasible to have in clinical settings, and there is need for trained personnel.

Mobile health technology can overcome these limitations by assessing multiple risk factors using widely available and affordable technology. Moreover, with smartphone applications (apps), users can self-assess and monitor their risk for falls. Questionnaires assessing factors such as fatigue or fear of falling can be implemented within a health app. Smartphones are also embedded with accelerometers and gyroscopes that can be leveraged to measure posture.[43,45] Previous evidence has suggested that smartphone accelerometers can assess postural control in pwMS and distinguish between assisted device users and non-assisted device users (see Chapter 2). Therefore, there is potential to use smartphone technology to objectively measure posture and assess self-reported symptoms that are related to fall risk.

Approximately 85% of pwMS own a mobile device, and ~45% of pwMS use a health app.[57] Mobile health apps are rapidly growing to improve monitoring and management of MS. With the high usage of health apps among the MS population, a fall risk app offers high potential increase accessibility to falls screening and improve treatment practices. Prior to developing a fall risk app, the first step is to develop an algorithm that can be employed in mobile technology and accurately measures fall risk in pwMS. Therefore, the purpose of this study was to develop an algorithm with the most influential risk factors associated with falls in pwMS that can be implemented through a smartphone app, and to determine the classification accuracy of the final algorithm. It was hypothesized that a multifactorial model will have greater classification accuracy in predicting fall status than a single risk factor.

Methods

Participants

Twenty-seven individuals with MS participated in the current study and are the same participants as study 1 (see Chapter 2). Participants were included if they were: a) 18 years or older; b) had a physician confirmed diagnosis of MS; b) normal or corrected to normal hearing and vision; c) capable of standing unaided for at least one minute; and d) scored ≤6.5 on the Expanded Disability Status Scale (EDSS). Participants were excluded if they had any neurological disorder other than MS.

Experimental Protocol

Participants completed standing balance tasks while holding a smartphone against their chest and standing on a force plate. Five standing balance tasks were performed on the following order for 30 seconds each: 1) eyes open, 2) eyes closed, 3) semi-tandem, 4) tandem, and 5) single leg. Two trials of each task were performed. Participants also completed two trials of the TUG and two trials of the 9-hole peg test with each hand.

Following the balance tasks, participants were asked to complete questionnaires related to their MS symptoms. Participants completed the Modified Impact Fatigue Scale (MIFS) which assesses fatigue over the last month,[37] Multiple Sclerosis Walking Scale (MSWS-12) which assesses perceived walking over the past two weeks,[38] Patient Determined Disease Steps (PDDS) and Expanded Disability Status Scale (EDSS) which assesses disability level,[79] Visual Functioning Questionnaire which assesses visual function,[80] Falls Efficacy Scale which assesses fear of falling, and Activities Balance Confidence Scale (ABC) which assesses perceived balance confidence.[81] Falls history over the last 6-months was also recorded, with a fall defined as an unintentional event in which a person coms to rest on the ground or lower level.[82]

Statistical Analysis

Statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 26 (IBM Corp, Armonk, NY). Acceleration was extracted from the smartphone and processed through a custom MATLAB code that has been previously described.[47] In brief, root mean square (RMS) acceleration was calculated from the smartphone for the anteroposterior and mediolateral directions for each condition. The Romberg Ratio, the ratio between eyes open and eyes closed conditions, was calculated for RMS acceleration. The Romberg Ratio was chosen because an elevated Romberg is an indicator of poor balance in pwMS[83], and using the ratio minimizes differences in accelerometry outcomes when using different smartphone accelerometers.

An independent samples t-test was performed to determine differences between fallers (≥1 fall) and non-fallers (<1 fall) for the Romberg Ratio and for self-reported MS symptoms. Outcomes that had a p value of 0.1 or below were inputted into a logistic regression model. A p value of 0.1 was chosen as opposed to the traditional 0.05 to avoid underfitting the model.[84]

A binary logistic regression analysis was performed to identify factors that are most associated with MS fallers. Model building was iterative and guided by interpretability and evaluation of the Wald statistic for each variable. This method is recommended over stepwise methods using *p*-value based decision making to improve the quality of the final model when using small data sets.[85] In addition to the variables entered to the model, fall history was also added into the final model as it has shown to be a significant predictor of future falls,[34] but was not entered into the regression analysis as it dampens the effect of other variables. After the model was created, coefficients for each variable were determined based on the beta value and Odds ratio.[84] Sensitivity, specificity, and classification accuracy were calculated for the final model.

Results

Demographic information and outcome measures of all participants is presented in Table 3.1. Overall, there were 17 fallers and 10 non-fallers. Age ranged from 27 to 75 years, and EDSS ranged from 2.5 to 6.5.

Table 3.1. Demographic information of all participants. Values are expressed in mean (standard deviation).

	Mean (Standard Deviation)
Age	53.4 (13.4) years
Gender	22 Females 5 Males
Expanded Disability Status Scale (median (IQR))	3.5 (2.5-6)
Assisted Device	12 Users 15 Non-users
Multiple Sclerosis Duration	15.7 (11.1) years
Type of Multiple Sclerosis	1 Primary Progressive 4 Secondary Progressive 22 Relapse Remitting

From the independent samples t-test, fallers had a significantly greater mediolateral postural instability as measured through the Romberg Ratio (p = 0.03), had worse perceived walking ability as measured through the Multiple Sclerosis Walking Scale (p = 0.02), used an assisted device (p = 0.05), had worse balance confidence as measured from the ABC-6 (p = 0.002), and had greater disability as represented through the PDDS (p = 0.04) and EDSS (p = 0.01). There were no significant differences between fallers and non-fallers for number of medications, amount of physical activity, fatigue, or age (Table 3.2).

Table 3.2. Independent samples t-test of mobility measures and questionnaires to assess Multiple Sclerosis symptoms. Values are expressed in mean (standard deviation). RMS = Root Mean Square

Measure	**Non-Fallers**	**Fallers**	***p* – value**
Age	48.1 (15.8)	56.6 (11.1)	0.11
Activities Balance Confidence Scale – Short Form	72.9 (12.9)	45.1 (23.6)	0.002
Falls Efficacy Scale	28.1 (9.2)	31.6 (9.2)	0.35
Modified Impact Fatigue Scale	56.5 (9.5)	59.2 (11.5)	0.53
Visual Functioning	91.9 (9.0)	91.6 (8.3)	0.94
Multiple Sclerosis Walking Scale	24.1 (27.5)	53.8 (31.2)	0.02
Patient Determined Disease Steps	1.4 (1.5)	2.7 (1.5)	0.04
Number of Medications	3.9 (2.9)	6.4 (3.6)	0.08
Timed Up and Go (sec)	9.5 (2.2)	14.4 (5.4)	0.01
9-Hole Peg Test (sec)	26.5 (10.9)	31.7 (14.4)	0.34
Assisted Device Usage	2 AD users 8 Non users	10 AD users 7 Non users	0.05
Romberg Ratio RMS Mediolateral	0.9 (0.4)	1.4 (0.5)	0.03
Romberg Ratio RMS Anteroposterior	1.0 (0.2E-3)	1.0 (0.1E-2)	0.28

The MSWS-12, ABC-6, PDDS, mediolateral sway from the Roberg Ratio, number of balance tasks completed, number of medications, and assisted device usage were inputted into a logistic regression model to predict fallers from non-fallers. Because PDDS and walking ability from the MSWS-12 were highly correlated and colinear (ρ = 0.85; p = <0.001), only the MSWS-12 was inputted into the regression model.

Based on the Wald statistic and beta values of each variable, the final model from logistic regression analysis included the ABC-6, MSWS-12, RMS Romberg Ratio in the mediolateral direction, and number of balance tasks completed (Table 3.3). Medications added little significance to the model (Wald = 0.001; ß = 0.007). Additionally, although assisted device usage had a high beta value, the Wald statistic was small (Wald = 1.0), and its relationship with the MS Walking Scale was high. There are also individuals who may not use an assisted device even though it is recommend by a clinician, and RMS acceleration has shown to discriminate between assisted device and non-assisted device users. As a result, the final model is:

Fall Risk = w1*Balance Confidence + w2*Walking Scale + w3*Mediolateral Sway + w4*Balance Tasks Completed + w5*Fall History

Table 3.3. Output from a logistic regression model to predict MS fallers. ABC = Activities Balance Confidence; MSWS = Multiple Sclerosis Walking Scale; RMS = Root Mean Square

Variable	**B**	**S.E.**	**Wald**	**Odds Ratio**	***p* – value**
ABC – 6	-0.33	0.24	2.11	0.72	0.15
MSWS-12	-0.34	0.25	1.89	0.74	0.17
Medications	0.01	0.21	0.001	1.007	0.98
Romberg Ratio RMS Mediolateral	3.39	2.38	2.02	29.64	0.16
Balance Completion Tasks	-5.30	3.86	1.87	0.005	0.17
Assisted Device Usage	4.97	4.97	1.0	144.36	0.32

The coefficients for each variable was determined from beta values and odds ratio within the regression results. Variables with Larger beta values and odds ratios were given larger coefficient values. For this final model, the overall classification accuracy of identifying fallers to non-fallers was 81.5%, which is greater than the classification accuracy of each individual variable which ranged from 70-78% (Table 3.4). The sensitivity of the model was 82.4% and specificity was 72.7%. The model also had an adequate fit (Hosmer and Lemeshow Test = 0.81; Negelkrete R^2 = 0.65).

Table 3.4. Classification accuracy predicting fallers and non-fallers in those with Multiple Sclerosis (MS) with individual and combined variables. RMS = Root Mean Square

Variable	**Classification Accuracy**
Activities Balance Confidence – 6	74.1%
MS Walking Scale	70.4%
Romberg Ratio RMS Mediolateral	70.4%
Balance Completion	77.8%
Activities Balance Confidence – 6 + Balance Completion + MS Walking Scale + Romberg Ratio	81.5%

Discussion

The purpose of this study was to develop a weighted algorithm to predict fall risk to embed within a mobile health app for individuals with MS. Results from a bivariate analysis and logistic regression analysis determined that balance confidence, self-reported walking ability, mediolateral sway, and the number of balance tasks completed from five balance tasks were the strongest predictors of fall status in those with MS. Moreover, postural stability as measured through mediolateral sway and number of completed balance tasks were the strongest predictors.

This weighted algorithm offers potential to be used to allow pwMS to self-assess and self-manage their risk of falling.

Falls in those with MS stem from a complex interplay of physiological and psychological factors. Therefore, it is important to assess for multiple risk factors when understanding fall risk. An advantage to the algorithm developed here is that it integrates multiple risk factors that are related to falls in pwMS, including physiological factors (i.e., postural stability, balance performance), and self-reported factors (i.e., balance confidence, walking perception). Additionally, this algorithm examines objective performance using smartphone accelerometry which is more sensitive than self-reported or clinical balance measures.[71] While there are additional measures that may be related to falls in pwMS, this algorithm is designed specifically to include factors that can be measured using a mobile health app.

Previous studies have also performed multivariate analysis to determine the best predictors of falls in pwMS. Our findings are in line with these previous studies. For instance, Tajali and colleagues[76] found that a combination of self-reported and performance measures of mobility are most related to falls in pwMS. Nisagard et al.[86] also found that the Multiple Sclerosis Walking Scale was a significant predictor of pwMS with a history of falls. Several studies have identified balance and walking as important predictors for falls.[61,72,86] In addition to mobility, balance confidence and a past history of falls are associated with future falls in those with MS from multivariate analysis.[34,76,87] Therefore, integrating both objective mobility measures and self-reported confidence measures in the final algorithm integrates multiple fall risk factors for those with MS.

There were also outcomes that did not significantly differ between fallers and non-fallers in our sample. For instance, fatigue and number of medications were not related to fall history in the current sample. Past studies have found mixed results on fatigue, as some studies indicate a relationship between fatigue and falls,[76,88] while others found no relationship.[66,86] Future studies with larger sample sizes may better understand the relationship between falls and fatigue. There is also conflicting evidence on medication use and falls in pwMS. For instance, two studies found significant associations between number of medications and falls in MS,[89,90] but others found no association[86,91]. The largest study to date of 100 pwMS found no significant relationship between number of medications and falls.[91] Our results are in line with this study, but future work examining medication use, such as the types of medication, is warranted.

This study provides a foundation for integrating fall risk factors into a mobile health app specific for pwMS. Because of constraints in current fall risk screening practice (i.e., clinicians have limited time, equipment is expensive, need for trained expertise), mobile technology offers potential to overcome these limitations and improve accessibility to fall risk screening. Additionally, bringing fall risk assessment to the users offers potential for pwMS to self-monitor and self-manage their fall risk. The results of the study present the first algorithm that incorporates multiple risk factors measurable with a smartphone to measure fall risk in pwMS. As more data is collected, it is expected that the algorithm will become more enhanced. For instance, assistive device usage may become a stronger predictor for falls, while other factors such as fatigue and sit-to-stand may be included. With a greater sample size, the algorithm can be further analyzed using *p*-values along with the beta values and odds ratio to develop an accurate, sensitive, and specific model. This algorithm though, is the first algorithm that includes multiple modifiable risk factors. With this algorithm, pwMS can understand which areas put them at the greatest risk for falls. Currently, falls prevention interventions utilize a cookie-cutter approach. By measuring multiple modifiable fall risk factors, this algorithm can guide personalized prescriptions to most effectively reduce fall risk in pwMS.

The results of this study are important to inform fall prevention practices, but this study is not without limitations. First, there was a small sample size used to develop the algorithm. While the sample size is small, the results are in agreement with previous studies. Future studies, though, should include a larger sample size to understand risk factors most important to integrate into a fall risk algorithm. Second, this study was limited to risk factors that could only be measured with a smartphone. While this algorithm did not include all risk factors related to falls, these risk factors can be measured outside a clinical setting and can potentially increase access to screening with mobile technology. Future directions include testing the validity of this weighted algorithm compared to standard fall risk assessments and understanding its reliability over time. This algorithm was also developed specifically for independent fall risk screening, but it can be modified for screening by a clinician or trained personnel. Tests such as the TUG or sit-to-stand can be added, and measuring postural control during these tests may provide a better fall risk measure than using time to completion.[92] With continued testing, future steps will aim to improve the algorithm to best capture fall risk in individuals with MS.

In conclusion, the purpose of this study was to develop a weighted algorithm to measure fall risk in pwMS that can be integrated into a mobile health app. Results suggest that postural sway measured through smartphone accelerometry, balance confidence, the Multiple Sclerosis Walking Scale, number of balance tasks completed, and a past history of falls are the best predictors of falls in pwMS. This algorithm provides an important step to provide tailored fall risk screening to pwMS and measuring a person's unique fall risk. Future steps are to integrate this algorithm into a fall risk app and to test the validity and reliability of the algorithm in those with MS.

CHAPTER 4: USABILITY OF A FALL RISK MOBILE HEALTH APP FOR INDIVIDUALS WITH MULTIPLE SCLEROSIS

Introduction

Multiple Sclerosis (MS) is a chronic, neurodegenerative disease of the central nervous system (CNS) that affects over a million people in the United States.[1] MS may affect the brain, spinal cord, brainstem, and/or optic nerves, and can result in a range of sensory (i.e., pain, loss of proprioception), motor (i.e., spasticity, muscle weakness, balance or gait impairments), and/or cognitive (i.e., slowed processing speed, memory loss) symptoms.[2,3] Depending on which areas of the CNS are affected, symptoms vary from one individual to another.[2,4] Furthermore, new symptoms may rise or current symptoms may worsen throughout the course of the disease.[4] There is currently no cure for MS, and clinicians focus on managing MS symptoms and minimizing disease progression. However, the heterogeneity of MS makes this a complex disease to treat and manage.

Mobile health applications (apps) have rapidly evolved in recent years to help individuals track, manage, and treat their health.[93] For instance, health apps have been developed to help individuals track their physical activity,[94,95] manage their medications,[96] or treat disease symptoms.[97,98] Due to the complexity of MS, there is increasing use of mobile health apps to support disease monitoring and symptom management.[57,99] Indeed, over 85% of people with MS (pwMS) own a mobile device, and 45% of pwMS use a mobile health app to help manage or treat MS.[57] Common health apps for pwMS include those that improve disease management or provide disease and treatment information.[60]

While there are MS health apps developed for symptom management and medication tracking,[54] there are limited health apps developed to assess and manage fall risk. Falls are a significant health concern for pwMS, with half of those falling in a six-month period and up to 50% of falls resulting in an injury.[4] Risk factors for falls stem from multiple MS symptoms including impaired walking and balance, cognitive declines, and fatigue.[100] While assessing fall risk can be performed clinically, clinicians have time constraints, may not have necessary equipment, and commonly only assess one aspect of fall risk.[101] A fall risk app overcomes these constraints by providing self-assessments using affordable and ubiquitous technology. Additionally, MS symptoms fluctuate throughout the course of the disease,[4] and changes in symptoms lead to changes in fall risk. A health app can help individuals measure and track changes in their fall risk. Moreover, due to the COVID-19 pandemic, there are even more barriers to access healthcare, and a health app can increase access to home-based screening.

A fall risk health app for pwMS offers potential to increase fall assessment in the home setting, improve fall risk self-management, and reduce fall-related injuries. A health app can measure fall risk by leveraging smartphone accelerometry to objectively measure postural control and assess MS symptoms related to falls through self-reported questionnaires. A critical step in the development of a health app is to understand the usability of the app for its intended users.[102] Usability testing ensures that those with MS can easily use and understand an app to improve their overall health. Moreover, a review of MS health apps indicated that most apps do not meet the needs of those with MS, leading to poor adherence and use.[60] Applying a user centered approach in the development of health apps can help improve adoption and usage.[103] Therefore, the purpose of this study was to develop a fall risk app for pwMS and to test the usability of the app through an iterative design process. A user centered approach will improve the development of an app to facilitate the needs of those with MS to increase falls screening and ultimately reduce fall-related injuries.[104]

Methods

Application Development

This app, Steady-MS, was developed in Android Studio 3.1.2 and was developed as an extension of a validated fall risk app for older adults, Steady^{TM}.[51] Steady-MS consists of two components: The first are 25 questions targeting demographic information and MS symptoms. These questions include age, gender, past history of falls, type of MS, history of MS, the Multiple Sclerosis Walking Scale (MSWS-12),[38] and the short form of the Activities Balance Confidence Scale (ABC-6) (Figure 4.1).[81] The second component is a progressive balance component, in which the app guides users through five progressively difficult standing balance tasks. In the following order, the tasks are: 1) eyes open, 2) eyes closed, 3) semi-tandem, 4) tandem, and 5) single leg. A text description and image guides users through each task (Figure 4.2). Each task takes 30 seconds, and users are instructed to hold the phone against their chest for the duration of the task to measure their postural sway. These tasks were chosen because worse performance on these tasks are associated with falls in pwMS.[21,71] After each task, users are asked to report if they completed the task, attempted but didn't complete, or did not attempt. These data, along with responses to the 25-item questionnaire, is inputted into a weighted algorithm and covered into a score ranging from 0-100, in which higher scores represent a higher risk for falls.

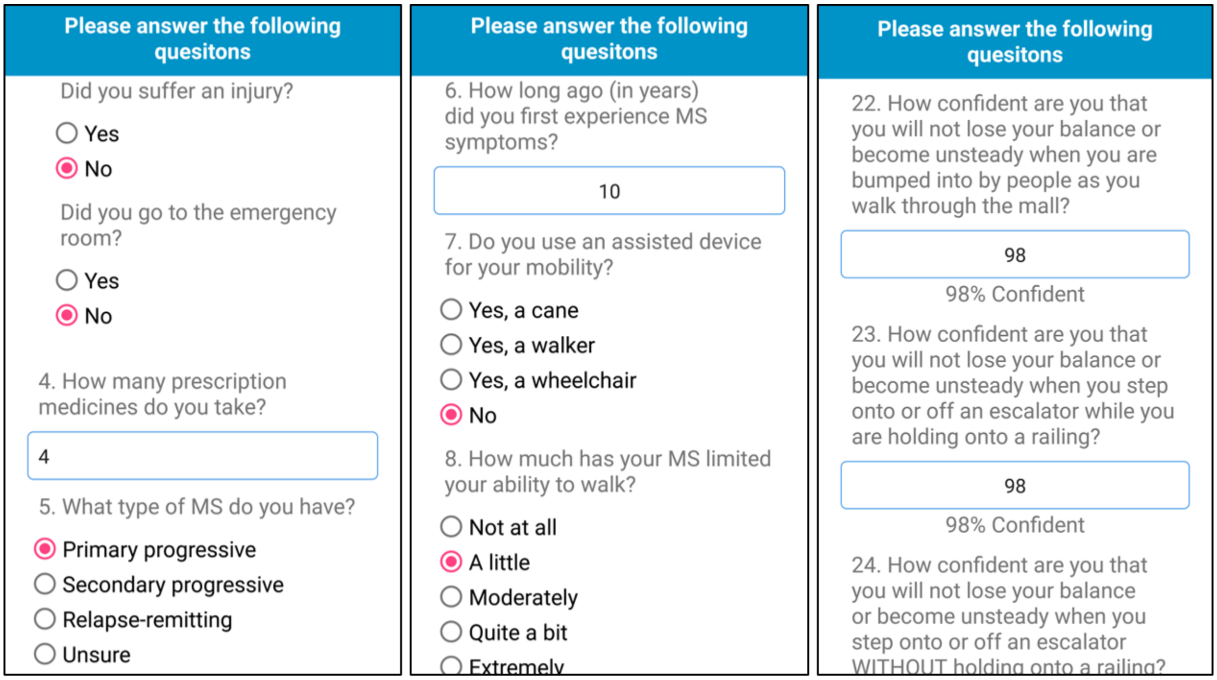


Figure 4.1. Steady-MS asks users to answer 25 questions related to their health, past falls, MS symptoms, and perceived balance.

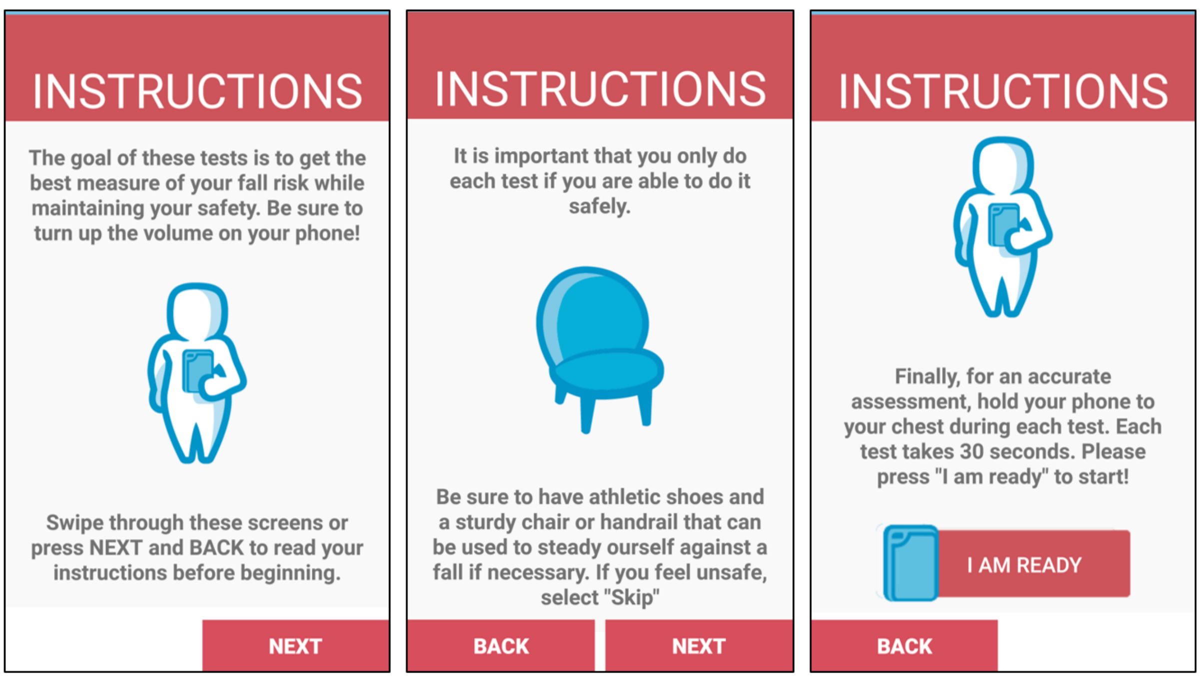


Figure 4.2. Steady-MS guides users to safely perform five standing balance tasks while holding the phone against their chest.

Steady-MS was also developed with consideration for common MS symptoms that may influence usability. For instance, fatigue is a common symptom that affects ~70% of pwMS.[105] To prevent fatigue, we included within the 25 questions those needed for the fall risk algorithm and asked only important additional questions (i.e., MS duration, type of assisted device) that relate to falls. We also limited balance tasks to one trial of five tasks. Vision impairments are also a MS symptom affecting ~30% of pwMS and may influence reading questionnaire and instructions.[106] Therefore, the font size was at least size 14, and all text was black text on a light background to improve contrast. Cognitive impairment including reduced processing speed and memory decline affects between 40-70% of pwMS.[107] We aimed to prevent cognitive overload by presenting one set of instructions per screen and keeping consistency throughout the app.

