Physiotherapy and exercise interventions for the treatment of people with Multiple Sclerosis with moderate to severe mobility impairment

A thesis submitted for the award of Doctor of Philosophy

Author: Neasa Mary Hogan, BSc. MISCP
University: University of Limerick
Supervisors: Dr Susan Coote and Prof. Sue Franklin
Submitted to the University of Limerick November 2011
Abstract

Title: Physiotherapy and exercise interventions for the treatment of people with Multiple Sclerosis with moderate to severe mobility impairment.

Author: Neasa Hogan

Multiple sclerosis (MS) is a disease of the central nervous system. It is characterised by both demyelination and degeneration. It is progressive in nature and can lead to severe disability, functional limitations and a poor quality of life (QoL). Many people with MS (PwMS) live with some form of physical impairment. Physiotherapy plays an important role in the management of physical symptoms.

A review of the literature highlighted that a multitude of physiotherapy and exercise interventions have been evaluated in PwMS. These studies, however, included PwMS with varying levels of mobility. No randomised controlled trial has previously evaluated the effect of a physiotherapy intervention specifically on PwMS with moderate to severe mobility impairment. The overall aim of this research was to evaluate the effect of three community based interventions on PwMS who mobilise with at least bilateral assistance.

Participants (n=111) were allocated to ten weekly hour long sessions of group physiotherapy, individual physiotherapy, yoga or a control group. The effect of treatment was analysed using baseline and post intervention (Week 12) data. The data at follow up (Week 24) was analysed separately. A post hoc analysis was performed to explore the variables that may influence outcome. Outcomes measures used at each time point were the Multiple Sclerosis Impact Scale-29v2 (MSIS-29v2), Modified Fatigue Impact Scale (MFIS), Berg Balance Scale (BBS), and the six minute walk test (6MWT).

The study revealed that there was a significant treatment effect for group physiotherapy, individual physiotherapy and yoga on the BBS (p<0.05). There were significant improvements on the MSIS-29v2 and the MFIS for group and individual physiotherapy (p<0.05). There was a trend for worsening for yoga and a trend for improvement in the control group. There was a significant improvement on the 6MWT for individual physiotherapy and a trend for improvement for group physiotherapy. These improvements were not maintained at week 24. Baseline scores on the BBS and sensation contributed significantly to a higher score on the BBS at outcome. The results of the analysis on falls revealed a high prevalence of falls in this cohort, a significant reduction in the number of falls and fallers post intervention for group physiotherapy.

The results of this research suggest group physiotherapy is as effective as individual physiotherapy in improving balance, impact of MS and fatigue and in reducing falls. This has implications for service delivery for this population of PwMS. Group therapy may reduce the financial cost for health care providers and have added benefits for PwMS. These results need to be confirmed by comparing them to a larger, matched control group. Future research needs to establish the effect of yoga in PwMS with moderate to severe mobility limitations and other variables that may predict outcome need to be explored.
Declaration

I declare that this thesis is entirely my own work and that it has not been submitted as an exercise for a degree at this or any other University.

I hereby give my permission for this thesis to be lent or copied on request, with the consent of the librarian, and with due acknowledgement of the author.

Signed: ______________________

Date: ______________________
Acknowledgements

First and foremost, I would like to acknowledge the contribution of Multiple Sclerosis Ireland (MSI). This project was made possible by MSI through the financial support of Tesco Ireland, through their Charity of the Year Programme and Pobal and through administration of the Dormant Accounts funding. I would like to thank all the staff and members of MSI for their support, help and time throughout the life of the project.

There are certain people I would like to acknowledge and thank individually:

My sincere thanks to my supervisor Dr Susan Coote, for her continued encouragement, support, knowledge, guidance and understanding through every step of the research process.

My second supervisor Prof. Sue Franklin for her advice and guidance and for bringing a different perspective to the table.

This thesis was examined by Prof. Alan Donnelly and Prof. Peter Feys and I would like to thank them for their time and for bringing their knowledge to an interesting discussion at the Viva Voce.

Aidan Larkin, national co-ordinator of the Getting the Balance Right Project (GTBR), for his contribution to the methodology and life of the project.

Dr Jean Saunders, director of the Statistical Consulting Unit at the University of Limerick, for her advice and input into the statistical analysis involved in this study.

Dr Maria Garrett, for her contribution to the methodology of the GTBR project and help with assessments and for her support during the research process.

All the staff of the Regional Offices of MSI for their work in stratifying participants and organising the delivery of the interventions locally.
The many people with MS who took part in the pilot study and the main study, without their participation this research would not have been possible.

The physiotherapists that attended the training days and were involved in the assessment and delivery of the interventions.

The yoga instructors involved in delivering the interventions.

Sandra Caulfield, Lindy Shinkwin, Ciara Hogan, who in addition to my supervisors, took the time to proofread chapters of this thesis.

Maria Garrett, Lonan Hughes, Catriona O’Dwyer and Elaine Toomey, fellow postgraduate students, for the company and laughs throughout my time in the University of Limerick.

All of my work colleagues in St Camillus’ hospital and St Ita’s hospital for being both supportive and accommodating especially during the last few months.

All of my friends and family for their patience and words of encouragement, support and motivation over the last four years.

To Mark for being there for me.

And finally to my parents, Nessa and Denis, for their continued support throughout everything I do.

For Levi…
Table of Contents

Abstract ............................................................................................................................ ii
Declaration ...................................................................................................................... iii
Acknowledgements ........................................................................................................ iv
Table of Contents .......................................................................................................... vi
List of Tables ................................................................................................................ xi
List of Figures ............................................................................................................... xiii

Chapter 1 Introduction ................................................................................................... 1
  1.0 Outline of chapter .................................................................................................. 1
  1.1 Multiple Sclerosis ............................................................................................... 1
  1.2 Epidemiology of MS .......................................................................................... 2
  1.3 Consequences of MS ....................................................................................... 2
  1.4 Treatment of MS ............................................................................................... 4
  1.5 Background to research project ....................................................................... 5
  1.6 Aims and objectives ......................................................................................... 6
  1.6 Thesis outline and summary ............................................................................ 7

Chapter 2 Physiotherapy and exercise interventions for People with Multiple Sclerosis with moderate to severe mobility impairment – A review of the literature ................................................................................................. 9
  2.0 Introduction ....................................................................................................... 9
  2.1 Methodology ..................................................................................................... 10
    2.1.1 Search Strategy .......................................................................................... 10
    2.1.2 Inclusion and exclusion criteria ................................................................. 10
    2.2.3 Assessment of Study Quality .................................................................. 11
  2.2 Results ............................................................................................................. 12
    2.2.1 Specific physiotherapy interventions ...................................................... 14
2.2.2 Aerobic Exercise

2.2.3 Physiotherapy V’s Aerobic exercise V’s Combined (physiotherapy and aerobic exercise)

2.2.4 Resistance Exercise

2.2.5 Other (Yoga, LTBWST, Rhythmic Auditory Stimulation)

2.3 Discussion

2.4 Conclusions

Chapter 3 Factors that affect outcome

3.1 Introduction

3.1 The natural history/progression of MS

3.1.1 Type of MS

3.1.2 Age

3.1.3 Gender

3.2 Clinically assessed Variables

3.2.1 Sensation

3.2.2 Tone/Spasticity

3.2.3 Balance

3.3 Conclusions and Implications for post hoc analysis

Chapter 4 Outcome measures and Physiotherapy Intervention

4.0 Introduction

4.1 Outcome Measurement

4.2 Selection of outcome measures

4.2.1 Multiple Sclerosis Impact Scale 29, version 2: Justification, Description and Psychometric properties

4.2.2 Modified Fatigue Impact Scale: Justification, Description and Psychometric properties

4.2.3 Berg Balance Scale: Justification, Description and Psychometric properties
9.2.3 Statistical Analysis ............................................................... 163

9.3 Results ..................................................................................... 165
  9.3.1 Prevalence ........................................................................... 165
  9.3.2 Risk factors ......................................................................... 165
  9.3.3 Effect of intervention ........................................................... 168

9.4 Discussion ................................................................................ 171
  9.4.1 Prevalence ........................................................................... 171
  9.4.2 Risk Factors for falls ............................................................ 172
  9.4.3 Effect of intervention on falls ................................................. 174

9.5 Conclusions ............................................................................ 176

Chapter 10 Conclusion .................................................................... 178

  10.0 Introduction .......................................................................... 178
  10.1 Summary of main findings .................................................... 178
  10.2 Implications for Clinical Practice ........................................... 181
  10.3 Implications for future research ............................................ 182

References .................................................................................... 185

Appendices .................................................................................. 201
List of Tables

Table 1 Assessment of overall study validity.......................................................12
Table 2. Studies evaluating specific physiotherapy interventions.........................16
Table 3 Quality Assessment of studies evaluating specific physiotherapy interventions ......................................................................................................................18
Table 4 Studies evaluating aerobic exercise..........................................................21
Table 5 Quality Assessment of studies evaluating aerobic exercise ......................23
Table 6 Studies comparing physiotherapy, aerobic exercise and a combined treatment of physiotherapy and aerobic exercise.........................................................24
Table 7 Quality Assessment of studies comparing physiotherapy, aerobic exercise and a combined treatment of physiotherapy and aerobic exercise .......................25
Table 8 Studies evaluating resistance training ......................................................27
Table 9 Quality Assessment of studies evaluating resistance training .................28
Table 10 Studies evaluating other interventions....................................................29
Table 11 Quality Assessment of studies evaluating other interventions ..............31
Table 12 Research Ethics Committees who approved the methodology for the main study.................................................................................................................74
Table 13 Reasons for dropouts (including relapses) at week 12 and week 24 ......86
Table 14 Baseline demographics for each group..................................................88
Table 15 Baseline scores for each group for all outcome measures ....................89
Table 16 Baseline medication usage for all groups (overall number and medications for specific symptoms)..............................................................................91
Table 17 Objectively assessed impairments at baseline for all of the groups .......92
Table 18 Median number of sessions attended by participants in each group .......95
Table 19 Descriptives and Paired t-tests for MSIS-29v2 physical component..... 101

Table 20 Descriptives and Wilcoxon Signed Rank tests for MSIS-29v2 psychological component................................................................. 103

Table 21 Descriptives and paired t-tests for MFIS ................................................. 105

Table 22 Descriptives and paired t-tests for BBS.................................................. 107

Table 23 Descriptives and Wilcoxon Signed Rank tests for 6MWT...................... 109

Table 24 Descriptives and post hoc analysis for MSIS-29v2 physical component113

Table 25 Descriptives and Friedman results for MSIS-29v2 psychological component ................................................................................................. 115

Table 26 Descriptives and post hoc analysis for MFIS ........................................... 117

Table 27 Descriptives and post hoc analysis for Berg Balance Scale ................. 119

Table 28 Descriptives and Friedman test p values for six minute walk test ........ 121

Table 29 Correlation coefficients between MSIS29v2 physical component outcome scores and outcome measures, demographics and symptoms at baseline........ 124

Table 30 Correlation coefficients between BBS outcome scores and outcome measures, demographics and symptoms at baseline........................................... 125

Table 31 Results for Multiple Regression analysis (Physical component of MSIS29v2) ..................................................................................................... 127

Table 32 Results for Multiple Regression analysis (Berg Balance Scale) ........... 129

Table 33 Studies evaluating prevalence of falls in PwMS................................. 160

Table 34 Characteristics of fallers and non fallers ............................................ 166

Table 35 Logistic regression results predicting likelihood of falling ............... 168

Table 36 Number of fallers, falls and p values for group physiotherapy, 1:1 physiotherapy, yoga and the control group ..................................................... 170
List of Figures

Figure 1 Flow chart of literature search for interventions for PwMS with an EDSS score of >6. ................................................................. 13

Figure 2 Sketchings of the group physiotherapy exercises used in information booklets ............................................................ 59

Figure 3 Scores before and after the intervention for the physical component of the MSIS-29 ................................................................. 65

Figure 4 Scores before and after the intervention for the psychological component of the MSIS-2 ................................................................. 66

Figure 5 Scores before and after the intervention for the MFIS ................................................................. 66

Figure 6 Scores before and after the intervention for the Berg Balance Scale .............. 67

Figure 7 Distance in metres (m) over 2 minutes before and after the intervention . 68

Figure 8 Scores on the DGI before and after the intervention ............................. 68

Figure 9 Participant Flow Chart .................................................................. 85

Figure 10 Number of participants reporting each problem ..................................... 94

Figure 11 Breakdown of sessions attended by participants in each of the groups ... 95

Figure 12 Mean MSIS29v2 physical component scores at week 1 and week 12 .. 101

Figure 13 Boxplot showing the MSIS29v2 psychological component scores at week 1 and week 12 ................................................................. 103

Figure 14 Mean MFIS scores at week 1 and week 12 ........................................ 105

Figure 15 Mean BBS scores at week 1 and week 12 ........................................... 106

Figure 16 Boxplot showing the 6MWT distance scores at week 1 and week 12 ... 108

Figure 17 Mean MSIS29v2 physical component scores at week 1, week 12 and week 24 ........................................................................ 112
Figure 18 Boxplot showing the MSIS29 psychological component scores at week 1, week 12 and week 24 ................................................... 114

Figure 19 Mean MFIS scores at week 1, week 12 and week 24 ....................... 116

Figure 20 Mean BBS scores at week 1, week 12 and week 24 ......................... 118

Figure 21 Boxplot showing the 6MWT distance scores at week 1, week 12 and week 24 ................................................................. 120
Chapter 1 Introduction

1.0 Outline of chapter

The aim of this introductory chapter is to provide an outline of the thesis. Multiple Sclerosis will be described in terms of its pathophysiology, epidemiology, consequences and treatment. The content of each chapter is also summarised briefly.

1.1 Multiple Sclerosis

Multiple sclerosis (MS) is a chronic debilitating disease of the central nervous system (CNS). It is characterised by the two simultaneous processes, inflammation leading to demyelination and degeneration of neuronal axons, resulting in the disruption of axon potentials in the brain and spinal cord (Compston and Coles, 2008). Depending on the area of the CNS affected MS can cause a multitude of motor, sensory, visual, psychological, sexual, and bladder and bowel symptoms.

Lublin and Reingold (1996) described four main types of MS, Relapsing Remitting MS (RRMS), Secondary Progressive MS (SPMS), Primary Progressive MS (PPMS) and Progressive Relapsing MS (PRMS). RRMS has a clearly defined disease course that includes relapses with full recovery or with residual deficits and there is a lack of disease progression during the period between relapses. SPPM has an initial relapsing-remitting disease course followed by progression with or without occasional relapses, minor remissions or plateaus. PPMS results in disease progression from onset with occasional plateaus and temporary minor improvements may be observed. PRMS has a progressive disease course from onset, with clear acute relapses, recovery may be complete or partial.

People with Multiple Sclerosis (PwMS) may experience difficulties with balance and mobility, fatigue, muscle weakness, spasticity, impaired sensation, altered
vision, cognitive difficulties and incontinence. The varying distribution of demyelination and degeneration throughout the CNS means that the symptoms experienced by PwMS can differ greatly for each individual and also over time (Compston, 2004). Typical onset of MS is during young adulthood and mortality rates are only slightly higher than those observed in the general population (Ragonese et al., 2008). Although the cause of MS remains unknown it is thought that a combination of immune, genetic and environmental factors result in the complex pathogenesis of the disease (Compston and Coles, 2008).

1.2 Epidemiology of MS

Europe has the highest estimated prevalence of MS in the world at 80 per 100,000 (Dua et al., 2008). The prevalence of MS varies across different geographical regions in the world. High prevalence rates have been identified in different areas in the Republic of Ireland. McGuigan et al, (2004) estimated prevalence rates of 120 per 100,000 in the south east of the country and 185 per 100,000 in the north west of the country.

The mean age at onset of MS is between 29 and 33 while the range of age at onset is broad and varies from 10 to 59 years of age (Dua et al., 2008). More women than men are affected by MS. The global female: male ratio is estimated at 3:1 (Dua et al., 2008). Recent evidence (Ramagopalan et al., 2010) suggests that the female: male ratio is increasing due to an increase in the numbers of female RR patients over time.

1.3 Consequences of MS

MS is a progressive disease that can lead to severe disability, functional limitations and a poor quality of life (QoL). PwMS have a near normal life expectancy, the median time to death from onset has been suggested as approximately 30 years, representing a reduction in life expectancy of between 5 and 10 years (Bronnum-
Hansen et al., 2004). Therefore, PwMS may have to live for many years with severe mobility problems and have a need for regular therapeutic intervention. Despite this PwMS have problems accessing health care (Benito-Leon et al., 2003). An Irish profiling study revealed that PwMS received on average three hours physiotherapy over a three month period (Coote et al., 2010) with 36% of participants receiving one hour or less and 9.5% of participants receiving more than 8 hours of treatment.

It is suggested that within 15 – 25 years of diagnosis approximately 50% of PwMS will require the use of a walking aid (Confavreux et al., 2003, Tremlett et al., 2006) and PwMS identify the continued loss of mobility as one of their greatest concerns for their future (Finlayson, 2004). This not only increases a person’s risk of falling but also has a socioeconomic effect. Naci et al (2010) conducted a review of the economic burden of MS and observed that as disease severity (as measured on the EDSS) increased there was a significant increase in costs associated with the care of that person. It has also been reported that even minor mobility impairment appeared to contribute to loss of productivity and income (Salter et al., 2009).

One of the most commonly reported symptoms in PwMS is loss of balance (Bakshi, 2003, Peterson et al., 2007a). Balance problems along with other symptoms of MS challenge a person’s physical mobility and their ability to ambulate safely in their community or at home, therefore, increase their risk of falling (Cattaneo et al., 2002). Recent literature has highlighted the high prevalence of falls in PwMS (Finlayson and Peterson, 2006, Peterson et al., 2007a). The cost of a fall to an individual with MS and to health services across the globe is significant. Consequences of a fall for that individual can include injuries, hip fractures being one of the most common, decreased confidence and increased fear of falling and a decrease in activity levels and social participation. The average cost of a hospitalisation for a falls related injury in North America was $17,500 in 2004 (Roudsari et al., 2005)
It is evident that mobility impairment, balance deficits and falls are a significant problem, both in terms of personal impact for PwMS and cost to health services, but access to services is limited in Ireland. This highlights the need for increased, more effective service provision for PwMS in this country.

1.4 Treatment of MS

There is currently no cure for MS and as previously described PwMS may experience a decrease in physical functioning and a worsening of symptoms over time. Physiotherapy plays an important role in the management of symptoms in MS but the specific outcome of these treatments on PwMS with moderate to severe mobility impairment has not been evaluated to date.

Exercise has been shown to be a beneficial treatment option for PwMS with minimal gait impairment. Interventions in the form of regular cardiovascular and strengthening exercise programmes have demonstrated significant improvements for PwMS (Rietberg et al., 2004, Motl and Gosney, 2008). Improvements have been observed in disease symptoms, general fitness and QoL. A recent review has been published highlighting the effect of exercise therapy in improving fatigue in PwMS with minimal gait impairment (Andreasen et al., 2011). The effectiveness of exercise as an intervention for people with more severe mobility impairment is not known as this research is focused mainly on PwMS who are more mobile (EDSS<6).

Very little is known about how this specific population of PwMS with moderate to severe mobility impairment respond to physiotherapy and exercise interventions. This research aims to add to the evidence base available surrounding this population of PwMS by evaluating the efficacy of three community based treatment options.
1.5 Background to research project

This research was conducted as part of the Getting the Balance Right Project (GTBR). The GTBR project was a collaboration between the Physiotherapy Department in the University of Limerick (UL) and Multiple Sclerosis Ireland (MSI). MSI has 5,000 members with MS, and it is estimated that there are up to 8,000 people with a diagnosis of MS in the Republic of Ireland. Research recently undertaken by MSI with its members clearly highlighted that physiotherapy and exercise related programmes were their top priority (Lansdowne Market Research Project, 2005) in terms of services required and not widely available either through the HSE or from MSI currently. The GTBR project was set up in response to this and aimed to both deliver and evaluate physiotherapy and exercise interventions for people with MS in Ireland.

The GTBR project stratified PwMS according to their mobility level and how much assistance they needed when mobilising. PwMS were stratified to one of three strands. Strand A concerned individuals who are ambulatory, Strand B concerned individuals who required significant assistance to walk and Strand C concerned individuals who were non-ambulatory. This thesis deals with Strand B - PwMS who mobilise with at least bilateral assistance (rollator, two sticks/crutches).
1.6 Aims and objectives

The overall aim of this research was to provide MSI with the information to inform their provision of services by evaluating the efficacy of three community based interventions in PwMS with moderate to severe mobility impairment.