Participants

A total of 10 individuals with MS participated in two usability rounds. It has been recommended that small groups (n=~5) is suitable to identify usability issues.[108] PwMS (n=5) interacted with Steady-MS and identified usability issues. Using their feedback, we improved the design of the app, and then another group of pwMS (n=5) interacted with the app to identify any additional usability issues. This iterative design approach centered around the user is most effective for identifying user challenges when developing health apps.[103,104] Inclusion criteria for participants included: a) physician confirmed diagnosis of MS, b) age 18 years or older, c) self-reported ability to use a touchscreen device, and d) ability to stand independently for at least one minute. Those with a neurological disorder other than MS were excluded from the study.

Procedures

An iterative design-evaluation process of videotaped, semi-structured interviews were used to determine the optimal usability of Steady-MS. Participants were presented with a smartphone (Samsung Galaxy S6) and asked to open the app and follow all instructions. Participants first completed the app independently with as little assistance as possible. They then completed the app a second time, but this time thinking aloud and narrating their thoughts. They were also encouraged to discuss their likes, dislikes, and recommendations for improvements. After receiving their fall risk score, participants were also asked to identify and draw different graphics of how they want to receive their score, such as on a circular chart or linear scale.

Following the semi-structured interview, participants completed the Systematic Usability Scale (SUS) to understand the overall usability of the app. The SUS is widely used to quantify the usability of user-machine interfaces, consisting of 10 standard questions on a 5-point Likert scale.[109] The SUS ranges from 0 to 100, with higher scores representing greater usability. Participants also completed the Mobile Device Proficiency Questionnaire (MDPQ) to understand general proficiency of using mobile devices. The MDPQ ranges from 5-40, with higher scores representing greater proficiency.[110]

After the first iterative cycle, changes were made to the design of the app based on issues identified from the interviews. The second cycle of semi-structured interviews were performed on five new participants with MS. Due to COVID-19, interviews in the second round were performed remotely. The procedures followed the same format as the first round, but participants were delivered a smartphone with Steady-MS installed, and interviews were conducted over a video call. This format allowed us to understand how Steady-MS is used in the home environment.

Data and Statistical Analysis

All videotapes and field notes taken during the interview were transcribed verbatim. Qualitative data from videotapes and field notes were analyzed to develop a coding system in MAXQDA (Version 12.3.3, Berlin, Germany). Based on their content, data was assigned with codes, and codes with similar content were grouped into themes. Codes and themes were reviewed and discussed by two researchers (KH and MF).

Scores from the SUS were used to complement the qualitative results. SUS scores were averaged for each participant and transformed into a score out of 100.

Results

Iteration 1

Usability Interviews

Participant characteristics are displayed in Table 4.1. From the semi-structured interviews and coding analysis, three main themes were identified: 1) intuitive navigation; 2) efficiency of use; and 3) perceived value. Table 4.2 summarizes main issues identified from the interviews and subsequent changes made to Steady-MS.

Table 4.1. Demographic information of all participants in the first and second iterations. Values are presented in mean (years). EDSS = Expanded Disability Status Scale

	Iteration 1	**Iteration 2**
Age	53.2 (13.1) years	54.6 (8.7) years
Gender	4 females; 1 male	3 females; 2 males
EDSS median (IQR)	3 (2.5-6)	2.5 (2.5-6)
MS Duration	14 (5.9) years	16.2 (9.2) years
Education	2 – Associate Degree 3 – Bachelor's Degree	1 – High School Diploma 1 – Associate Degree 1 – Bachelor's Degree 2 – Master's Degree
Mobile Device Usage	5 – Owns smartphone 2 – Owns tablet	4 – Owns smartphone 3 – Owns tablet
Mobile Device Proficiency Scale	36.8 (3.3)	38.3 (1.1)

Intuitive Navigation

The most common usability issue during the first iteration was related to intuitive navigation. For example, when participants finish completing their self-reported questionnaires and moved onto the balance tasks, they are promoted to re-enter their ID. Two of the five participants had asked for clarification if they should re-enter their ID, or if the app was finished. It was not intuitive for these participants to re-enter their ID prior to moving onto the balance tasks. To address this issue, participants are no longer required to enter their ID to complete the balance tasks. Additionally, participants who use an assistive device asked for clarification whether the questionnaires referred to using or not using their assisted device. Therefore, for questions such as the short form of the ABC, we included instructions regarding assisted device usage.

There was also difficulty navigating through the 5 balance tests. Two of the participants asked clarification if eyes were open or closed, while two different participants performed the semi-tandem and tandem conditions incorrectly. While there was a text description instructing each balance stance, these participants reported that preferred having a clear image rather than reading text. Additionally, following each balance task, participants are asked to rate if they completed each test with one of three options. Of these options, participants reported that the last option, "I did not attempt to complete the test", was not intuitive. Participants indicated that if they were to select this option, they would have chosen to skip the test. To address these issues, we modified the images to indicate of eyes should be open or closed for each task (Figure 4.3). We also eliminated the option, "I did not attempt to complete the test".

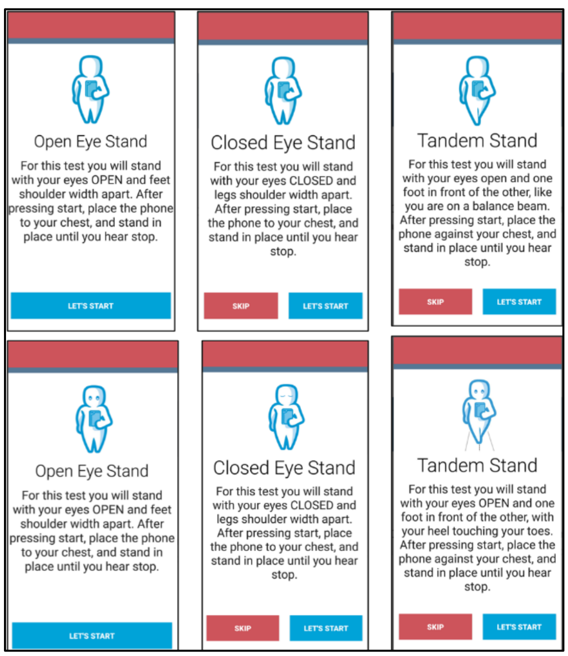


Figure 4.3. Steady-MS guides users through progressive balance tasks. The top panel of screenshots depict the first iteration of images and text, and the bottom panel depict the second iteration of images and text. Images of eyes and re-wording of text were edited to improve clarity and reduce cognitive overload.

For the final fall risk score, participants also reported that they liked receiving an overall score, but using a scale to present their score would be the most intuitive to improve their understanding. Three of participants preferred using a horizontal or vertical scale as opposed to a circular chart. They reported that they understood their score better on a linear scale with "low risk" on one end and "high risk" at the opposite end. Therefore, we added a horizontal scale depicting user's final fall risk score (Figure 4.4). The scale slides from 0-100, with a green color corresponding to lower fall risk, and a red color corresponding to higher fall risk.

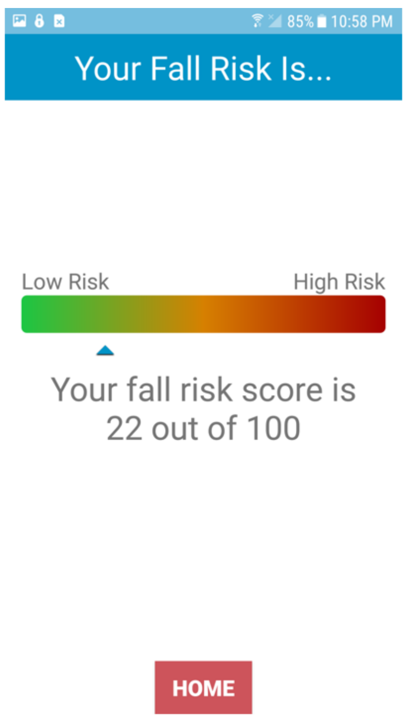


Figure 4.4. After completing the balance tests, Steady-MS outputs an overall fall risk score ranging from 0-100, in which higher scores represent higher fall risk.

"I'm a visual person, and when I have to read something, I will default to looking at the picture. I mean, I can read an instruction manual all day and, but if you show me a picture or video on how to do it, I'll probably pick it up faster." - Male, 36 years old

"You know, like they do on emojis. You just have those little circles for your eyes if they are closed or open. Maybe it's just me, but it's reading all these words or looking at the picture. I could see what I was supposed to do without reading all that. -Female, 57 years old

"I don't understand 'I did not attempt to complete the test' because if you didn't attempt to complete it, why wouldn't you just skip it?" -Female, 46 years old

"I enter my ID again and hit the 'Get Started'?" -Female, 76 years old

Efficiency of Use

Overall, all participants found that Steady-MS was efficient and easy to use. Participants reported that the app walks them through each question and balance test, and they reported that they could use it independently on their own. One participant reported that the Multiple Sclerosis Walking Scale questionnaire felt redundant, but none of the participants felt that the total number of questions or number of balance tasks needed to be reduced.

"I mean, it is pretty easy and seems to walk you through it, in my opinion. It's pretty straight forward." -Male, 36 years old

"Everything was quite clear when I was going through that." -Female, 51 years old

"I could do that on my own." -Female, 57 years old

Perceived Value

The last theme was related to the value of having a fall risk app. All of the participants reported that having an app would be beneficial for them to understand their risk of falling. Two of the participants found that having a fall risk score can provide confirmation or reassurance in their perceived changes in symptoms, especially during a relapse. These participants said that they would want to use Steady-MS to gauge their changes prior to seeing a physician. Participants with a higher fall risk found value in learning about their score, but they also wanted exercises or other prevention strategies. One participant also reported that she sees value in monitoring her fall risk at home rather than having to travel to a clinician.

Other participants reported that going through the app helped them realize factors that are related to falls. One participant, for instance, learned the importance of vision for fall risk and can be more aware of this in the future. Another participant reported that the tandem stance was a balance task she wanted to improve on.

"I guess I didn't realize the factors if your eyes open or closed or your stance can increase your fall risk. I guess I can be more conscious about those types of things because it seems to me now with that feedback about my vision, it plays a pretty important role in my balance. – Female, 57 years old

"But when I get feeling bad, boy, that number [the fall risk score] *shoots up. You know? It's not just my mind, you know, the app kind of confirms it. So maybe I'll use a cane instead*." -Male, 36 years old

"I like to gauge without having to go all the way to the doctor." -Female, 46 years old

Iteration 2

Usability Interviews

After the second round of interviews, transcript analysis and coding revealed three themes related to intuitive navigation, efficiency of use, and perceived value.

Intuitive Navigation

After modifying Steady-MS, participants in the second round of interviews reported little difficulty navigating through the app. After editing images and text for the balance tasks, four of the five participants performed all of the balance tasks correctly. One participant asked for clarification for the semi-tandem stance to confirm if she was standing correctly. After completing the 'About Me' questions, one participant returned to the questionnaires again, realized there were no more additional questions, and proceeded to complete the balance tests. To indicate this section is completed, we dimmed the 'About Me' section after users are finished (Figure 4.5). Overall, participants reported that Steady-MS was intuitive and easy to navigate.

Figure 4.5. After completing the 'About Me', this section is dimmed, and users are prompted to click on the 'Test' section.

"I didn't know if there was more about me, like if there were more categories within it. So I chose it again and then I kind of knew enough to be able to scroll through and go back."

-Female, 56 years old

"[Referring to the fall risk scale] *The green and the red colors pretty self-explanatory to me."*

-Female, 53 years old

Efficiency of Use

Similar to the first round of interviews, participants reported that Steady-MS was efficient and simple to use. They found that navigating through the questions and balance tasks were straightforward. Participants reported that if there was any confusion on the balance tasks or questionnaires, they understood the instructions after re-reading a second time. Participants also reported that they could use Steady-MS independently on their own without additional guidance.

“It seems simple enough to use and I’m not tech savvy as some are. There wasn’t anything if I read through it twice I wouldn’t understand.” -Male, 61 years old

“It's very easy to read. I liked that part, and the contrast is good too. I'm actually reading without my reading glasses, so that's a good sign” -Female, 53 years old

“I thought it was pretty good and straightforward.” -Male, 64 years old

Perceived Value

All participants reported that Steady-MS can provide them many benefits. Participants indicated that the most beneficial component was seeing their fall risk score. One participant, for instance, said that when she sees her neurologist, she may be asked to perform static balance tasks, but doesn’t receive feedback on her performance. With Steady-MS, she can see a score that gives her measurable feedback. Another participant reported that Steady-MS may be useful to understand her changes in fall risk with lifestyle changes. Because of COVID-19, her yoga classes have been canceled. She can feel changes in her balance and walking as a result, but seeing a score to confirm these changes may motivate her to try online yoga.

“I think it's neat to gauge your risk. Like when I go to the neurologist, she'll have me do stuff, and she'll say hmm or uh huh. And I don't know what any of that means. So it's kind of nice to have it be like, oh, your score is this.” -Female, 39 years old

"They're doing a lot of yoga online and whatnot. But we all know we don't do those, or I don't anyway, as much as I would if I were going to class. So it might be a way for me to say, hey, you need to do a little bit more with your yoga because your balances are getting a little bit more, you know, unstable, I suppose. -Female, 43 years old

"*You live with yourself all day, every day, and sometimes it's hard to tell if you feel like, you know, like I'm not getting around as well. And if you could look at* [the app] *and would it show you, oh yeah, it does say I have more of a fall risk*." -Female, 56 years old

Table 4.2. Summary of main issues identified in the first round of interviews, sample quotes from each issue, and solutions implemented to improve the app.

Domain	Issue	Sample quotes	Solution
Intuitive Navigation	Unclear if eyes are open or closed for balance tests	I have to keep my eyes closed, don't I?	Added eyes to icons to depict if eyes are open or closed.
	Confusion between semi-tandem and tandem stances	Maybe a picture or description because the one that said balance beam made more sense	Modified pictures to clarify semi-tandem and tandem stances. Re-worded description of each stance.
	Re-entering ID prior to balance tests	I just hit the 'Get Started' again?	After completing 'About Me', users are no longer prompted to re-enter their ID.
	Redundant option of completing test	I don't understand 'I did not attempt to complete the test' because if you didn't attempt to complete it, why wouldn't you just skip it?	The 'I did not attempt to complete the test' option was removed, as users are able to skip any balance task.
	Assisted device usage	This was to think about this as if I'm using my crutch, right?	Added instructions to answer the Activities Balance Confidence Scale as if you were to have your assisted device.
Efficiency of Use	Easy to use	I find that easy to use my own	
Perceived Value	Tracking score over time	If they can learn and improve their score, it would help them feel confident.	

System Usability Scale

In the first iteration, the average SUS score was 95.5 with a standard deviation of 3.3. In the second iteration, the average SUS score was 95.5 with a standard deviation of 2.9. While the SUS score did not change between iterations, this is likely because of a ceiling effect with a maximum score of 100. Previous work has indicated that the average technology SUS score is

60, and scores of 80 or above indicate that users are more likely to recommend the device to others.[111]

Discussion

The purpose of this study was to test the usability of a fall risk health application for individuals with MS through a user-centered design approach. After the first round of usability testing, participants identified issues navigating through the app, but reported that it was overall easy to use and found value in undergoing a fall risk assessment. We modified the app to improve navigation, and after the second round of testing, participants reported that the app was easy to navigate and could use the app on their own. These results suggest that Steady-MS is a usable health app that pwMS can use to self-assess their risk for falling. High scores on the SUS also indicate high usability among pwMS.

The main issues identified from semi-structured interviews were related to intuitive navigation. These were issues were related to understanding the entire instructions of a balance task (i.e., the position of the feet and if eyes are open or closed). Cognitive impairment is a common symptom resulting from MS,[112] and the instructions for each balance task may have resulted in cognitive overload for pwMS. To reduce cognitive overload, we improved the visuals and text to depict each balance task. Indeed, during the second round of testing, 4 participants completed all balance tasks correctly without asking for clarification. For future developments, it is important to consider the cognitive demands on pwMS to prevent cognitive overload.

Participants in both rounds of testing reported that they found the app clear, simple to use, and useful in learning their risk for falling. This suggests that pwMS can independently use Steady-MS and learn about their fall risk. Participants also reported that they value receiving a fall risk score, because they can identify if their score improves with exercise or declines with the onset of symptoms. Steady-MS offers potential for pwMS to self-assess and self-monitor their fall risk using a smartphone. Because MS symptoms fluctuate throughout the course of the disease, fall risk also changes.[4] Therefore, tracking and monitoring fall risk can help pwMS increase their awareness in their fall risk and take part in prevention strategies before a fall occurs. Unlike traditional fall risk assessments performed in clinics or lab-based settings, Steady-MS provides a tool to increase access to fall risk assessments that can be performed at home.

Steady-MS is designed and developed to measure fall risk specific to those with MS, but there are also additional features that can improve the quality of the app to prevent falls. Because participants reported the importance of tracking and monitoring their fall risk, a future feature is to develop a 'history' of scores that users can view. With a 'history' feature, users can compare their scores to a baseline level. Additionally, participants, particularly those at a higher risk for falls, reported they would want to receive exercises to complement their score. There are currently exercise apps specific to pwMS, such as MS Gym and NeuroNation. A feature that links Steady-MS to a validated and safe exercise app can allow pwMS to seek exercise based treatment strategies. Adding targeted treatments like exercise may be critical for those at higher fall risk to feel empowered from Steady-MS rather than fearful. Participants also reported that in addition to receiving an overall fall risk score, they wanted to understand their performance on each balance task and how they compare to others. As more data is collected on balance performance through the smartphone, a future addition may include adding performance on each task with a comparison to age and gender-matched individuals.

When developing future mobile health apps for pwMS, there are important aspects to ensure high usability. First, it is important to prevent cognitive overload in pwMS, as cognitive impairment is a common MS symptom.[112] Within Steady-MS, this was found when participants were asked to follow two separate instructions for a balance task. Using clear visuals and simple text is important to avoid cognitive overload. Second, when presenting a score or number to pwMS, it is important to make sure the score is easily understandable. Participants in the study reported that they preferred receiving a number because it is measurable, and they can track improvements over time. However, it is important that pwMS interpret scores accurately. When using a scale from 0-100, it was important to depict, both visually and through text, that 0 represents low risk and 100 represents high risk. Following these two guidelines can improve the development of future health apps to maximize usability for pwSM.

While there are many health apps developed for pwMS, ranging from medication management to improving cognition, Steady-MS is the first health app designed to measure fall risk specific to the MS population.[57] Because pwMS have unique fall risk factors and usability challenges, it is important to design an app that is specific for this population. There have been other fall risk apps developed for older adults[113-115] and for those with Parkinson's disease.[116] Unlike most fall risk apps, Steady-MS incorporates multiple fall risk factors into consideration rather than only one risk factor. This is important given that fall risk is multifactor for pwMS.[77] Moreover, unlike many of the health apps developed to improve self-management of MS symptoms, undergoing usability testing ensures that Steady-MS is usable for the targeted population.[117] As demonstrated in a review of MS-related health apps, most health apps have low usage and adherence because they lack user-centered testing and design.[60] By undergoing usability testing to ensure that pwMS find the app usable and useful, there is potential to increase fall risk self-assessments.

This is the first study to develop and test a MS fall risk app, but there are also limitations to this study. The participants in this study have high mobile technology usage and scored high on the MDPQ. Those with less technology experience may have additional usability issues that were not identified in this study. However, MS commonly affects younger adults, and over 80% of pwMS own a smartphone.[57] Therefore, it is likely that a person with MS will already have mobile device experience. Additionally, while Steady-MS measures overall fall risk, it currently does not offer fall prevention strategies. Seeking treatment after understanding individual risk is the next step to prevent falls, and future iterations of Steady-MS will aim to incorporate prevention strategies. Last, participants in this study have participated in pervious and falls prevention studies. Therefore, they may remember these balance tasks and how to perform them correctly. Future steps should include an additional usability round with participants without falls prevention research experience.

In conclusion, the purpose of this study was to determine the usability of a fall risk health app for pwMS. After one round of semi-structured interviews, we made modifications to improve users' intuitive navigation when answering their health-related questionnaires and performing five balance tasks. After a second round of interviews, users reported that the app was straightforward to use, easy to navigate, and found value in learning about their fall risk. SUS scores averaged 95.5 after the second round of testing, suggesting high usability. These results provide support in using a fall risk app to provide pwMS a tool to self-assess and self-manage their fall risk. With the numerous barriers in receiving fall risk screening (i.e., transportation, equipment, clinician time constraints), Steady-MS offers potential for home-based, independent assessment.

CHAPTER 5: FEASIBILITY OF HOME-BASED PROCEDURES FOR INDEPENDENT FALL RISK SCREENING

Introduction

Multiple Sclerosis (MS) is a chronic, neurodegenerative disease of the central nervous system that affects over one million individuals in the United States.[97] MS causes a range of symptoms, such as vision impairments, muscle spasticity, and impaired walking and balance.[2] Several MS symptoms put pwMS at a higher risk for falling.[7] Indeed, falls are highly prevalent among pwMS, with one in two pwMS falling in a six-month period.[4,7] Up to half of those falls will result in an injury, ranging from bruises to fractures.[4]

A widely adopted paradigm for falls prevention involves screening for multiple fall risk factors followed by prescribing targeted treatment strategies.[9] The first step of assessing risk factors can incorporate multiple types of measurement. For instance, fall risk factors may be assessed through validated self-report measures, such the Modified Impact Fatigue Scale to assess fatigue[37] and the Multiple Sclerosis Walking Scale[38] to assess perceived walking ability. While simple to use, self-report measures are prone to subjective bias.[39] Fall risk factors may also be assessed through performance measures. The Berg Balance Scale or Timed Up and Go are tests that measure balance and mobility.[118] They involve little instrumentation and can be performed in clinics, but they are prone to ceiling effects and may not always capture underlying mobility impairments in those with MS.[17] Technology such as force plates, pressure sensitive mats, or motion capture systems also measure mobility.[74] They are more robust and can capture minute changes in movement, but they are expensive and require trained personnel.[62] In addition to these limitations, clinicians also have time constraints, and access to in-person clinical visits are restricted because of the COVID-19 pandemic. Because of these limitations, pwMS may not receive appropriate screening. Without measuring fall risk factors, pwMS may not receive tailored prevention strategies and remain vulnerable to falls and fall related injuries.

Mobile technology offers potential to increase access to falls screening and treatment strategies with affordable, portable, and ubiquitous technology. Mobile technology can also help individuals monitor changes in fall risk and improve self-management of symptoms from the home environment. As access to healthcare remains even more limited during the COVID-19 pandemic,[119] it is critical for pwMS to be able to objectively self-assess their symptoms and fall risk from their homes. Mobile technology offers potential to bring falls screening to the individual's control.

Health applications (apps) are also commonly used among those with MS. Approximately 80% of pwMS own a smartphone, and 45% use a health app.[57] Providing pwMS with a familiar tool may improve their adoption and adherence.[55] To measure fall risk, a health app can incorporate fall risk questionnaires, and the accelerometer embedded within smartphones can objectively measure postural control.[46]

Indeed, we have developed a fall risk app, Steady-MS, that assesses multiple risk factors and measures overall fall risk for pwMS (see Chapter 3). We have tested the usability of the app with pwMS and ensured that it is both usable and useful (see Chapter 4). Ultimately, with Steady-MS, pwMS will be able to independently measure their fall risk in their homes and be equipped to manage their own fall risk. However, the feasibility of using Steady-MS in the home environment must first be determined. Additionally, with the increasing need to perform of remote-based testing to follow social distancing restrictions, the feasibility of performing remote study procedures must be understood. The purpose of this study was to understand the feasibility of pwMS independently using Steady-MS in the home-setting, examining aspects of recruitment, suitability of study procedures, and study resources. The secondary aim was to determine the validity of the fall risk score calculated from Steady-MS as compared to validated self-report fall risk measures. This home-based study identifies challenges and barriers for pwMS using the app in their own homes, and it helps understand the advantages and challenges of performing home-based research projects. We hypothesize that using Steady-MS is safe and feasible in the home setting, and we hypothesize that the fall risk score is comparable to fall risk questionnaires.

Methods

Participants

Thirteen individuals with MS that were recruited from a convenience sample participated in this study. Participants recruited were different than those who participated in studies 1-3. Participant demographics are displayed in Table 1. Participants were included if they: a) have a physician confirmed diagnosis of MS, b) are 18 years or older, c) self-report the ability to use a touchscreen device, d) have ability to stand independently for at least 1 minute, and e) have access to home internet and a webcam. Participants included were separate from those who participated in study one and study three.

Table 5.1. Demographic information for 13 study participants. Values are presented in mean (standard deviation)

Age	57.9 (9.0) years
Gender	4 males; 9 females
Highest Level of Education	1 – High school diploma 3 – Associate's degree 6 – Bachelor's degree 1 – Master's degree 2 – PhD or equivalent
Multiple Sclerosis Duration	19.1 (9.8) years
Assisted Device Usage	8 – none 4 - cane 1 - walker
Mobile Technology Usage	12 smartphone users 8 tablet users

Procedures

Because of restrictions placed on human subject research due to the COVID-19 pandemic, all testing procedures were performed in the participants' home. The steps for the study procedures are depicted in Figure 1. Participants were recruited through emails to MS support groups in central Illinois and through emails from the research team's database (Figure 1A). Following screening for inclusion and exclusion criteria (Figure 1B), a researcher hand delivered or mailed a smartphone (Samsung Galaxy) to all participants with the app, Steady-MS, installed (Figure 1C). For deliveries, the phone was dropped off at the participant's front porch and picked back up following testing. For mailing, the phone was mailed through the United States post office to the participant. Participants were asked to mail the phone back in a supplied box following testing at their earliest convivence.

After delivering the phone, participants and a researcher met over a video call (Figure 1D). After providing informed verbal consent, participants were asked to open Steady-MS on the smartphone and follow the guided instructions until they received a fall risk score. A researcher watched participants use Steady-MS through the video call, and any questions were addressed through video. Steady-MS first instructs participants to answer 25 questions related to their demographic information (i.e., age, gender), their MS (i.e., type of MS, MS duration), perceived walking ability through the Multiple Sclerosis Walking Scale-12,[38] and balance confidence through the short form of the Activities Balance Confidence Scale.[81] Steady-MS then instructs participants to complete 5 standing balance tasks in the following order for 30 seconds each: 1) eyes open, 2) eyes closed, 3) semi-tandem, 4) tandem, and 5) single leg. For participants' safety, Steady-MS instructs them to stand near a sturdy object during these balance tasks (i.e., table, countertop). Participants also have the option to skip any balance task. After completing each task, participants are asked to rate if they completed the task or if they lost their balance. Performance on the balance tasks and responses to the 25-item questionnaire are inputted into a weighted algorithm and converted to score from 0-100, where higher scores represent greater fall risk.

After completing the balance tasks, participants completed questionnaires online that are related to fall risk (Qualtrics^{XM}, Provo, UT). Participants completed the Falls Efficacy Scale International (FES-I) to assess their fear of falling,[78] the Multiple Sclerosis Walking Scale (MSWS-12) to assess their self-reported walking ability,[38] and Patient Determined Disease Steps (PDDS) to determine disability level,[79] and a falls survey about their past history of falls. These questionnaires were chosen because they have shown to be associated with fall risk in pwMS.[34,86,120]

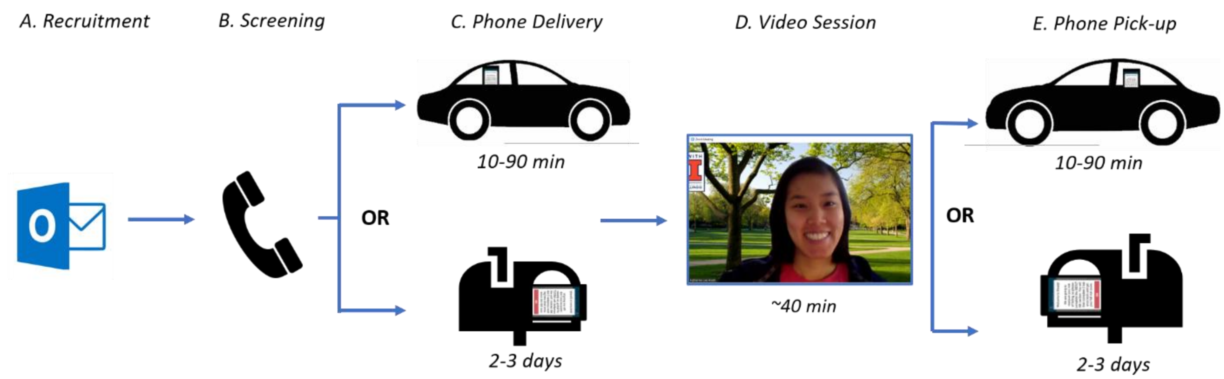


Figure 5.1. For the study procedures, participants were recruited through support groups and from a convivence sample (A). Participants were screened over the phone for inclusion and exclusion criteria (B). A researcher delivered smartphones to eligible participants through drop off or mail (C) and met the participant through a video call (D). Following the video call, a researcher picked the phone back up or the participant mailed the phone back (E).

Data Analysis

To determine the feasibility of the study, outcomes were grouped into four categories as recommended to evaluate feasibility[121]: 1) recruitment, 2) data collection procedures and outcome measures, 3) acceptability and suitability, and 4) evaluation of resources.

To understand the validity of the fall risk score, statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) for Windows, version 26 (IBM Corp, Armonk, NY). Scores in the FES-I and MSWS-12 were summed and averaged across participants. Scores on the PDDS and the number of falls in the past year were averaged across all participants. Spearman's correlations were performed between the fall risk score from Steady-MS and scores on the FES-I, PDDS, MSWS-12, and number of falls in the past year. Significance was set at $\alpha = 0.05$.

Results

Recruitment

It was anticipated that recruiting the sample population would be simple, as participants could complete all testing procedures in their homes. The research team also has experience working with individuals with MS throughout the state. To reach a different sample apart from studies one, two, and three, support groups in Bloomington, IL, Peoria, IL, and Savoy, IL were contacted. Support group leaders emailed members of the support group regarding this study. Participants were also recruited from the research team's database. Approximately 100 individuals with MS were contacted for the study, and 13 individuals were screened and enrolled. Low recruitment is likely due to the COVID-19 pandemic. With concerns related to health, personal finances, and overall well-being during the global pandemic, it is likely that pwMS were not interested in volunteering for a research study. It is also possible that pwMS may be less interested in home-based studies compared to in-person lab-based studies. It is difficult to determine the direct cause of low recruitment, but given the high success of recruitment from study one, low recruitment is most likely to be related to COVID-19.

Data Collection Procedures and Outcome Measures

The remote procedures for this study were necessary due to social distancing restrictions, but it was unclear if these remote procedures were feasible. Overall, the procedures and outcome measures for this study were appropriate to conduct for pwMS. Hand delivering phones to participants was faster and more reliable than mailing phones. By delivering a phone, a single session was completed within a day. Delivering phones was also faster and more efficient for participants, as they grabbed the phone from their front porch and left it on their front porch after finishing the study. However, delivering phones limited recruiting participants who live further away and puts more burden (i.e., time and effort) on the researchers. For example, internet was required for the researcher for the video call, and because coffee shops and restaurants with public internet were closed due to COVID-19, roundtrip visits were needed to both deliver and pick up the phone. This entailed up to 6 hours of driving for one session for those living out of town (recall Figure 1). Therefore, for participants out of town, it was more feasible to mail phones. Even though it took up to three days for mail delivery, there was substantially less time spent driving. Four phones were mailed, and all phones arrived back within ten days from data collection without damage or loss of data.

For video calls, Zoom Video Communications was used. Zoom was chosen over other software because of its simplicity. Participants clicked a link to open a video session and were not required to make a personal account. Approximately half of the participants reported using Zoom in the past and were familiar with its interface. Some participants, however, had technical issues with Zoom, such as enabling audio or enabling video. Therefore for some participants, extra time was spent configuring Zoom.

Using Steady-MS in the home setting was successful for pwMS. Participants had little to no issues or questions when navigating through the app. Participants followed instructions guided by the app to answer questions about their MS symptoms and safely performed the five balance tasks. Participants followed safety instructions to stand near a sturdy object, and participants skipped tasks if they felt unsafe. There were no adverse events reported. There were also few issues with answering the online questionnaires.

Acceptability and Suitability of Study Procedures

The study procedures were both acceptable and suitable for the participants. Given the social distancing regulations, participants found it acceptable to perform the study procedures through video. The home-based procedures also reduced burden on participants (i.e., time, travel), increasing the acceptability of these procedures. After receiving the phone, participants had little difficulty using Steady-MS in their homes and obtaining their fall risk score. Participants were able to easily open Steady-MS on the phone, answer the 25 questions about their health, and perform the balance tasks while ensuring their safety. This suggests that pwMS may potentially be able to use Steady-MS independently in their homes. There was also little difficulty in answering questionnaires through Qualtrics™. Following phone delivery, the study was completed within 30-45 minutes, which was a suitable length for participants. Time spent delivering and picking up the phone ranged from 10-180 minutes for the researcher.

Evaluation of resources and ability to manage and implement the study

To efficiently deliver and mail phones to multiple participants within a given week, the research team had multiple phones available to use. For this remote study, it was important to have at least five phones available. This allowed for multiple data collections to take place each week, as well as having at least one backup phone available. Additionally, the majority of the phones were hand-delivered rather than mailed due to concerns about phones being damaged or lost during the shipping process. After mailing and receiving four phones back without damages and with full data, having more phones available to mail can increase the number of sessions each week. A future procedure may also include sending participants the app to download on their own phone. This reduces needing multiple phones. Because data is stored on the hardware of the phone, a simple way for participants to transfer data to the research team should first be investigated prior to sharing the app.

While all participants were able to use Zoom on their own personal devices, a future consideration may be to deliver a tablet with a video app installed. This may reduce technical difficulties with using a novel video app, and this may also increase recruitment of participants who do not own a personal webcam.

Validity

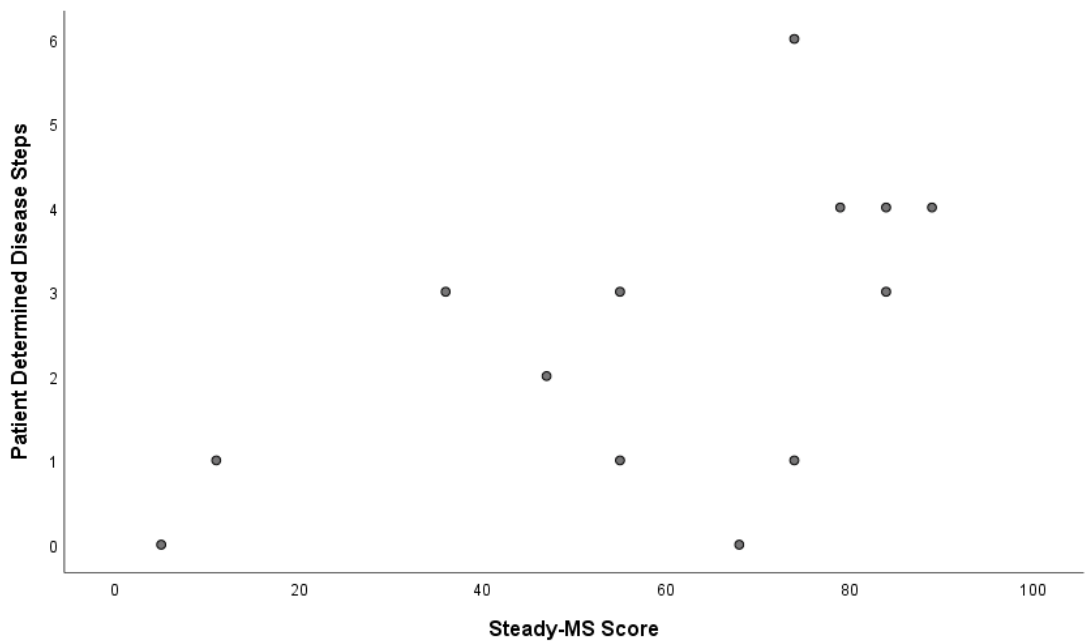
Outcome measures for the self-reported fall risk measures are displayed in Table 2. There was a moderate correlation between Steady-MS and disability level as measured through the PDDS ($\rho = 0.64$; $p = 0.02$; Figure 2A), perceived walking as measured through the MSWS-12 ($\rho = 0.70$; $p = 0.01$; Figure 2B). There were strong correlations between Steady-MS and falls in the last year ($\rho = 0.82$; $p < 0.001$; Figure 2C) and fear of falling as measured through the FES-I ($\rho = 0.88$; $p < 0.001$; Figure 2D).

Table 5.2. Mean and standard deviation of outcomes from fall risk questionnaires

Questionnaire	**Mean (standard deviation)**
Patient Determined Disease Steps Median (IQR)	3 (1-4)
Fall Efficacy Scale International	31.54 (12.30)
Multiple Sclerosis Walking Scale	31.69 (13.27)
Falls in the past year Median (range)	2 (0-17)

Figure 5.2. Scatter plots depicting the relationship between Steady-MS and the Patient Determined Disease Steps (A), Multiple Sclerosis Walking Scale (B), number of falls in the past year (C), and Falls Efficacy Scale (D).

A.



B.

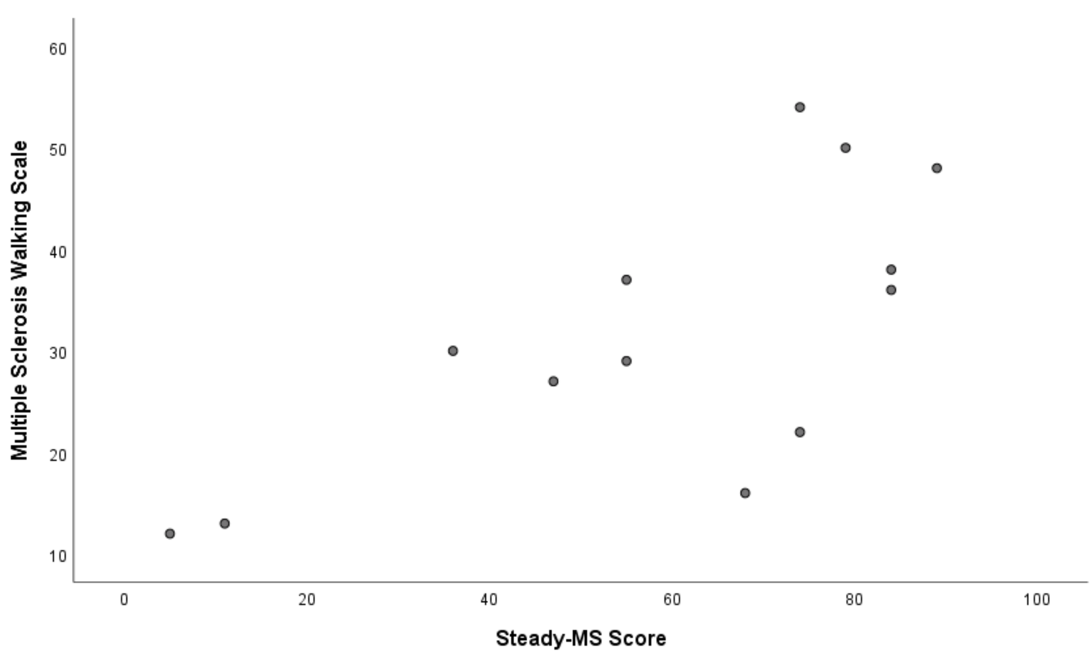
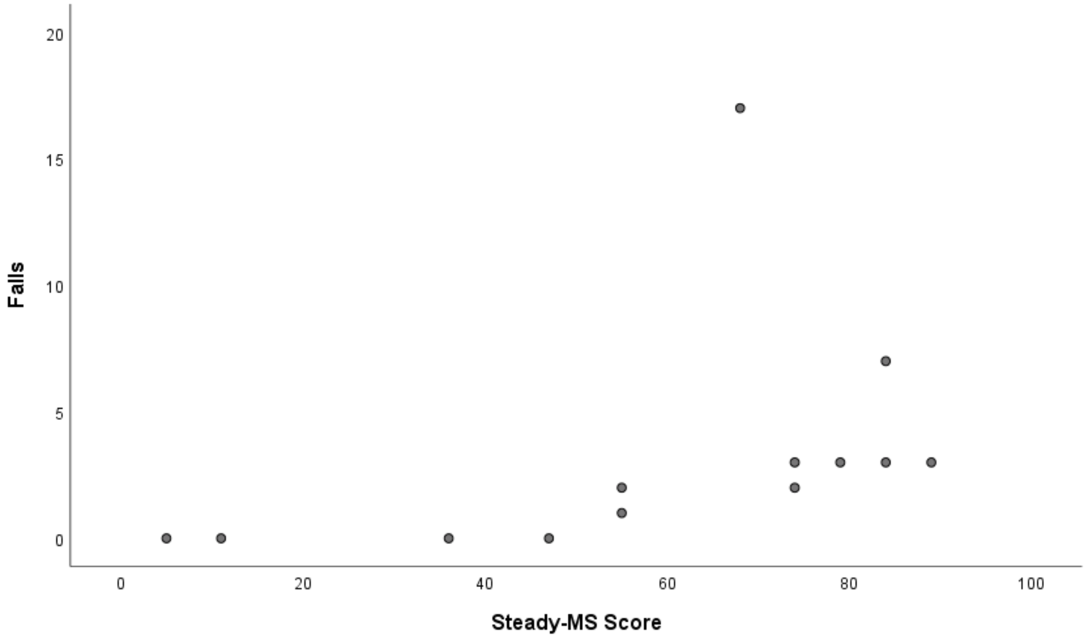
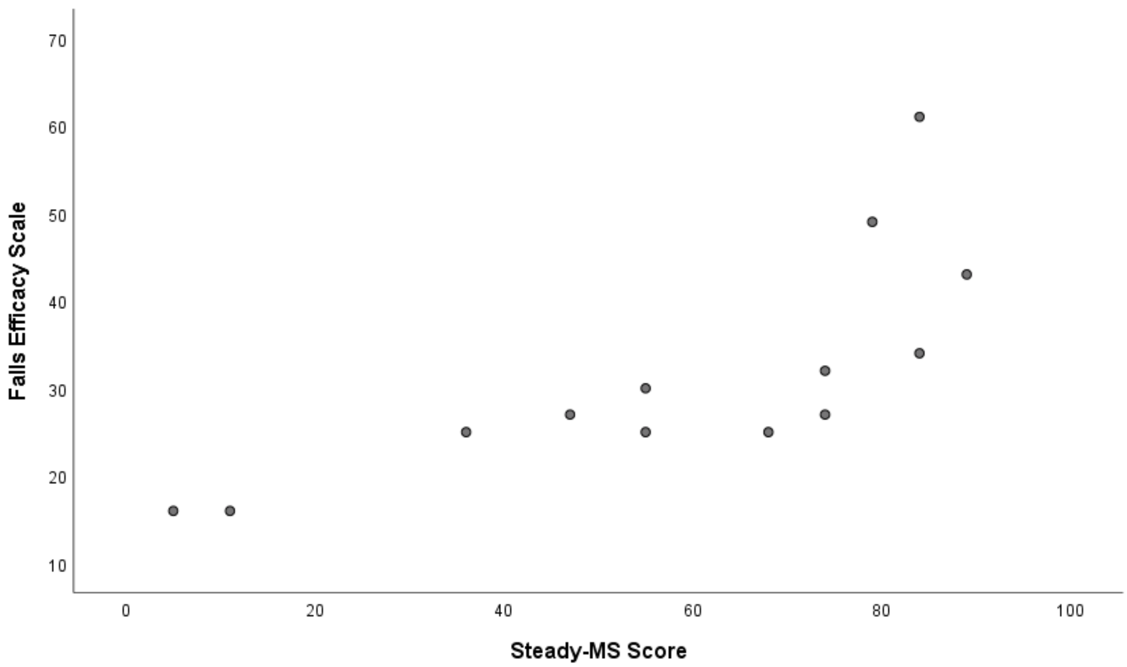


Figure 5.2 (Cont.)

C.



D.



Discussion

The purpose of this study was to determine the feasibility of performing home-based procedures to use a MS fall risk mobile health app in the home setting. The secondary aim was to determine if the fall risk score is comparable to validated fall risk self-reports. Our results suggest that it is feasible for pwMS to independently use Steady-MS in their homes. Delivering smartphones and meeting over a video call was accepted by participants. While there were some difficulties for participants connecting to a video call, participants were able to answer a 25-item questionnaire about their health and undergo five balance tasks in their homes with minimal instructions. There is also preliminary evidence that the Steady-MS fall risk score is comparable to self-report measures.

The results suggest that the study procedures were suitable and appropriate for home-based fall risk assessments in pwMS. While recruitment of participants was difficult, it is likely that recruitment issues were due to factors related to COVID-19 but may also be due to other factors. In the future as daily schedules return to normal, recruitment approaches should be re-evaluated. Despite low recruitment, this study demonstrates that remote-based study procedures with pwMS can be performed successfully and safely, which may be critical if social distancing restrictions continue. In addition, pwMS independently and safely self-assessed their risk for falling, suggesting that there is potential that Steady-MS can be used for home-based fall risk assessments. With barriers in receiving fall risk screening in a clinic, and with the increasingly limited access to healthcare due to COVID-19,[119] it is important for pwMS to have access to fall risk assessments from their homes. Moreover, not only does Steady-MS offer independent fall assessments, but Steady-MS also offers potential for home-based treatments targeted for each individual.

The results of this study are comparable to other feasibility studies examining technology use for pwMS in the home setting. A previous study evaluated the feasibility of using a smartphone app to improve fatigue in a 12-week telerehabilitation intervention.[122] PwMS reported that telerehabilitation was feasible, and their fatigue levels improved following the intervention. Another study performed a home-based computer program for cognitive rehabilitation, and pwMS reported enjoying the convivence of home training.[123] These studies suggest that there is potential to deliver a telerehabilitation falls prevention intervention paired with Steady-MS. Steady-MS improves access to screening, and telerehabilitation may prevent falls through tailored treatment strategies. Performing these steps in the home setting adds convenience while reducing travel barriers.

This study suggests that home-based use of a fall risk mobile health app is feasible for pwMS. However, modifications to study procedures can improve the efficiency of conducting home-based studies. First, the majority of phones in this study were delivered by hand. Mailing phones to four participants was found to be safe and effective to those who lived further away. Therefore, to increase recruitment and enrollment for pwMS who live out of state, mailing phones should be considered as potential form of delivery. Second, access to internet was important for both participants and the research team to conduct video calls. Having a mobile hot-spot may greatly reduce time on the researcher when hand delivering phones. A mobile hot-spot offers potential to perform a video call inside a car without needing to drive back to the researcher's home. A hot-spot provided to participants may also help those who do not have access to internet. Third, one issue during home-based testing was that participants often did not show up to the video call on time. When the participant was called as a reminder, they often reported that they lost track of time being at home all day. Therefore, reminders with notifications may improve on-time data collection.

The validity of the fall risk score was found to be moderate compared to the fall risk self-reports. There were moderate, significant correlations between the fall risk score and disability level, fear of falling, self-reported walking ability, and number of falls in the past year. These questionnaires have previously shown to be associated with falls in pwMS.[77,88,124] The moderate correlations suggest that the fall risk score is comparable to validated self-reports used to evaluate fall risk. However, a limitation to self-reported questionnaires is that they are prone to subjective bias and may not accurately reflect objective performance.[39] For instance, pwMS may underreport the PDDS indicating that they have mild disability, but in actuality demonstrate walking impairments. Future studies should compare the fall risk score from Steady-MS to objective performance measures, such as the Physiological Profile Assessment, Timed Up and Go, or Berg Balance Scale to better understand the validity of the fall risk score.

While return-to-work policies are slowly being implemented, many remote studies will continue to be encouraged during the COVID-19 pandemic. There were important lessons learned from these remote study procedures that can apply to future remote studies. First, providing participants with a simple and clear health app minimized confusion. A video-call prohibits pointing or demonstrating to participants about specific instructions. Therefore, any instructions or clarifications were verbal. By using a health app that has been modified through two iterations, this minimized difficulties using the app that may have required seeing the participant's phone. Second, clear communication was critical to successfully perform remote testing. Communication to participants about the date and time of a data collection, how to access the video call, and receiving and returning the phone is important to ensure a smooth data collection. Confirming instructions with participants was helpful to ensure that each step would run smoothly. Third, flexibility and adaptability appeared more important during remote testing than in-person testing. Technology issues may arise, mailing phones may be delayed, and typical recruitment strategies may not be as effective. Being flexible, creative, and adaptable will help overcome these unique challenges during remote testing.

The results of this study suggest that these study procedures were feasible to perform, and that Steady-MS is feasible to use in home settings, but there are also limitations that should be considered. First is a small sample size. Thirteen participants were included in this study but may not be representative of the MS population. Feasibility with a larger and more diverse sample should be examined. Second, participants were delivered a phone with Steady-MS pre-installed. Future steps should determine whether pwMS are able to install Steady-MS from their own mobile device and use on their own. Third, this study was limited to those who had home internet access and access to a webcam. Providing participants with a tablet with mobile data may overcome the need for internet and a webcam for video calls. Last, while participants in this study were different than those in studies 1-3, these participants were previously recruited for fall prevention-related studies in the past. Therefore, they may have more experience with balance exercises and Steady-MS may have seemed more intuitive for these participants.