The specific objectives of this thesis are:

- To review the available literature surrounding interventions for PwMS with moderate to severe mobility impairment and the possible factors that may influence the outcome of an intervention
- To detail the methodology used to evaluate and compare group physiotherapy, which consisted of circuit style class of balance and strength exercises, individual physiotherapy and yoga in a community based setting.
- To establish the effects of the above interventions immediately after their completion
- To investigate the maintenance of these effects three months after the completion of the interventions
- To explore signs and symptoms that may be associated with outcome after the intervention period
- To review the literature surrounding falls in PwMS and establish the effect of the above interventions on falls and to describe the prevalence rates and risk factors for falling in this cohort of PwMS
Chapter 2 presents a review of the available literature surrounding physiotherapy and exercise interventions in PwMS with moderate to severe mobility impairment. A multitude of different interventions were evaluated and the results of the included studies suggested possible beneficial effects. These studies, however, included PwMS of varying mobility levels and the effect of the interventions specifically on PwMS with more significant mobility impairment could not be established. The studies included had a moderate to high risk of bias due to methodological weaknesses.

A further exploration of the literature surrounding variables that may influence the outcome of an intervention in this population of PwMS is presented in Chapter 3. A pilot study and a main study were conducted. The outcome measures and group physiotherapy intervention were common to both studies and are presented in Chapter 4. Chapter 5 describes the methodology, results and recommendations of the pilot study. The main study methodology is described in detail in Chapter 6.

The main study results are presented in Chapter 7 of this document. These include the results surrounding the effects of the interventions, the maintenance of these effects at follow up and the results of a post hoc analysis to identify factors that may influence outcome. A detailed demographic profile of the participants is also included in this chapter.

The main findings of the study are discussed in relation to other literature and in terms of their clinical significance in Chapter 8. The limitations to the research are also detailed here.
Chapter 9 includes a review of the literature regarding falls in PwMS. Due to interesting results observed for balance a secondary analysis was performed evaluating the prevalence of falls in the total cohort of participants in this study along with the risk factors associated with falling and the effect of the above interventions on number of falls and fallers.

The main conclusions of this research and the implications for clinical practice, health service delivery and future research are presented together in Chapter 10. The dissemination of the results, in terms of publications and conference presentations can be seen in the Appendix A.

This research is novel in many ways. It is the first known randomised controlled trial evaluating community based interventions specifically in PwMS with moderate to severe mobility impairment. It adds to the limited knowledge base available on the treatment of this population and provides new information on how PwMS with respond to physiotherapy interventions and yoga. It is the first study in an MS population to compare the effects of group physiotherapy and individual physiotherapy. This is important for health service delivery at present due to budgetary restraints in all aspects of health care. This research looks at the effect of the interventions at follow up, which to date only 3 studies have addressed. This is important information relevant to all clinicians and service providers involved in the management of MS as it is a chronic and progressive condition. In addition, it is also the first study to explore the efficacy of physiotherapy and yoga intervention on outcome at participation, activity and impairment level.
Chapter 2 Physiotherapy and exercise interventions for People with Multiple Sclerosis with moderate to severe mobility impairment – A review of the literature

2.0 Introduction

In recent years it has been established that exercise interventions in the form of regular cardiovascular and strengthening exercise programmes have been very beneficial for PwMS (Rietberg et al., 2004) with meta analyses suggesting that exercise has a positive influence on both quality of life (QoL) (Motl and Gosney, 2008) and mobility (Snook and Motl, 2009). Improvements have been seen in disease symptoms, general fitness and fatigue. However, this research is focused mainly on PwMS who are more mobile (EDSS < 6) and the consensus on the effect of exercise interventions on people who are more severely disabled remains unclear. There are, however, no current recommendations or reviews looking solely at interventions for PwMS who have moderate to severe mobility problems (EDSS > 6). Thus, the aim of this literature review is to review current quantitative literature published evaluating all types of physical interventions for PwMS who mobilise with assistive devices (EDSS > 6) in order to identify possible treatment options for this population.

The specific objectives of this review are to identify possible treatment options for PwMS with moderate to severe mobility limitations, to describe the interventions and outcome measures used, discuss the results and assess the quality of the studies using the Cochrane tool for evaluating trials. It is the first known review to be conducted in this area.
2.1 Methodology

2.1.1 Search Strategy

The following electronic databases were searched for studies that looked at physical or exercise interventions for people with moderate to severe MS (EDSS > 6); Amed, Biomedical References Collection: Expanded, Nursing Allied Health Collection: Basic, Embase, Cinahl, Medline, PsychINFO, SPORTdiscus. The key words used to develop the search strategy for the databases included multiple sclerosis, MS, exercise, physiotherapy, physical therapy, rehabilitation. Different combinations of all these terms were used to source the articles. In addition to the electronic search the reference lists of relevant articles were checked for further articles. One reviewer performed the article search, selected the relevant articles and performed the quality assessment of the studies.

2.1.2 Inclusion and exclusion criteria

The titles of the articles were screened and potentially relevant articles were retrieved for full-text assessment. Articles were included in this review if they incorporated participants with an EDSS of greater than 6. If a person has an EDSS score of greater than 6 it means the person needs constant bilateral support to walk 20 metres. If disability rating was not reported studies were included if some or all of the participants used a walking aid. Studies were excluded if all participants’ EDSS scores were less than 6. Only quantitative studies were included in this review. The participants in the trials all had a definite diagnosis of MS and did not recently experience a relapse or exacerbation (time from relapse varied from 1 to 6 months). Non English language studies were also excluded.
2.2.3 Assessment of Study Quality

The quality of the studies was assessed using the recommendations from The Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2008). This involved rating the validity of each study using criteria regarding four categories of systematic errors – selection bias, performance bias, attrition bias and detection bias.

Selection bias refers to any systematic differences in comparison groups; not randomising participants adequately can lead to selection bias. Performance bias refers to any systematic differences in the care provided to each group apart from the intervention being evaluated, therefore, duration and frequency of treatments should be consistent across treatment groups to prevent performance bias. Attrition bias refers to any systematic differences in withdrawals from the trial, therefore, all dropouts and the reasons for these dropouts should be clearly reported and explained to prevent attrition bias. Detection bias refers to any systematic differences in outcome assessment. Non–blinded assessment of outcomes of intervention may lead to detection bias. These biases can seriously affect the validity of the results.

In this review each of the studies was rated for each of the four categories. The studies met, didn’t meet or partly met the criteria. When all of the criteria are met there is a low risk of bias and this is unlikely to affect the validity of the results. When one or more of the criteria are partly met there is a moderate risk of bias and there may be some doubt about the results. Finally when one or more criteria are not met then there is a high risk of bias and this can seriously affect the validity of the results. This is summarised in Table 1. (Higgins and Green, 2008). By including all studies regardless of quality, and guiding the reader as to the level of validity, this review aims to present the evidence to date which cumulatively may be of use in clinical decision making.
Table 1 Assessment of overall study validity

<table>
<thead>
<tr>
<th>Risk of bias</th>
<th>Interpretation</th>
<th>Relationship to individual criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk of bias</td>
<td>Plausible bias unlikely to seriously alter the results</td>
<td>All of the criteria met</td>
</tr>
<tr>
<td>Moderate risk of bias</td>
<td>Plausible bias that raises some doubt about the results</td>
<td>One or more criteria partly met</td>
</tr>
<tr>
<td>High risk of bias</td>
<td>Plausible bias that seriously weakens confidence in the results</td>
<td>One or more criteria not met</td>
</tr>
</tbody>
</table>

2.2 Results

A total of 183 articles were retrieved from the electronic search (see Figure 1 for flow chart of literature search). A total of 14 studies fulfilled the inclusion criteria and were included in this review. These included different physical interventions; specific physiotherapy treatments and balance interventions (n =4), resistance exercises (n=2), aerobic exercise (n =4), and others (n=4) such as yoga, treadmill training with body weight support and rhythmical auditory stimulation. Each of these interventions will be discussed separately in the following sections.
Figure 1 Flow chart of literature search for interventions for PwMS with an EDSS score of >6.

Articles generated by search
\( (n = 183) \)

Studies excluded (non experimental design, non-English language)
\( (n = 127) \)

Studies retrieved for more detailed evaluation
\( (n = 56) \)

Studies excluded if participants included had EDSS of <6
\( (n = 42) \)

Studies included in review
\( (n = 14) \)
2.2.1 Specific physiotherapy interventions

Table 1 summarises four studies that looked at specific physiotherapy treatments for PwMS with mobility problems (Cattaneo et al., 2007b, Smedal et al., 2006, Wiles et al., 2001, Lord et al., 1998). The level of mobility of the participants was consistent for the studies with some or all of the participants using a walking aid. The type of aids was not described except in the study by Smedal et al (2006) where both subjects used unilateral assistance.

The interventions mainly focused on improving balance and mobility. This is evident from the outcome measures used with all four studies using different measures of mobility and similar measures of balance. Three out of the four studies used the Berg Balance Scale (BBS) and it showed some significant improvements in all three studies (Cattaneo et al., 2007b, Smedal et al., 2006, Lord et al., 1998). This suggests the BBS is sensitive to change when evaluating a physiotherapy treatment in PwMS with mobility problems. The variety of mobility measures used was much greater and so were the results observed. This could be due to the different treatment techniques used or because some outcome measures used were more responsive to change.

Lord et al, (1998) compared two different treatment approaches. A task orientated (disability based) approach was compared to an approach using facilitation techniques (impairment based). Significant improvements were seen for both groups in all outcome measures except walking time in the facilitation based groups but no significant difference were seen between the groups. Wiles et al, (2001) had similar findings when a facilitation based intervention was compared with a more functional task orientated intervention. There was improvements seen in both groups post treatment but no difference between groups suggesting that the type of treatment does not affect the results and all physiotherapy input was beneficial.
In contrast to this Cattaneo et al (2007b) found that when two different types of balance rehabilitation programmes, one based on motor strategies and one based on sensory strategies, were compared with conventional physiotherapy not specifically aimed at balance there was a significant difference between both balance groups and the conventional therapy group for the BBS. The actual change in the group aimed at motor and sensory strategies was 7 points on the BBS. This was slightly lower, 4 points, for the group aimed at motor strategies alone. The exact content of the conventional therapy, however, was not reported decreasing the external validity of this result. This evidence suggests that there is a need for specificity of training e.g. specific balance exercises to improve balance.

Although these results are mostly positive there are some other factors that need to be considered. Table 3 shows that the studies have a moderate or a high risk of bias, questioning the validity of the results. All the studies had small sample sizes, two had no control group and in all but one of the studies the type of mobility aid used by participants is unknown, therefore, decreasing the extent to which the results can be generalised. It should be noted that all physiotherapy treatments were well tolerated by the participants and did not have any negative effects.
<table>
<thead>
<tr>
<th>Study Design</th>
<th>Sample (mobility)</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattaneo et al 2007</td>
<td>RCT</td>
<td>n = 44 EDSS not reported (15 used walking aid)</td>
<td>Group 1: Balance rehabilitation (motor and sensory strategies), Group 2: Balance rehabilitation (motor strategies), Group 3: Conventional therapy</td>
<td>10 or 12 sessions, 45 mins over 3 weeks</td>
</tr>
<tr>
<td>Smedal et al 2006</td>
<td>Single-subject experimental study design with ABAA phases</td>
<td>n = 2 EDSS 6 both used walking aids</td>
<td>One on one physiotherapy based on the Bobath concept for 4 3 week periods</td>
<td>BBS, Gait parameters using GAITRite, TUG, RVGA, VAS for perceived gait problems, RMI, PGIC</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Sample Size</td>
<td>EDSS</td>
<td>Treatment</td>
</tr>
<tr>
<td>-------</td>
<td>--------</td>
<td>-------------</td>
<td>------</td>
<td>-----------</td>
</tr>
<tr>
<td>Wiles et al 2002</td>
<td>Randomised Controlled Crossover Trial</td>
<td>n = 42</td>
<td>EDSS not reported</td>
<td>3 week therapy periods 1. at home 2. at hospital 3. no therapy</td>
</tr>
<tr>
<td>Lord et al 1998</td>
<td>Pilot Randomised Comparison Study</td>
<td>n = 23</td>
<td>EDSS not reported</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection Bias</th>
<th>Performance Bias</th>
<th>Attrition Bias</th>
<th>Detection Bias</th>
<th>Overall risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattaneo et al 2007</td>
<td>Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Moderate</td>
</tr>
<tr>
<td>Smedal et al 2006</td>
<td>Not Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>Wiles et al 2002</td>
<td>Met</td>
<td>Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Moderate</td>
</tr>
<tr>
<td>Lord et al 1998</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
</tbody>
</table>
2.2.2 Aerobic Exercise

Four studies, depicted in table 4, evaluated aerobic exercise in PwMS with an EDSS score of up to 6.5 (Van den Berg et al., 2007, Mostert and Kesselring, 2002, Rodgers et al., 1999, Sosnoff et al., 2009). The EDSS score was not reported in one study (Van den Berg et al., 2007) but it was stated that 14 out of the 16 participants used a walking aid, however, the exact type of walking aid was not disclosed. The aerobic exercise was in the form of bicycle ergometry (Mostert and Kesselring, 2002, Rodgers et al., 1999, Sosnoff et al., 2009) and treadmill training (Van den Berg et al., 2007) The frequency and duration of the interventions varied from 4 weeks (Van den Berg et al., 2007, Mostert and Kesselring, 2002, Sosnoff et al., 2009) to 6 months (Rodgers et al., 1999). It cannot be determined if the length or frequency of the intervention correlated with the results as the outcome measures used were largely variable.

Fatigue was assessed in two of the studies using the FSS which showed no significant improvement in either study (Van den Berg et al., 2007, Mostert and Kesselring, 2002). This might be because the FSS may not be sensitive to change in this population or that the treatment had no effect on fatigue. There was a greater absolute change observed (-4.5) observed in the study by Van den Berg et al, (2007) than that observed in the study by Mostert and Kesselring (2002). This may be due to the differences in content and intensity of the aerobic interventions. FSS scores decreased more following three weekly half hour sessions of treadmill training than those observed following five weekly half hour sessions of cycle ergometry. This suggests that allowing time for muscle recovery may be an important component of aerobic interventions aiming to reduce fatigue in PwMS. Sosnoff et al (2009) evaluated the effects of unloaded leg cycling on spasticity in 22 PwMS and similarly to Mostert and Kesselring (2002) no improvements were observed using the Ashworth Scale. These studies suggest that aerobic exercise can improve health related quality of life, is well tolerated by PwMS, does not have an effect on gait parameters with the outcome measures used, and its effect on spasticity remains unknown. This may be due to the outcomes used and not because the intervention had no effect. There are, however, limitations to the studies which
include small sample sizes, the training protocols are not clearly defined and the training intensities are not well controlled and one of the studies does not include a control group. All the studies also have a high risk of bias seriously weakening the validity of the results (Table. 5)

2.2.3 Physiotherapy V’s Aerobic exercise V’s Combined (physiotherapy and aerobic exercise)

The results of the study described in Table 6 show that the three intervention groups improved their fatigue scores in comparison to the control group (Rasova et al., 2006b). All three intervention groups received twice weekly treatment sessions for two months. The control group did not change their current habits. The physiotherapy based intervention had a greater impact on neurological impairment (EDSS) whereas the aerobic exercise had a greater impact on spirometric properties. The number of participants using walking aids or the type of walking aid used was not disclosed, therefore affecting the amount to which the results can be generalised. The study also has some methodological weaknesses, there was no randomisation and the control group was significantly smaller to begin with. The study also has a high risk of bias (Table 7).
Table 4 Studies evaluating aerobic exercise

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample (mobility/disability)</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sosnoff et al 2009</td>
<td>Pilot Study</td>
<td>n = 22  mean EDSS = 3.5 ±1.7</td>
<td>Exercise Group unloaded leg cycling for 4 weeks x 3 30 mins sessions</td>
<td>MAS, H-Reflex, MSSS-88</td>
<td>Reduction in perception of spasticity (MSSS-88) No reduction in electrophysiological (H-Reflex) or clinical (MAS) measures of spasticity</td>
</tr>
<tr>
<td>Van den Berg et al 2006</td>
<td>Randomised Crossover Trial</td>
<td>n = 16  EDSS not reported (14 used a walking aid)</td>
<td>Group 1 (immediate) weeks 3-6 Group 2 (delayed) weeks 8-11. Supervised treadmill training x 3 a week (increased to a max 30 mins as tolerated @ 55-85% of APMHR with max 3 rest periods)</td>
<td>2 min walk, 10 m timed walk, Rivermead Mobility Index, Fatigue Severity Scale, @ baseline, 7 &amp; 12 weeks</td>
<td>significant ↑ in speed in the trained group compared to untrained at crossover time (p&gt;0.05) non significant increase in endurance. FSS-non significant change. No changes in overall disability-GNDS</td>
</tr>
<tr>
<td>Study</td>
<td>Design</td>
<td>Participants</td>
<td>Interventions</td>
<td>Outcomes</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>---------------------------------</td>
<td>--------------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
</tbody>
</table>
| Mostert & Kesselring  | RCT                             | n = 26       | **Exercise Group:** 5 x 30 min sessions a week-bike (individualised intensity)  
**Non-exercise Group:** normal rehab program  
**Non MS controls** (4 weeks) | FSS-no significant difference in any of the groups, SF-36-significant improvement in MS exercise groups in vitality and social functioning index, no significant changes in MS non intervention group. No significant improvement in VO2 max |
| & 2002                |                                 | EDSS 1 - 6.5 | Mean = 4.6 (±1.9)                                                                                                                                                                                                  |                                                                                                                                                           |
|                       |                                 |              |                                                                                                           |                                                                                                                                                           |
| Rodgers et al 1999   | Experimental group Design       | n = 18       | **Exercise Group:** 3 x/week for 30 mins @ 60% of age predicted max HR 24 weeks duration  
**PROM LL, gait analysis using video based 3-D motion measurement, VO2 max, EDSS** | APHRM – Age predicted heart rate max, FSS – Fatigue severity scale, GNDS – Guy’s Neurological Disability Scale, RCT – Randomised controlled trial, PROM LL – Passive range of movement lower limb, EDSS – Expanded Disability Status Scale, FVC – Forced vital capacity, FEV1 – forced expiratory volume in 1 second, HR – Heart rate |
|                       |                                 | EDSS 1 - 6.5 | Mean = 3.8 (±2.2)  
8 used walking aid                                                                                                                                                                                   |                                                                                                                                                           |
<p>| | | | | |
|                       |                                 |              |                                                                                                           |                                                                                                                                                           |</p>
<table>
<thead>
<tr>
<th></th>
<th>Selection Bias</th>
<th>Performance Bias</th>
<th>Attrition Bias</th>
<th>Detection Bias</th>
<th>Overall risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sosnoff et al 2009</td>
<td>Not Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>Van den Berg et al 2006</td>
<td>Met</td>
<td>Partly Met</td>
<td>Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>Mostert and Kesselring 2002</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Not Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>Rodgers et al 1999</td>
<td>Met</td>
<td>Partly Met</td>
<td>Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
</tbody>
</table>
### Table 6 Studies comparing physiotherapy, aerobic exercise and a combined treatment of physiotherapy and aerobic exercise

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample (mobility/disability)</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rasova et al 2006</td>
<td>Controlled trial</td>
<td>n=112 EDSS = 1.0 - 6.5</td>
<td><strong>Group 1</strong>: neurophysiologically based physiotherapy, <strong>Group 2</strong>: bicycle ergometer-intensity and length of load individualised, <strong>Group 3</strong>: mix of 1 and 2, <strong>Group 4</strong>: no change to their current habits. All groups twice weekly for 2 months</td>
<td>EDSS, Barthel Index, Environment Status Scale, MS QoL, MFIS, Back Depression Inventory Scale, respiratory function and physical fitness</td>
<td>improvements in fatigue, depression &amp; spirometric &amp; spiroergonomic parameters in groups 1, 2 and 3, significant impairment (EDSS) improvements in groups 1 &amp; 3 not in 2 &amp; 4</td>
</tr>
</tbody>
</table>

EDSS – Expanded disability status scale, MS Qol – Multiple Sclerosis quality of life questionnaire, MFIS – Modified fatigue impact scale
Table 7 Quality Assessment of studies comparing physiotherapy, aerobic exercise and a combined treatment of physiotherapy and aerobic exercise

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection Bias</th>
<th>Performance Bias</th>
<th>Attrition Bias</th>
<th>Detection Bias</th>
<th>Overall risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rasova et al 2006</td>
<td>Not Met</td>
<td>Met</td>
<td>Not Met</td>
<td>Met</td>
<td>High</td>
</tr>
</tbody>
</table>

### 2.2.4 Resistance Exercise

Three studies looked at resistance exercises in this population of PwMS (Harvey et al., 1999, DeBolt and McCubbin, 2004, Filipi et al., 2010). An RCT by De Bolt and McCubbin (2004) examined the differences between a non exercise group and a group who performed an 8 week home based resistance programme, Harvey et al (1999) compared the differences between resistance exercises, mobility exercises and no exercise and Filipi et al (2010) investigated the effect of resistance training using stationary machines, dumbbells and Swiss balls on balance and gait in 33 PwMS.