In conclusion, this study suggests that it is feasible for pwMS to meet over a video call and self-assess their fall risk with Steady-MS in their homes. With the growing demand for home-based research to follow social distancing restrictions, it was feasible to continue to collect data with mobile technology in the home environment. The fall risk score is also comparable to validated fall risk self-report measures. There is potential for pwMS to safely and independently use a health app to assess their risk for falling. Steady-MS offers a critical step increase access to fall risk screening and improve self-management of their symptoms and fall risk.

CHAPTER 6: CONCLUSIONS

Multiple Sclerosis (MS) is a chronic, progressive disease of the central nervous system that impairs the ability to walk and maintain balance, putting people with MS (pwMS) at a higher risk for falls.[4] One in two pwMS fall in a six-month period, and up to half of those falls lead to injuries, ranging from contusions to fractures.[7] The first step in falls prevention is to assess multiple risk factors specific to pwMS.[9] However, pwMS seldomly receive fall risk screening due to clinician time constraints, expensive equipment, and the need for trained personnel. Moreover, pwMS need routine screening throughout the course of the disease. Mobility technology is affordable, ubiquitous, and offers a solution to increase access to screening in the home setting.[57,60] The overarching purpose of this study was to leverage the power of smartphone technology to develop a fall risk mobile health app for pwMS to independently assess their risk for falling. Bringing individualized and independent falls screening to the hands of those with MS is a critical step in the falls prevention paradigm to improve overall function and quality of life.

Four studies were performed contributing to the development a fall risk app for pwMS. In study one, results demonstrated that smartphone accelerometry can be used to measure postural control in pwMS. These results were also used to develop an algorithm in study two to measure overall fall risk incorporating risk factors measured with a smartphone. This algorithm included assessing postural control, balance confidence, walking ability, and past fall history. In study three, the health application, Steady-MS, was developed integrating the fall risk algorithm, and usability testing identified challenges for pwMS. After making iterative changes to the app, Steady-MS was found to be both usable and useful for the targeted population. Feasibility testing in study four found that not only were remote study procedures using Steady-MS accepted among pwMS, but it was also it is feasible for pwMS to independently and safely use Steady-MS in the home environment. Overall, results from these four studies suggest that pwMS can independently use a smartphone app to measure their risk for falls from their homes.

Because of multiple constraints in receiving fall risk assessments (i.e., time, equipment costs, trained personnel), Steady-MS offers strong potential for pwMS to self-assess and self-monitor their risk for falling. Because MS symptoms fluctuate throughout the course of the disease,[2] monitoring these changes as they relate to fall risk can prevent falls before symptoms become severe. Moreover, with limited access to healthcare due to the COVID-19 pandemic, there is an increasing need for telehealth and telecare to maintain overall health and well-being.[119] Steady-MS provides, for the first time, a home-based tool for pwMS to self-assess their fall risk. Moreover, Steady-MS assesses multiple risk factors to provide pwMS their overall fall risk. With a fall risk app, pwMS can both measure and manage their fall risk from their homes.

The aim of this project was to develop a usable fall risk health app for pwMS, but the results of the studies also provide important falls prevention information for researchers and clinicians. Study 1 demonstrated that RMS and CEA as measured through a smartphone accelerometer discriminated assisted device users and non-assisted device users. Smartphone accelerometry can potentially be used in clinical settings to objectively identify balance impairments before a fall occurs. PwMS with minimal disability have shown to have balance impairments as measured with COP outputs from a force plate, [21,125] and levering smartphone accelerometry can potentially identify those with balance deficits. Early treatment can reduce future falls and injuries. In study 2, a fall risk algorithm was developed to include modifiable fall risk factors most associated with falls in pwMS. This algorithm provides a tool that can be used to provide personalized and tailored treatments for pwMS. Rather than providing broad interventions for all pwMS, this algorithm provides an important start to identify specific areas to target. Additionally, this algorithm can be further modified to fit the needs of clinicians and researchers who may want to include additional tests (i.e., walking, vision, manual dexterity). In study 3, the usability of Steady-MS was determined. From this study, it was found that cognitive overload was a critical usability consideration. In developing mobile health apps for pwMS, user-centered design to prevent cognitive overload is critical to ensure high usability. Last, from study 4, it was found that clear communication and using user-center designed technology improved the feasibility of performing remote study procedures.

Not only does Steady-MS bring fall risk assessment to the hands of the individual, but Steady-MS also provides potential to improve the quality of care for pwMS. As telehealth and telecare is becoming more prevalent, Steady-MS can help clinicians objectively assess postural control and measure overall fall risk.[126,127] With information that Steady-MS provides, clinicians can offer recommendations to improve their overall health. Additionally, Steady-MS offers potential for targeted telerehabilitation. Home-based exercise has shown to improve balance and overall function in pwMS.[128,129] Paired with Steady-MS, targeted rehabilitation specific for each individual can be prescribed and may improve fall prevention treatment. Additionally, intervention studies can take place in homes as Steady-MS can measure fall risk and functional outcomes for pre and post-assessments. PwMS can also gauge participants' progress during an intervention using the app. Steady-MS opens opportunities to improve overall function and well-being in the home setting.

There are also limitations of this project to consider. The population that participated in the development of the algorithm and usability testing was a small sample that has also participated in previous fall-prevention based studies. This may have influenced the usability results and the fall risk factors incorporated into the algorithm. Steady-MS was also designed specifically for independent testing in the home setting. Therefore, the algorithm may not be the best algorithm for clinic-based or research-based fall risk assessments. As more data is collected to improve the algorithm, factors to include for clinical testing should be incorporated. Steady-MS also does not include environmental fall risk factors. A future home environment check list may help pwMS identify areas within their home to improve to reduce their fall risk.

Future steps will further improve the use of Steady-MS. First, the validity and reliability of the fall risk score should be determined. The fall risk score calculated Steady-MS should be compared to clinical fall risk assessments (i.e., Physiological Profile Assessment, Berg Balance Scale). This will determine how the fall risk score compares to scores on clinical fall risk tests.[46] Test re-test reliability of the score should also be examined. Second, as more data is collected with Steady-MS, the fall risk output could provide both an overall score and scores on individual components of the test with comparisons to age and gender-matched individuals. This will inform users of their performance and individual risk factors to improve upon. Last, in addition to measuring fall risk, prevention strategies should be included to empower pwMS to reduce their fall risk. Home-based exercise programs or home modification strategies can be included as treatment plans. Therefore, not only will pwMS be able to self-assess their fall risk, but they can also take part in strategies to prevent fall-related injuries.

In conclusion, Steady-MS is a usable mobile health app that measures overall fall risk in pwMS. There is evidence that pwMS can self-assess their fall risk in their homes, giving potential to improve self-management and monitoring of MS symptoms and fall risk. Steady-MS overcomes limitations to current falls screening and brings fall risk assessment to the hands of the individual. Moreover, Steady-MS offers potential for targeted telerehabilitation to prevent fall related injuries. This important tool increases access to fall risk assessments, and with future steps to further enhance its use, Steady-MS can help prevent fall related injuries and maximize functional independence in pwMS.

REFERENCES

1. Wallin MT, Culpepper WJ, Campbell JD, et al. The Prevalence of MM in the United States. *Neurology.* 2019:10.1212/WNL.0000000000007035.
2. Filippi M, Bar-Or A, Piehl F, et al. Multiple Sclerosis. *Nature Reviews Disease Primers.* 2018;4(1):43.
3. Frohman EM, Racke MK, Raine CS. Multiple Sclerosis—the Plaque and Its Pathogenesis. *New England Journal of Medicine.* 2006;354(9):942-955.
4. Cameron MH, Nilsagard Y. Chapter 15 - Balance, Gait, and Falls in Multiple Sclerosis. In: Day BL, Lord SR, eds. *Handbook of Clinical Neurology.* Vol 159: Elsevier; 2018:237-250.
5. Rae-Grant AD, Eckert NJ, Bartz S, Reed JF. Sensory Symptoms of Multiple Sclerosis: A Hidden Reservoir of Morbidity. *Multiple Sclerosis (Houndmills, Basingstoke, England).* 1999;5(3):179-183.
6. Nilsagård Y, Gunn H, Freeman J, et al. Falls in People with Ms—an Individual Data Meta-Analysis from Studies from Australia, Sweden, United Kingdom and the United States. *Multiple Sclerosis Journal.* 2015;21(1):92-100.
7. Matsuda PN, Shumway-Cook A, Bamer AM, Johnson SL, Amtmann D, Kraft GH. Falls in Multiple Sclerosis. *PM&R : The Journal of Injury, Function, and Rehabilitation.* 2011;3(7):624-632; quiz 632.
8. Peterson EW, Cho CC, Finlayson ML. Fear of Falling and Associated Activity Curtailment Among Middle Aged and Older Adults with Multiple Sclerosis. *Multiple Sclerosis (Houndmills, Basingstoke, England).* 2007;13(9):1168-1175.
9. Palumbo P, Palmerini L, Bandinelli S, Chiari L. Fall Risk Assessment Tools for Elderly Living in the Community: Can We Do Better? *PloS One.* 2015;10(12):e0146247-e0146247.
10. Sosnoff JJ, Sung J. Reducing Falls and Improving Mobility in Multiple Sclerosis. *Expert Review of Neurotherapeutics.* 2015;15(6):655-666.
11. Gunn H, Markevics S, Haas B, Marsden J, Freeman J. Systematic Review: The Effectiveness of Interventions to Reduce Falls and Improve Balance in Adults with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2015;96(10):1898-1912.
12. Finlayson ML, Peterson EW. Falls, Aging, and Disability. *Physical Medicine and Rehabilitation Clinics of North America.* 2010;21(2):357-373.
13. Peterka RJ. Chapter 2 - Sensory Integration for Human Balance Control. In: Day BL, Lord SR, eds. *Handbook of Clinical Neurology.* Vol 159: Elsevier; 2018:27-42.
14. Dendrou CA, Fugger L, Friese MA. Immunopathology of Multiple Sclerosis. *Nature Reviews Immunology.* 2015;15:545.
15. Fjeldstad C, Pardo G, Frederiksen C, Bemben D, Bemben M. Assessment of Postural Balance in Multiple Sclerosis. *International Journal of MS Care.* 2009;11(1):1-5.
16. Ganesan M, Kanekar N, Aruin AS. Direction-Specific Impairments of Limits of Stability in Individuals with Multiple Sclerosis. *Annals of Physical and Rehabilitation Medicine.* 2015;58(3):145-150.
17. Kanekar N, Aruin AS. The Role of Clinical and Instrumented Outcome Measures in Balance Control of Individuals with Multiple Sclerosis. *Multiple Sclerosis International.* 2013;2013:190162-190162.
18. Frzovic D, Morris ME, Vowels L. Clinical Tests of Standing Balance: Performance of Persons with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2000;81(2):215-221.
19. Martin CL, Phillips B, Kilpatrick T, et al. Gait and Balance Impairment in Early Multiple Sclerosis in the Absence of Clinical Disability. *Multiple Sclerosis Journal.* 2006;12(5):620-628.

20. Soyuer F, Mirza M, Erkorkmaz U. Balance Performance in Three Forms of Multiple Sclerosis. *Neurological Research.* 2006;28(5):555-562.
21. Comber L, Sosnoff JJ, Galvin R, Coote S. Postural Control Deficits in People with Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Gait & Posture.* 2018.
22. LaRocca NG. Impact of Walking Impairment in Multiple Sclerosis. *The Patient: Patient-Centered Outcomes Research.* 2011;4(3):189-201.
23. Hausdorff JM. Gait Dynamics, Fractals and Falls: Finding Meaning in the Stride-to-Stride Fluctuations of Human Walking. *Human Movement Science.* 2007;26(4):555-589.
24. Givon U, Zeilig G, Achiron A. Gait Analysis in Multiple Sclerosis: Characterization of Temporal–Spatial Parameters Using Gaitrite Functional Ambulation System. *Gait & Posture.* 2009;29(1):138-142.
25. Block VJ, Lizee A, Crabtree-Hartman E, et al. Continuous Daily Assessment of Multiple Sclerosis Disability Using Remote Step Count Monitoring. *Journal of Neurology.* 2017;264(2):316-326.
26. Sosnoff JJ, Weikert M, Dlugonski D, Smith DC, Motl RW. Quantifying Gait Impairment in Multiple Sclerosis Using Gaitrite Technology. *Gait & Posture.* 2011;34(1):145-147.
27. Socie MJ, Motl RW, Pula JH, Sandroff BM, Sosnoff JJ. Gait Variability and Disability in Multiple Sclerosis. *Gait & Posture.* 2013;38(1):51-55.
28. Moon Y, Sung J, An R, Hernandez ME, Sosnoff JJ. Gait Variability in People with Neurological Disorders: A Systematic Review and Meta-Analysis. *Human Movement Science.* 2016;47:197-208.
29. Day BL, Bancroft MJ. Chapter 6 - Voluntary Steps and Gait Initiation. In: Day BL, Lord SR, eds. *Handbook of Clinical Neurology.* Vol 159: Elsevier; 2018:107-118.
30. Herman R, Cook T, Cozzens B, Freedman W. Control of Postural Reactions in Man: The Initiation of Gait. In: Stein RB, Pearson KG, Smith RS, Redford JB, eds. *Control of Posture and Locomotion*. Boston, MA: Springer US; 1973:363-388.
31. Comber L, Galvin R, Coote S. Gait Deficits in People with Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Gait & Posture.* 2017;51:25-35.
32. Flegel M, Knox K, Nickel D. Step-Length Variability in Minimally Disabled Women with Multiple Sclerosis or Clinically Isolated Syndrome. *Int J MS Care.* 2012;14(1):26-30.
33. Socie MJ, Sosnoff JJ. Gait Variability and Multiple Sclerosis. *Multiple Sclerosis International.* 2013;2013:7.
34. Cameron MH, Thielman E, Mazumder R, Bourdette D. Predicting Falls in People with Multiple Sclerosis: Fall History Is as Accurate as More Complex Measures. *Multiple Sclerosis International.* 2013;2013:496325.
35. Ytterberg C, Einarsson U, Holmqvist LW, Peterson EW. A Population-Based Study of Fall Risk Ractors Among People with Multiple Sclerosis in Stockholm County. *Journal of Rehabilitation Medicine.* 2013;45(5):452-457.
36. Coote S, Hogan N, Franklin S. Falls in People with Multiple Sclerosis Who Use a Walking Aid: Prevalence, Factors, and Effect of Strength and Balance Interventions. *Archives of Physical Medicine and Rehabilitation.* 2013;94(4):616-621.
37. Téllez N, Río J, Tintoré M, Nos C, Galán I, Montalban X. Does the Modified Fatigue Impact Scale Offer a More Comprehensive Assessment of Fatigue in Ms? *Multiple Sclerosis Journal.* 2005;11(2):198-202.
38. Hobart J, Riazi A, Lamping D, Fitzpatrick R, Thompson A. Measuring the Impact of MS on Walking Ability: The 12-Item Ms Walking Scale (Msws-12). *Neurology.* 2003;60(1):31-36.
39. Rosenman R, Tennekoon V, Hill LG. Measuring Bias in Self-Reported Data. *Int J Behav Healthc Res.* 2011;2(4):320-332.

40. Quinn G, Comber L, Galvin R, Coote S. The Ability of Clinical Balance Measures to Identify Falls Risk in Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Clinical Rehabilitation.* 2018;32(5):571-582.
41. Sun R, McGinnis R, Sosnoff JJ. Novel Technology for Mobility and Balance Tracking in Patients with Multiple Sclerosis: A Systematic Review. *Expert Review of Neurotherapeutics.* 2018;18(11):887-898.
42. Sun R, Sosnoff JJ. Novel Sensing Technology in Fall Risk Assessment in Older Adults: A Systematic Review. *BMC Geriatrics.* 2018;18(1):14.
43. Alberts JL, Hirsch JR, Koop MM, et al. Using Accelerometer and Gyroscopic Measures to Quantify Postural Stability. *Journal of Athletic Training.* 2015;50(6):578-588.
44. Center PR. Mobile Fact Sheet. 2018; http://www.pewinternet.org/fact-sheet/mobile/.
45. del Rosario MB, Redmond SJ, Lovell NH. Tracking the Evolution of Smartphone Sensing for Monitoring Human Movement. *Sensors (Basel, Switzerland).* 2015;15(8):18901-18933.
46. Roeing KL, Hsieh KL, Sosnoff JJ. A Systematic Review of Balance and Fall Risk Assessments with Mobile Phone Technology. *Archives of Gerontology and Geriatrics.* 2017;73:222-226.
47. Hsieh KL, Roach KL, Wajda DA, Sosnoff JJ. Smartphone Technology Can Measure Postural Stability and Discriminate Fall Risk in Older Adults. *Gait & Posture.* 2019;67:160-165.
48. Mellone S, Tacconi C, Schwickert L, Klenk J, Becker C, Chiari L. Smartphone-Based Solutions for Fall Detection and Prevention: The Farseeing Approach. *Zeitschrift für Gerontologie und Geriatrie.* 2012;45(8):722-727.
49. Rasche P, Mertens A, Brohl C, et al. The "Aachen Fall Prevention App" - a Smartphone Application App for the Self-Assessment of Elderly Patients at Risk for Ground Level Falls. *Patient Safety In Surgery.* 2017;11:14.
50. Hayes N. Fallcheck. *Nursing Standard (Royal College of Nursing (Great Britain):1987.* 2015;29(35):27.
51. Hsieh KL, Fanning JT, Rogers WA, Wood TA, Sosnoff JJ. A Fall Risk Mhealth App for Older Adults: Development and Usability Study. *JMIR Aging.* 2018;1(2):e11569.
52. Hsieh KL, Fanning JT, Sosnoff JJ. A Smartphone Application Is Valid and Reliable in Older Adults During Real World Testing. *Gerontechnology.* 2019;18(1):29-35.
53. Koch-Henriksen N, Sørensen PS. The Changing Demographic Pattern of Multiple Sclerosis Epidemiology. *The Lancet Neurology.* 2010;9(5):520-532.
54. Marziniak M, Brichetto G, Feys P, Meyding-Lamadé U, Vernon K, Meuth SG. The Use of Digital and Remote Communication Technologies as a Tool for Multiple Sclerosis Management: Narrative Review. *JMIR Rehabilitation and Assistive Technologies.* 2018;5(1):e5-e5.
55. Apolinário-Hagen J, Menzel M, Hennemann S, Salewski C. Acceptance of Mobile Health Apps for Disease Management among People with Multiple Sclerosis: Web-Based Survey Study. *JMIR Formative Research.* 2018;2(2):e11977-e11977.
56. Haase R, Schultheiss T, Kempcke R, Thomas K, Ziemssen T. Use and Acceptance of Electronic Communication by Patients with Multiple Sclerosis: A Multicenter Questionnaire Study. *Journal of Medical Internet Research.* 2012;14(5):e135-e135.
57. Marrie RA, Leung S, Tyry T, Cutter GR, Fox R, Salter A. Use of Ehealth and Mhealth Technology by Persons with Multiple Sclerosis. *Multiple Sclerosis and Related Disorders.* 2019;27:13-19.
58. Lejbkowicz I, Paperna T, Stein N, Dishon S, Miller A. Internet Usage by Patients with Multiple Sclerosis: Implications to Participatory Medicine and Personalized Healthcare. *Multiple Sclerosis International.* 2010;2010:640749-640749.
59. Van Kessel K, Babbage DR, Reay N, Miner-Williams WM, Kersten P. Mobile Technology Use by People Experiencing Multiple Sclerosis Fatigue: Survey Methodology. *JMIR mHealth and uHealth.* 2017;5(2):e6.

60. Giunti G, Guisado Fernández E, Dorronzoro Zubiete E, Rivera Romero O. Supply and Demand in Mhealth Apps for Persons with Multiple Sclerosis: Systematic Search in App Stores and Scoping Literature Review. *JMIR mHealth and uHealth.* 2018;6(5):e10512-e10512.
61. Cattaneo D, De Nuzzo C, Fascia T, Macalli M, Pisoni I, Cardini R. Risks of Falls in Subjects with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2002;83(6):864-867.
62. Prosperini L, Castelli L. Spotlight on Postural Control in Patients with Multiple Sclerosis. *Degenerative Neurological and Neuromuscular Disease.* 2018;8:25-34.
63. Cameron MH, Lord S. Postural Control in Multiple Sclerosis: Implications for Fall Prevention. *Current Neurology and Neuroscience Reports.* 2010;10(5):407-412.
64. Ozinga SJ, Alberts JL. Quantification of Postural Stability in Older Adults Using Mobile Technology. *Experimental Brain Research.* 2014;232(12):3861-3872.
65. Ozinga SJ, Machado AG, Miller Koop M, Rosenfeldt AB, Alberts JL. Objective Assessment of Postural Stability in Parkinson's Disease Using Mobile Technology. *Movement Disorders.* 2015;30(9):1214-1221.
66. Peterson EW, Ben Ari E, Asano M, Finlayson ML. Fall Attributions among Middle-Aged and Older Adults with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2013;94(5):890-895.
67. Mukaka MM. A Guide to Appropriate Use of Correlation Coefficient in Medical Research. *Malawi Medical Journal.* 2012;24(3):69-71.
68. Lamkin-Kennard KA, Popovic MB. 4 - Sensors: Natural and Synthetic Sensors. In: Popovic MB, ed. *Biomechatronics*: Academic Press; 2019:81-107.
69. Boes MK, Sosnoff JJ, Socie MJ, Sandroff BM, Pula JH, Motl RW. Postural Control in Multiple Sclerosis: Effects of Disability Status and Dual Task. *Journal of the Neurological Sciences.* 2012;315(1):44-48.
70. Hou Y-R, Chiu Y-L, Chiang S-L, Chen H-Y, Sung W-H. Development of a Smartphone-Based Balance Assessment System for Subjects with Stroke. *Sensors.* 2019;20(1):88.
71. Prosperini L, Fortuna D, Giannì C, Leonardi L, Pozzilli C. The Diagnostic Accuracy of Static Posturography in Predicting Accidental Falls in People with Multiple Sclerosis. *Neurorehabilitation and Neural Repair.* 2013;27(1):45-52.
72. Peterson EW, Cho CC, von Koch L, Finlayson ML. Injurious Falls among Middle Aged and Older Adults with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2008;89(6):1031-1037.
73. Montalban X, Mulero P, Midaglia L, et al. Floodlight: Remote Self-Monitoring Is Accepted by Patients and Provides Meaningful, Continuous Sensor-Based Outcomes Consistent with and Augmenting Conventional in-Clinic Measures (P4.382). *Neurology.* 2018;90(15 Supplement):P4.382.
74. Shanahan CJ, Boonstra FMC, Cofré Lizama LE, et al. Technologies for Advanced Gait and Balance Assessments in People with Multiple Sclerosis. *Frontiers in Neurology.* 2018;8:708-708.
75. Matsuda PN, Shumway-Cook A, Ciol MA, Bombardier CH, Kartin DA. Understanding Falls in Multiple Sclerosis: Association of Mobility Status, Concerns About Falling, and Accumulated Impairments. *Phys Ther.* 2012;92(3):407-415.
76. Tajali S, Shaterzadeh-Yazdi M-J, Negahban H, et al. Predicting Falls among Patients with Multiple Sclerosis: Comparison of Patient-Reported Outcomes and Performance-Based Measures of Lower Extremity Functions. *Multiple Sclerosis and Related Disorders.* 2017;17:69-74.
77. Gunn HJ, Newell P, Haas B, Marsden JF, Freeman JA. Identification of Risk Factors for Falls in Multiple Sclerosis: A Systematic Review and Meta-Analysis. *Physical Therapy.* 2013;93(4):504-513.

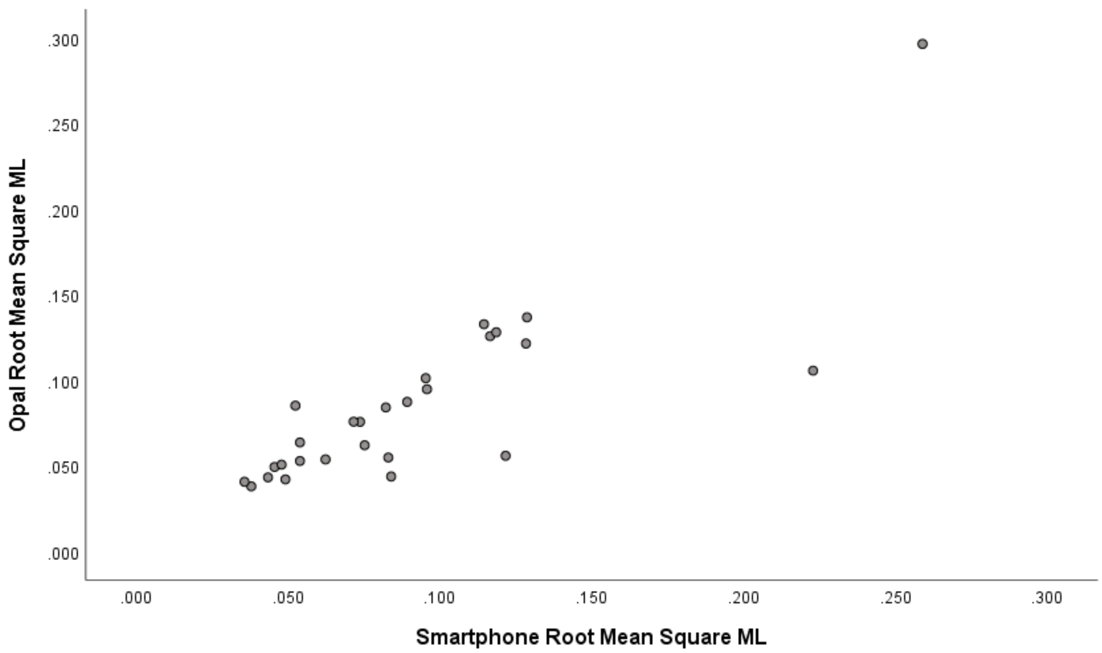
78. van Vliet R, Hoang P, Lord S, Gandevia S, Delbaere K. Falls Efficacy Scale-International: A Cross-Sectional Validation in People with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2013;94(5):883-889.
79. Learmonth YC, Motl RW, Sandroff BM, Pula JH, Cadavid D. Validation of Patient Determined Disease Steps (Pdds) Scale Scores in Persons with Multiple Sclerosis. *BMC Neurology.* 2013;13(1):37.
80. Massof RW, Fletcher DC. Evaluation of the Nei Visual Functioning Questionnaire as an Interval Measure of Visual Ability in Low Vision. *Vision Research.* 2001;41(3):397-413.
81. Wood TA, Wajda DA, Sosnoff JJ. Use of a Short Version of the Activities-Specific Balance Confidence Scale in Multiple Sclerosis. *International Journal of MS Care.* 2019.
82. Organization WH. Falls. 2018; http://www.who.int/news-room/fact-sheets/detail/falls. Accessed August 16, 2018.
83. Kalron A. The Romberg Ratio in People with Multiple Sclerosis. *Gait & Posture.* 2017;54:209-213.
84. Lee YH, Bang H, Kim DJ. How to Establish Clinical Prediction Models. *Endocrinology Metab (Seoul).* 2016;31(1):38-44.
85. Steyerberg EW, Eijkemans MJC, Harrell Jr FE, Habbema JDF. Prognostic Modelling with Logistic Regression Analysis: A Comparison of Selection and Estimation Methods in Small Data Sets. *Statistics in Medicine.* 2000;19(8):1059-1079.
86. Nilsagård Y, Lundholm C, Denison E, Gunnarsson L-G. Predicting Accidental Falls in People with Multiple Sclerosis—a Longitudinal Study. *Clinical Rehabilitation.* 2009;23(3):259-269.
87. Beghi E, Gervasoni E, Pupillo E, et al. Prediction of Falls in Subjects Suffering from Parkinson Disease, Multiple Sclerosis, and Stroke. *Archives of Physical Medicine and Rehabilitation.* 2018;99(4):641-651.
88. Nilsagard Y, Denison E, Gunnarsson LG, Bostrom K. Factors Perceived as Being Related to Accidental Falls by Persons with Multiple Sclerosis. *Disability and Rehabilitation.* 2009;31(16):1301-1310.
89. Cameron MH, Karstens L, Hoang P, Bourdette D, Lord S. Medications Are Associated with Falls in People with Multiple Sclerosis: A Prospective Cohort Study. *Int J MS Care.* 2015;17(5):207-214.
90. Gunn H, Creanor S, Haas B, Marsden J, Freeman J. Risk Factors for Falls in Multiple Sclerosis: An Observational Study. *Multiple Sclerosis Journal.* 2013;19(14):1913-1922.
91. Comber L, Quinn G, McGuigan C, Galvin R, Coote S. Medication Usage and Falls in People with Multiple Sclerosis. *Multiple sclerosis (Houndmills, Basingstoke, England).* 2018;24(7):995-998.
92. Witchel HJ, Oberndorfer C, Needham R, et al. Thigh-Derived Inertial Sensor Metrics to Assess the Sit-to-Stand and Stand-to-Sit Transitions in the Timed up and Go (Tug) Task for Quantifying Mobility Impairment in Multiple Sclerosis. *Frontiers in Neurology.* 2018;9(684).
93. Martínez-Pérez B, de la Torre-Díez I, López-Coronado M. Mobile Health Applications for the Most Prevalent Conditions by the World Health Organization: Review and Analysis. *J Medical Internet Research.* 2013;15(6):e120.
94. Bort-Roig J, Gilson ND, Puig-Ribera A, Contreras RS, Trost SG. Measuring and Influencing Physical Activity with Smartphone Technology: A Systematic Review. *Sports Medicine (Auckland, NZ).* 2014;44(5):671-686.
95. Carter DD, Robinson K, Forbes J, Hayes S. Experiences of Mobile Health in Promoting Physical Activity: A Qualitative Systematic Review and Meta-Ethnography. *PloS One.* 2018;13(12):e0208759.
96. Armitage LC, Kassavou A, Sutton S. Do Mobile Device Apps Designed to Support Medication Adherence Demonstrate Efficacy? A Systematic Review of Randomised Controlled Trials, with Meta-Analysis. *BMJ Open.* 2020;10(1):e032045.

97. Whitehead L, Seaton P. The Effectiveness of Self-Management Mobile Phone and Tablet Apps in Long-Term Condition Management: A Systematic Review. *Journal Medical Internet Research.* 2016;18(5):e97.
98. Jupp JCY, Sultani H, Cooper CA, Peterson KA, Truong TH. Evaluation of Mobile Phone Applications to Support Medication Adherence and Symptom Management in Oncology Patients. *Pediatric Blood & Cancer.* 2018;65(11):e27278.
99. Lowe-Strong A, McCullagh PJ. Monitoring of Symptoms and Interventions Associated with Multiple Sclerosis. *Studies in Health Technology and Informatics.* 2005;117:223-228.
100. Giannì C, Prosperini L, Jonsdottir J, Cattaneo D. A Systematic Review of Factors Associated with Accidental Falls in People with Multiple Sclerosis: A Meta-Analytic Approach. *Clinical Rehabilitation.* 2014;28(7):704-716.
101. Rae-Grant A, Bennett A, Sanders AE, Phipps M, Cheng E, Bever C. Quality Improvement in Neurology: Multiple Sclerosis Quality Measures. *Neurology.* 2015;85(21):1904.
102. Broekhuis M, van Velsen L, Hermens H. Assessing Usability of Ehealth Technology: A Comparison of Usability Benchmarking Instruments. *International Journal of Medical Informatics.* 2019;128:24-31.
103. McCurdie T, Taneva S, Casselman M, et al. Mhealth Consumer Apps: The Case for User-Centered Design. *Biomedical Instrumentation & Technology.* 2012;46(s2):49-56.
104. Schnall R, Rojas M, Bakken S, et al. A User-Centered Model for Designing Consumer Mobile Health (Mhealth) Applications (Apps). *Journal of Biomedical Informatics.* 2016;60:243-251.
105. Lerdal A, Celius EG, Krupp L, Dahl AA. A Prospective Study of Patterns of Fatigue in Multiple Sclerosis. *European Journal of Neurology.* 2007;14(12):1338-1343.
106. Balcer LJ, Miller DH, Reingold SC, Cohen JA. Vision and Vision-Related Outcome Measures in Multiple Sclerosis. *Brain.* 2014;138(1):11-27.
107. Langdon DW. Cognition in Multiple Sclerosis. *Current Opinion in Neurology.* 2011;24(3):244-249.
108. Nielsen J. How Many Test Users in a Usability Study. *Nielsen Norman Group.* 2012;4(06).
109. Brooke J. *SUS-A Quick and Dirty Usability Scale.* 1996:4-7.
110. Roque NA, Boot WR. A New Tool for Assessing Mobile Device Proficiency in Older Adults: The Mobile Device Proficiency Questionnaire. *Journal of Applied Gerontology: The Official Journal of the Southern Gerontological Society.* 2018;37(2):131-156.
111. Sauro J. Measuring Usability with the System Usability Scale. 2011; https://measuringu.com/sus/.
112. Sumowski JF, Benedict R, Enzinger C, et al. Cognition in Multiple Sclerosis: State of the Field and Priorities for the Future. *Neurology.* 2018;90(6):278-288.
113. Pergolotti M, Deal AM, Bryant AL, et al. Senior Sway: Using a Mobile Application to Measure Fall Risk. *Journal of Geriatric Physical Therapy (2001).* 2019;42(3):E101-e107.
114. Rasche P, Mertens A, Bröhl C, et al. The “Aachen Fall Prevention App” – a Smartphone Application App for the Self-Assessment of Elderly Patients at Risk for Ground Level Falls. *Patient Safety in Surgery.* 2017;11:14.
115. Rabe S, Azhand A, Pommer W, Muller S, Steinert A. Descriptive Evaluation and Accuracy of a Mobile App to Assess Fall Risk in Seniors: Retrospective Case-Control Study. *JMIR Aging.* 2020;3(1):e16131.
116. Fiems CL, Miller SA, Buchanan N, et al. Does a Sway-Based Mobile Application Predict Future Falls in People with Parkinson Disease? *Archives of Physical Medicine and Rehabilitation.* 2020;101(3):472-478.
117. Ruzic L, Sanford JA. Usability of Mobile Consumer Applications for Individuals Aging with Multiple Sclerosis. Paper presented at: International Conference on Universal Access in Human-Computer Interaction2017.

118. Bennie S, Bruner K, Dizon A, Fritz H, Goodman B, Peterson S. Measurements of Balance: Comparison of the Timed Up and Go Test and Functional Reach Test with the Berg Balance Scale. *Journal of Physical Therapy Science.* 2003;15(2):93-97.
119. Murthy S, Gomersall CD, Fowler RA. Care for Critically Ill Patients with Covid-19. *JAMA.* 2020;323(15):1499-1500.
120. Mazumder R, Lambert WE, Nguyen T, Bourdette DN, Cameron MH. Fear of Falling Is Associated with Recurrent Falls in People with Multiple Sclerosis: A Longitudinal Cohort Study. *International Journal of MS Care.* 2015;17(4):164-170.
121. Orsmond GI, Cohn ES. The Distinctive Features of a Feasibility Study: Objectives and Guiding Questions. *OTJR: Occupation, Participation and Health.* 2015;35(3):169-177.
122. D'Hooghe M, Van Gassen G, Kos D, et al. Improving Fatigue in Multiple Sclerosis by Smartphone-Supported Energy Management: The MS Telecoach Feasibility Study. *Multiple Sclerosis and Related Disorders.* 2018;22:90-96.
123. Stuifbergen A, Becker H, Morgan S, Morrison J, Perez F. Home-Based Computer-Assisted Cognitive Training. *International Journal of MS Care.* 2011;13(4):189-198.
124. Finlayson ML, Peterson EW, Cho CC. Risk Factors for Falling among People Aged 45 to 90 Years with Multiple Sclerosis. *Archives of Physical Medicine and Rehabilitation.* 2006;87(9):1274-1279.
125. Karst GM, Venema DM, Roehrs TG, Tyler AE. Center of Pressure Measures During Standing Tasks in Minimally Impaired Persons with Multiple Sclerosis. *Journal of Neurologic Physical Therapy: JNPT.* 2005;29(4):170-180.
126. Lee A. Covid-19 and the Advancement of Digital Physical Therapist Practice and Telehealth. *Physical Therapy.* 2020.
127. Turolla A, Rossettini G, Viceconti A, Palese A, Geri T. Musculoskeletal Physical Therapy During the Covid-19 Pandemic: Is Telerehabilitation the Answer? *Physical Therapy.* 2020.
128. Finkelstein J, Lapshin O, Castro H, Cha E, Provance PG. Home-Based Physical Telerehabilitation in Patients with Multiple Sclerosis: A Pilot Study. *J Rehabilitation Research Dev.* 2008;45(9):1361-1373.
129. Sosnoff JJ, Finlayson M, McAuley E, Morrison S, Motl RW. Home-Based Exercise Program and Fall-Risk Reduction in Older Adults with Multiple Sclerosis: Phase 1 Randomized Controlled Trial. *Clinical Rehabilitation.* 2014;28(3):254-263.

APPENDIX A: SMARTPHONE ACCELEROMETRY AND OPAL SCATTER PLOTS

Figure A1. Scatter plots for root mean square and confidence ellipse area acceleration derived from the smartphone and Opal accelerometer during **eyes open** condition for 27 participants. ML = mediolateral; AP = anteroposterior



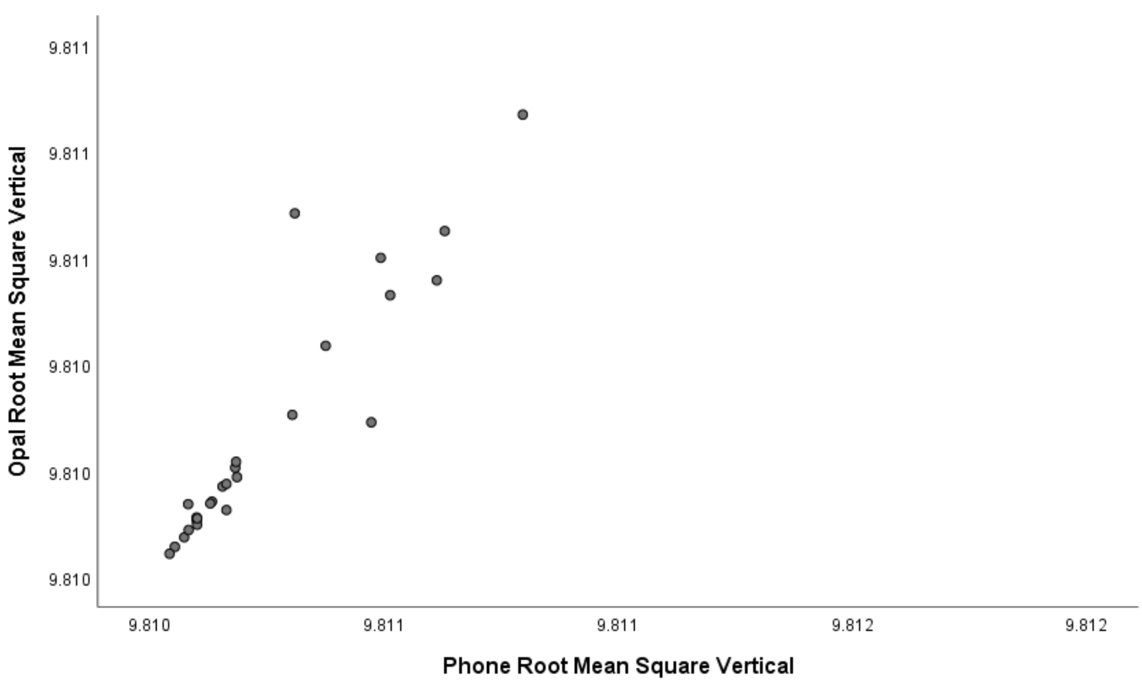
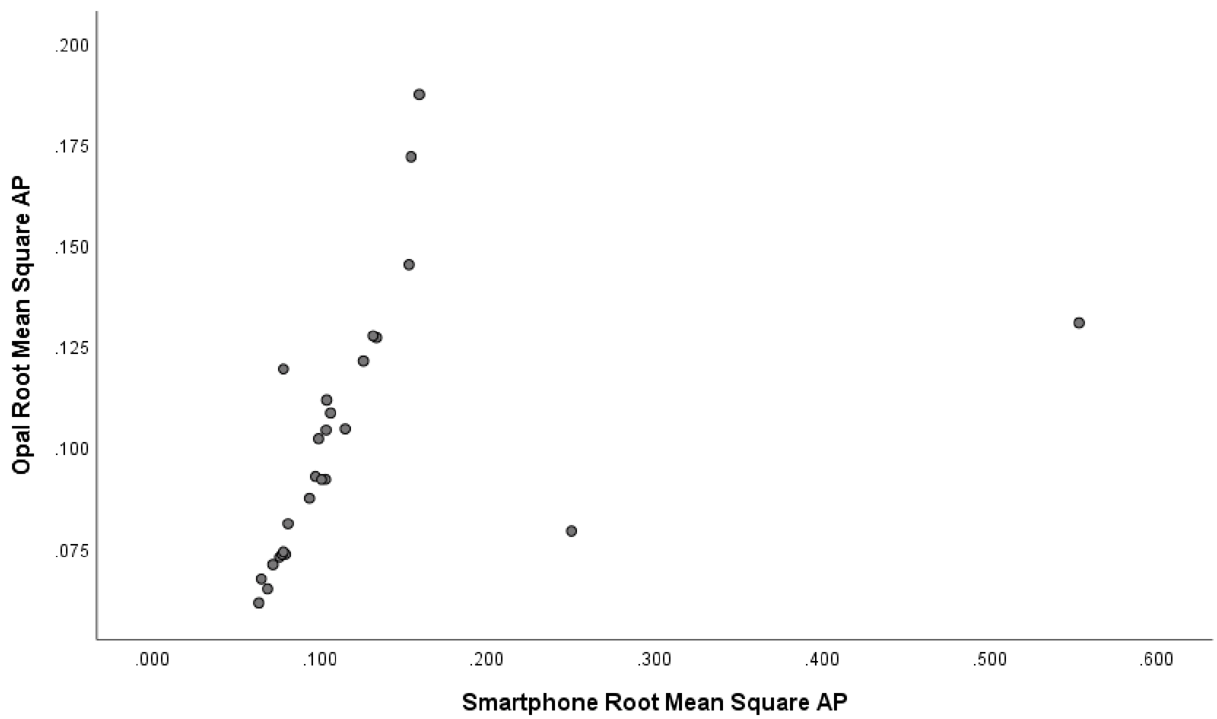


Figure A1 (Cont.)



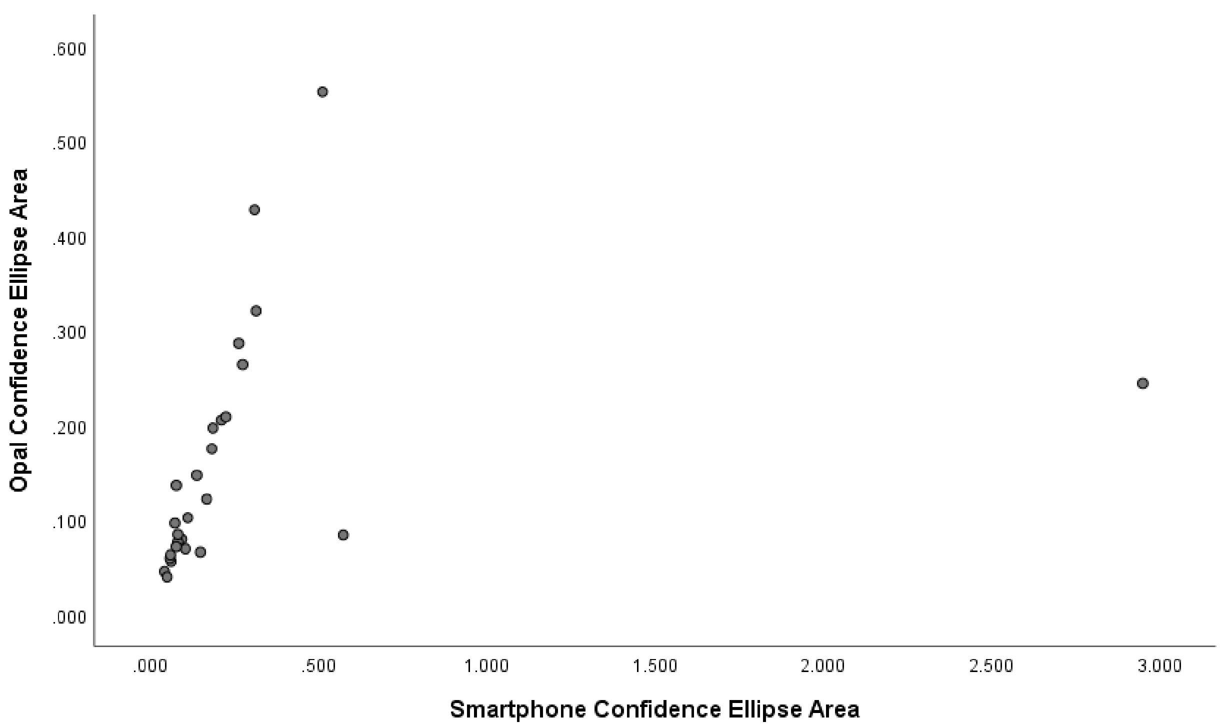
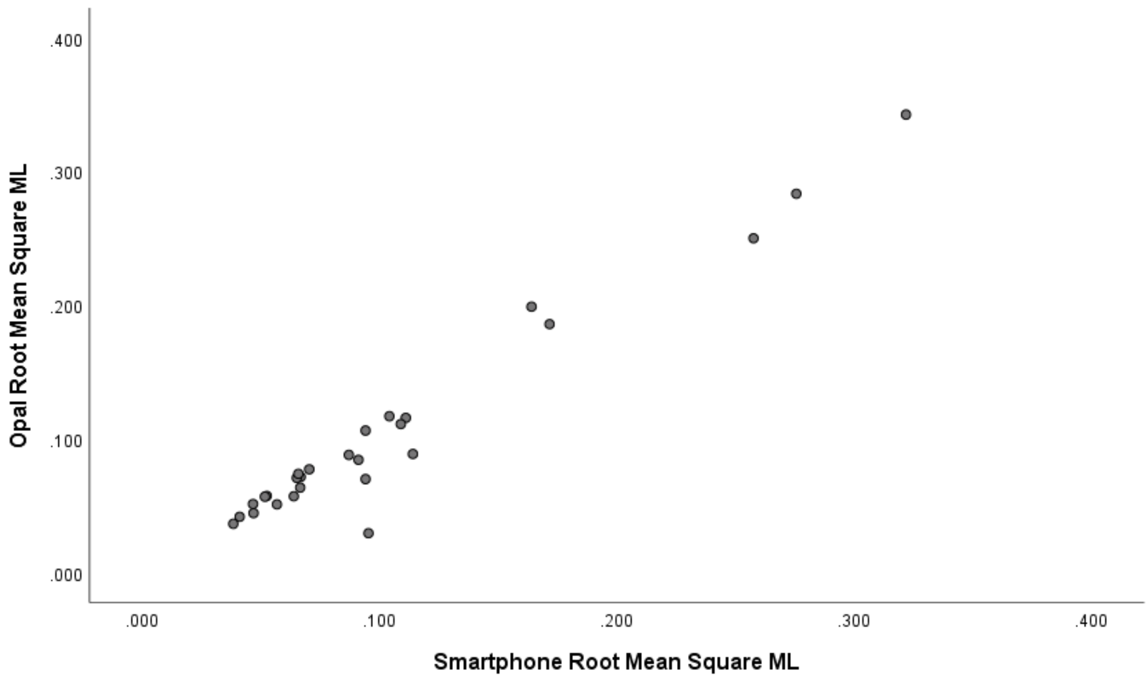


Figure A2. Scatter plots for root mean square and confidence ellipse area acceleration derived from the smartphone and Opal accelerometer during **eyes closed** condition for 27 participants. ML = mediolateral; AP = anteroposterior



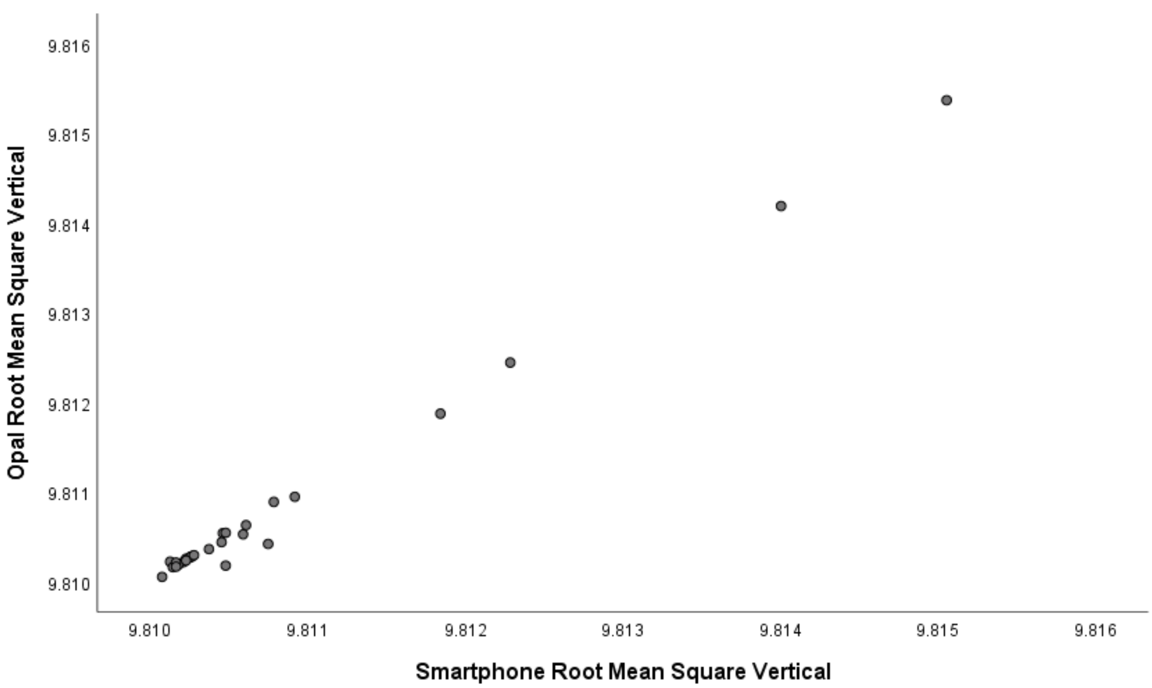
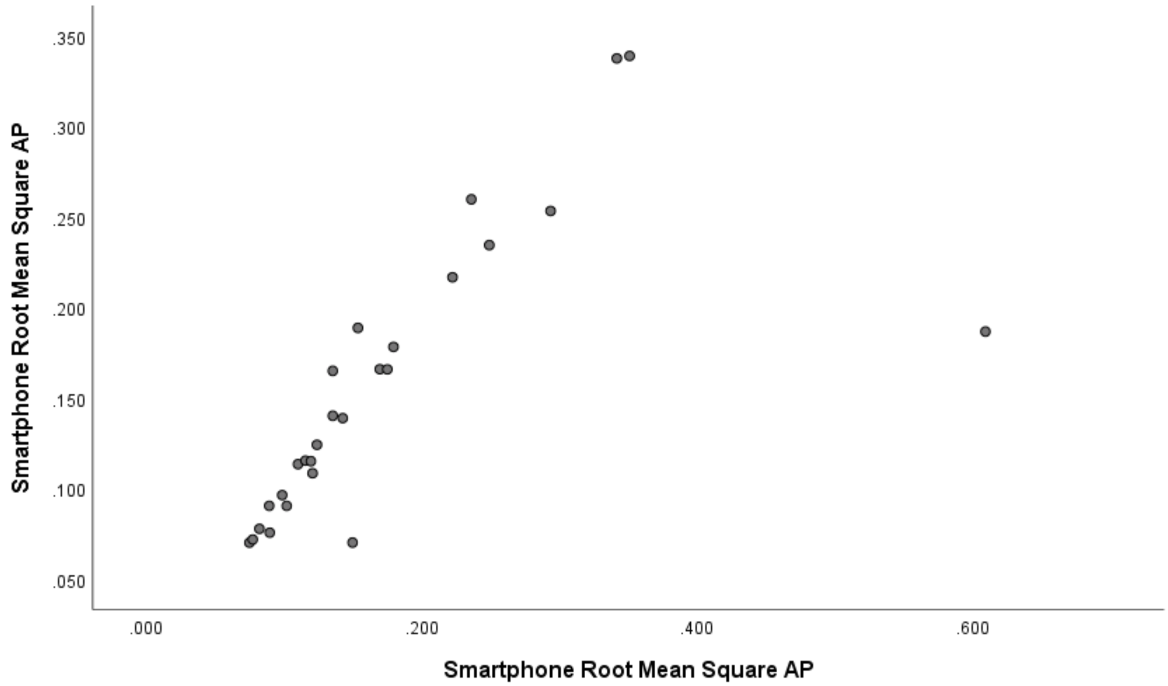


Figure A2 (Cont.)