The studies looked at different types of resistance exercises. Harvey et al (1999) used progressive weighted knee extensions in sitting, similarly, Filipi et al (2010) evaluated progressive resistance exercises using stationary machines and dumbbells whereas, DeBolt and McCubbin (2004) used a more functional approach with task orientated strength exercises which were also progressive e.g. sit to stands and stepping. All studies concentrated on lower limb strengthening which is probably due to the clinical observation of a more marked decrease in strength in the lower limbs as opposed to the upper limbs in PwMS.

DeBolt and McCubbin (2004) reported that leg extensor power increased by 37% but this improvement did not carryover to the functional measures and there was no significant improvement in either balance or transfers. In contrast to this, transfer speed increased by 23% in the study by Harvey et al (1999) and there was no significant improvement in knee extensor power. This could be due to the small
sample size in the strengthening group (n = 8) or because the exercises being performed were not functionally specific. Filipi et al (2010) demonstrated improvements in memory and concentration which were not assessed in the other studies. The results of this study need to be interpreted with caution as there was no control comparison, the sample was not randomised, the assessors were not blind to the participants’ intervention and all of the results were not reported.

The level of disability of the participants must be considered when evaluating these results. There was a huge variety of EDSS scores (1.0 – 6.5) in the De Bolt and McCubbin (2004) study and the study by Filipi et al (2010). This meant that people who had no disability and people who used constant bilateral support were given the same intervention. This could have affected the results as the needs of these two types of people would vary greatly. It is also not known which of them benefited more from the intervention. Eleven people used a walking stick in the study by Harvey et al (2009) none used bilateral support. No conclusions can be drawn from this evidence in relation to the use of resistance exercises in PwMS with more severe mobility problems (bilateral support). There is, however, a suggestion that it may be beneficial for PwMS who are more mobile. These studies also have a high risk of bias (Table 9) suggesting the results may not be valid.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample (mobility/disability)</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filipi et al 2010</td>
<td>Experimental Study Design</td>
<td>n = 33 EDSS = 1.0 – 6.5</td>
<td>Twice weekly resistance exercise sessions for 6 months, 50 mins duration</td>
<td>MFES, MFIS, BBS, TUG, MSFC, NeuroCom Balance Master, 3D Gait analysis</td>
<td>No improvement in speed of walking. Significant improvement of hip and knee extensors. Improved concentration (PASAT) and decreased fatigue (MFIS)</td>
</tr>
<tr>
<td>DeBolt and McCubbin 2004</td>
<td>RCT</td>
<td>n = 37 EDSS = 1.0 – 6.5</td>
<td>8 wk home based resistance training 1. 5-10 m warm-up, 2. 25-30 m exs, 3. 5-10 whole body stretching</td>
<td>Balance-AP sway, ML sway &amp; sway speed using Accusway⁺, Modified Ashworth Scale, Leg extensor power rig, Up and Go test</td>
<td>No significant changes for balance, Up and Go test or spasticity. Leg extensor power ↑37% in treatment group</td>
</tr>
</tbody>
</table>
Harvey et al 1999 RCT  

- **Group A**: no exercise  
- **Group B**: mobility and balance exercises x1 a day  
- **Group C**: weighted leg exercise (seated leg extensions through angle of 45°) 5 sets of 10 x2 a day  

Pulse rate & timed 10m walk, EMG & MVC of quadriceps, timed transfer (modified up & go test)  


Table 9 Quality Assessment of studies evaluating resistance training

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection Bias</th>
<th>Performance Bias</th>
<th>Attrition Bias</th>
<th>Detection Bias</th>
<th>Overall risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filipi et al 2010</td>
<td>Not Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>DeBolt and McCubbin 2004</td>
<td>Met</td>
<td>Not Met</td>
<td>Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>Harvey et al 1999</td>
<td>Met</td>
<td>Partly Met</td>
<td>Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
</tbody>
</table>
### Table 10 Studies evaluating other interventions

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Sample (mobility/disability)</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Main Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oken et al 2004</td>
<td>RCT</td>
<td>n= 69 mean EDSS = 3.1 (± 2.1)</td>
<td>Iyangar Yoga 90-m x1 a week Aerobic Exercise 90-m x1 a week, HEP, bicycling on stationary bicycles (2-3 0n Borg RPE) Waiting list control 6 months</td>
<td>Stroop Colour-Word Interference, EEG Median Power Frequency, SF-36 Health Survey, MFI, POMS CESD-10, STAI, SSS</td>
<td>no significant diff in primary outcome measures, improvements for both treatment groups for fatigue</td>
</tr>
</tbody>
</table>
### Conklyn et al 2010
**Exploratory pilot design**

- **n = 10** EDSS not reported (3 used 1 WS, 1 used 2 WS, 6 used a rollator) PPMS
- **Group 1** - 4 weeks, home based walking programme with rhythmic auditory stimulation
- **Group 2** - 2 weeks control, 2 weeks of above treatment
- GAITRite system, Timed 25-Foot Walk Test, MAS, MMT, NPRS, PDDS
- Statistically significant improvements in gait parameters after treatment. No statistically significant changes in MAS, MMT NPRS or PDDS.

### Pilutti et al 2011
**Pre and Post experimental design**

- **n = 6** mean EDSS = 6.9 (±1.7)
- **BWSTT** - 12 weeks x 1 a week for 30 minutes
- EDSS, MSFC, MSQoL, MFIS
- No change on EDSS, improvements on MSFC, statistically significant improvements on MSQoL, non significant improvements on MFIS.

Table 11 Quality Assessment of studies evaluating other interventions

<table>
<thead>
<tr>
<th>Study</th>
<th>Selection Bias</th>
<th>Performance Bias</th>
<th>Attrition Bias</th>
<th>Detection Bias</th>
<th>Overall risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giesser et al 2007</td>
<td>Met</td>
<td>Met</td>
<td>Partly Met</td>
<td>Not Met</td>
<td>High</td>
</tr>
<tr>
<td>Oken et al 2004</td>
<td>Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Met</td>
<td>Moderate</td>
</tr>
<tr>
<td>Conklyon et al 2010</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>Not Met</td>
<td>Partly Met</td>
<td>High</td>
</tr>
<tr>
<td>Pilutti et al 2011</td>
<td>Not Met</td>
<td>Met</td>
<td>Partly Met</td>
<td>Partly Met</td>
<td>High</td>
</tr>
</tbody>
</table>
2.2.5 Other (Yoga, LTBWST, Rhythmic Auditory Stimulation)

Four studies that used other interventions in this population of PwMS are described in Table 10. Yoga was compared to aerobic exercise and a waitlist control in one study (Oken et al., 2004) and LTBWST (Locomotor training with body weight support on a treadmill) was evaluated in two studies with four and six participants respectively (Giesser et al., 2007, Pilutti et al., 2011). The results were positive for LTBWST with three out of the four participants showing improvements in balance and mobility measures in the study by Giesser et al (2007). The amount of body weight support required by participants reduced over the 12 week intervention in the study by Pilutti et al (2011). They observed significant improvements for the physical and mental subscales of the MSQoL (P=0.02 and 0.01 respectively). Due to the small sample size and the fact that in one study the participants had primarily MS lesions in the spinal cord the results cannot be generalised to a larger population of PwMS. Comparisons between the results in both studies cannot be made due to the lack of similar outcomes reported.

Oken et al (2004) found that there was improvements in fatigue for both the yoga and aerobic exercise group compared to the control. There was, however, no significant difference between both treatment groups for any of the measures. The intensity at which the aerobic exercise was performed was 2 to 3 on a perceived exertion scale. This could have affected the results of this treatment group as other studies have documented exercise intensities using ratings from 11 to 14 on the Borg Rate of Perceived Exertion scale (Mostert and Kesselring, 2002). The novel approach of rhythmical auditory stimulation was evaluated in 10 PwMS by Conklyn et al (2010). There were no negative effects to this treatment. The changes observed on the outcome measures were not statistically significant but moderate to large effect sizes (0.51 – 0.89) were observed indicating the study was underpowered. There is a high and moderate risk of bias in these studies (Table 11) which could negatively affect the results.
2.3 Discussion

Results of the studies in general were positive and well tolerated by PwMS. The variety of interventions used showed that physiotherapy, aerobic exercise, resistance exercise, yoga, LTBWST all had the potential to be effective for PwMS with mobility problems.

Studies evaluating physiotherapy conveyed improvements in balance and mobility. They did not, however, assess the effect of the intervention on QoL which has been shown to be compromised in PwMS (Benito-Leon et al., 2003). Therefore, it is unknown if an improvement in function due to physiotherapy intervention can additionally cause an improvement in QoL. As MS is such a diverse and varied condition in each individual self reported QoL measures are important when evaluating MS as they may serve to alert clinicians to areas that might otherwise be overlooked. There was also a lack of consistency with the measures used to assess mobility, making it hard to determine which type of physiotherapy intervention was the most effective in evaluating mobility. The importance of a complete assessment evaluating outcome at the level of impairment of body structure and function, activity and participation is recommended by the World Health Organisation’s International Classification of Functioning (WHO-ICF, 2001).

At least 80% of PwMS report fatigue as a symptom at sometime during the course of their condition and it is described by up to 40% of PwMS as the most debilitating symptom ahead of spasticity, weakness or bladder or bowel problems (Bakshi, 2003). The majority of studies evaluating aerobic exercise showed no significant decrease in fatigue post intervention. The mechanisms of fatigue in MS may be particularly complex, therefore, making it hard to quantify and assess (Smith and Hale, 2007). These studies (Van den Berg et al., 2007, Mostert and Kesselring, 2002) used the FSS to assess fatigue, whereas, when the MFIS was used (Rasova et al., 2006a) an improvement in fatigue was observed. This could suggest that the FSS is lacking sensitivity to detect changes in the many dimensions of fatigue or that the differing content of intervention did not affect the fatigue of these participants.
Resistance exercise showed improvements in leg extensor strength but did not improve balance or mobility. Further investigation is needed to assess the relationship between strength increases and function. Other interventions (LTBWST and yoga) also showed some positive results but more research is needed in these areas if recommendations are to be made regarding their use in the treatment of PwMS.

The overall methodological quality of the studies is poor. Generally sample sizes are small and therefore the statistical power is low. Blinding and randomisation procedures are poorly reported as is the exact content of the interventions making reproducibility difficult. Meaningful comparisons between the studies are limited by these methodological weaknesses and other methodological differences such as the use of different outcome measures, populations, study designs and interventions used. All the studies in this review had a high or moderate risk of bias, therefore, affecting the validity of the results.

In all but two of the studies included in this review (Smedal et al., 2006, Giesser et al., 2007), participants of varying levels of mobility were included in the same treatment groups. PwMS with an EDSS score of 1 (no disability) and 6.5 (constant bilateral support required) were given the same intervention despite having hugely different treatment needs and there was a lack of analysis of subgroups of mobility. These two studies only contained 8 participants in total. Therefore, it is unclear from the results of this literature review which participants benefited most from the interventions used, participants that were independently mobile or participants that required bilateral assistance to walk. The optimal treatment and treatment parameters still remain unknown for PwMS with an EDSS score of >6.

There appears to be an indirect relationship between physical activity and disability in PwMS (Motl et al., 2007). Individuals who are more physically active tend to have less functional and disability limitations (Motl et al., 2007). This corresponds to the findings of this review. Even though it is unknown which intervention is best for this population a multitude of physical interventions can be beneficial and some type of physical activity should be incorporated into the treatment of a person with
MS. The multitude of interventions used in these studies reflect the complex nature of MS. Due to the variable nature of symptom presentation and mechanisms of recovery there are rationales behind the use of these different interventions. Improvements following balance and resistance training may be explained by increases in strength, which have been shown to be correlated with postural sway (Yahia et al., 2011), or by enhanced somatosensory conduction (Cameron and Lord, 2010). Aerobic exercise interventions may be beneficial for PwMS as they attend to the negative physiological profile associated with MS (Dalgas et al., 2008).

The recommendations from this review for future research are similar to those from the Cochrane Review on exercise therapy for PwMS (Rietberg et al., 2004). Methodological weaknesses, such as such as small sample sizes, lack of randomisation and blinding, and inadequate reporting of intervention protocols are still as evident in the current literature as they were in 2004. This review reiterates the need for better quality studies that have larger sample sizes, appropriate randomisation and blinding procedures, control comparisons and reproducible interventions.

The Cochrane Review also recommended that the WHO – ICF framework should be used as a basis for outcome measurement. In agreement, this review also highlights the need for outcome measures that assess the impact of disease at impairment, activity and participation levels. Some studies included in this review did not include a measure of QoL, therefore, the intervention’s effect on participation was not known. It would also be beneficial to clinicians if the use of outcome measures was more consistent across studies, allowing comparability of results.

Current research that looks at physical interventions for PwMS groups individuals of all levels of mobility together. Individuals who mobilise with bilateral assistance are given the same intervention as individuals who mobilise independently and have no gait abnormalities even though the treatment needs of these individuals would be hugely different, thus making it hard for clinicians to use the results to inform clinical practice. Research surrounding interventions and their effectiveness in PwMS is challenging because of the varying presentations of each individual
with MS. This review recommends that future research in this area should stratify PwMS according to their mobility in order to determine what intervention would be most effective when treating PwMS who have different mobility problems.

2.4 Conclusions

This review found that a collection of studies with a moderate to high level of bias suggest positive results for PwMS, but these need to be supported by larger well designed studies. As participants are not stratified according to gait ability or level of the various impairments they present with, it is still remains unknown what intervention is most suitable for which patients. The optimal type, frequency and duration of intervention for this population remains unclear and further research is needed to develop treatment recommendations for clinicians treating PwMS with moderate to severe mobility problems.

It also remains unclear how PwMS with moderate to severe mobility limitations respond to physical interventions. The evidence base for PwMS who mobilise with bilateral assistance is limited and there are no clear recommendations about the optimal interventions. Thus, the physiotherapy interventions that were to be evaluated in the current study for use by Multiple Sclerosis Ireland were developed using some of the information in this review to address outcomes that are relevant and important to this population of PwMS. The development and content of these interventions will be described in Chapter 4.
Chapter 3 Factors that affect outcome

3.1 Introduction

It is evident from previous studies evaluating physiotherapy interventions (Chapter 2) some participants improve, whereas, other participants don’t and participants with varying levels of mobility impairment or given the same treatments so it remains unknown which participants benefit from which intervention. The aim of this chapter is to explore the available literature on factors that may be responsible for the outcome of physiotherapy or exercise interventions. This information will inform a post hoc analysis which will aim to establish any factors that may be associated with a positive outcome.

In order to attempt to understand the effect of different treatments on PwMS the natural history of the disease needs to be recognized and understood. Factors that may affect the outcome of the disease over time due to the natural progression of the disease may also affect the response to an intervention. Previous studies have explored how type of MS, age and gender has affected outcome. Other factors that may influence the outcome of physiotherapy or exercise interventions include symptoms of MS that are routinely assessed by clinicians and researchers in the treatment of PwMS. These include sensation, spasticity/tone and balance.

Pharmaceutical intervention is common in the treatment of PwMS and in recent years has increased the complexity of evaluating the natural history of MS. The pharmaceutical interventions may also have an effect on disease progression and disability and, therefore, may also impact on the outcome of a physiotherapy and exercise intervention. Research evaluating drug therapy in MS predominantly focuses on Relapsing Remitting MS (RRMS) and the effect subcutaneous administration of interferon beta 1a. The aim of this drug is to decrease the rate and severity of relapses and to delay the progression of disability by prevention lesion formation in the central nervous system (CNS) (Hartung et al 2009). A recent study by Uitdehaag et al (2011) analysed the long term effects interferon beta 1a in 191
participants with RRMS and found that mean annualised relapse rates were lower for participants with long-term use of this drug. Clinical outcomes demonstrated shorter time to accumulation of an EDSS score of > 6 in the control group compared to the drug therapy group.

Recently oral medications have been researched as alternatives to subcutaneously administered medications. Oral Fingolimod has been evaluated as a treatment option for RRMS. This is a sphingosine-1-phosphate modulator that acts by preventing lymphocyte departure from lymph nodes and works on reducing the amount of infiltration of potentially auto-aggressive lymphocytes into the CNS. A study by Kappos et al (2010) found that when compared to a placebo in 1033 participants with RRMS oral Fingolimod significantly reduced the amount of disability progression (measured using EDSS) over a 24 month period.

Sustained release oral Fampridine and its effect on walking has been evaluated for use in all types of MS (Goodman et al., 2009). The proposed mechanism of action of Fampridine is that it is a voltage dependent potassium-channel blocker that improves the conduction in demyelinated pathways which is impaired in MS. Goodman et al (2009) demonstrated clinically meaningful improvements in walking (measured using the Timed 25ft walk and the Multiple Sclerosis Walking Scale 12) following 13 weeks of treatment with Fampridine compared to a placebo. Research to date suggests that pharmaceutical interventions may have an impact on disease progression, disability and walking. Further research is needed into their effect on the outcome of a rehabilitation or exercise programme and the combined effects of drug and exercise therapy.

3.1 The natural history/progression of MS

Literature exploring the natural history of MS has looked at the time taken to reach specific disability milestones as measured on the EDSS. Several studies have evaluated how type of MS, age and gender influence the time taken to arrive at these disability milestones.
3.1.1 Type of MS

MS is a complex disease with four main types as described in chapter 1, Relapsing remitting MS (RRMS), Secondary Progressive MS (SPMS), Primary Relapsing MS (PRMS) and Primary Progressive MS (PPMS).

Confavreux and Vukusic (2006) compared people with a relapsing course of MS with those who had a progressive form of the disease. They found that participants with a progressive form of the disease had a significantly shorter time from onset of MS to EDSS scores of 4 (able to walk without aid or rest for 500m), 6 (intermittent or constant unilateral assistance needed to walk 100 meters with or without rest) and 7 (unable to walk further than 5m with aid, uses wheelchair but can transfer alone). Participants with a relapsing course of MS took an average of 33.1 years to reach an EDSS score of 7, whereas, participants with a progressive course of MS took an average of 13.4 years to reach the same disability level. Similar findings were observed in other studies (Cottrell et al., 1999, Tremlett et al., 2006, Debouverie et al., 2008) where people with PPMS required the use of a walking stick and wheelchair sooner.

The literature suggests that people with RRMS may experience a more favourable disease course and people with a progressive form of the disease have a poorer outcome of disease progression. A review of the literature (Tremlett et al., 2010) found that once the progressive phase of the disease was reached, time to higher levels of disability were similar (among SPMS and PPMS) in the majority of the research. Disease progression to EDSS of 4, 6 and 10 was similar in people with SPMS and people with PPMS (Kremenchutzky et al., 2006). Confavreux and Vukusic (2006) also found that the time between assignment of EDSS 4 to EDSS 6 and 7 was similar between relapsing and progressive forms of MS.
3.1.2 Age

Natural history studies have consistently shown that a younger age at onset is associated with longer times to disability markers and that older age at onset is associated with shorter times to the acquisition of the same disability. Several studies have showed that a younger age at onset is associated with a shorter time to reach an EDSS score of 6 ((Tremlett et al., 2006, Confavreux et al., 2003).

Confavreux and Vukusic (2006) showed that people with a relapsing form of MS were significantly younger (mean age = 29.6 ±9.5) at onset than those who had a progressive form of MS (mean age = 39.3 ±11.3). Participants that had a relapsing form of MS were significantly younger at onset of EDSS scores of 4 and 6 but there was no significant difference observed for age at onset of EDSS score 7.

Recently late onset MS has become more common (Tremlett et al., 2010). Approximately 55 -80% of people diagnosed with MS over the age of 50 are diagnosed with primary progressive MS (Kis et al., 2008), which is indicative of a poorer outcome.

3.1.3 Gender

There is conflicting evidence surrounding the influence of gender on disease progression. More men have been shown to have PPMS (Confavreux and Vukusic, 2006) which has been shown to be indicative of a poorer outcome. A previous study by the same authors (Confavreux and Vukusic, 2006) found that females took significantly longer to reach disability milestones (scores of 4, 6 and 7 on the EDSS).

Female gender has been associated with a longer time to an EDSS score of 6 in other studies ((Tremlett et al., 2006, Confavreux et al., 2003). Being female has also been associated with a longer time to diagnosis of SPMS from RRMS (Koch et al., 2009). The effect of gender on outcome in people with PPMS in that study showed that gender was not associated with a longer time to an EDSS of 6.
There is considerable debate in the natural history of MS studies surrounding these factors and their influence on disease outcome and prognosis in PwMS. The literature suggests that a relapsing form of the disease, a younger age at onset and female gender are indicative of a positive outcome.

3.2 Clinically assessed Variables

Symptoms that are commonly experienced among PwMS may also affect the outcome of an intervention. Signs and symptoms that predict a positive outcome following rehabilitation have not been established in PwMS. This has been researched in Stroke populations and the available evidence will be extrapolated from these studies. Balance, sensation and tone are impairments frequently assessed in a clinical setting. Establishing if these factors are indicative of a positive outcome may help clinicians in selecting appropriate intervention options. It may also provide information regarding matching treatments with impairments. The literature surrounding the effects of, sensation, tone and balance impairment on outcome will be discussed in the following sections.

3.2.1 Sensation

The literature surrounding the incidence of sensory symptoms in PwMS is minimal. Subjectively, 10% of participants (n=24) reported altered sensation as their worst symptom, whereas, 78% of participants (n=78) were found to have abnormal vibration sensation in their toes (Rae-Grant et al., 1999). As a result of the lack of literature available specific to MS populations, evidence surrounding stroke populations was consulted due to the widespread incidence of sensory dysfunction reported in this population and due to the manifestation of sensory symptoms in the clinical presentation of both MS and Stroke. The incidence of sensory dysfunction can be as high as 85% in people following Stroke (Sullivan and Hedman, 2008).
Trojano et al (1995) found that in 60 patients with progressive MS the time taken to reach an EDSS score of 6 was negatively influenced by sensory involvement at onset (p < 0.01). Therefore, if a person had sensory symptoms at onset the time taken for them to need intermittent or constant unilateral assistance to walk 100 metres with or without rest was shorter than those with no sensory symptoms.

Tyson et al (2008) reported that tactile and proprioceptive sensation was related to mobility independence and recovery in activities of daily living in 102 participants in the acute stage following a stroke. Sensation was measured using the Rivermead Assessment of Somatosensory performance and the relationship between this and the Barthel Index (BI) and the Rivermead Mobility Index (RMI) was explored. Results revealed that the associations were statistically significant and moderate in magnitude (r = 0.515, p < 0.005 for RMI and r = 0.416, p < 0.005 for BI). In 115 stroke patients, the relationship between proprioceptive function and mobility, as measured on the RMI was explored (Welmer et al., 2007). Proprioception was measured using the Thumb Localisation Test. This test examines the position of a passively fixed thumb in relation to the body axis, as measured with motor tasks performed by the opposite reaching limb. Multivariate logistic regression analyses revealed that normal proprioception was significantly associated with better mobility according to the RMI (OR=3.4, 95% CI=1.1–10.6). A review by Sullivan and Hedman (2008) also showed that sensory loss following stroke was associated with poorer outcomes in motor capacity, functional abilities and quality of life.

This available evidence from the stroke literature suggests that participants with normal sensation may have a better outcome following a physical intervention than those with impaired sensation.
3.2.2 Tone/Spasticity

Spasticity occurs when there is an abnormal increase in muscle tone and clinically presents as muscle stiffness with increased resistance to passive movements. Spasticity can be defined as “an inappropriate, velocity dependent increase in muscle tonic stretch reflexes, caused by the amplified reactivity of motor segments to sensory input” (Hobart et al., 2006).

The incidence of spasticity in PwMS has been reported to be as high as 84%, n=413 (Rizzo et al., 2004). Of these participants 17% reported that spasticity frequently affects their activities, 13% reported that they are forced to modify their activities daily and 4% reported that spasticity prevented their activities on a daily basis. Participants with spasticity had significantly lower score on the physical component of the SF-36 than those without spasticity.

In a study of 68 PwMS 47% had clinically significant spasticity, defined as a Modified Ashworth Scale (MAS) score of 2, 3, 4, or 5 (Barnes et al., 2003). Individuals with reported spasticity were found to have significantly higher levels of disability (as measured on the EDSS) than those who had no spasticity or those who did not have clinically significant spasticity.

Ryu et al (2010) observed that motor functional gains in participants without spasticity were greater than participants with spasticity following in a stroke population. Motor function was assessed using the Functional independence measure before and after a period of multidisciplinary rehabilitation. The Modified Ashworth Scale (MAS) was used to assess spasticity.

This evidence suggests that spasticity may negatively affect the outcome of an intervention, however, previous literature has shown that repetitive exercise can reduce spasticity in a stroke population who have moderate spasticity (Diserens et al., 2007). This suggests that depending on the treatment type people with moderate spasticity may respond well to a physical intervention.
3.2.3 Balance

Balance deficits may be caused by impairments in the sensory system or motor systems or lesion of spinal cord and brain. Adequate balance depends on the integration of input from visual, somatosensory, and vestibular systems and on appropriate motor responses (Cattaneo et al., 2002). PwMS have been shown to have slowed somatosensory conduction and this presents clinically with a decreased ability to maintain an upright position and delayed responses to postural perturbations (Cameron and Lord, 2010). These impairments are common in PwMS and may affect the outcome of an exercise intervention.

Balance impairment in a population of people who had experienced a stroke was a strong predictor of function following a rehabilitation programme (Tyson et al., 2007). Better balance scores, as measured using the Brunel Balance Assessment were associated with increased recovery of activities of daily living (assessed using the BI) and mobility disability (measured using the RMI).

Balance impairment, measured objectively (Cattaneo et al., 2002) and subjectively (Nilsagard et al., 2009) has been shown to be associated with falls in PwMS. Increased balance deficits and experiences of falling may contribute to Fear of Falling (FOF) in PwMS. In a sample of 1064 PwMS, 63.5% of participants reported experiencing FOF and 83% of this group reported that they curtail their physical activities (Peterson et al., 2007b). This FOF due to balance deficits and the associated limitations in physical activity may impact on the results of a physical intervention programme.
3.3 Conclusions and Implications for post hoc analysis

Some of the factors that may affect outcome were discussed in this chapter. These included demographic factors researched in the natural history of MS studies, gender, age and type of MS, and clinically assessed variables such as, tone, sensation and balance.

The evidence suggests that gender, age and type of MS may affect outcome and will be considered as variables in the post hoc analysis. Type of MS will be categorised into either, relapsing or progressive MS as the literature suggests the most significant differences are observed between these disease courses. The effect of these factors once an EDSS score of 7 is reached is questionable but as this is an exploratory data analysis and not all participants have an EDSS score of 7 they will used in the post hoc analysis.

The evidence surrounding somatosensory functions in stroke patients highlights the specific importance of considering abnormal sensation in the evaluation of a rehabilitation program. Normal sensation, less than moderate spasticity and less balance impairment are potentially favourable clinical factors and, therefore will be considered when exploring the factors that may be associated with the outcome of the interventions used in this research.
Chapter 4 Outcome measures and Physiotherapy Intervention

4.0 Introduction

The principle aim of this research which was to provide information for MSI regarding the efficacy of community based interventions for the treatment of PwMS who mobilise with at least bilateral assistance and in order to address this aim two studies were undertaken. A small pilot study was conducted to inform a second, larger multi-centred study.

The aim of this chapter is to describe the outcome measures and the group physiotherapy intervention as these elements were common to both studies. The following two chapters will present the results of the pilot study, how these results informed the main study and describe the main study methodology.

4.1 Outcome Measurement

The selection of appropriate outcome measures involved the evaluation of the psychometric properties of the measure itself. An outcome measure must provide accurate results in order to be purposeful to clinicians and researchers. Accuracy of a measure is determined by its measurement properties which include reliability, validity and responsiveness to change. This section describes the psychometric properties of reliability, validity and responsiveness to change.

Reliability

In order for an outcome measure to be reliable it must be able to demonstrate consistency and be capable of differentiating between the participants on whom the measurements are being applied (Finch et al., 2002). There are two ways of expressing reliability, relative and absolute. Relative reliability is used to depict a measure’s ability to distinguish among participants and is usually expressed as an
intracl s correlation coefficient (ICC). ICC’s vary from 0 to 1 with higher values representing higher reliability.

Absolute reliability represents the reliability of a measure by expressing the measurement error in the same units as the original measurement. The standard error of the measurement (SEM) is used to quantify absolute reliability and can be defined as the standard deviation of the error scores. If you know the SEM you can determine the confidence interval around any true score or the confidence interval of a predicted true score given an obtained score. The formula for the standard error of measurement is:

\[
\text{SEM} = \text{SD} \times \sqrt{1-r}
\]

where SD = the standard deviation of the measure, and 
\( r \) = the reliability coefficient of the measure, typically the ICC.

There are three types of reliability, internal consistency, test-retest reliability and interrater reliability. Internal consistency is important when multi-item measures are summarized into a total score, therefore, they are mostly associated with questionnaires. Test-retest reliability is the reliability of a measure when it is used on different occasions. Interrater reliability describes the reliability of a measure when assessments are performed by different individuals and are important when looking at attributes that need hands-on or observational assessment to gain a participants’ score, for example the Berg balance Scale.

**Validity**

The validity of a measure refers to the extent to which a measure assesses what it is intended to measure. There are four types of validity; face validity, content validity, criterion validity and construct validity (Finch et al., 2002). Face validity simply deems whether a measure seems to be measuring what it is intended to measure. Content validity refers to the extent to which a measure represents all facets of a given construct. Criterion validity assesses the extent to which a measure provides results that are consistent with a gold standard measure. When there is no gold standard measure available a measure can be compared to other measures intended to measure the same attribute and this represents construct validity.
**Responsiveness to Change.**

The responsiveness of an outcome measure focuses on clinically important change and is important for the interpretation and application in the clinical setting. Receiver operating characteristics (ROC) curves, minimal clinically important difference (MCID) and effect size are all ways of expressing a measure’s responsiveness. The area under the ROC curve is a measure of responsiveness, a score of at least .70 is acceptable (Terwee et al., 2007). MCID is defined as the smallest difference in a score in a domain of interest that patients perceive as beneficial and that would mandate, in the absence of side-effects and a change in the patient's management (Jaeschke et al., 1989). It is expressed in the same units as the unit of measurement.

**4.2 Selection of outcome measures**

A Cochrane Review (Rietberg et al., 2004) evaluating the evidence for exercise interventions in PwMS recommended that the World Health Organisation’s International Classification of Functioning, Disability and Health (WHO-ICF, 2001), should be used as a basis for outcome measurement. The preceding literature review (Chapter 2) also highlighted the need for outcome measures that assess the impact of disease at impairment, activity and participation levels.

Outcome measures were chosen based on their psychometric properties and on their relevance and importance as outcomes for PwMS. The Multiple Sclerosis Impact Scale-29 (MSIS-29v2), Modified Fatigue Impact Scale (MFIS), Berg Balance Scale, Six Minute Walk Test (6MWT), and Hand Held Dynamometry (HHD) were selected as outcomes for this study. The MSIS-29v2 was chosen as the primary outcome measure for two reasons; 1) it has strong psychometric properties and 2) because the WHO-ICF framework recommends the measurement of outcome at participation level.
4.2.1 Multiple Sclerosis Impact Scale 29, version 2: Justification, Description and Psychometric properties

Justification

Previous studies evaluating physiotherapy interventions in PwMS with varying levels of mobility failed to assess outcome at participation level. Studies evaluating aerobic and resistance exercise in this population have used the MS-QoL and the generic SF-36. Generic measures have been shown to be less sensitive to change than MS specific measures (Riazi, 2006). A meta-analysis by Motl and Gosney (2008) showed that there is a greater effect of exercise observed when you use a disease specific measure. The MSIS-29 was chosen above other outcome measures such as the MS-QOL and the SF-36 because of its specificity to MS and because of its psychometric properties. The development of the questionnaire involved interviewing PwMS increasing the relevance of the outcome measure to PwMS (Hobart et al., 2001).

Description

The MSIS-29 is a 29 item questionnaire which is intended to measure the physical and psychological impact of MS from a patient’s perspective. It contains two subscales – a 20 item physical scale and a 9 item psychological scale. All items have 5 response categories (not at all, a little, moderately, quite a bit and extremely) that are assigned sequential integers (1, 2, 3, 4, 5). The scores for the two scales are attained by summing the item scores for the 20 item physical scale and the 9 item psychological scale. The physical scale score ranges from 20 - 100 and the psychological scale score ranges from 9 to 45. A higher score on this scale indicates a greater impact of MS on a person’s physical or psychological functioning.

The MSIS-29 was developed using a rigid psychometric approach. It was developed in three stages (Hobart et al., 2001). Questionnaire items were generated from 30 interviews with PwMS regarding the impact of MS on their lives. Health care professionals involved in the care of PwMS were also interviewed and further items were generated. The preliminary version of the questionnaire had 129 items
and was administered by postal survey to 1530 PwMS and standard item reduction techniques were used to develop the 29 item scale.

**Reliability**

The relative and absolute reliability of the MSIS-29 has been established. Two studies by the same research group (Riazi et al., 2002, Riazi et al., 2003) showed a reliability coefficient of 0.81 and 0.94 respectively for the physical component and 0.87 and 0.89 for the psychological component. These values are for 2 rehabilitation groups with participants with a mean EDSS score of 7.1 (±.8) and 6.4 (±1.2) respectively. The SEMs obtained from these studies ranged from 5.3 to 6 for the physical component and from 7.6 to 9.2 for the psychological component, indicating that a change above these values be a true change and not due to measurement errors. These studies included a wide range of EDSS scores and were not specific to the population in this study meaning the SEMs had to be interpreted with caution when the results were being analysed.

**Validity**

The validity of the MSIS-29 was established by a study (McGuigan and Hutchinson, 2004) with a large number of participants n = 200. They found that the physical component of the MSIS-29 correlated highly with the EDSS (0.704) and the London Handicap Scale (.843) whereas the psychological component correlated very poorly with the EDSS (0.095) but highly with the Back Depression Inventory-II (0.799). This is as expected as the EDSS is based on the physical task of walking, whereas the BD1 – II is based on the psychological problem of depression.

**Responsiveness**

A study looking at the responsiveness of the MSIS-29 (Hoogervorst et al., 2004) found that the area under the curve for PwMS with an EDSS of 5.5 to 8 was 0.845. This a moderate score of responsiveness. The MCID of the physical component of the MSIS-29 was reported as 9 in PwMS with an EDSS of between 5.5 and 8.5
(Costelloe et al., 2007). However, the MCID was established by comparing its change score to change scores on the EDSS, which has been shown to lack responsiveness to change. The MSIS-29 has been shown to be more responsive than other measures that measure physical impact of MS. The physical component of the MSIS-29 had an effect size of 0.64, the Short-Form 36 Health Survey had an effect size of .45 and the Functional assessment of MS had an effect of 0.61 in a rehabilitation group (Hobart et al., 2005).

**MSIS-29 version 2**

The authors of the MSIS-29 performed a Rasch analysis on the above outcome measure that was used in the pilot study. Hobart and Cano (2009) found that participants were less able consistently distinguish between ‘moderately’, ‘quite a bit’ and ‘extremely’ for 9 items in the physical component and 1 item in the psychological component. The ‘quite a bit’ option was, therefore, removed from the scale leaving the choice of four answers instead of five. The MSIS – 29 version two was used for the main study (Appendix B). This change should, in theory, increase internal consistency of the measure. The scores for the physical component of the MSIS-29v2 range from 20 – 80 and 9 – 36 for the psychological component.

**4.2.2 Modified Fatigue Impact Scale: Justification, Description and Psychometric properties**

**Justification**

Fatigue is a silent and disabling symptom of MS. It has been reported that at least 65% of PwMS experience fatigue on a daily basis (Krupp et al., 1994). A large survey of over nine thousand PwMS in North America revealed that 74 % of participants reported severe fatigue (Hadjimichael et al., 2008). Fatigue can limit a person’s activities of daily living and their ability to work (Trisolini et al., 2010). It has also been shown to be a self reported risk factor for falls in PwMS (Nilsagard et al., 2009). Fatigue in MS is poorly understood and multi-factorial, therefore, the assessment, evaluation and treatment of fatigue in PwMS remains challenging.
The literature review in Chapter 2 highlighted that the effect of specific physiotherapy intervention on fatigue was not assessed previously. The studies evaluating exercise interventions used either the MFIS or the FSS. No statistically significant improvements were observed for the Fatigue Severity Scale (FSS), whereas, the MFIS appeared more sensitive to change and therefore, was selected for use in this research (Appendix C).

**Description**

The MFIS is a structured self report questionnaire. It measures the impact of fatigue on the day to day functioning of a person living with MS. It is a 21 item scale of which each item is scored from 0 (never) to 4 (almost always), thus ranging from 0 – 84 and the higher the score the greater the impact of fatigue. It has been classified as a multidimensional scale and is intended to analyse different aspects of fatigue by assessing impact on physical, cognitive and psychosocial functioning.

**Reliability**

The inter-rater reliability of the MFIS was evaluated in a sample of PwMS with a range of EDSS scores (3 – 8.5) (Kos et al., 2005). They assessed the reliability by performing the MFIS on two occasions three days apart and also by using the control period of an intervention study. The reported ICC’s (0.68 and 0.85) demonstrated moderate to high reliability. No measure of absolute reliability for the MFIS was established in these studies.

**Validity**

The MFIS has demonstrated the ability to discriminate between a group of PwMS with fatigue and a group of those that don’t indicating good construct validity (Flachenecker et al., 2002). A cut off score of 38 has been shown to indicate clinically relevant fatigue. Good convergent validity has been shown between the MFIS and the FSS, r = 0.68. This indicates that the MFIS and the FSS are measuring the same constructs.
Responsiveness to change

No study to date has evaluated the responsiveness of the MFIS. As previously mentioned in the review of the literature (Chapter 2) the MFIS has demonstrated the ability to detect change following exercise interventions, whereas, the FSS has not.

4.2.3 Berg Balance Scale: Justification, Description and Psychometric properties

Justification

Balance impairment is common in PwMS. There is a high prevalence of self reported balance problems (Bakshi, 2003) and objectively measured balance impairment (Frzovic et al., 2000) in studies evaluating balance in PwMS. Balance impairment has been shown to be a risk factor for falls in PwMS (Cattaneo et al., 2002, Nilsagard et al., 2009) and challenges their ability to mobilise safely.

Previous studies evaluating specific physiotherapy interventions have used the BBS to measure balance (Cattaneo et al., 2007b, Smedal., et al 2006, Lord et al., 1998). The BBS was chosen as a measure of impairment for this study because of its high quality psychometric properties and to allow for comparisons to other studies. Another study (DeBolt and McCubbin, 2004) used platform technology to assess balance sway but as the current study was community based this would not have been feasible.
Description

The BBS is a clinical scale that evaluates balance in sitting and standing and rates performance from 0 (cannot perform) to 4 (normal performance). It is a fourteen item instrument intended for individuals with some degree of balance impairment. The items explore a person’s ability to sit, stand, lean, turn and maintain the upright position on one leg. The higher the score the greater the participants performance of the balance tasks and the highest possible score is 56. Time to complete takes ten to twenty minutes depending on the ability of the subject. It is widely used by physiotherapists in the clinical setting (Appendix D).

Reliability

The relative reliability of the BBS has been well established in the elderly and stroke populations. One study (Cattaneo et al., 2007a) looked at the relative reliability of the BBS in a group of PwMS who used walking aids, similar to the population of the current research. The test – retest reliability and the inter-rater reliability were assessed and both had ICC values of 0.96, indicating a high level of relative reliability. Paltamaa et al (2005) suggested that the SEM for the BBS in people with MS was 0.85 but the participants in this study had a mean score of 50 on the BBS indicating minimal balance impairment, unlike the participants involved in the current research.

Validity

In a study evaluating the validity (Cattaneo et al., 2006) of the BBS for use in PwMS it showed good construct validity in the prediction of patients who used an assistive device. It was also shown to have good concurrent validity and a cut off score of 44 was suggested as a criterion to identify PwMS who have a risk of falls.

Responsiveness
Minimal clinical important difference (MCID) on the BBS has been established for PwMS but the values available are for PwMS who are more mobile (Paltamaa et al., 2007). The change score required to show clinically meaningful change was identified as 2.33. This score, however, was obtained using PwMS with less balance and mobility impairment. In a stroke population if a change of ± 6 is observed then one can be 90% confident of genuine change (Stevenson, 2001). The BBS showed statistically significant change in the studies evaluating interventions in PwMS indicating that it is sensitive to change in this population.

4.2.4 Six Minute Walk Test: Justification, Description and Psychometric properties

Justification

Walking impairment is a common consequence of MS. Previous literature has shown that PwMS have a slower speed of walking and decreases step length and cadence than healthy controls (Morris et al., 2002, Hamilton et al., 2009). Disease progression is associated with increased mobility impairment and 50% of PwMS will require the use of a walking aid within 15 – 25 years of their diagnosis (Confavreux et al., 2003). PwMS consider mobility related problems as the second greatest barrier to retaining employment (Chandraratna, 2010).

There is a lack of consistency surrounding the use of timed walks in the previous studies of PwMS. The shorter timed walks did not appear sensitive to change in these studies, therefore, the 6MWT was chosen to measure at the level of activity according to the ICF framework to allow for greater comparisons between other studies of PwMS and other populations. Gijbels et al (2010) suggests that the 6MWT is better at predicting habitual walking performance than shorter walking tests.
Description

The 6MWT was originally developed from the twelve minute walk test and was used to assess exercise tolerance in individuals with respiratory disease. It is now widely used in many different populations (Heart Disease, Chronic Heart Failure, Fibromyalgia, elderly, stroke and other neurological conditions). It is a performance based measure of functional exercise capacity. The distance walked in six minutes is recorded and the further the distance walked the better the performance. Participants in the main study were instructed to walk “as fast and as safely” as they could (Fry and Pfalzer, 2006). Rest periods were allowed and documented. A ten metre walkway was used with a chair at each end in order for the participant to rest when they needed to. The participants were advised to wear comfortable walking shoes and to wear the same shoes for all assessments.