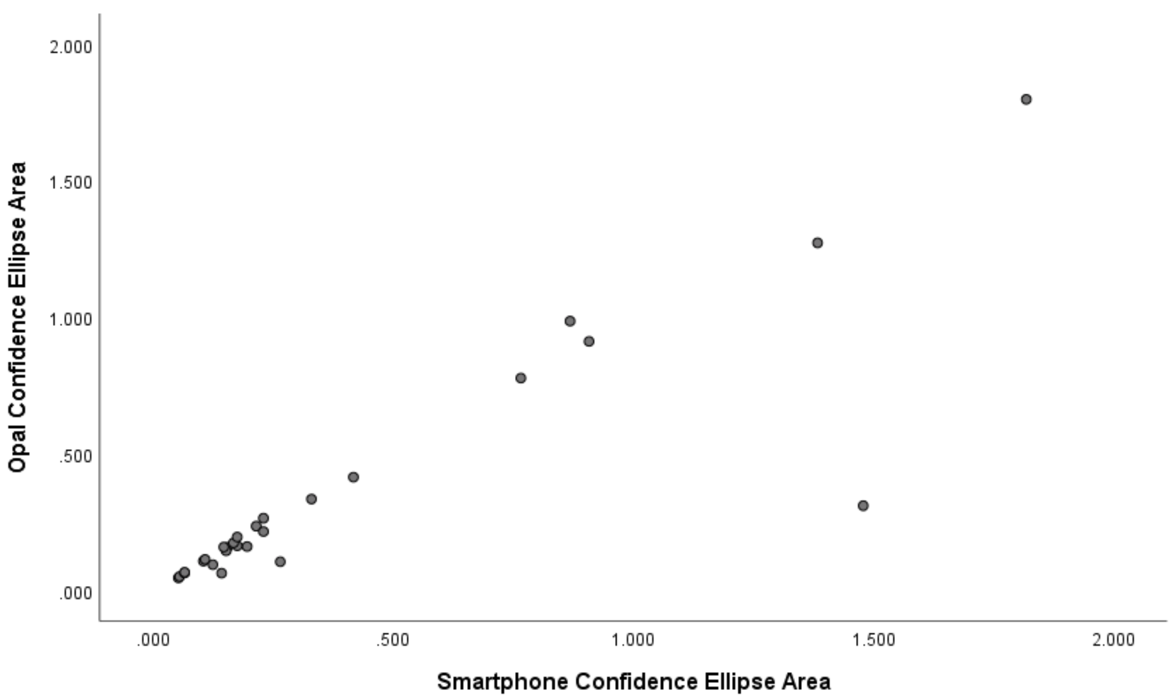
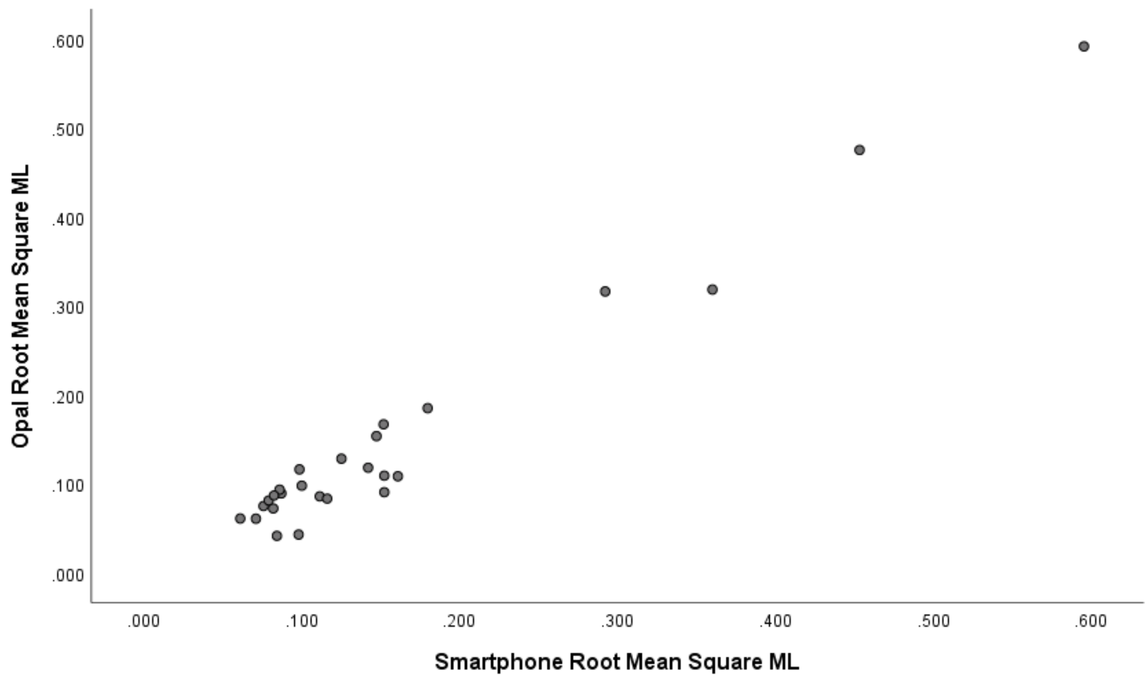


Figure A3. Scatter plots for root mean square and confidence ellipse area acceleration derived from the smartphone and Opal accelerometer during **semi-tandem** condition for 27 participants. ML = mediolateral; AP = anteroposterior



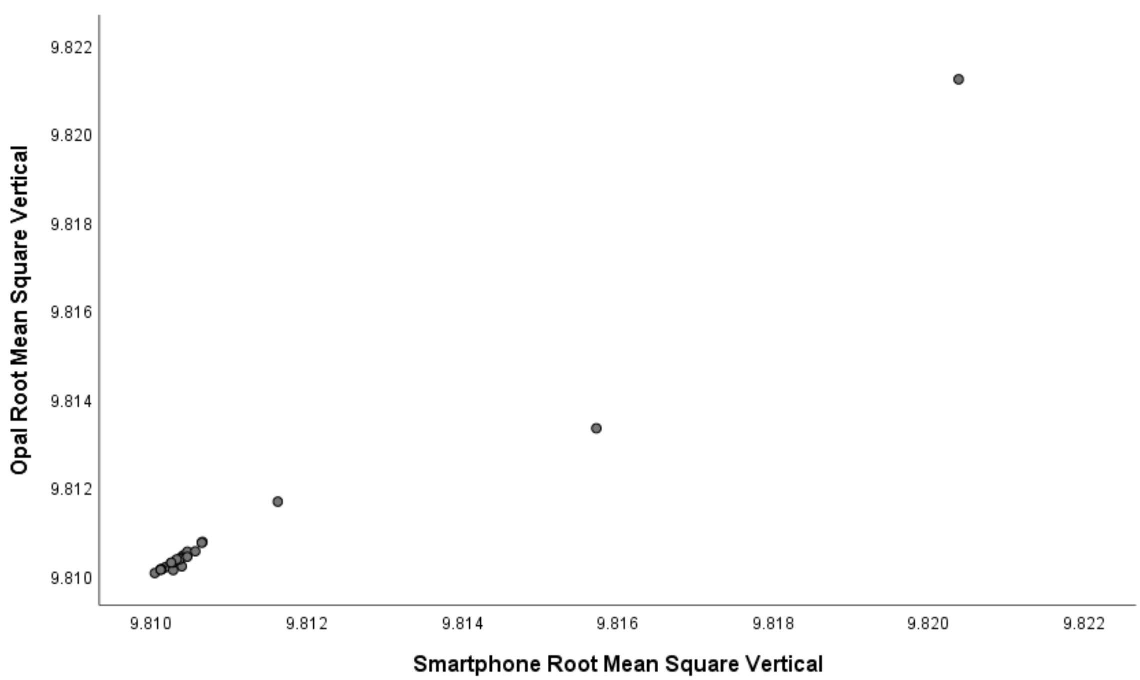
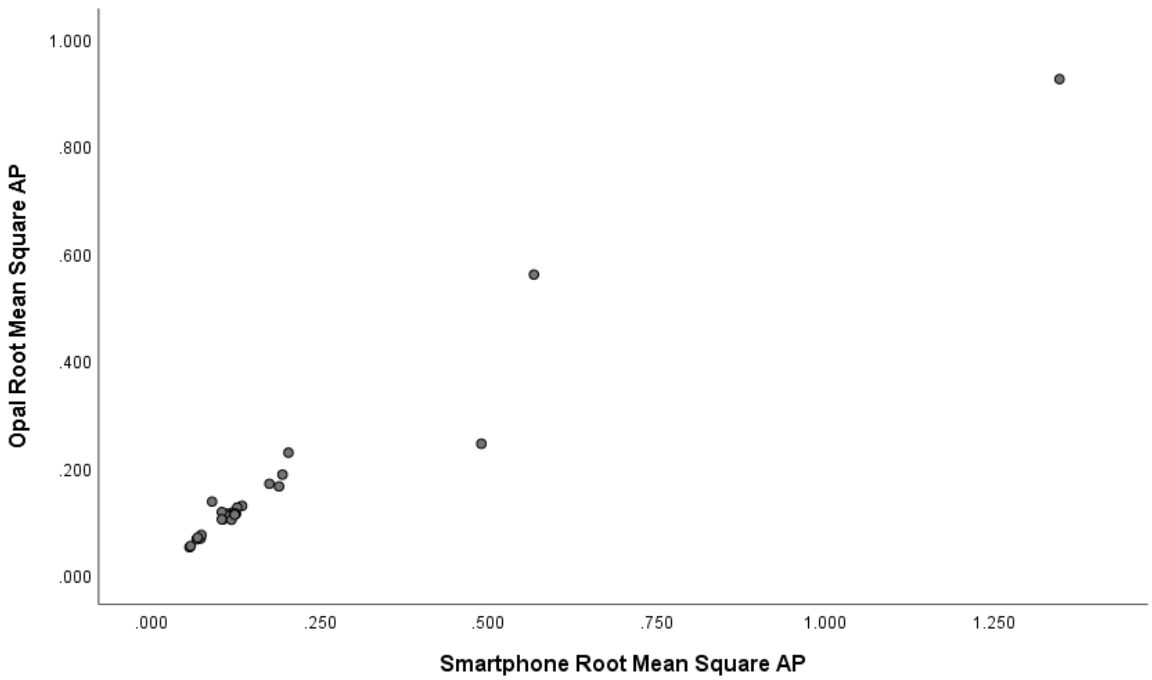


Figure A3 (Cont.)



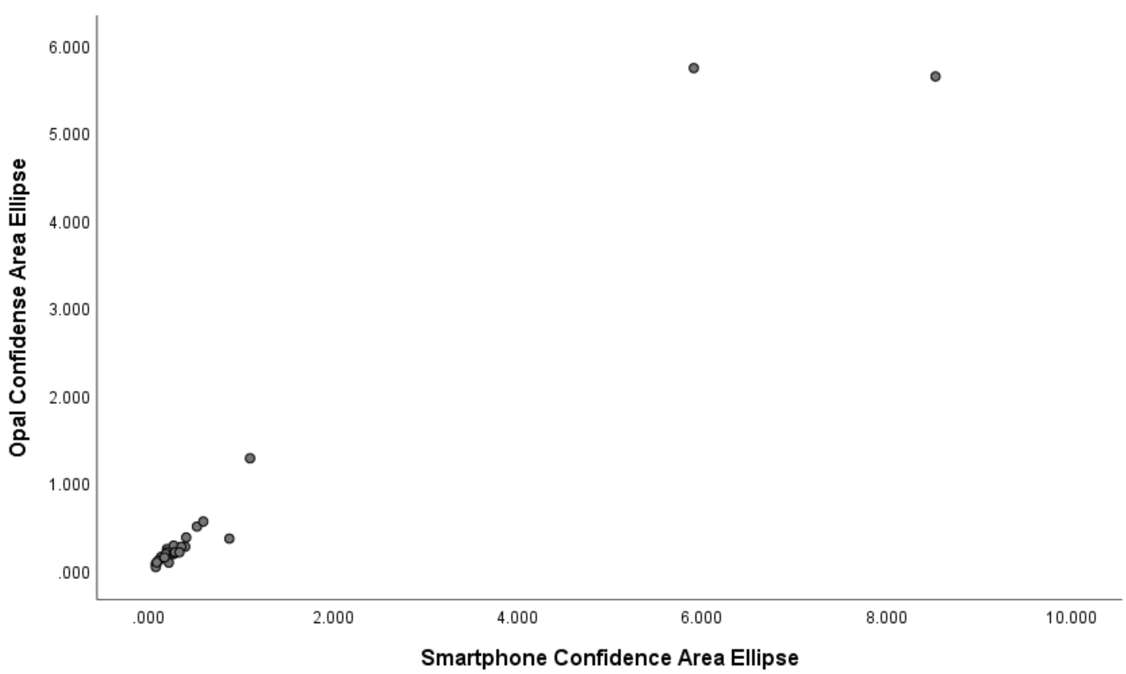
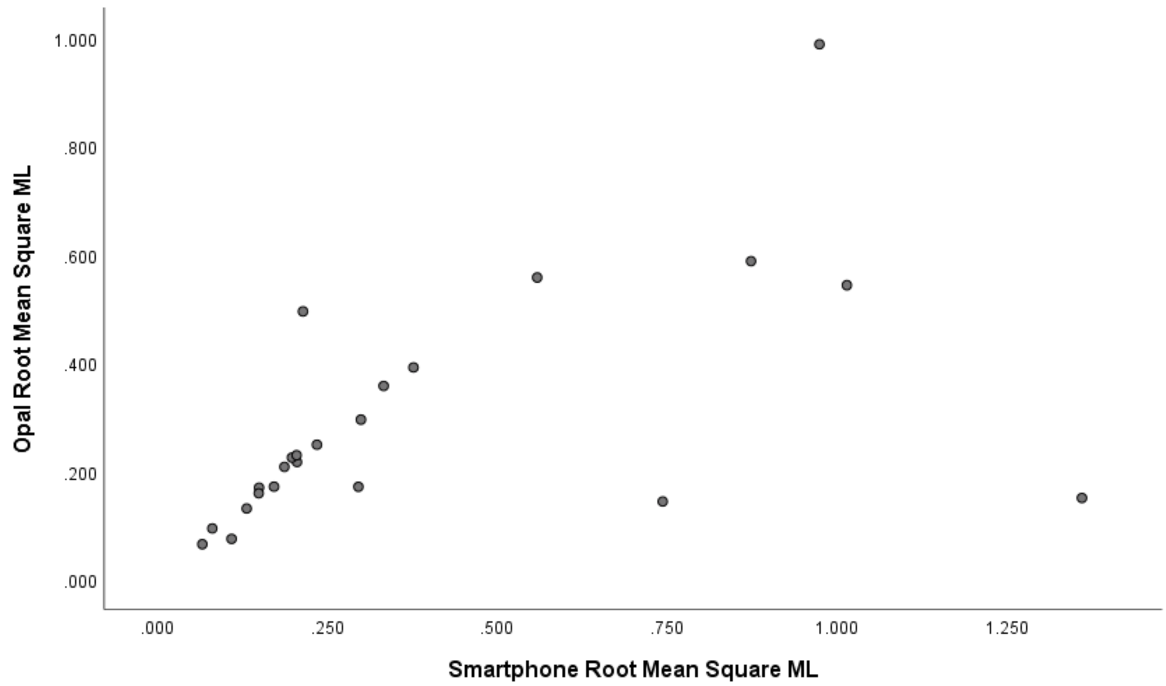


Figure A4. Scatter plots for root mean square and confidence ellipse area acceleration derived from the smartphone and Opal accelerometer during **tandem** condition for 23 participants. ML = mediolateral; AP = anteroposterior



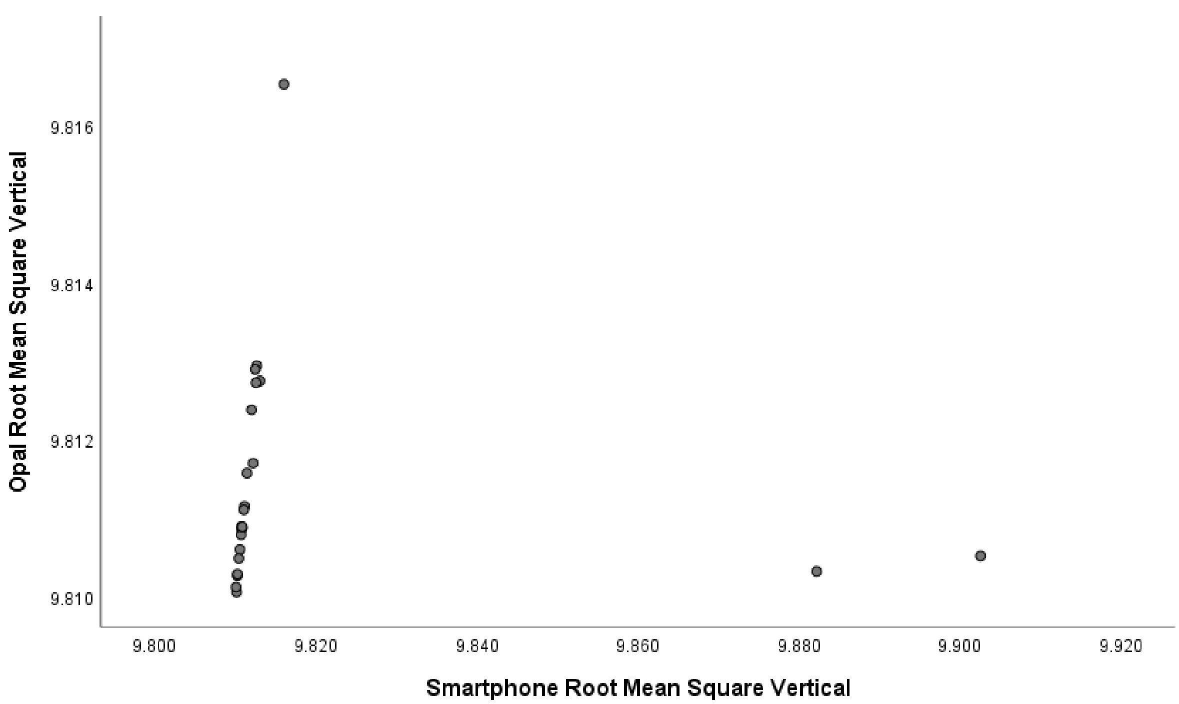
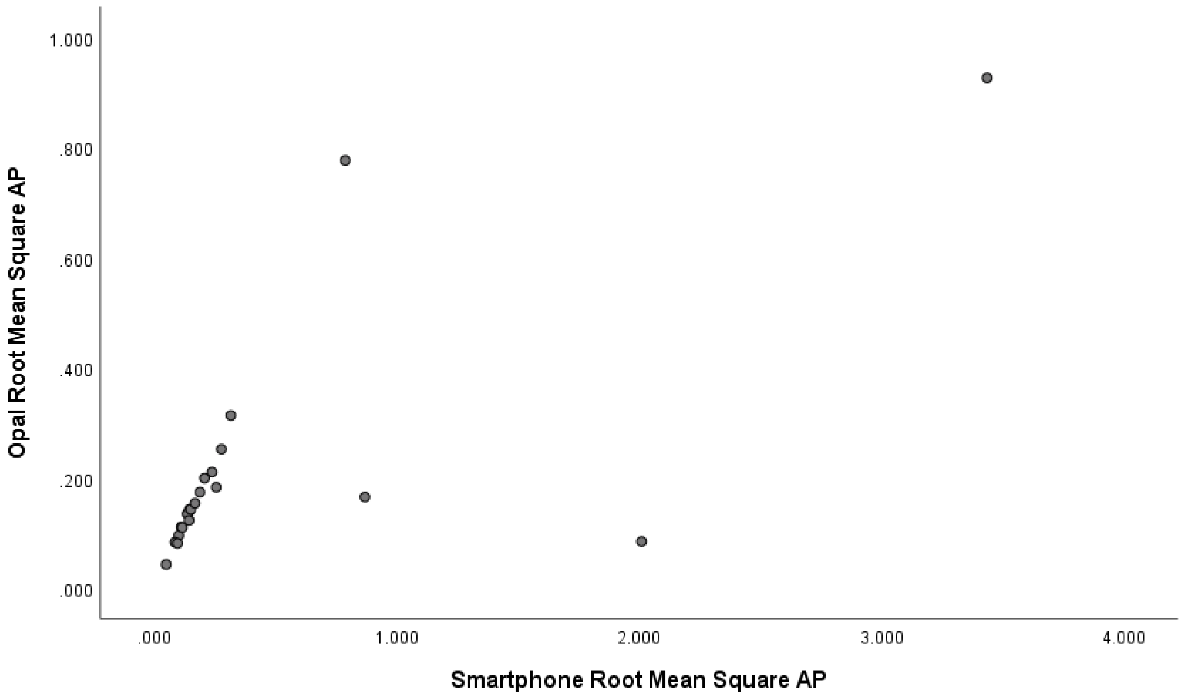


Figure A4 (Cont.)