Reliability

The relative reliability of the 6MWT has been evaluated in two studies (Goldman et al., 2008, Paltamaa et al., 2005). Both studies showed a high level of test re-test and inter-rater reliability with ICC values of 0.96 and 0.95 respectively for test re-test reliability and 0.91 and 0.93 respectively for inter-rater reliability. The absolute reliability was also established in the study by Paltamaa (2005) and SEM values of 30.65 metres for test re-test reliability and 35.85m.

Validity

The construct validity of the 6MWT has been evaluated in 40 PwMS and it has been shown to correlate better with the Timed 25ft walk (r = 0.83) and the Multiple Sclerosis walking scale (r = 0.81) than the EDSS (Goldman et al., 2008). Gibjels et al (2010) found that the 6MWT correlated significantly with habitual walking performance (HWP) in 21 participants with moderate MS (r = 0.73, p<0.001). HWP was measured using the Step Watch Activity Monitor.
Responsiveness

A MCID value of 85 metres has been established for PwMS (Paltamaa et al., 2005). However, this value was obtained using participants who were more mobile (EDSS of between 1 and 6) than the population involved in this research project who require more assistance when walking. In theory, if participants walking distances were shorter at baseline the amount of change needed to be clinically relevant should be smaller.

4.2.5 Hand Held Dynamometry: Justification, Description and Psychometric properties

Justification

The isokinetic dynamometer is the gold standard for assessing strength. It is an expensive piece of apparatus that is not widely available in clinical sites in Ireland and it is not portable. HHD and manual muscle testing (MMT) are two other options for assessing strength. MMT is widely acknowledged as being unreliable and inadequate. Therefore, HHD was chosen to measure strength in this study as it was practical option for use in a community based study.

HHD involves the use of a portable device that displays a reading in Newtons when pressure is applied to it. An extensive review of the literature regarding the reliability and validity of HHD (Kolber and Cleland, 2005) has reported high relative reliability. The studies are limited by the omission of any measure of absolute reliability. The same review reveals moderate to high criterion validity when compared to isokinetic dynamometry. Standardised positions were used to increase the reliability and comparability of the results obtained (Andrews et al., 1996). No study has evaluated the responsiveness of HHD.
4.3 Physiotherapy Intervention

As previously reported in Chapter 2 of this document the exact content of the interventions was not documented in previous studies evaluating balance programmes in PwMS. Balance is a commonly reported symptom in PwMS and prevalence rates of falls in PwMS have been shown to be greater than 50% in recent studies (Nilsagard et al., 2009, Finlayson and Peterson, 2006, Cattaneo et al., 2002).

A search was conducted on the literature surrounding falls prevention programmes in the elderly population. Both populations (elderly and PwMS) share similar symptoms, such as, weakness and balance deficits, therefore, this study used the extensive research in the elderly to inform the intervention. It is applicable for this population of PwMS who are at a high risk of falling due to balance problems, the use of a walking aid and lower limb weakness.

It has been shown that PwMS have less leg strength than healthy controls (Andrews et al., 1996) and that reduced muscle strength is a major impairment that limits activities of daily living (White and Dressendorfer, 2004). Therefore, the group physiotherapy intervention was adapted from a combination of the falls prevention in the elderly literature (Means et al., 2005), balance training in PwMS and strengthening in PwMS (DeBolt and McCubbin, 2004). The group format was adapted from Means et al (2005) in which balance improved and falls were reduced following balance retraining in groups of 6 – 8 participants.

A circuit style format was used that consisted of a mixture of balance and strengthening exercises (See figure 2). The exercises and possible progressions are described below. Exercises were performed in sets of 12. If participants were able to perform 12 repetitions of an exercise safely and easily then the aim of the participant at this point was to be failing at the last repetition. The load was increased by 2 – 5 % when a participant could easily achieve 12 repetitions. Not all participants progressed through all the exercises. The progression was dependent on the ability of the participant and their safety while performing the exercises.
Figure 2 Sketchings of the group physiotherapy exercises used in information booklets
1. Sit to Stand, progressed by altering;
   Hand Positioning – Participants may have initially needed to use hands for support to rise from chair, then progressing to hands by side and then to hands across chest.
   Seat Height – Participants may have initially required a higher seat height which was lowered to increase the intensity of the exercise.
   Repetitions – Was performed in sets of 12 and number of sets increased to 3 as participant progressed.
   Weights – Handheld weights were given to participants who needed further progression.

2. Squat, progressed by altering;
   Support – Participants may have initially needed bilateral support, this was decreased to unilateral and then to no support as participants’ ability increased.
   Repetitions – Was performed in sets of 12 and number of sets was increased to 3 as participant progressed.
   Weights – Handheld weights were given to participants who are able to perform 3 sets of 12 squats safely with no support.

3. Heel Raises, progressed by altering;
   Support – Participants may have initially needed bilateral support, this was decreased to unilateral support and then to independent calf raises as participant progressed.
   Repetitions - Was performed in sets of 12 and number of sets increased as participant progressed.
   Other options – If participants were able they performed single leg calf raises or if they could perform 3 sets of 12 independent calf raises weights were added as further progression.

   The following three exercises were completed within parallel bars.

4. Step ups, progressed by altering;
   Support – Participants may have started with bilateral support, and then decreased to unilateral support, then to no support.
Stepping – Initially participants may have stepped onto step and back to starting position, then stepped onto step and over, and then onto step, over and backwards to starting position.

Step Height – When participants were comfortable with all directions of stepping step height was increased.

5. Tandem Stepping/Walking – progressed by altering;
Support – Participants may have started with bilateral support, and then decreased to unilateral support, then to no support.
Stepping – Participants may have initially just placed one foot in front of the other and held this position. The number of steps was increased as the participant progressed.

6. Side Stepping – progressed by altering;
Support – Participants may have started with bilateral support, and then decreased to unilateral support, then to no support.
Number of steps – Initially participants may have only taken one step in each direction. This was increased as participants’ ability increased.
If a participant was unable to take a step to the side, weight shifting from side to side in standing was performed and progressed to stepping when the participant was able.
Chapter 5 - Pilot Study

5.0 Introduction

A pilot study was conducted to inform the methodology of the main study. The principal aim of this pilot study was to assess the feasibility and suitability of a set of outcome measures and a physiotherapy intervention for use in a larger study of PwMS with moderate to severe mobility impairment. The secondary aim of the pilot study was to obtain preliminary data on the effects of a group physiotherapy intervention on balance and mobility in a sample of people with MS.

This chapter details the methodology and results of the pilot study, and concludes with recommendations for the main study.

5.1 Methodology

A comparative pre- and post-intervention study design was used. A convenience sample of 6 PwMS who mobilised with at least bilateral assistance was recruited through the Multiple Sclerosis Ireland (MSI) database. An information leaflet (Appendix E) was given to potential participants and consent forms (Appendix F) were signed prior to enrolment in the study.

Assessment

Participants were assessed one week before and one week after a six week intervention by the treating physiotherapist. The outcome measures used were the Multiple Sclerosis Impact Scale-29 (MSIS-29), the Modified Fatigue Impact Scale (MFIS), the Berg Balance Scale (BBS), the two minute walk test (2MWT) and the Dynamic Gait Index (DGI).
A semi structured informal interview was conducted at the end of the follow up assessment. It consisted of six lead in questions that were designed to gain information from the participants’ perspectives on the class structure itself, any possible benefits of the class, and on the effects of exercising in a group. Qualitative information was obtained to confirm that changes described by participants were captured by the outcome measures in order to establish the suitability of the outcome measures for use in the main study.

The question route for the interview was:

1. Have you noticed any physical changes or changes to your daily activities since you started the exercise class?
2. Could you tell me the positive aspects of the class (if any) and the negative aspects of the class (if any)?
3. Did you think the venue was suitable?
4. How did you feel exercising in a group?
5. Is there anything you would change about the class?
6. What would be your ideal exercise class?

**Intervention**

The intervention used in the pilot study was as described in Chapter 4 of this thesis. It was a circuit style class of balance and strengthening exercises. Participants attended an hour long class once a week for a period of six weeks.

**Data Analysis**

Graphs were used to visually depict the results. Medians and Semi Interquartile Range (SIR) were used to describe the data and non parametric data analysis was used as the sample size was small and the assumptions for normality were not met. The Wilcoxon Signed Rank test was performed for each measure to assess the significance of any change seen.
5.2 Results

Participants

Five females and one male with a mean age of 52.33 (±13.12) years took part in this study. At baseline the mean length of time since diagnosis was 15.68 (±9.11) years. Three of the participants had Relapsing-Remitting MS (RRMS), two had Secondary Progressive MS (SPMS) and the type of MS for the remaining participant was unknown. All participants mobilised with at least bilateral aid outdoors. All participants had a self reported history of falling with an average of 1.83(±0.75) falls in the three months prior to the baseline assessment. Participants attended an average of 4.33 classes over the 6 week period.

Intervention

The intervention and individual exercises were well tolerated by all participants. There were no adverse effects or events recorded during the class. Classes lasted for approximately one hour and were completed once a week for 6 weeks. Attendance was recorded at each class. There was 100% attendance for 5 of the 6 participants and the mean number of sessions attended was 5.8. The level of difficulty was different for each of the participants and the exercises were modified or progressed accordingly. All participants were able to complete all the exercises. Exercises were progressed on a weekly basis depending on the ability of the participant to perform a specific exercise. Exercises were progressed for all participants over the course of the intervention.

Outcome Measures

MSIS -29

Figure 3 shows the scores of the MSIS-29 physical component before and after the intervention for each individual participant. For the physical component all of the scores decreased indicating that the impact of MS on their physical functioning decreased. The median scores before and after were 59 (7.5) and 46.5 (3.6) respectively. This change was statistically significant (p = 0.028). Sample size
calculations suggested that in order to have 90% power and to detect a similar change using a Wilcoxon rank-sum test with a 0.05 two-sided significance level a sample size of 22 in each group would be required.

Figure 3 Scores before and after the intervention for the physical component of the MSIS-29

For the psychological component four of the participants scores decreased, one stayed the same and one increased (Figure 4). The median scores before and after were 22 (4) and 19 (1.6) respectively. This change was not deemed statistically significant (p = 0.78).
Modified Fatigue Impact Scale (MFIS)

It is evident from Figure 5 that the MFIS score decreased after the intervention in four of the participants and increased in two. The median score before was 40.5 (3.5) and the median score after was 36.5 (8.875). This change was not statistically significant ($p = 0.344$)
The Berg Balance Scale

It can be seen from figure 6 that all participants’ scores increased for the BBS after the intervention. The median score before was 26.5 with a semi interquartile range (SIQR) of 6.625 and the median score after was 34.5 with a SIQR of 9. This change was statistically significant (p =0.027). The alpha level was set at 0.05.

Figure 6 Scores before and after the intervention for the Berg Balance Scale

The Two Minute Walk Test (2MWT)

The distance walked over two minutes before and after the intervention for each participant can be seen in Figure 7. It is evident from this graph there were only minimal changes to the distance walked following the intervention period. The median distances walked before and after the intervention were 34.5m (11.12) and 39m (14.375) respectively. This change was not statistically significant p=0.5. The 2MWT was originally chosen for use in the pilot study as participants had moderate to severe mobility impairment and their ability to mobilise for 6 minutes was not known. All participants used bilateral aid during the 2MWT but two participants seemed to perform better than the others. To allow for greater change and variability to be assessed the 6MWT was chosen as the measure of walking for the
larger study. Literature published following the pilot study also supported the use of the 6MWT instead of shorter walk tests to assess habitual walking in PwMS with moderate mobility impairment (Goldman et al., 2008).

Figure 7 Distance in metres (m) over 2 minutes before and after the intervention

![Distance in metres (m) over 2 minutes before and after the intervention](image)

**The Dynamic Gait Index (DGI)**

Figure 8 illustrates that there was no change on the DGI for any of the participants. Their scores at baseline equalled their scores after the 6 week intervention.

Figure 8 Scores on the DGI before and after the intervention

![Scores on the Dynamic Gait Index (DGI)](image)
Qualitative Findings

The following two sections are reflective of the answers and discussions with the participants during the interviews. Quotations are used to illustrate the themes that emerged from the interviews.

Balance

Five out of the six participants felt their balance had improved. Two of the participants reported that they were quicker to react to a sudden loss of balance, and for one of those participants the frequency of these incidents was reduced.

“I still lose my balance but much less often and now I’m quicker to react and correct myself and save myself”

Another participant felt that the improvements in their balance led to increased independence with transfers.

“Before I used to worry a lot about my balance, I’m a bit more confident now before I used wait for someone to help (with transfers) but now I don’t”

No participant reported a decrease in their balance abilities.

Group exercising

When asked about the positive aspects of the class all of the participants spoke about the group setting. They felt that they did not need to be self conscious as they would be in a gym and that they had a shared understanding and similar symptoms and experiences.

“We all understand each other, because we’re all in the same boat”

Two participants also felt that exercising in a group provided motivation to do the exercises and made it more appealing.

“Exercise used be a chore, the group has a great atmosphere”

One of the participants also felt that the group was still small enough for personal attention. Overall the participants felt that exercising in a group was more beneficial than doing it their own.
5.3 Implications for main study

The main aim of this pilot study was to assess the feasibility and suitability of a set of outcome measures for use in a larger scale study. The MSIS-29, MFIS, BBS appeared to be feasible for use in this population of PwMS who mobilise with bilateral assistance.

The DGI (Appendix G) is a task based measure that evaluates dynamic balance in people who have balance impairments. It involves completing different tasks while walking and has been used in to evaluate the effects of balance retraining in PwMS with varying levels of mobility (Cattaneo et al., 2007b). The results showed that there was no change in score observed after intervention for any of the participants suggesting it may not be sensitive to change in a this particular population of PwMS. The highest possible score on the DGI is 24 and the highest score of any of the participants in this study was 12. As participants in this study had moderate to severe mobility impairments it may be possible that the DGI was too challenging for them. As a result of this it was decided that the DGI would not be used as an outcome measure for the GTBR study.

As this was a pilot study little was known about the capabilities of this group of PwMS. The 6MWT was used in previous studies evaluating exercise interventions in PwMS but as these studies contained people of all levels of mobility it was not known if the more impaired population would be able to complete a 6MWT so a 2MWT was used in this pilot study. Only minor changes were observed in the distance walked over the two minute period and the participants were able to complete the test with minimum difficulty. The 6MWT is more widely used and would allow for greater comparisons with other studies and other populations. It also provides information about the impact of increased walking on symptoms, for example the onset of drop foot with fatigue and walking endurance. For these reasons the 6MWT was chosen for use in the main study.
The secondary aim of this pilot study was to obtain preliminary data on the effectiveness of a balance and strength intervention in this population of PwMS. As there were only six participants statistically significant changes were not expected but were observed for two of the outcome measures, the BBS and the physical component of the MSIS-29. This pilot study also used the novel approach of collecting qualitative data by using an informal semi-structured interview. This approach was used to assess whether the objective improvements seen on the outcome measures were reflected in how the participants themselves felt. The improvements seen on the BBS and on the physical component of the MSIS-29 correlated with the subjective reports of improved balance and transfers. The importance of the group setting was also evident from the semi structured interviews.

The pilot study did not include a measure of strength. The intervention included strength exercises and any changes in strength that may have occurred were not captured. For the main study strength was assessed using hand held dynamometry (HHD) to evaluate any increases or decreases in strength that may have occurred. Lower limb strength was assessed as the exercises in this intervention specifically targeted the lower limb.

The fact that this was a pilot study with only six participants must be considered when interpreting the results. It did, however, provide useful information and implications for the development of the larger, national, multi-centred study.
5.4 Conclusions

- This pilot study suggested that the MSIS-29, the MFIS and the BBS were feasible and suitable for use in a population of PwMS who have moderate to severe mobility problems and were used in the main study.
- The DGI was not sensitive to change in this sample of PwMS and was not used in the GTBR project.
- In order to allow for more change and greater comparability with other studies the 6MWT was used in the main study instead of the 2MWT.
- A strength measure (HHD) as previously described in Chapter 4 was planned for use in the main study.
Chapter 6 – Main Study Methodology

6.0 Introduction

This chapter will outline the aims and objectives of this study, and describe in detail the methodological procedures that were undertaken.

6.1 Aim and Objectives

The principle aim of this research was to evaluate the efficacy of community based physiotherapy and yoga interventions for PwMS with moderate to severe mobility impairment in order to inform Multiple Sclerosis Ireland (MSI).

The objectives of the main study were

1. To evaluate the immediate and follow up effects of two types of physiotherapy interventions (group and individual) and yoga on PwMS who mobilise with at least bilateral assistance.

2. To compare the effectiveness of these interventions in order to establish the most effective treatment option for this population of PwMS.

3. To explore signs and symptoms of MS that may be associated with the outcome of the above interventions.

6.2 Study Design

The study was conducted as a multi-centred, single-blinded, block randomised, controlled trial. Assessments were performed before (week 1) and after (week 12) the intervention period and at three month follow up (week 24).
6.3 Study Settings

The assessments and interventions for the main study were conducted in venues sourced by MSI. These included community centres, local gyms and hotels that were accessible to PwMS.

6.4 Ethical Approval

This methodological protocol was approved by 11 Research and Ethics Committees in Ireland. These are detailed in Table 12.

Table 12 Research Ethics Committees who approved the methodology for the main study

<table>
<thead>
<tr>
<th>Research Ethics Committees</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cork University Hospital</td>
<td>Cork</td>
</tr>
<tr>
<td>HSE Dublin North East</td>
<td>Drogheda</td>
</tr>
<tr>
<td>Mater Misericordiae Hospital</td>
<td>Dublin</td>
</tr>
<tr>
<td>St James Hospital</td>
<td>Dublin</td>
</tr>
<tr>
<td>Beaumont Hospital</td>
<td>Dublin</td>
</tr>
<tr>
<td>Adelaide and Meath Hospital</td>
<td>Dublin</td>
</tr>
<tr>
<td>Galway Regional Hospitals</td>
<td>Galway</td>
</tr>
<tr>
<td>Mid West Regional Hospital</td>
<td>Limerick</td>
</tr>
<tr>
<td>Sligo General Hospital</td>
<td>Sligo</td>
</tr>
<tr>
<td>HSE- Dublin Mid Leinster</td>
<td>Tullamore</td>
</tr>
<tr>
<td>Waterford regional Hospital</td>
<td>Waterford</td>
</tr>
</tbody>
</table>
6.5 Recruitment

Participants were referred to the study by themselves, their carers, MSI, Chartered Physiotherapists, Neurologists, GPs or Clinical nurse specialists. Referrals were made to the ten regional offices of MSI. A form completed over the telephone (Appendix H) was used to screen for exclusion criteria and to stratify according to mobility level using the GNDS mobility component score. Participants were then sent the information leaflet (Appendix I) and a consent form (Appendix J). The signed consent form was returned to the regional office. The participants’ General Practitioners were sent a letter (Appendix K) informing them of their participation and the relevant information leaflet was enclosed.

6.6 Inclusion criteria

Participants who met the following criteria were eligible for inclusion in the main study;

1. Confirmed diagnosis of MS from a Neurologist or Physician.

2. A Guys Neurological Disability Scale lower limb mobility component score of three or four. A score of three indicates that a person usually uses bilateral support (two sticks or crutches, frame, rollator) to walk outdoors and a score of four indicates that a person usually uses a wheelchair to travel outdoors, but is able to stand and walk a few steps with or without help (Sharrack and Hughes, 1999) (Appendix L). The mobility component of the GNDS was chosen over the EDSS as the means for stratifying participants in this study. It can be administered easily over the phone unlike the EDSS which needs to be performed by a neurologist and provided a screening tool to allow for the allocation of participants to the appropriate strand.

3. Over 18 years of age
Participants with all types of MS were included in this study and it was not necessary for participants to be members of MSI.

3.7 Exclusion Criteria

Participants were excluded from the study if they met one of the following criteria at the time of assessment:

1. Currently experiencing an exacerbation of symptoms due to relapse

2. Received steroid treatment or had a relapse within 3 months of the baseline assessment

3. Pregnant at the time of referral

4. Under 18 years of age

6.8 Randomisation

Once consent for 6 people was obtained in a geographical area, the regional office contacted the National Coordinator who allocated that block of subjects to the control or an intervention condition. In order to ensure that there were equal numbers randomised to the three intervention groups and the control group a sealed envelope containing the four group options written on pieces of paper was used. These were randomly withdrawn as soon as a block of participants was available and returned to the envelope after four blocks had been allocated to each of the groups. Allocation was disclosed to the regional coordinators before commencement of the assessments.
6.9 Interventions

Participants were allocated to one of the three intervention groups (group physiotherapy individual physiotherapy, yoga) or the control group. The duration of each intervention was one hour a week for ten weeks.

Group Physiotherapy

Group physiotherapy consisted of a circuit style class of lower limb strengthening and balance exercises adapted from previous literature. The exercises included were: sit to stands, step ups, squats, calf raises, step ups, and side stepping. These exercises are described in more detail in Chapter 4 of this document. The group physiotherapy intervention was pre-defined and standardised in order to allow reproduction of the programmes. Deliverers of the group physiotherapy interventions attended a training day and were provided with an information letter and a handbook of the class content (Appendices M and N).

Individual Physiotherapy

Participants allocated to individual physiotherapy received individualised treatments depending on the problem list and goals established by the Chartered Physiotherapist who was treating them. This was done to represent individualised physiotherapy practice. The content of the intervention was recorded for each individual treatment session using notes written by the treating physiotherapist. These notes were sent via registered post to the University of Limerick when the treatments were finished. The individualised physiotherapy interventions were not a continuation of previous community physiotherapy. Physiotherapists had no contact with the participants prior to the commencement of the intervention. If participants were currently receiving physiotherapy they were not included in the research arm of this project. The content of the individual physiotherapy interventions was different to the content of the group physiotherapy interventions and was not
standardised in order to reflect routine physiotherapy practice and to allow for comparisons to be made between a standardised class format and one on one individualised treatment sessions.

**Yoga**

Yoga was not assessed as part of the pilot study but is frequently provided to its members by Multiple Sclerosis Ireland (MSI). Prior to the commencement of this trial Yoga had only been evaluated by one study (Oken et al., 2004) which did not find conclusive results and did not evaluate the effect for participants who used walking aids separately to the main cohort of participants who mobilised independently. Members of MSI anecdotally report benefits from taking part in Yoga and the Getting the Balance Right Project provided an opportunity to formally evaluate yoga for MSI and to explore the effects of this intervention specifically for PwMS with moderate to severe mobility limitations as this had not been established in previous literature. Participants attended a weekly yoga class of approximately one hour’s duration. All yoga instructors were members of The Yoga Federation of Ireland. The yoga intervention was not specified, in order to represent routine practice. Instructors were given a standardised pack in order to document the interventions.

**Control Group**

The control group did not receive an intervention for the 12 weeks and were advised not to change their exercise habits. Physiotherapy services at this time were extremely limited and most people with MS were waiting significant time periods for physiotherapy intervention (Coote et al., 2010), therefore, the 3 month control period was not considered significantly disadvantageous. Once the control period was over participants received the treatment of their choice but the response to this was not assessed as part of this trial.
6.10 Assessment

Each participant was assessed by a blinded assessor who was unaware of group allocation.

Assessments were carried out at week 1, week 12 and at week 24 using the following outcome measures: Multiple Sclerosis Impact Scale 29 version 2 (MSIS-29), Berg Balance Scale (BBS), Modified Fatigue Impact Scale (MFIS), six minute walk test (6MWT), hand held dynamometry (HHD). The more physically demanding outcome measures were separated to avoid fatigue and so the order of testing was 6MWT, MSIS, BBS, MFIS, HHD. A standardised assessment form was also used at baseline and follow up assessments.

Baseline Assessment Form

Neurological assessment forms from senior physiotherapists who were members of the PIMS (Physiotherapists interested in MS) group were gathered from different clinical sites around the country. They were reviewed by the research team in the University of Limerick and a detailed assessment form (Appendix O) was created including questions about any confounding variables that might have influenced the results. These included mobility level using the GNDS, any abnormalities in sensation, history and frequency of falls, type of MS, length of time since diagnosis and first symptoms, medication, proprioception, co-ordination, ankle range of motion, current exercise habits and previous physiotherapy. This information was obtained by interview and physical assessment in Week 1.

Follow up Assessment Form

Prior to repeating the outcome measures at follow up a brief assessment form was used (Appendix P) to establish if the participants had fallen, changed or started new medication or had other interventions over the course of the study.
6.11 Standardisation

Assessors attended training days in Limerick and Dublin in order to standardise the measurements. To ensure standardisation of physiotherapy interventions, training days for those physiotherapists delivering the programmes were held on three occasions. Supporting documentation was provided and follow-up advice and information for deliverers was supplied as necessary by e-mail and telephone. Standardised documentation was used to record attendance, description and completion of the interventions (Appendix Q).

6.12 Data Analyses

All data was analysed using the statistical software package, Predictive Analytic Software (PASW) version 18.

Normality Testing

All baseline measures were summarised and tested for normality. In order to assess the normality of the data histograms and Quantile-Quantile plots were used to describe the frequency distribution. The shape of the histogram revealed if the distribution of the data was normal or non-normal. If the distribution was normal a bell shaped symmetrical curve would be observed. The Shapiro Wilk test for normality was also performed in order to calculate the probability that the data had come from a normal distribution. The higher the probability (>0.05) the closer the data is to a normal distribution.

Baseline differences

One-way ANOVA was used to assess any significant differences between groups at baseline when the data was normally distributed and the Kruschal-Wallis test was used when the data was not normally distributed. Chi square tests for independence were used for categorical data.
The main effects

The descriptive statistics used for normally distributed data were means, standard deviations and 95% confidence intervals (CI). This data was analysed using a repeated measures ANOVA to establish if there was a significant effect of time and group. Paired t-tests were used when a significant effect for time was observed in order to establish where this effect occurred. To address the issue of multiple testing the p value was adjusted using the Bonferroni correction method. For this method the p value set for significance was divided by the number of statistical comparisons performed. Effect sizes were calculated using the formula Mean difference/SD baseline (Cohen 1988).

Medians, semi-interquartile ranges (SIR) and boxplots were used to describe non normal data. Wilcoxon signed rank tests were used to assess the change seen over time. In order to assess any differences between groups a change score was computed and Kruschal Wallis and Mann Whitney U tests were performed.

Post hoc analysis

A multiple regression analysis was performed to explore the variables that may influence outcome. The data set collected as part of the baseline assessment was extensive and considered a range of impairments of body structures and functions, activities and participation restrictions. This was informed by the literature review in Chapter 3 which identified the signs and symptoms that may affect the outcome of an intervention and these were used as the independent variables.

Two multiple regression analyses were performed using a subjective/patient report outcome (MSIS-29v2 physical component outcome score) and an objective outcome (BBS). Each independent variable had to reach statistical significance in order to significantly contribute to the variance.
Chapter 7 – Results

7.0 Introduction

The objectives of the main study were to establish the effect of group physiotherapy, one to one physiotherapy and yoga over time, to compare the differences between these intervention groups and a control group and to establish a set of signs and symptoms associated with a positive outcome.

This chapter will begin with a detailed demographic profile of the participants involved and describe the attrition rate and the content of the interventions. The baseline data for groups will be presented and compared firstly. Secondly, the principal study results and the results of the post hoc analysis will be presented.

In this chapter the results of the principal study will be presented and described by outcome measures; MSIS-29 v 2 physical and psychological components, Berg Balance Scale, Modified Fatigue Impact Scale and Six Minute Walk Test. The outcome measures were analysed to assess any differences between the treatment groups at baseline, any changes over time within each of the allocation groups and the differences between these groups were also evaluated. The maintenance of effect at week 24 was analysed separately.
7.1 Research Participants and flow through study

One hundred and sixty-one participants were recruited and assessed for eligibility between June and October 2008. Fifteen participants were excluded and one hundred and forty six were allocated to one of the four groups, group physiotherapy, one on one physiotherapy, yoga or control. Figure 9 shows the flow of participants from baseline assessment to 12-week follow up and to 24 week follow up.

Excluded Participants and dropouts

Participants were excluded at baseline if they did not meet the inclusion criteria. Reasons for exclusion at this time point included the use of steroids in the previous three months (n=7) and not meeting the mobility criteria of Strand B (3 or 4) on the Guys Neurological Disability Scale mobility component (n=8). Three participants were moved to Strand A (PwMS who mobilise with up to one stick/crutch) and five were moved to Strand C (non ambulatory PwMS).

Lost to follow up – Week 12

Following the twelve week intervention period data was available to analyse for one hundred and eleven participants. The reasons participants were lost to follow up or discontinued the intervention can be seen in Table 13. The proportion of dropouts for each group was; 27% for group physiotherapy, 22% for one to one physiotherapy, 18% for yoga and 21% for the control group. There were more dropouts in the physiotherapy intervention but this may be explained by the larger sample sizes in these groups. The number of dropouts due to relapses was low in all of the groups. This may be partially explained by the low percentage of participants with RRMS. There were, however, 2 relapses in the control group despite the small number of participants. The overall attrition at week twelve was 22%.
Lost to follow up – Week 24

There was an increase in the number of dropouts between week 12 and week 24. Reasons for these can be seen in the in Table 13. This decrease in numbers was taken into account during the data analysis and a separate analysis examining the follow up effect was conducted using only data from participants who attended all three assessments. The number of relapses increased for the participants in group physiotherapy and yoga and decreased for one to one physiotherapy. The overall attrition from week 1 to week 24 was 54%.

Participants’ randomisation to each group

It is evident from the flow chart (Figure 9) that there are uneven numbers in the three intervention groups and the control group. The yoga and control groups have smaller numbers compared to the two physiotherapy interventions. If the randomisation procedure had been implemented as outlined in the methodology chapter there would have been similar numbers in the four groups. The regional offices were consulted and the reasons why this happened were explored. This further evaluation revealed a number of explanations. Some of the MS society’s regional offices reported that a portion of their participants expressed that they did not want to take part in yoga classes while participants originally allocated to the control group requested physiotherapy intervention. At this point those participants were randomised to one of the physiotherapy interventions. Another reason for the small numbers in the yoga group was due to difficulty in finding suitable yoga instructors in certain areas. How this affects the interpretation of the results will be considered in the discussion chapter of this document. The collection of more control data was discussed as a possibility to address this limitation. At this time, however, a sample of people with MS who had not taken part in the Getting the Balance Right Project exercise programmes was difficult to recruit and data collected would have been subject to contamination due to confounding variables such as knowledge, experience and benefits of these programmes.
Figure 9 Participant Flow Chart

Assessed for eligibility
n = (161)

Excluded (n = 15)
Not meeting inclusion criteria
(n = 7)
Moved to Strand A
(n = 3)
Moved to Strand C
(n = 5)

Randomised (n =146)

Allocated to group physiotherapy
(n = 66)

Discontinued intervention
(n = 8)
Lost to follow up 1
(n = 10)
Analysed at week 12
(n = 48)
Lost to follow up 2
(n = 12)
Analysed at week 24
(n = 36)

Allocated to 1:1 physiotherapy
(n = 45)

Discontinued intervention
(n = 8)
Lost to follow up 1
(n = 2)
Analysed at week 12
(n = 35)
Lost to follow up 2
(n = 10)
Analysed at week 24
(n = 25)

Allocated to yoga
(n = 16)

Discontinued intervention
(n = 2)
Lost to follow up 1
(n = 1)
Analysed at week 12
(n = 13)
Lost to follow up 2
(n = 4)
Analysed at week 24
(n = 9)

Allocated to control group
(n = 19)
Table 13 Reasons for dropouts (including relapses) at week 12 and week 24

<table>
<thead>
<tr>
<th></th>
<th>Group Physiotherapy</th>
<th>Individual Physiotherapy</th>
<th>Yoga</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Week 12</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Discontinued</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 due to relapse,</td>
<td>1 due to relapse,</td>
<td>2 due to relapse,</td>
<td>1 unknown reason,</td>
<td>2 due to relapse,</td>
</tr>
<tr>
<td>1 requested 1:1</td>
<td>1 due to pneumonia,</td>
<td>1 due to relapse,</td>
<td>1 did not like intervention so stopped attending</td>
<td>1 due to rapidly progressing MS</td>
</tr>
<tr>
<td>treatment,</td>
<td>1 travelled to the</td>
<td>1 weather too cold</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 not able for group physio,</td>
<td>1 USA,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 unwell unable to attend,</td>
<td>3 moved to Strand C,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 moved to Strand C,</td>
<td>1 weather too cold</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 stopped due to fall</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lost to follow up 1</td>
<td>1 steroids for LBP,</td>
<td>1 on holidays for follow up assessment</td>
<td>DNA follow up assessment</td>
<td>Assessment date clashed with hospital appointment</td>
</tr>
<tr>
<td>3 DNA follow up assessment,</td>
<td>1 on holidays for follow up assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 on holidays for follow up assessment,</td>
<td>1 DNA follow up assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 sick at follow up assessment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Week 24</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Lost to follow up 2</strong></td>
<td>6 DNA follow up assessment, 2 Relapses,</td>
<td>4 DNA follow up assessment, 1 relapse, 5 unwell, 1 on holidays</td>
<td>2 DNA follow up assessment, 1 Relapse, 1 on holidays</td>
<td></td>
</tr>
<tr>
<td>Lost to follow up 2</td>
<td>6 DNA follow up assessment, 2 Relapses,</td>
<td>4 DNA follow up assessment, 1 relapse, 5 unwell, 1 on holidays</td>
<td>2 DNA follow up assessment, 1 Relapse, 1 on holidays</td>
<td></td>
</tr>
</tbody>
</table>
7.2 Baseline profile and differences between groups at baseline

Information from the baseline assessment was used to establish a profile of participants for each of the groups.

**Demographic profile of participants**

The mean age of the participants for the total cohort was 54.9 years (±10.1). Seventy two (64.3%) were female and forty (35.7%) were male. The largest percentage of the cohort had Secondary Progressive MS (41.4%). Relapsing Remitting MS and Primary Progressive MS were reported by 27% and 22% of the participants respectively, and 8.1% did not know what type of MS they had. Gender, age, duration since diagnosis and onset of symptoms, type of MS and GNDS for each of the groups is displayed in Table 14. It is evident that the control group were significantly younger and had a significantly shorter time since diagnosis (p<0.05).
Table 14 Baseline demographics for each group

<table>
<thead>
<tr>
<th></th>
<th>Group Physiotherapy</th>
<th>1:1 Physiotherapy</th>
<th>Yoga</th>
<th>Control</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (N) / Female (N)</td>
<td>18 / 30</td>
<td>15 / 20</td>
<td>5/8</td>
<td>2/13</td>
<td>0.247c</td>
</tr>
<tr>
<td>Age in years (SIR)</td>
<td>57(10)</td>
<td>52(11)</td>
<td>58(8)</td>
<td>49(6)</td>
<td>0.029b</td>
</tr>
<tr>
<td>Duration since diagnosis in yrs (SD)</td>
<td>18(9)</td>
<td>13(8)</td>
<td>15(8)</td>
<td>10(3)</td>
<td>0.002a</td>
</tr>
<tr>
<td>Duration since Symptoms in yrs (SD)</td>
<td>22(11)</td>
<td>20(13)</td>
<td>21(14)</td>
<td>15(7)</td>
<td>0.233a</td>
</tr>
<tr>
<td>Type of MS (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RR</td>
<td>13</td>
<td>7</td>
<td>4</td>
<td>5</td>
<td>0.152c</td>
</tr>
<tr>
<td>SP</td>
<td>20</td>
<td>16</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>PP</td>
<td>8</td>
<td>11</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>7</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>GNDS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>28 (58)</td>
<td>21(60)</td>
<td>9(69)</td>
<td>0.256c</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>17 (35)</td>
<td>13(37)</td>
<td>4(30)</td>
<td></td>
</tr>
</tbody>
</table>

a One way ANOVA  
b Kruskal Wallis test  
c Chi-square test for independence
Table 15 Baseline scores for each group for all outcome measures

<table>
<thead>
<tr>
<th></th>
<th>Group Physio</th>
<th>1:1 Physio</th>
<th>Yoga</th>
<th>Control</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSIS-29 physical (±SD)</td>
<td>50.5(±9)</td>
<td>53.9(±11.3)</td>
<td>48(±10)</td>
<td>55(±9)</td>
<td>0.107a</td>
</tr>
<tr>
<td>MSIS-29v2 psychological (SIR)</td>
<td>18(5.5)</td>
<td>18(5)</td>
<td>15(3)</td>
<td>16.5(3.25)</td>
<td>0.293</td>
</tr>
<tr>
<td>BBS (±SD)</td>
<td>28.5(±9)</td>
<td>30(±11.5)</td>
<td>22(±13)</td>
<td>18(±6)</td>
<td>0.391a</td>
</tr>
<tr>
<td>MFIS (±SD)</td>
<td>40.7(±16)</td>
<td>46.7(±14)</td>
<td>30.4(±17)</td>
<td>47(±15)</td>
<td><strong>0.034a</strong></td>
</tr>
<tr>
<td>6MWT(±SIR)</td>
<td>105.5(56)</td>
<td>89(63)</td>
<td>66(57)</td>
<td>79(49)</td>
<td>0.103a</td>
</tr>
</tbody>
</table>

*One way ANOVA  bKruskal Wallis test*
Outcome Measures at Baseline

Scores at baseline for all outcome measures in each group can be seen in Table 15. In order to be able to interpret the difference between groups, scores at baseline should be similar. This is not the case for the yoga group. Participants in this group were significantly less fatigued than those in the one to one physiotherapy and the control groups.

Baseline Medication usage

The median number of medications used by each group can be seen in Table 16. The usage of medications for specific symptoms can also be seen here. Thirteen percent of the total cohort reported not taking any medication, the majority of the cohort (87%) reported taking one or more medications. For three of the four groups the percentage of participants taking disease modifying medication was larger than the percentage of participants in those groups that had RRMS. There were no statistically significant differences between the groups for medication usage at baseline (p>0.05)
Table 16 Baseline medication usage for all groups (overall number and medications for specific symptoms)

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Number of Medications (SIR)</th>
<th>Disease Modifying n (%)</th>
<th>Spasticity n (%)</th>
<th>Fatigue n (%)</th>
<th>Pain n (%)</th>
<th>Continence n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy</td>
<td>2.4 (1.9)</td>
<td>21 (43.8)</td>
<td>17 (35.4)</td>
<td>1 (2.1)</td>
<td>11 (23)</td>
<td>9 (18.7)</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>2.5 (1.5)</td>
<td>10 (28.6)</td>
<td>14 (40)</td>
<td>3 (8.6)</td>
<td>6 (17.1)</td>
<td>9 (25.7)</td>
</tr>
<tr>
<td>Yoga</td>
<td>3 (2)</td>
<td>4 (30.7)</td>
<td>7 (53.8)</td>
<td>2 (15.4)</td>
<td>4 (30.7)</td>
<td>2 (15.4)</td>
</tr>
<tr>
<td>Control</td>
<td>4 (2)</td>
<td>9 (60)</td>
<td>8 (53)</td>
<td>3 (20)</td>
<td>4 (26.7)</td>
<td>4 (26.7)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.146&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.119&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.675&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.142&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.846&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.792&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Kruskal Wallis Test  <sup>b</sup>Chi-square test for independence
Table 17 Objectively assessed impairments at baseline for all of the groups

<table>
<thead>
<tr>
<th></th>
<th>Group Physiotherapy n (%)</th>
<th>1:1 Physiotherapy n (%)</th>
<th>Yoga n (%)</th>
<th>Control n (%)</th>
<th>p-value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UL Sensation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>38(79.1)</td>
<td>25(71.4)</td>
<td>9(69.2)</td>
<td>11(73.3)</td>
<td>0.234</td>
</tr>
<tr>
<td>impaired</td>
<td>6(12.5)</td>
<td>10(28.6)</td>
<td>4(30.8)</td>
<td>4(26.7)</td>
<td></td>
</tr>
<tr>
<td><strong>LL Sensation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.960</td>
</tr>
<tr>
<td>normal</td>
<td>24(50)</td>
<td>18(51.4)</td>
<td>7(53.8)</td>
<td>9(60)</td>
<td></td>
</tr>
<tr>
<td>impaired</td>
<td>20(46.7)</td>
<td>16(45.7)</td>
<td>6(46.2)</td>
<td>6(40)</td>
<td></td>
</tr>
<tr>
<td><strong>Tone knee (MAS)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.465</td>
</tr>
<tr>
<td>0</td>
<td>10(20.8)</td>
<td>9(25.7)</td>
<td>3(23.1)</td>
<td>7(46.7)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>18(37.5)</td>
<td>8(22.8)</td>
<td>3(23.1)</td>
<td>2(13.3)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4(8.3)</td>
<td>7(20)</td>
<td>3(23.1)</td>
<td>2(13.3)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>9(18.7)</td>
<td>4(11.4)</td>
<td>1(7.7)</td>
<td>2(13.3)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>4(8.3)</td>
<td>6(17.1)</td>
<td>1(7.7)</td>
<td>1(6.7)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>UL Proprioception</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.468</td>
</tr>
<tr>
<td>normal</td>
<td>41(85.4)</td>
<td>31(88.6)</td>
<td>10(76.9)</td>
<td>15(100)</td>
<td></td>
</tr>
<tr>
<td>abnormal</td>
<td>4(14.6)</td>
<td>4(11.4)</td>
<td>2(15.4)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td><strong>LL Proprioception</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.427</td>
</tr>
<tr>
<td>normal</td>
<td>35(72.9)</td>
<td>24(68.5)</td>
<td>6(46.2)</td>
<td>8(53.3)</td>
<td></td>
</tr>
<tr>
<td>abnormal</td>
<td>13(27.1)</td>
<td>10(28.5)</td>
<td>6(46.2)</td>
<td>6(46.7)</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Chi-square test for independence
Profile of Impairments at Baseline

Upper and lower limb sensation and proprioception were assessed at baseline. Sensation was assessed using light touch with a tissue. Participants were asked to rate the normality of the sensation from 0 – 10 for three sites on the upper limb and three sites on the lower limb, with a maximum score of 60 indicating normal sensation. Proprioception was assessed by placing participants’ big-toe (LL) and finger in different positions with asking participants to identify these positions with their eyes closed. Tone at the knee joint was assessed using the Modified Ashworth Scale (MAS) which has six categories ranging in severity from 0 – 5. The response rate for each category can be seen in Table 17. It is evident from the results shown here that abnormal sensation and proprioception is more common in the lower limb than the upper limb. There were no statistically significant differences for sensation, tone or proprioception between the groups at baseline.