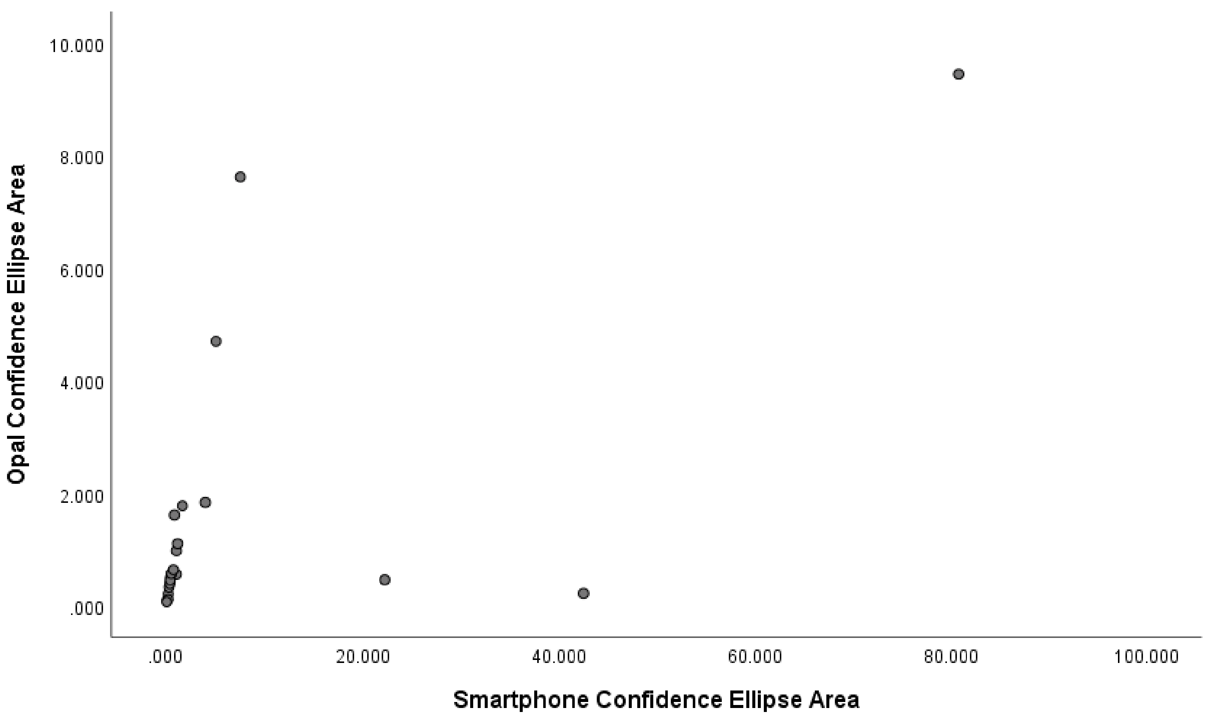
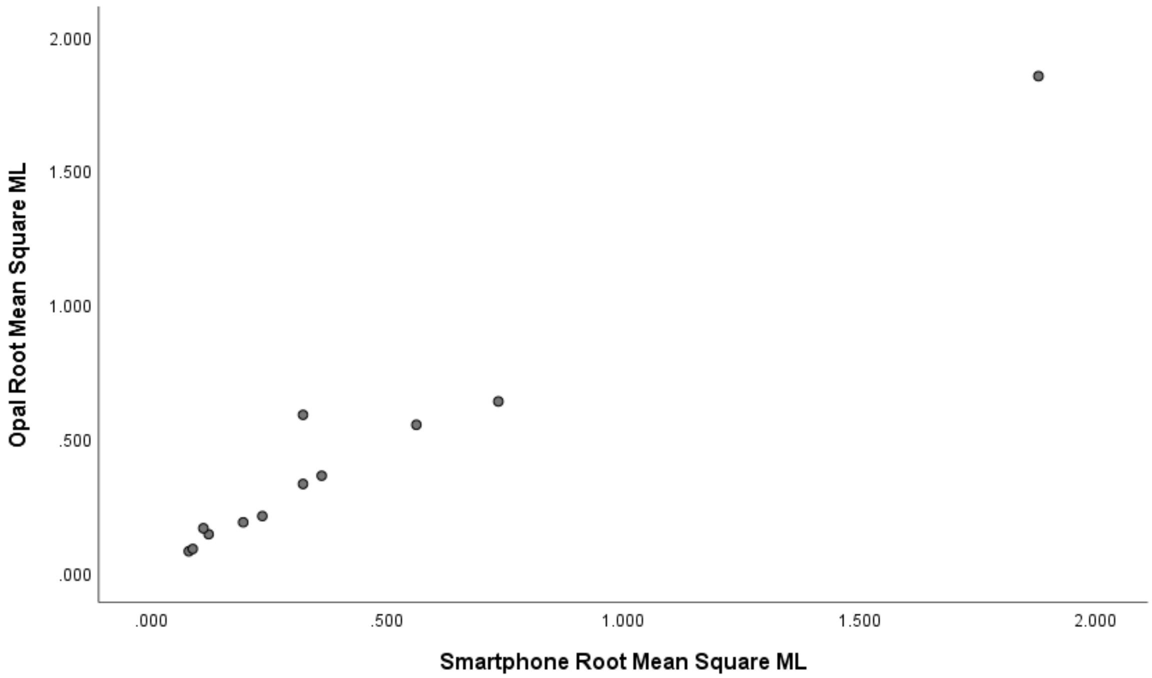


Figure A5. Scatter plots for root mean square and confidence ellipse area acceleration derived from the smartphone and Opal accelerometer during **singe leg** condition for 12 participants. ML = mediolateral; AP = anteroposterior



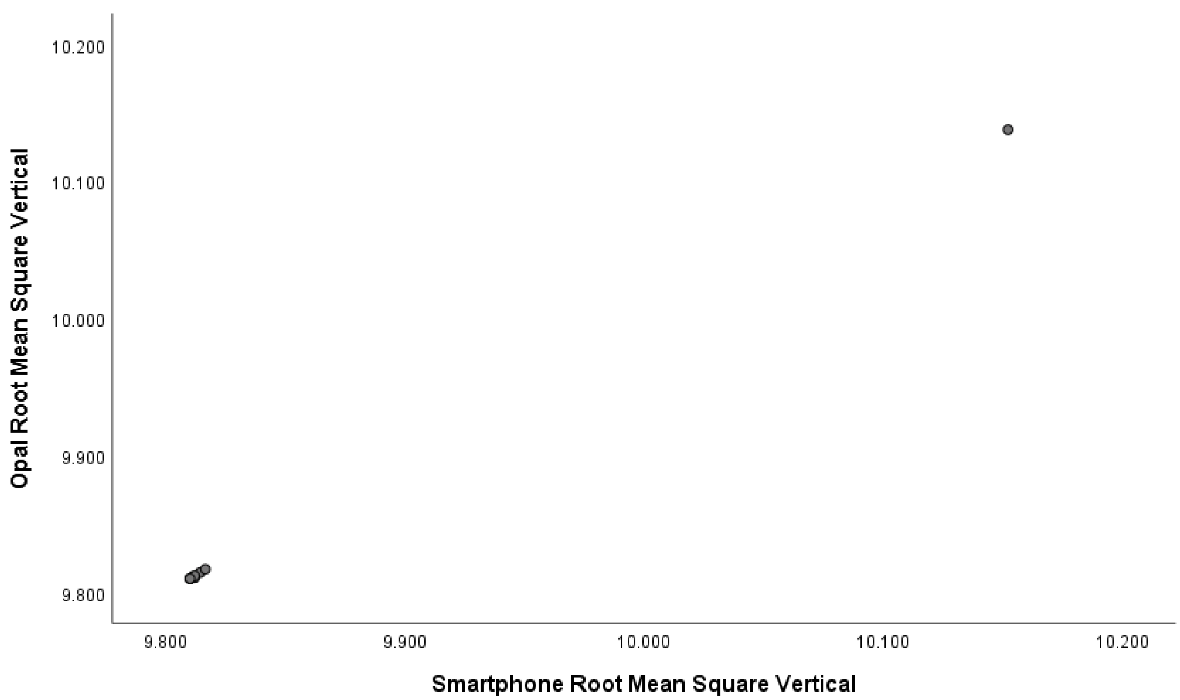
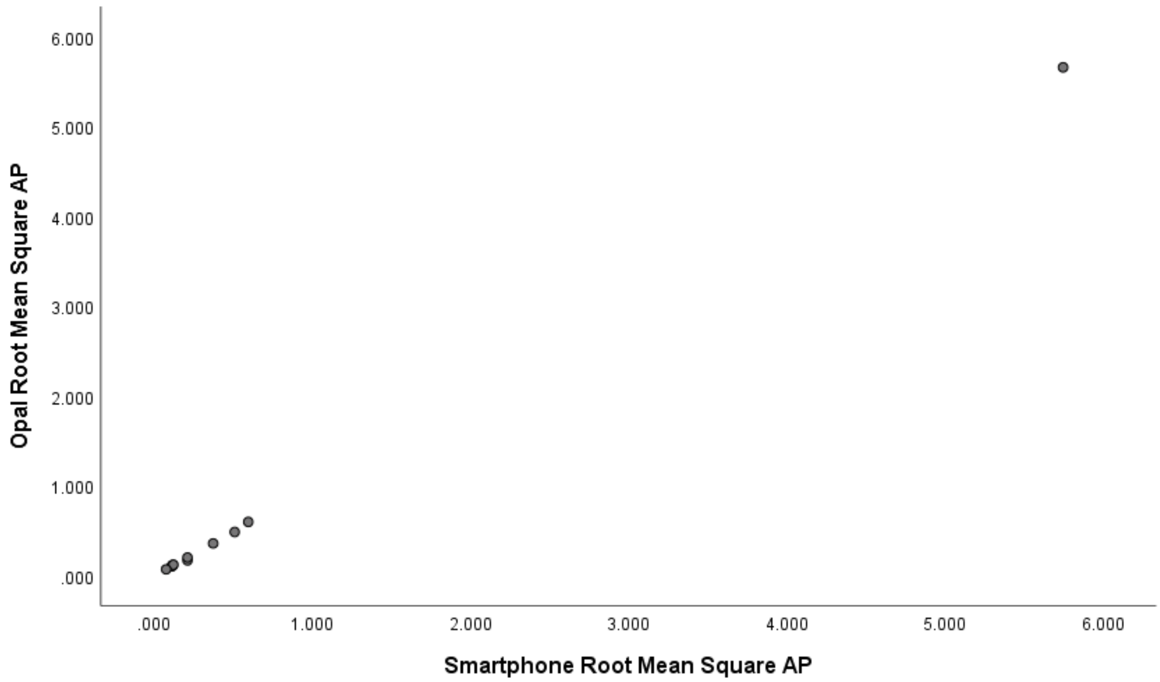
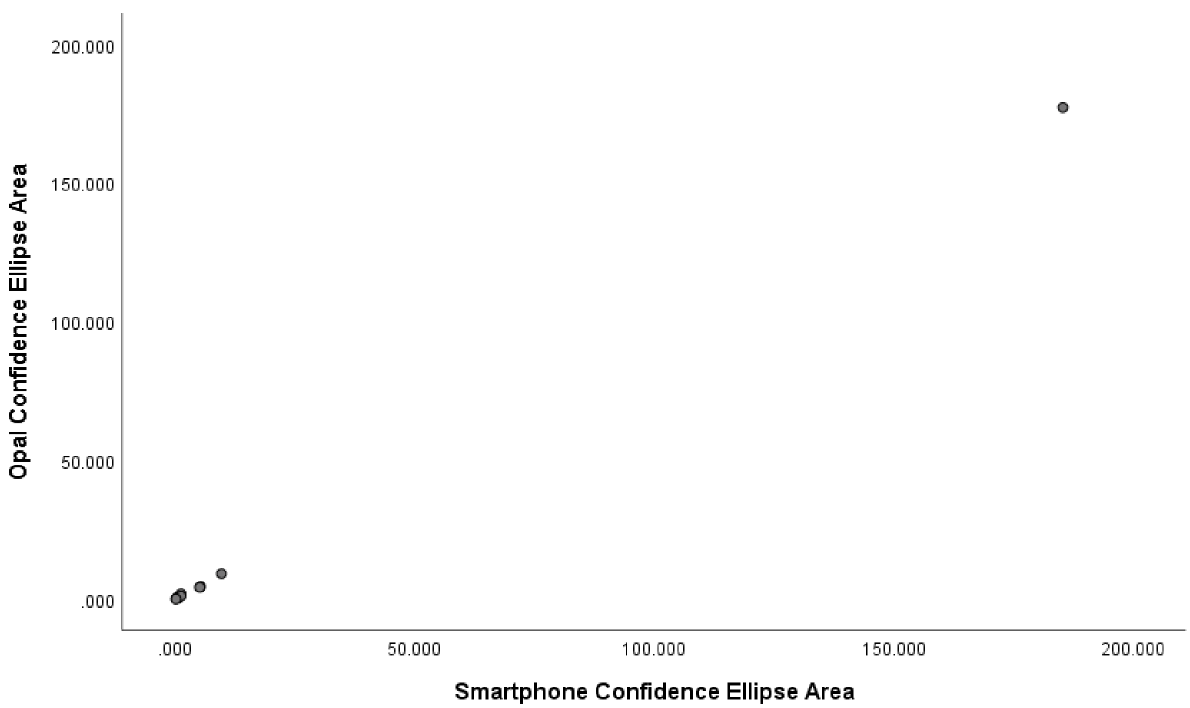


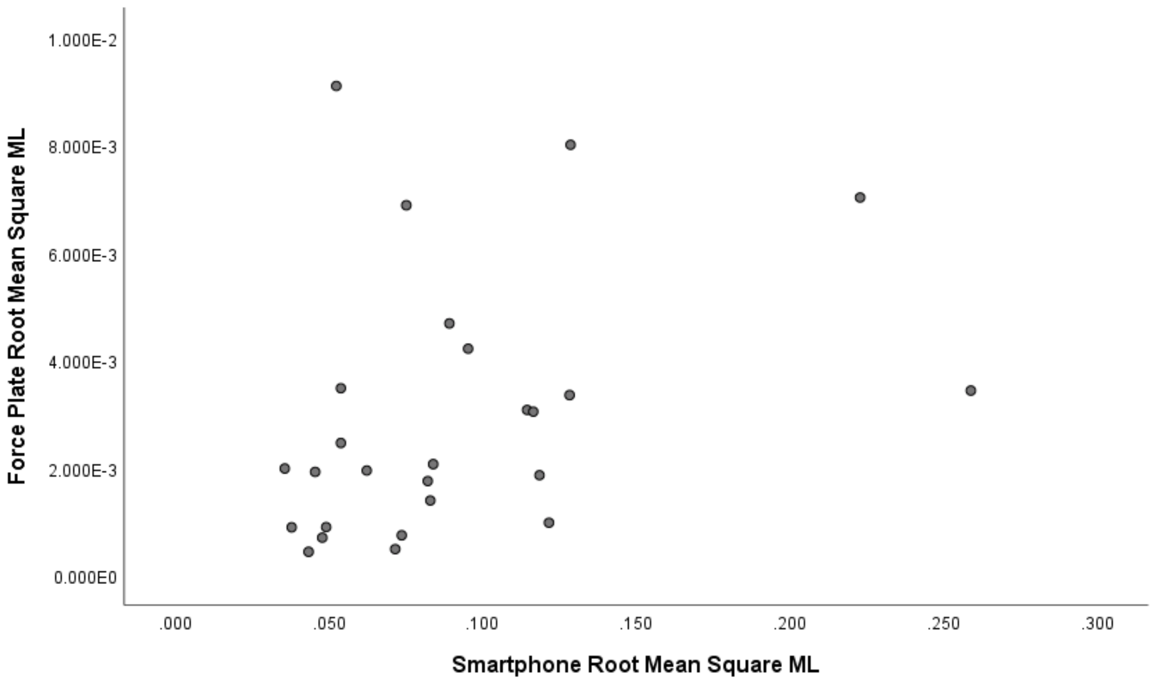
Figure A5 (Cont.)





APPENDIX B: SMARTPHONE ACCELEROMETRY AND FORCE PLATE SCATTER PLOTS

Figure B1. Scatter plots for root mean square and confidence ellipse area derived from the smartphone accelerometer and force plate during **eyes open** condition for 27 participants. ML = mediolateral; AP = anteroposterior



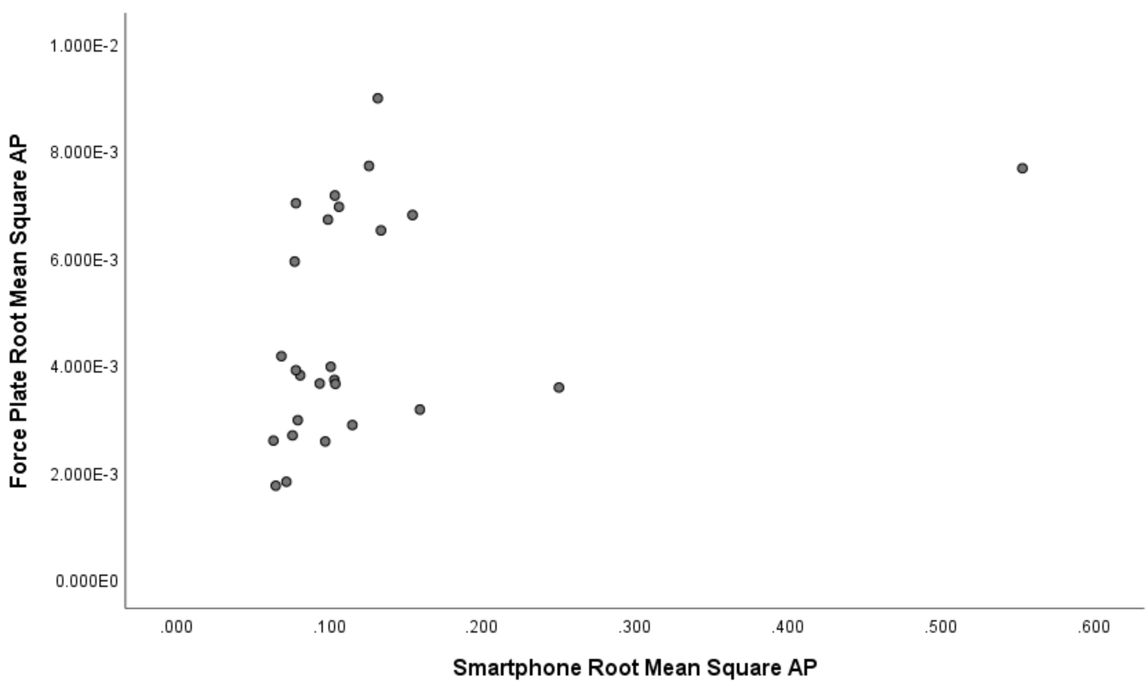


Figure B1 (Cont.)

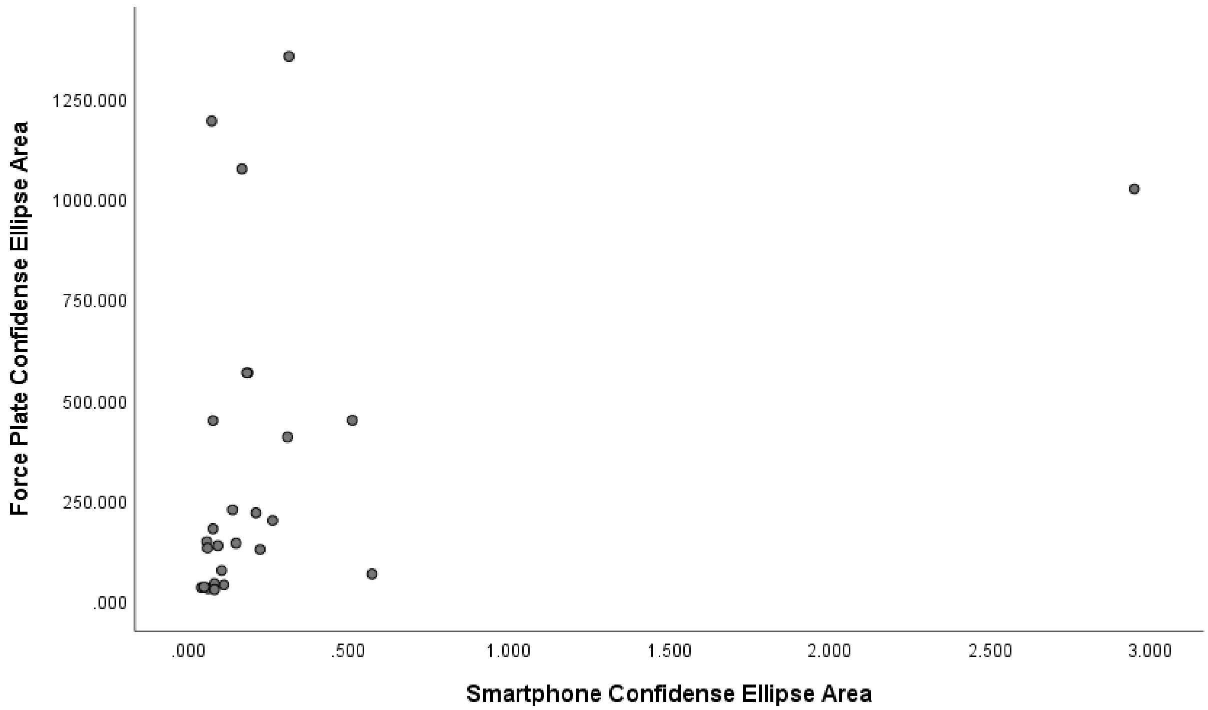


Figure B2. Scatter plots for root mean square and confidence ellipse area derived from the smartphone accelerometer and force plate during **<u>eyes closed</u>** condition for 27 participants. ML = mediolateral; AP = anteroposterior

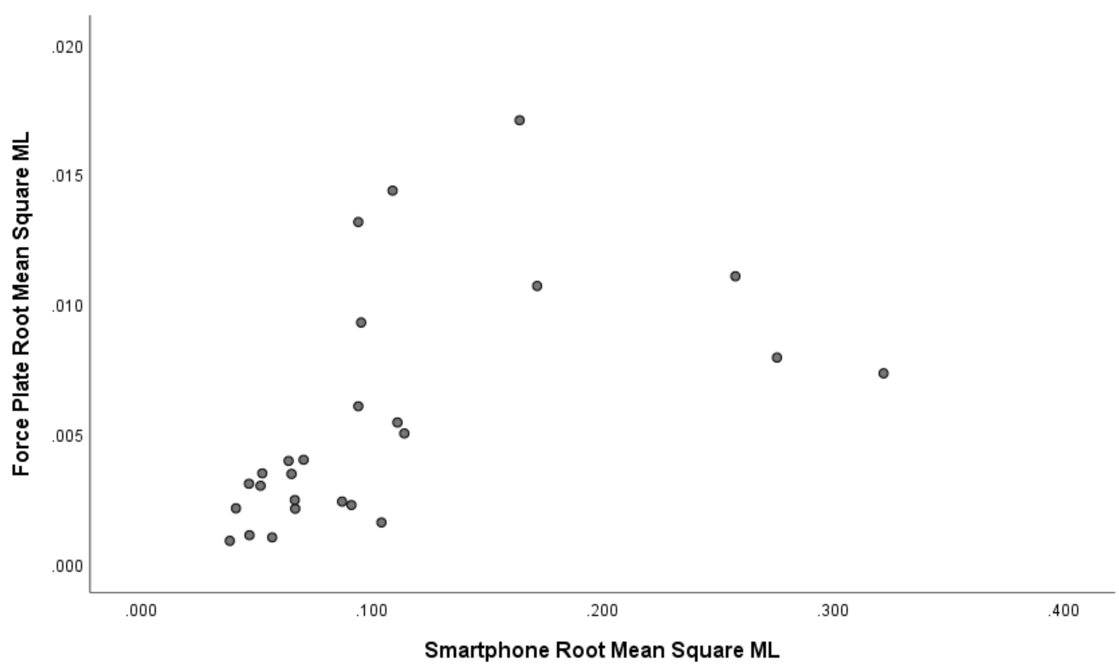
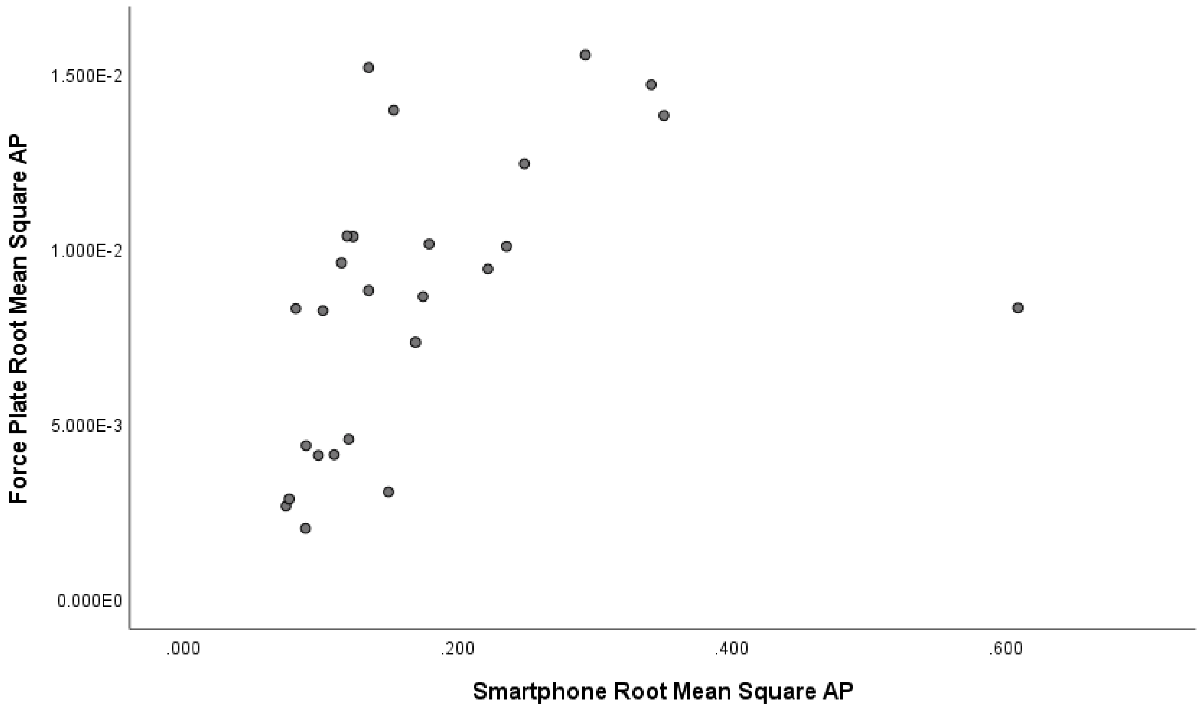


Figure B2 (Cont.)