Participants Main Problems

Participants were asked to name the top three problems they have due to their MS. The most frequent responses can be seen in Figure 10. The top four most commonly reported problems for this cohort of Strand B participants were difficulty with their mobility, fatigue, balance and weakness.
7.3 Attendance

Each physiotherapist or yoga deliver was issued with a standardised documentation pack. The attendance of participants and the exercises performed at each session were documented.

Deliverers recorded the number of sessions each participant attended. The median number of sessions attended was 8, 9 and 8, for group physiotherapy, one on one physiotherapy and yoga respectively. There was no significant difference between the three intervention groups for the number of sessions attended. This data was not normally distributed so the difference between the groups was assessed using the Kruskal-Wallis test.
Table 18 Median number of sessions attended by participants in each group

<table>
<thead>
<tr>
<th></th>
<th>Group Physiotherapy</th>
<th>One on One Physiotherapy</th>
<th>Yoga</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Sessions</td>
<td>8(1.5)</td>
<td>9(1)</td>
<td>8(2.25)</td>
<td>0.139</td>
</tr>
<tr>
<td>Attended (SIR)</td>
<td>6(4 - 10)</td>
<td>3(7-10)</td>
<td>7(3 - 10)</td>
<td></td>
</tr>
<tr>
<td>Range(min - max)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Breakdown of sessions attended**

Figure 11 conveys the percentage of participants that attended each number of the sessions. The majority of participants in each of the intervention groups attended 6 or more sessions.

Figure 11 Breakdown of sessions attended by participants in each of the groups
7.4 Content of Interventions

Each physiotherapist or yoga deliverer recorded the programme of exercises completed by each participant on a weekly basis.

Group Physiotherapy

There were seven different deliverers of group physiotherapy. Treatment fidelity was ensured by documentation and it revealed high adherence to the programme. Two participants received specific lower limb stretching which was not a component of the prescribed class. The exercises were progressed and modified according to participants’ ability and this was documented. A fall was documented in one of the classes but no other adverse effects were documented during the classes.

One to One Physiotherapy

Participants in the individualised physiotherapy group had not received community physiotherapy in the three months prior to the commencement of this trial. The individualised treatments were not a continuation of previously provided therapy and were performed following a new assessment by the treating physiotherapist who had no previous contact with the participants. Documentation was analysed for four of the five deliverers of one to one physiotherapy. One set of documentation was not returned. Three out of the four physiotherapists delivered the exercises that were prescribed for the group physiotherapy. These exercises were completed during the sessions as well as other treatments specific to the individual. Additional components included pacing techniques, specific lower back exercises, walking, stretching and bridging exercises. The remaining physiotherapist did not use the elements of the group programme. Treatments consisting of a combination of the above additional exercises were carried out specifically for each participant.
Yoga

There were three yoga led groups. One of the three classes included squatting, which was one of the prescribed exercises for the group physiotherapy intervention. Relaxation, meditation, breathing techniques and stretching were common to all three classes. Other components that made up the yoga classes included maintaining different poses, for example, the mountain pose, the cat pose and the tailor pose (2 classes) and self massage (1 class).
7.5 Main Study Findings

Strength data was collected using Hand Held Dynamometry (HHD) as described in the methodology but a subsequent analysis of the reliability of HHD in 8 PwMS suggested poor between rater reliability and large SEM values, for example, the SEM for knee extension was 40.95N, 31.7% of the mean strength measured for the PwMS in the study.

All data was initially tested for a normal distribution. This was done using visual analysis of histograms in conjunction with the Shapiro Wilk normality test (n<50 per group). Non-normally distributed data was assessed using non parametric tests while normally distributed data was assessed using parametric tests. Data was assessed for normality in order to perform the most appropriate statistical tests for that data distribution and to establish if the data met or violated the assumptions of parametric analyses. Parametric techniques are considered more powerful than non parametric alternatives but applying these techniques to non-normally distributed data may lead to problems and may affect the validity of the findings. Parametric tests such as ANOVA and t-tests are procedures based on comparing means with reference to a normal distribution. When data is non-normally distributed or skewed the mean no longer reflects the appropriate measure of centrality and thus, performing parametric tests may lead to biased results.

The analysis was performed in three stages in order to answer the three research questions:

1. What was the effect of the interventions between baseline and week 12?
2. What was the follow up effect (Week 24)?
3. What signs and symptoms influence outcome?
7.6 Stage 1 - Analysis of data between Week 1 and Week 12

The descriptive statistics used for normally distributed data were means, standard deviations and 95% confidence intervals (CI). This data was analysed using a repeated measures ANOVA. All the assumptions of this form of analysis were met. If there was any significant time or group interactions these were examined further using post-hoc paired t-tests. Paired t-tests were used to establish if there was a statistically significant difference in the mean scores between week 1 and week 12. Other statistical methods may also have been performed as alternatives for this post hoc analysis, for example, the Tukey test which is based on the same principle as the t-test and addresses the issue of multiple testing. Conducting multiple paired t-tests may not have been the most effective method of analysis and may have increased the likelihood of Type 1 error. In order to address this and decrease the possibility of Type 1 error the p value was adjusted using the Bonferroni correction method. For this method the p value set for significance was divided by the number of statistical comparisons performed. If there was not a significant time with group interaction the plot of the means was consulted to guide the interpretation of the results and possible post-hoc analysis. Medians and semi-interquartile ranges (SIR) were used to describe not normally distributed data. Wilcoxin signed rank tests were used to assess the change seen over time. In order to assess any differences between groups a change score was computed and Kruschal Wallis tests were performed.
Multiple Sclerosis Impact Scale-29 v2 Physical Component

A decrease in score on this scale indicates a decrease in the physical impact of MS. A repeated measures ANOVA (between-within) was performed to assess the effect of having one of three interventions (Group physiotherapy, one on one physiotherapy, yoga) or having no intervention (control) on the MSIS-29v2 physical component across two time periods (Week 1 and Week 12). There was no significant interaction between intervention type and time, Wilks’ Lambda = 0.965, F = 1.285, df = 3, 107 and p = 0.238. There was a significant main effect for time, (Wilks’ Lambda = 0.930, F = 7.993, df = 1, 107 and p = 0.006) with the two physiotherapy interventions and the control group showing a reduction in score at week 12 (see Figure 12). The mean score for the yoga group increased at week 12. Post hoc analysis was conducted after consulting the plot of the mean scores to establish where there was a significant change over time (see Table 19). The main effect comparing the groups was not significant, p = 0.228.
Figure 12 Mean MSIS29v2 physical component scores at week 1 and week 12

![Graph showing mean MSIS29v2 physical component scores over time for different groups.]

Table 19 Descriptives and Paired t-tests for MSIS-29v2 physical component

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Week 1 (SD)</th>
<th>Mean Week 12 (SD)</th>
<th>Mean Change (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Physiotherapy</td>
<td>50.5 (9.49)</td>
<td>45.95 (10.52)</td>
<td>4.54 (1.5, 7.5)</td>
<td>8.9</td>
<td>0.48</td>
<td>0.004*</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>54.05 (11.49)</td>
<td>49.42 (12.02)</td>
<td>4.52 (1.1, 7.9)</td>
<td>8.4</td>
<td>0.4</td>
<td>0.012*</td>
</tr>
<tr>
<td>Yoga</td>
<td>48.31 (10.53)</td>
<td>49.61 (11.62)</td>
<td>-1.31 (-7.3, 4.7)</td>
<td>2.7</td>
<td>0.12</td>
<td>0.645</td>
</tr>
<tr>
<td>Control</td>
<td>55.33 (9.51)</td>
<td>50.47 (11.28)</td>
<td>4.86 (-0.6, 10.4)</td>
<td>8.7</td>
<td>0.43</td>
<td>0.08</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.0125
Multiple Sclerosis Impact Scale-29 v2 Psychological Component

A decrease in score on this scale indicates a decrease in the psychological impact of MS. Repeated measures ANOVA is the preferred method of analysing randomised controlled trials with baseline and post-intervention measures, however the data failed to meet the key assumptions for this technique (normality, sphericity and equality of variances). Thus, non-parametric statistics were used. Median values and semi interquartile ranges (SIR) were used as descriptive statistics. The change over time was visually depicted using a boxplot containing the median values at week 1 week 12 (Figure 13). The dark line represents the median value. The boxes represent the 25th and 75th percentile and the whiskers represent the range. Scores on the psychological component of the MSIS-29v2 decreased for group physiotherapy, one on one physiotherapy and the control group by 16.7, 5 and 11.6 percent respectively. The significance of these changes was assessed using the Wilcoxon signed rank test and only the group physiotherapy showed a statistically significant change $p = 0.005$ (Table 20). The differences between the groups were assessed by computing a change score and performing a Kruskal Wallis test. There was no statistical significant change between the groups, $p = 0.17$. 
Figure 13 Boxplot showing the MSIS29v2 psychological component scores at week 1 and week 12.

Table 20 Descriptives and Wilcoxon Signed Rank tests for MSIS-29v2 psychological component

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Week 1 (SIR)</th>
<th>Median Week 12 (SIR)</th>
<th>Median Change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Physiotherapy</td>
<td>18 (5.5)</td>
<td>15 (4.75)</td>
<td>-3</td>
<td>0.005*</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>18 (5.38)</td>
<td>17 (4.88)</td>
<td>-1</td>
<td>0.057</td>
</tr>
<tr>
<td>Yoga</td>
<td>14 (2.25)</td>
<td>15 (4)</td>
<td>1</td>
<td>0.281</td>
</tr>
<tr>
<td>Control</td>
<td>17 (4)</td>
<td>15 (4.5)</td>
<td>-2</td>
<td>0.507</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.0125
Modified Fatigue Impact Scale

There was no significant time by group interaction when a repeated measures ANOVA was performed on the MFIS data, Wilks’ Lambda = 0.951, F = 1.814, df = 3, 105 and p = 0.149. There was, however, a significant main effect for time, Wilks Lambda = 0.924, F = 8.605, df = 1, 105 and p=0.004. Figure 14 shows that the mean scores decreased (indicating an improvement) for group physiotherapy, individual physiotherapy and the control group. These improvements were statistically significant for both physiotherapy interventions. The mean scores increased for yoga increased indicating a worsening of the effects of fatigue.

The main results of the repeated measures ANOVA showed a significant effect for group, p=0.035. This was explored further by performing a one way ANOVA to assess any differences between the groups. The results showed that the differences between the groups were not statistically significant, p=0.128.
Figure 14 Mean MFIS scores at week 1 and week 12

Table 21 Descriptives and paired t-tests for MFIS

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Week 1 (SD)</th>
<th>Mean Week 12 (SD)</th>
<th>Mean Change (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Physiotherapy</td>
<td>40.71 (16.22)</td>
<td>35.56 (15.66)</td>
<td>5.14 (1.2 - 9.1)</td>
<td>12.6</td>
<td>0.33</td>
<td>0.011</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>46.6 (14.8)</td>
<td>39.51 (13.66)</td>
<td>7.4 (3.2, 11.6)</td>
<td>15.9</td>
<td>0.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Yoga</td>
<td>30.38 (17.17)</td>
<td>32.53 (19.54)</td>
<td>-2.15 (-7.2, 2.9)</td>
<td>7.1</td>
<td>0.13</td>
<td>0.374</td>
</tr>
<tr>
<td>Control</td>
<td>49 (15.47)</td>
<td>42.6 (17.13)</td>
<td>6.38 (-0.4, 13.1)</td>
<td>13</td>
<td>0.37</td>
<td>0.062</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.0125
The results of a repeated measures ANOVA indicated that there was a significant time by group interaction (Wilks’ Lambda = 0.869, F = 4.391, df = 3, 87 and p = 0.006). The plot of the means was used as a guide to interpret the results due to this. The three intervention groups increased their scores on the scale (indicating an improvement) while the control showed a decrease in the average score (Figure 15). All three interventions showed statistically significant improvements and medium to large effect sizes (Table 22). The largest effect size was for the group physiotherapy intervention (0.6).

The graph suggested there may have been a significant difference between the control group and the intervention groups. This was assessed using a one way ANOVA which indicated a significant difference between the groups. Further analysis was performed using independent t-tests and statistically significant differences were found between the control group and group physiotherapy, individual physiotherapy and yoga (p = 0.002, 0.016 and 0.005 respectively).

Figure 15 Mean BBS scores at week 1 and week 12
Table 22 Descriptives and paired t-tests for BBS

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Week 1 (SD)</th>
<th>Mean Week 12 (SD)</th>
<th>Mean Change (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td>28.75 (9.51)</td>
<td>34.47 (9.87)</td>
<td>-5.71 (-7.8, -3.6)</td>
<td>19.9</td>
<td>0.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>30.44 (11.56)</td>
<td>34.15 (9.82)</td>
<td>-3.68 (-6.3, 1.0)</td>
<td>12.1</td>
<td>0.32</td>
<td>0.008</td>
</tr>
<tr>
<td>Yoga</td>
<td>22.6 (12.56)</td>
<td>27.9 (11.49)</td>
<td>-5.3 (-7.5, 3.1)</td>
<td>23</td>
<td>0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Control</td>
<td>24.89 (11.61)</td>
<td>21.77 (11.91)</td>
<td>3.11 (-2.8, 9.0)</td>
<td>↓12</td>
<td>0.26</td>
<td>0.258</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.0125

**Six Minute Walk Test**

The data for the six minute walk test was skewed and included outliers. Non parametric data analysis was used. The range of walking distance varied hugely with some participants walking less than ten metres and others walking more than 200 metres. The greatest median score increases were seen for group and individual physiotherapy (Figure 16). This increase was statistically significant for individual physiotherapy, p = 0.001 (See Table 23 for significance values). The control group’s median score improved by 7.8% and the yoga group’s median score decreased by 25%.
The graph showed that there may have been a statistically significant difference between yoga and the other groups. Change scores were computed subtracting the scores at baseline from the scores after the intervention. A Kruskal Wallis test was then performed and this indicated that there was no statistically significant difference between the groups, $p=0.528$.

Figure 16 Boxplot showing the 6MWT distance scores at week 1 and week 12
### Table 23 Descriptives and Wilcoxon Signed Rank tests for 6MWT

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Week 1 (SIR)</th>
<th>Median Week 12 (SIR)</th>
<th>Median Change</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy</td>
<td>101 (39.5)</td>
<td>121.2 (47.38)</td>
<td>20.2</td>
<td>0.08</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>83.75 (39.88)</td>
<td>100 (55)</td>
<td>16.25</td>
<td>0.002*</td>
</tr>
<tr>
<td>Yoga</td>
<td>70 (30)</td>
<td>45 (54.5)</td>
<td>-25</td>
<td>0.553</td>
</tr>
<tr>
<td>Control</td>
<td>83.5 (44)</td>
<td>90 (35)</td>
<td>6.5</td>
<td>0.363</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.0125

### 7.7 Summary of results so far

The results revealed that there were smaller numbers in the yoga and control group than in the physiotherapy intervention groups. This was due to participants not wanting to partake in yoga and a lack of yoga instructors.

The percentage of dropouts was similar across the three intervention groups and the control group. The number of dropouts due to relapses was small in all four groups.

The control group were significantly younger at baseline the length of time since their diagnosis was significantly shorter. The impact of fatigue (as measured on the MFIS) was significantly lower for the yoga group. There were no significant differences between the groups at baseline for medications used, sensation, tone or proprioception.

The results showed a significant treatment effect for the BBS. The three intervention groups improved significantly between week 1 and week 12 and there was a significant difference between the intervention groups and the control group.
There was no treatment effect observed for the subjective, self report outcome measures. There was, however, a significant improvement over time for both physiotherapy interventions observed on the MSIS-29v2 physical component and the MFIS and for group physiotherapy alone on the MSIS-29v2 psychological component. The mean scores on these measures were reduced (suggesting a decrease in the physical and psychological impact of MS and the impact of fatigue) for the control group, whereas, the mean scores increased for the yoga group (suggesting an increase in the physical and psychological impact of MS and the impact of fatigue).

There was a large range of walking distances recorded for the six minute walk test. The median distance walked decreased at week 24 for the yoga group and increased for the two physiotherapy interventions and the control group. This was statistically significant for the 1:1 physiotherapy group. There was no statistically significant difference between the groups.
7.8 Stage 2 – Follow up results week 1, week 12 and week 24

Participants who took part in group physiotherapy, individual physiotherapy and yoga were reassessed twelve weeks after the interventions to establish if the effects of the interventions were maintained. The control group were not reassessed at this time. The follow up data (Week 24) was analysed separately due to the increased number of dropouts at this time point. Only data from participants who were present for all three assessments was analysed to establish the time effect at follow up. Repeated measures ANOVAs were performed on the data that was normally distributed and Friedman’s Tests were performed on the data that was not normally distributed.

Multiple Sclerosis Impact Scale-29 v2 Physical Component

A repeated measures ANOVA was performed to assess the effect of the three interventions (Group physiotherapy, individual physiotherapy and yoga) on participants’ scores on the physical component of the MSIS29v2 across the three time points. There was a significant main effect for time, Wilks’ Lambda = 0.868, F = 5.037, df = 2, 66 and p=0.009.

Figure 17 shows the mean scores at each time point. A post hoc analysis was performed using paired t-tests to establish where this significant time effect occurred (See Table 24). There was a statistically significant improvement for group and individual physiotherapy between pre intervention and post intervention, p=0.001 and 0.005 respectively. The mean scores for the two physiotherapy interventions increased between post intervention and follow up (indicating an increase in the physical impact of MS) but not significantly. The yoga group’s scores increased post intervention and decreased at twenty four week follow up. These changes were not statistically significant.
Figure 17 Mean MSIS29v2 physical component scores at week 1, week 12 and week 24

P values represent significant changes over time (between week 1 and week 12) using paired t-tests.
Table 24 Descriptives and post hoc analysis for MSIS-29v2 physical component

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Week 1 (SD)</th>
<th>Mean Week 12 (SD)</th>
<th>Mean Week 24 (SD)</th>
<th>Mean Change 1 - 12 (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
<th>Mean Change 12 - 24 (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>51.8 (9.8)</td>
<td>45.9 (10)</td>
<td>48.75 (9.9)</td>
<td>-5.9 (-2.59, -9.1)</td>
<td>11.4</td>
<td>0.6</td>
<td>0.001*</td>
<td>2.85 (5.26, 0.35)</td>
<td>6.2</td>
<td>0.28</td>
<td>0.027</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>52.6 (12.6)</td>
<td>46.4 (11.7)</td>
<td>48.1 (13.4)</td>
<td>-6.2 (-2.1, -0.39)</td>
<td>11.8</td>
<td>0.49</td>
<td>0.005*</td>
<td>1.7 (4.2, -0.81)</td>
<td>3.6</td>
<td>0.14</td>
<td>0.174</td>
</tr>
<tr>
<td>Yoga</td>
<td>48.2 (9.9)</td>
<td>49.8 (7.6)</td>
<td>43.1 (7.5)</td>
<td>1.6 (10.31, -7.2)</td>
<td>3.3</td>
<td>0.16</td>
<td>0.693</td>
<td>-6.7 (1.2, -14.5)</td>
<td>13.4</td>
<td>0.88</td>
<td>0.86</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.008
Multiple Sclerosis Impact Scale-29 v2 Psychological Component

The data for the psychological component of the MSIS-29 v2 was abnormally distributed. In order to establish any significant differences over the three time points the Friedman Test was used. It can be seen from Figure 18 that the median score is reduced between week 12 and 14 for 1:1 physiotherapy and yoga (decrease in the psychological impact of MS) and is increased for group physiotherapy (increase in the psychological impact of MS). The changes observed are small. The results of the Friedman test (See table 25) indicated that there was a statistically significant difference in the scores across the three time points for group physiotherapy, $p = 0.012$. A post hoc analysis was conducted using the Wilcoxon signed rank test and a significant difference was found between week 1 and week 12 $p = 0.007$. There was no statistically significant difference between week 12 and week 24.