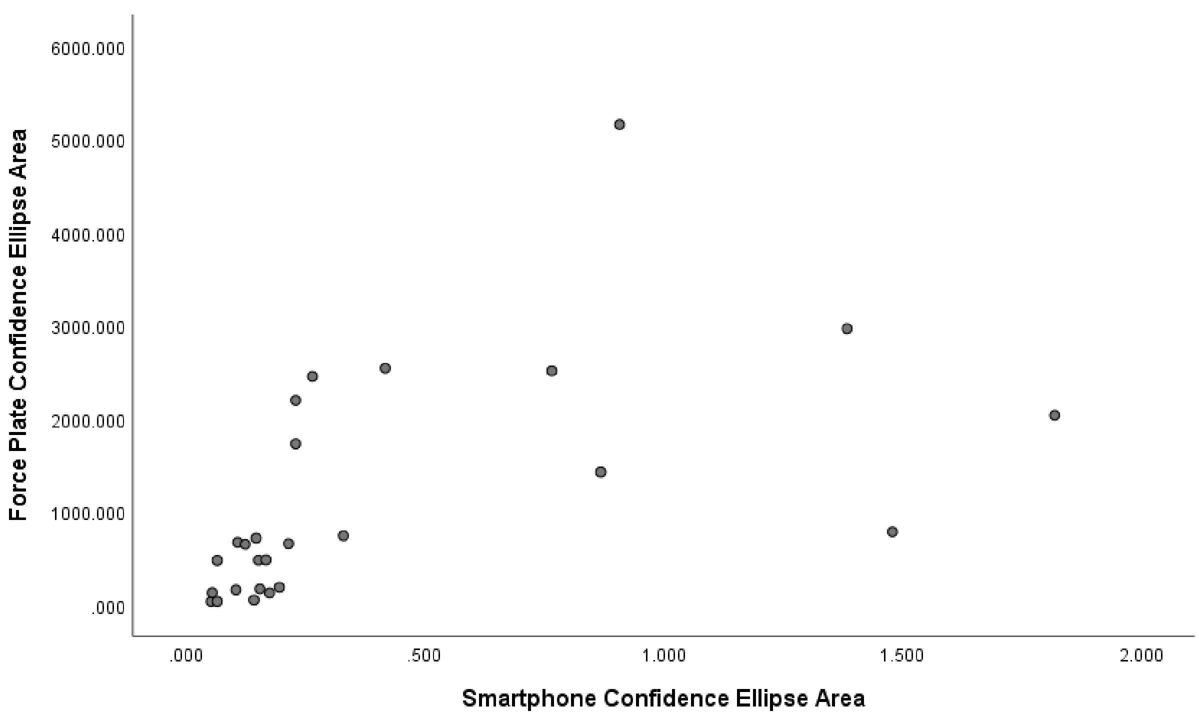
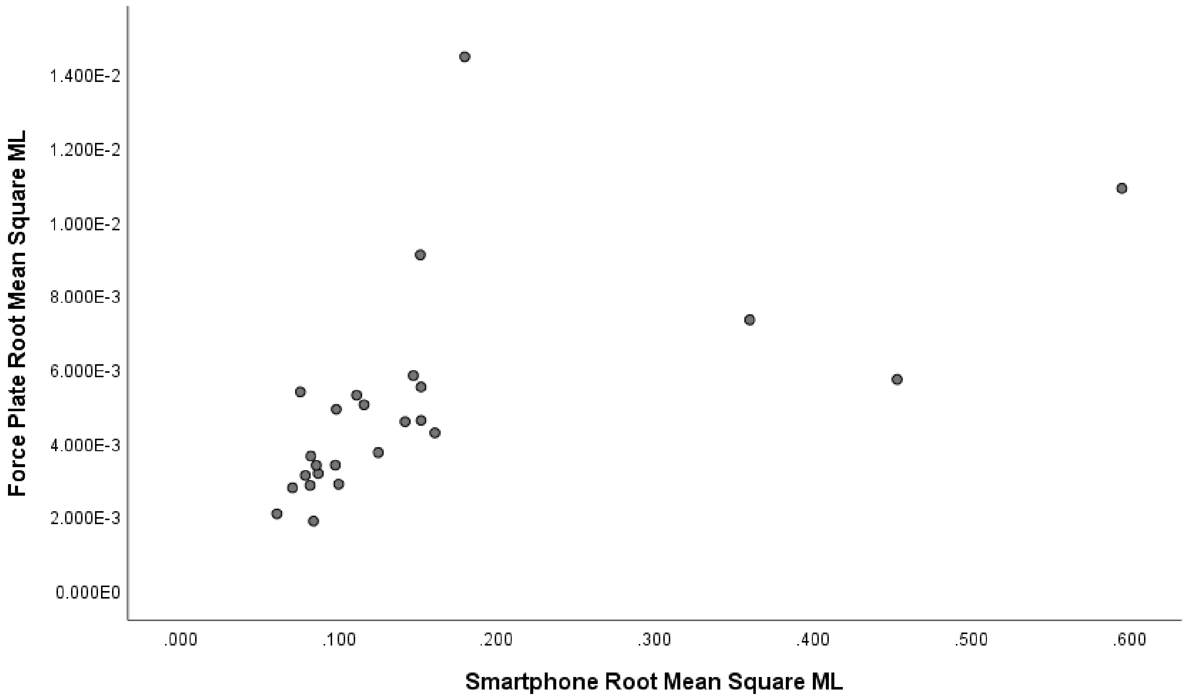


Figure B3. Scatter plots for root mean square and confidence ellipse area derived from the smartphone accelerometer and force plate during **semi-tandem** condition for 27 participants. ML = mediolateral; AP = anteroposterior



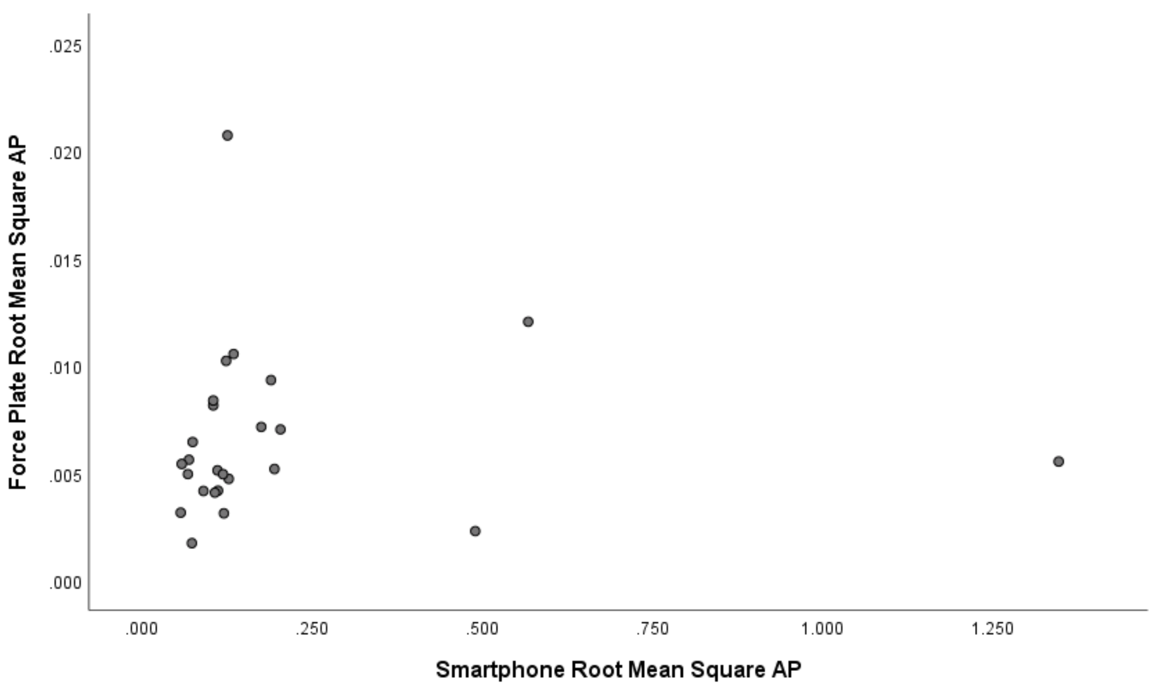


Figure B3 (Cont.)

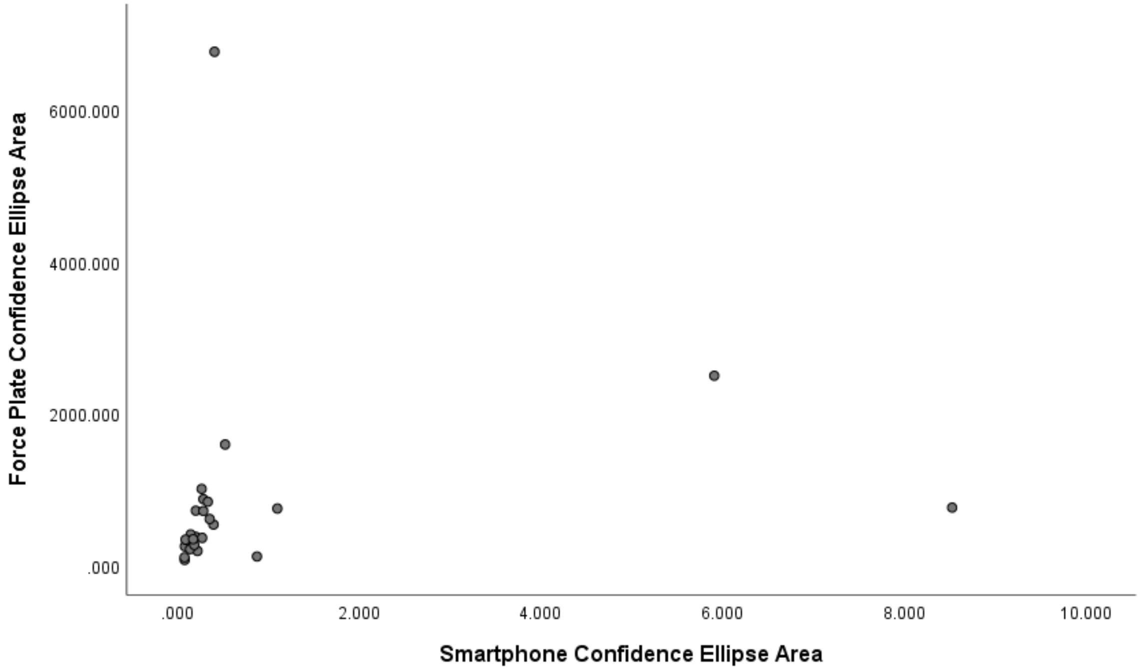


Figure B4. Scatter plots for root mean square and confidence ellipse area derived from the smartphone accelerometer and force plate during **<u>tandem</u>** condition for 23 participants. ML = mediolateral; AP = anteroposterior

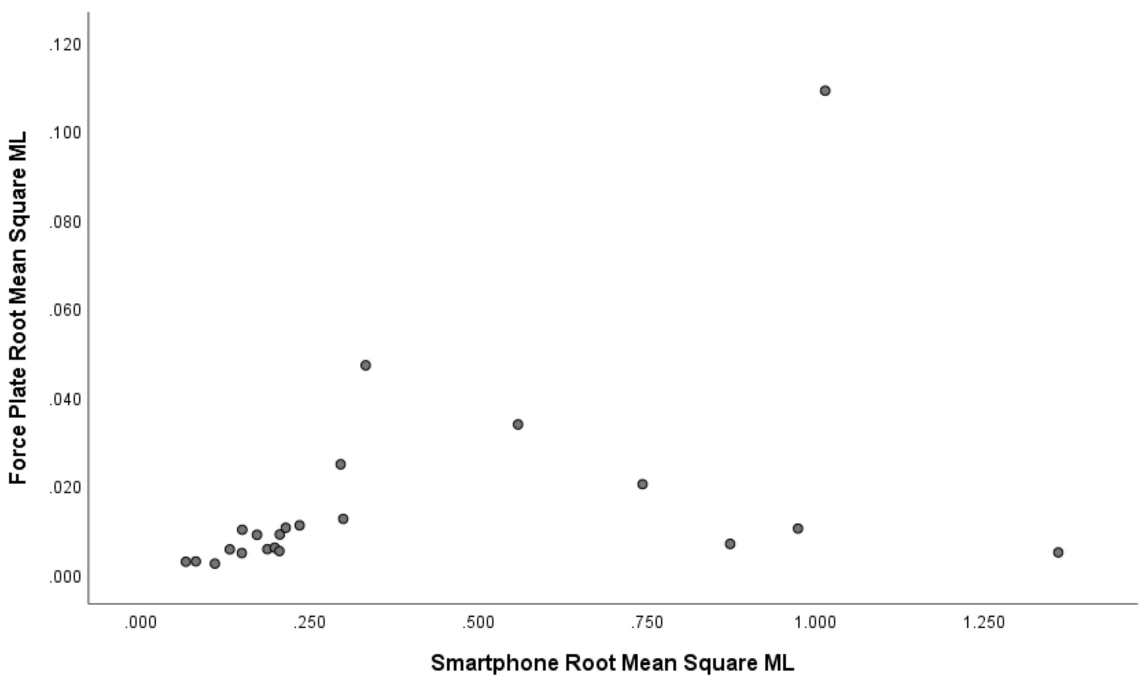
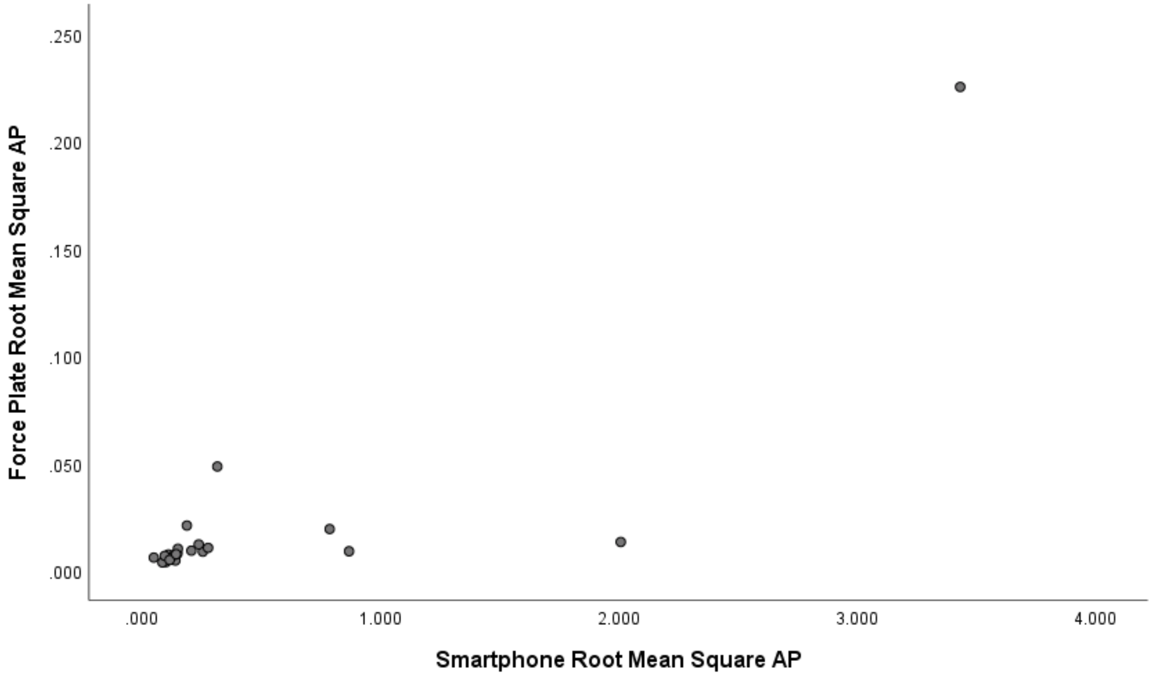


Figure B4 (Cont.)



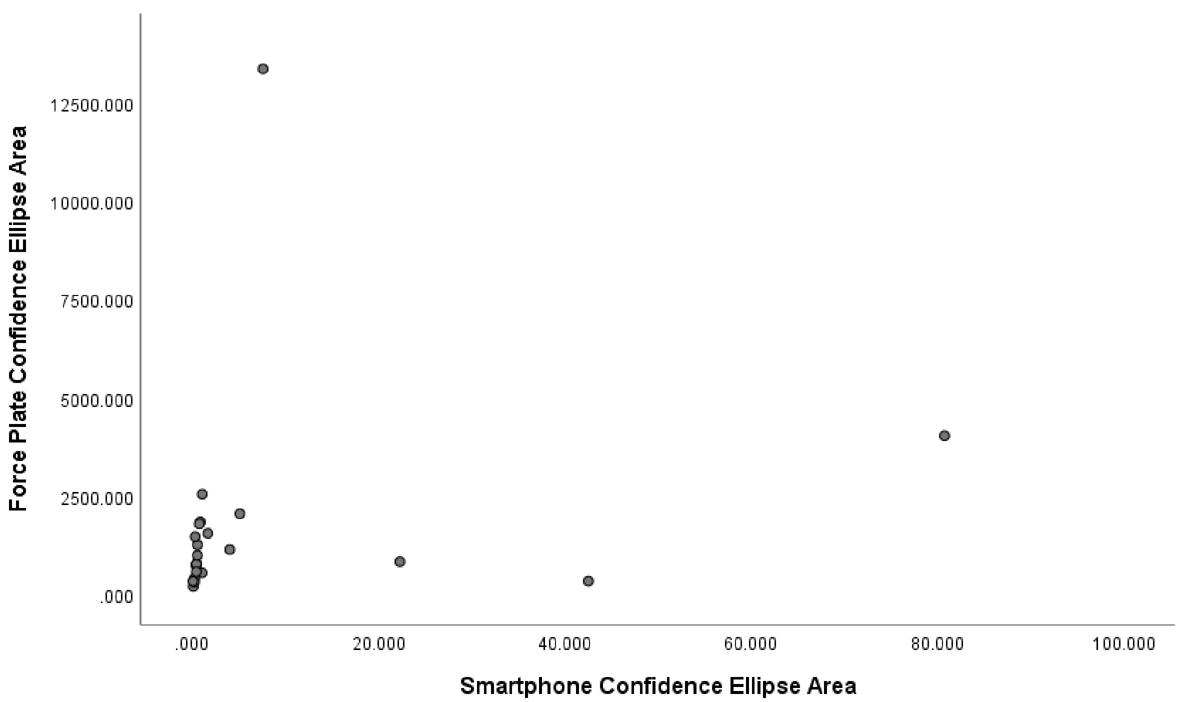
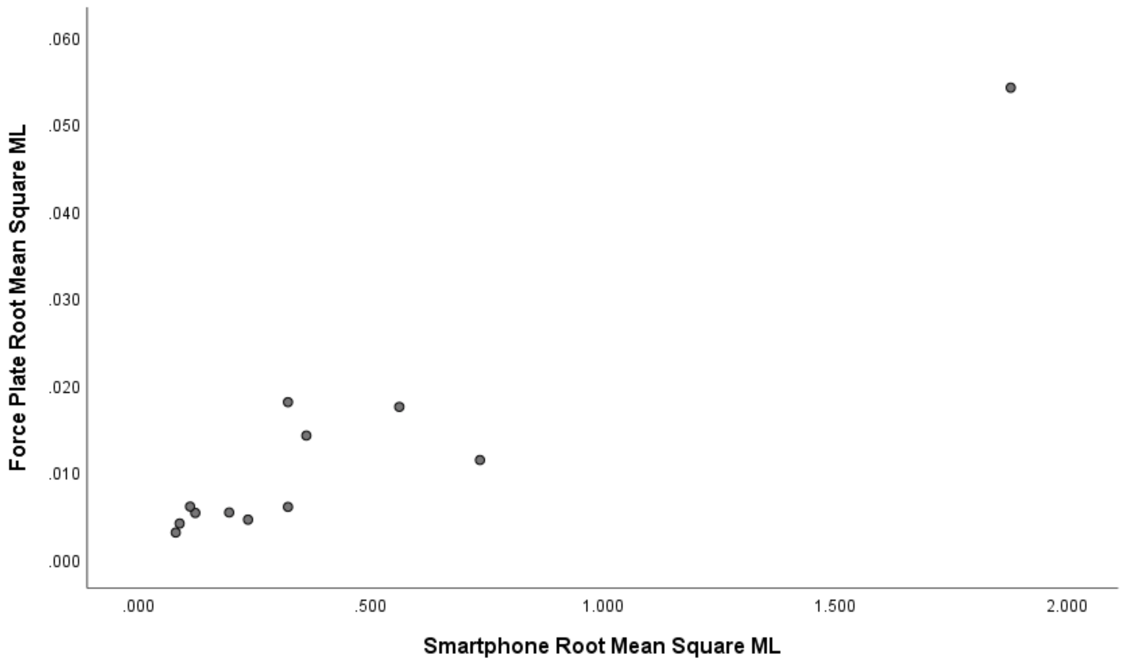


Figure B5. Scatter plots for root mean square and confidence ellipse area derived from the smartphone accelerometer and force plate during **single leg** condition for 12 participants. ML = mediolateral; AP = anteroposterior



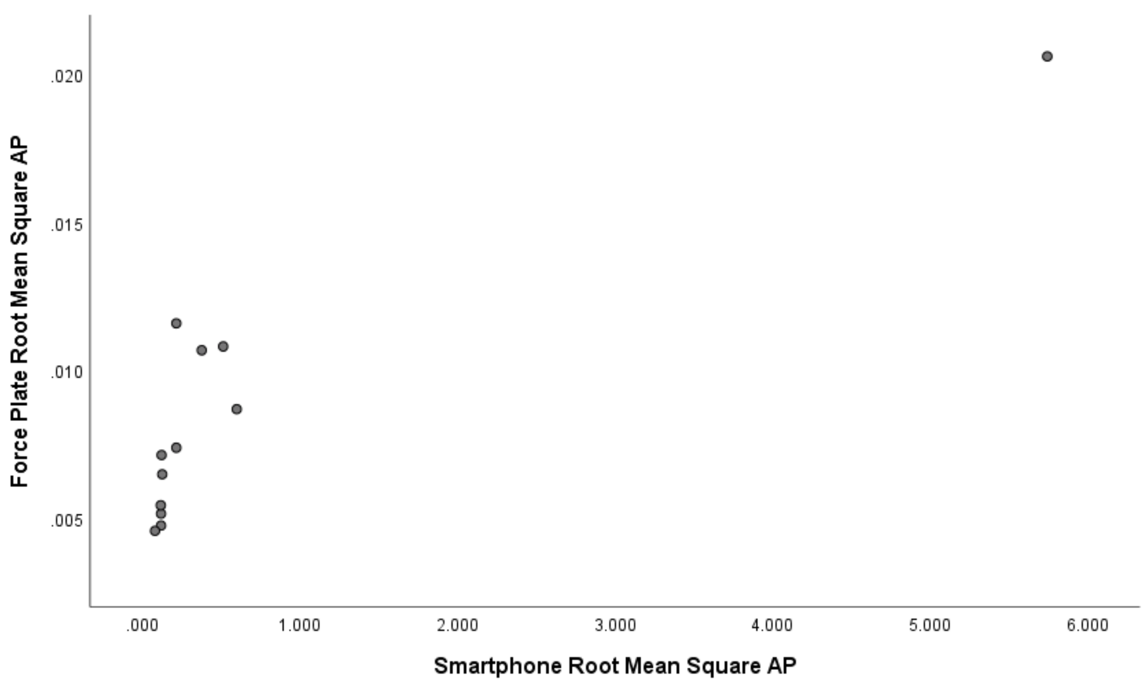


Figure B5 (Cont.)