Figure 18 Boxplot showing the MSIS29 psychological component scores at week 1, week 12 and week 24
Table 25 Descriptives and Friedman results for MSIS-29v2 psychological component

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Week 1 (SIR)</th>
<th>Median Week 12 (SIR)</th>
<th>Median Week 24 (SIR)</th>
<th>Median Change 1 - 12</th>
<th>Median Change 12 -24</th>
<th>p value (Friedman)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy</td>
<td>18 (5.8)</td>
<td>15 (4.75)</td>
<td>15.5 (3.75)</td>
<td>-3</td>
<td>0.5</td>
<td>0.012*</td>
</tr>
<tr>
<td>Yoga</td>
<td>14 (2.75)</td>
<td>15 (4)</td>
<td>13 (3)</td>
<td>1</td>
<td>-2</td>
<td>0.239</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>18 (4.25)</td>
<td>16 (4.75)</td>
<td>15 (4)</td>
<td>-2</td>
<td>-1</td>
<td>0.12</td>
</tr>
</tbody>
</table>

**Modified Fatigue Impact Scale**

There was no significant overall group and time interaction observed when a repeated measures ANOVA was performed on the MFIS data, Wilk’s Lambda = 0.953, F = 1.132, df = 4, 132 and p = 0.344. Analysing the graph led to the evaluation of the main effect of time which was significant, Wilk’s Lambda = 0.872, F = 4.841, df = 2, 66 and p = 0.011. The impact of fatigue increased at week 24 for both physiotherapy groups and decreased for the yoga group. There was no statistically significant differences for any of the interventions between weeks 12 and 24 (see Table 26 for post hoc analysis).
Figure 19 Mean MFIS scores at week 1, week 12 and week 24

$p=0.002$

P value represents significant change over time (between week 1 and week 12) using paired t-test.
Table 26 Descriptives and post hoc analysis for MFIS

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Week 1 (SD)</th>
<th>Mean Week 12 (SD)</th>
<th>Mean Week 24 (SD)</th>
<th>Mean Change 1 - 12 (SD)</th>
<th>Mean Change 12 - 24 (SD)</th>
<th>% Change 1 - 12 (95% CI)</th>
<th>Effect Size</th>
<th>p value</th>
<th>% Change 12 - 24 (95% CI)</th>
<th>Effect Size</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy</td>
<td>42.1 (15.2)</td>
<td>36.1 (16.7)</td>
<td>39.1 (17.8)</td>
<td>-6 (-1.59, 10.29)</td>
<td>-8 (-3.4, -13.77)</td>
<td>14.25</td>
<td>0.39</td>
<td>0.009</td>
<td>3 (7.8, -1.91)</td>
<td>0.17</td>
<td>0.227</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>47.2 (14.5)</td>
<td>38.6 (12.5)</td>
<td>29.9 (16.5)</td>
<td>-8.6 (-3.4, -13.77)</td>
<td>-8.7 (6.9, -4.27)</td>
<td>18.2</td>
<td>0.59</td>
<td>0.002*</td>
<td>22.5 (0.53)</td>
<td>0.623</td>
<td></td>
</tr>
<tr>
<td>Yoga</td>
<td>28.9 (15.5)</td>
<td>28.9 (14.7)</td>
<td>27.4 (13.9)</td>
<td>0 (4.69, -4.69)</td>
<td>-1.5 (4.9, -7.81)</td>
<td>0.0</td>
<td>0</td>
<td>1</td>
<td>5 (0.1)</td>
<td>0.615</td>
<td></td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.008
Berg Balance Scale

The results of the repeated measures ANOVA for the BBS data showed that there was no significant time and group interaction, Wilk’s Lambda = 0.750, F = 0.795, df = 4, 108 and p = 0.531. The main effect for time was significant, Wilk’s Lambda = 0.750, F = 8.984, df = 2, 54, and p < 0.000. A post hoc analysis (see table 27) was performed to establish where this time interaction took place. It is evident from the graph (Figure 20) that the scores for the physiotherapy intervention groups decreased between weeks 12 and 24. There was no statistically significant change between these time points and the mean score at week 24 was higher than the mean score at Week 1. The average score in the yoga group increased slightly at week 24.

Figure 20 Mean BBS scores at week 1, week 12 and week 24

![Graph showing mean BBS scores at different time points with p-value and significance](image-url)
Table 27 Descriptives and post hoc analysis for Berg Balance Scale

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean Week 1 (SD)</th>
<th>Mean Week 12 (SD)</th>
<th>Mean Week 24 (SD)</th>
<th>Mean Change 1 - 12 (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
<th>Mean Change 12 - 24 (95% CI)</th>
<th>% Change</th>
<th>Effect Size</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiotherapy</td>
<td>29.2 (9.9)</td>
<td>34.5 (10.4)</td>
<td>32.3 (11.5)</td>
<td>5.3 (7.95, 2.7)</td>
<td>18.1</td>
<td>0.53</td>
<td>&gt;0.001*</td>
<td>-2.2 (0.4, -4.89)</td>
<td>6.3</td>
<td>0.21</td>
<td>0.102</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>31.2 (10.9)</td>
<td>34.9 (9.9)</td>
<td>31.8 (11.1)</td>
<td>3.7 (7.13, 0.31)</td>
<td>11.9</td>
<td>0.33</td>
<td>0.034</td>
<td>-3.1 (0.4, -6.89)</td>
<td>8.8</td>
<td>0.31</td>
<td>0.085</td>
</tr>
<tr>
<td>Yoga</td>
<td>20.3 (10.9)</td>
<td>25.8 (10.3)</td>
<td>26.5 (10.6)</td>
<td>5.5 (9.41, 1.58)</td>
<td>27</td>
<td>0.5</td>
<td>0.015</td>
<td>0.7 (10.9, -9.56)</td>
<td>2.7</td>
<td>0.06</td>
<td>0.874</td>
</tr>
</tbody>
</table>

*Bonferroni correction – adjusted p value set at 0.008
Six Minute Walk Test

The Friedman test was used to assess the change in distance walked over six minutes at the three time points because the data was abnormally distributed. The results can be seen in Table 28. Distance walked decreased between week 12 and week 24 for both physiotherapy groups and increased for the yoga group (See Figure 21). The boxplot shows a number of outliers and a large amount of variability. The results of the Friedman Test indicated that there was a statistically significant difference in distance walked across the three time points for 1:1 physiotherapy, $p = 0.001$. A post hoc analysis using Wilcoxon Signed Rank tests revealed that there was no statistically significant difference between week 12 and 24 (follow up) but the change observed between week 1 and 12 for 1:1 physiotherapy was statistically significant, $p = 0.002$.

Figure 21 Boxplot showing the 6MWT distance scores at week 1, week 12 and week 24
Table 28 Descriptives and Friedman test p values for six minute walk test

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Week 1 (SIR)</th>
<th>Median Week 12 (SIR)</th>
<th>Median Week 24 (SIR)</th>
<th>Median Change 1 - 12</th>
<th>Median Change 12 - 24</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Physiotherapy</td>
<td>124.5 (39.37)</td>
<td>140 (60.75)</td>
<td>111.75 (54.5)</td>
<td>15.5</td>
<td>-28.25</td>
<td>0.850</td>
</tr>
<tr>
<td>1:1 Physiotherapy</td>
<td>87.5 (58)</td>
<td>110 (61)</td>
<td>100 44</td>
<td>32.5</td>
<td>-10</td>
<td>0.001</td>
</tr>
<tr>
<td>Yoga</td>
<td>42 (25)</td>
<td>35 (31)</td>
<td>66 (55)</td>
<td>-7</td>
<td>31</td>
<td>0.183</td>
</tr>
</tbody>
</table>
7.9 Summary of results between week 1, week 12 and week 24

There was less data included in the follow up analysis due to dropouts. The baseline scores for the participants who attended all three assessments were similar to the larger data set for all outcome measures except for the 6MWT. The median distance walked at baseline was greater for the participants in group physiotherapy that attended all three assessments and shorter for the yoga participants.

The yoga group scores suggested improvements on all the outcome measures between week 12 and week 24 but the number of participants who attended all three assessment was small (n=9).

There was a suggested worsening observed on the BBS, MFIS and the MSIS29v2 physical component for both physiotherapy intervention groups between week 12 and week 24. They did not, however, return to their baseline scores (week 1). The differences in scores on the psychological component of the MSIS29v2 between week 12 and week 24 were very small for both group and individual physiotherapy. The median distance walked was reduced at week 24 for both physiotherapy intervention groups. The changes observed between weeks 12 and 24 were not statistically significant.

7.10 Stage 3 Factors that influence outcome

A literature review (Chapter 2) evaluating the different interventions used in the treatment of PwMS with moderate to severe mobility difficulties found that there was a lack of conclusive evidence of the optimum intervention. It also showed that PwMS with varying levels of mobility and other symptoms were given the same treatments and it remained unknown which participants benefited from such which treatments.
An exploratory data analysis was performed in order to establish which signs and symptoms may be associated with a positive outcome. Data for both physiotherapy interventions was combined to increase the number of participants as the effects of the two interventions were similar.

**Dependent Variables**

The score at week 24 of the primary outcome measure (Physical component of the MSIS-29v2) was chosen as the dependent variable. Due to the disparity between the subjective self report measures and the objective measures the BBS score at week 24 was chosen as the dependent variable for a second multiple regression analysis. Both variables are continuous and their scores at baseline were entered into the analysis in order to incorporate the change in the scores over time.

**Independent Variables**

In order to establish what signs and symptoms may be associated with a positive outcome a literature review was conducted (Chapter 3) that looked at the natural history and progression in MS and the capacity of specific signs and symptoms to affect or predict the outcome of a rehabilitation programme. The number of participants included in this analysis was 81. The number of independent variables included in the model was kept to 8 at a time in order to maintain an adequate number of cases per variable and increase generalisability. Some of the variables were divided into two categories, normal and abnormal. This was done for lower limb proprioception, tone and sensation. Tone was measured using the Modified Ashworth Scale which ranges from 0 (no tone increase) to 4 (unable to move limb). This meant that scores of 0 equalled normal tone and any other scores equalled abnormal tone. Type of MS was categorised into either relapsing or progressive.
Correlation analysis

An initial correlation analysis was performed to establish the relationships between the dependent and the independent variables. The following tables show the correlation coefficients, using Pearsons for data that was normally distributed and Spearman’s Rho for data that was not normally distributed and for categorical data.

The results show that significant correlations were observed between the MSIS-29v2 physical score at outcome and the scores on the physical and psychological components at baseline and MFIS scores at baseline. The only significant correlations for the BBS at outcome were with and the baseline score on the BBS and the 6MWT.

Table 29 Correlation coefficients between MSIS29v2 physical component outcome scores and outcome measures, demographics and symptoms at baseline

<table>
<thead>
<tr>
<th>MSIS-29v2 physical scores at week 12 - correlations with baseline variables</th>
<th>Correlation Coefficient (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSIS29v2 Physical Baseline</td>
<td>0.555*(&lt;0.01)</td>
</tr>
<tr>
<td>MFIS</td>
<td>0.312*(0.004)</td>
</tr>
<tr>
<td>MSIS29v2 Psychological Baseline</td>
<td>0.443*(&lt;0.01)</td>
</tr>
<tr>
<td>BBS</td>
<td>0.106 (0.344)</td>
</tr>
<tr>
<td>6MWT</td>
<td>-0.185 (0.106)</td>
</tr>
<tr>
<td>Age</td>
<td>0.05 (0.654)</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.169 (0.126)</td>
</tr>
<tr>
<td>Type of MS</td>
<td>0.166 (0.156)</td>
</tr>
<tr>
<td>GNDS</td>
<td>0.117 (0.294)</td>
</tr>
<tr>
<td>Treatment</td>
<td>-0.158 (0.155)</td>
</tr>
<tr>
<td>Tone</td>
<td>0.108 (0.334)</td>
</tr>
<tr>
<td>LL sensation</td>
<td>0.015 (0.899)</td>
</tr>
<tr>
<td>LL proprioception</td>
<td>0.7 (0.533)</td>
</tr>
</tbody>
</table>

* Correlation is significant at the 0.01 level (2-tailed).
Table 30 Correlation coefficients between BBS outcome scores and outcome measures, demographics and symptoms at baseline

<table>
<thead>
<tr>
<th>BBS scores at week 12 correlations with baseline variables</th>
<th>Correlation Coefficient (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSIS29 Physical Baseline</td>
<td>-0.06 (0.613)</td>
</tr>
<tr>
<td>MFIS</td>
<td>-0.039 (0.746)</td>
</tr>
<tr>
<td>BBS Baseline</td>
<td>0.757* (&lt;0.01)</td>
</tr>
<tr>
<td>MSIS29 Psychological Baseline</td>
<td>0.036 (0.763)</td>
</tr>
<tr>
<td>6MWT</td>
<td>0.494* (&lt;0.01)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.018 (0.833)</td>
</tr>
<tr>
<td>Gender</td>
<td>-0.261 (0.26)</td>
</tr>
<tr>
<td>Type of MS</td>
<td>-0.007 (0.957)</td>
</tr>
<tr>
<td>GNDS</td>
<td>0.249 (0.012)</td>
</tr>
<tr>
<td>Treatment</td>
<td>-0.012 (0.861)</td>
</tr>
<tr>
<td>Tone</td>
<td>-0.062 (0.607)</td>
</tr>
<tr>
<td>LL sensation</td>
<td>0.009 (0.945)</td>
</tr>
<tr>
<td>LL proprioception</td>
<td>-0.143 (0.232)</td>
</tr>
</tbody>
</table>
Assumptions of Multiple Regression Analysis

Preliminary analyses were conducted to ensure there was no violation of the assumptions of linearity, multicollinearity and homoscedasticity. The dependent variables were normally distributed. Of the independent variables the six minute walk test alone had outliers. The analysis was performed with these outliers included and excluded. There was no change in the contribution of the six minute walk test with or without the outliers for both analyses. A correlation analysis was performed amongst all the independent variables and the assumption of multicollinearity was not violated.

Predicting Physical Impact of MS

The total variance on the MSIS29v2 outcome score explained by the best model as a whole was 34.3%, $F(9, 59) = 4.077$, $p<0.001$. Only one variable was statistically significant. This was the MSISv2 physical component score at baseline, $p <0.001$. The other variables did not contribute significantly to the model (See Table 31). The analysis was performed without the baseline score of the physical component of the MSIS-29v2 and with other combinations of the variables and none of them were found to contribute significantly to the model.
Table 31 Results for Multiple Regression analysis (Physical component of MSIS29v2)

<table>
<thead>
<tr>
<th>Model</th>
<th>b</th>
<th>SE B</th>
<th>Beta</th>
<th>Sig</th>
<th>95.0% Confidence Interval for b</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>18.991</td>
<td>9.302</td>
<td>0.045</td>
<td>0.045</td>
<td>(0.378, 37.605)</td>
</tr>
<tr>
<td>MSIS29 Physical Baseline</td>
<td>0.528</td>
<td>0.152</td>
<td>0.491</td>
<td>0.0001*</td>
<td>(0.223, 0.833)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-0.031</td>
<td>0.106</td>
<td>-0.043</td>
<td>0.769</td>
<td>(-0.244, 0.181)</td>
</tr>
<tr>
<td>MSIS29 Psychological Baseline</td>
<td>0.232</td>
<td>0.276</td>
<td>0.134</td>
<td>0.403</td>
<td>(-0.320, 0.784)</td>
</tr>
<tr>
<td>BBS</td>
<td>0.089</td>
<td>0.12</td>
<td>0.082</td>
<td>0.459</td>
<td>(-0.151, 0.330)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.087</td>
<td>0.111</td>
<td>-0.084</td>
<td>0.436</td>
<td>(-0.311, 0.163)</td>
</tr>
<tr>
<td>Gender</td>
<td>-1.469</td>
<td>2.559</td>
<td>-0.064</td>
<td>0.567</td>
<td>(-6.589, 3.650)</td>
</tr>
<tr>
<td>Type MS</td>
<td>1.905</td>
<td>2.939</td>
<td>0.071</td>
<td>0.519</td>
<td>(-3.976, 7.786)</td>
</tr>
<tr>
<td>LL sensation</td>
<td>-0.61</td>
<td>2.418</td>
<td>-0.027</td>
<td>0.801</td>
<td>(-5.448, 4.227)</td>
</tr>
<tr>
<td>6MWT</td>
<td>-0.035</td>
<td>0.023</td>
<td>-0.197</td>
<td>0.132</td>
<td>(-0.082, 0.011)</td>
</tr>
<tr>
<td>GNDS</td>
<td>2.985</td>
<td>2.656</td>
<td>0.129</td>
<td>0.266</td>
<td>(-2.329, 8.300)</td>
</tr>
</tbody>
</table>
Predicting Balance Scores

The total variance on the BBS outcome score explained by the best model as a whole was 63%, $F(8, 55) = 12.171$, $p<0.001$. Two variables contributed significantly to the model. These were the baseline score of the BBS and sensation (normal or abnormal), $p<0.001$ and 0.027 respectively (See Table 32). In order to establish and compare the contribution of each of the independent variables the Beta values were consulted. The Beta values in Table 32 represent the standardised coefficients, this means that values for each of the independent variables are standardised and converted to the same scale to allow for comparisons. The largest Beta value can be seen for the BBS at baseline (0.817) indicating that this variable makes the strongest unique contribution to explaining the dependent variable. The second largest Beta value is observed for lower limb sensation (-0.189). The part correlation coefficient for both these variables was squared to obtain an indication of their contribution to the total R square (0.63). The BBS at baseline and lower limb sensation explained 53% and 6% of the total variance in the dependent variable respectively.
Table 32 Results for Multiple Regression analysis (Berg Balance Scale)

<table>
<thead>
<tr>
<th>Model</th>
<th>b</th>
<th>SE B</th>
<th>Beta</th>
<th>Sig.</th>
<th>95.0% Confidence Interval for b</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Constant)</td>
<td>15.446</td>
<td>5.075</td>
<td></td>
<td>0.004</td>
<td>(5.277, 25.616)</td>
</tr>
<tr>
<td>BBS Baseline</td>
<td>0.776</td>
<td>0.08</td>
<td>0.817</td>
<td>0.000*</td>
<td>(0.615, 0.936)</td>
</tr>
<tr>
<td>MSIS29 Physical Baseline</td>
<td>0.02</td>
<td>0.094</td>
<td>0.002</td>
<td>0.983</td>
<td>(-0.187, 0.191)</td>
</tr>
<tr>
<td>MSIS29 Psychological Baseline</td>
<td>-0.129</td>
<td>0.192</td>
<td>-0.086</td>
<td>0.504</td>
<td>(-0.515, 0.256)</td>
</tr>
<tr>
<td>6MWT</td>
<td>0.021</td>
<td>0.016</td>
<td>0.132</td>
<td>0.213</td>
<td>(-0.012, 0.054)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>-0.04</td>
<td>0.062</td>
<td>0.064</td>
<td>0.523</td>
<td>(-0.163, 0.084)</td>
</tr>
<tr>
<td>LL Sensation</td>
<td>-3.701</td>
<td>1.624</td>
<td>-0.189</td>
<td>0.027*</td>
<td>(-0.189, 0.446)</td>
</tr>
<tr>
<td>LL Proprioception</td>
<td>1.578</td>
<td>1.864</td>
<td>0.072</td>
<td>0.401</td>
<td>(-2.157, 5.313)</td>
</tr>
<tr>
<td>Tone</td>
<td>-2.632</td>
<td>1.722</td>
<td>-0.126</td>
<td>0.132</td>
<td>(-6.083, 0.818)</td>
</tr>
<tr>
<td>Gender</td>
<td>-3.545</td>
<td>1.777</td>
<td>-0.168</td>
<td>0.071</td>
<td>(-7.107, 0.017)</td>
</tr>
<tr>
<td>GNDS</td>
<td>-0.958</td>
<td>1.887</td>
<td>-0.047</td>
<td>0.641</td>
<td>(-4.742, 2.825)</td>
</tr>
</tbody>
</table>
7.11 Summary of multiple regression analysis

The MSIS-29v2 and BBS scores at outcome were poorly correlated with the independent variables at baseline. Variables were still entered into the regression model as this was exploratory analysis. For the physical component of the MSIS-29v2 the baseline score on that measure was the only variable that influenced the outcome score. For the BBS two variables significantly contributed to the outcome scores, the baseline BBS score and sensation. The amount of variance explained by the variables was greater for the objectively assessed BBS than for the subjectively assessed physical component of the MSIS29v2.
Chapter 8 - Discussion

8.1 Introduction

The aim of this chapter is to discuss the main findings of this study. The effect of the treatment immediately after the intervention and at twenty four week follow up will be discussed in terms of other literature and clinical significance. The methodological issues that may have affected the results will also be discussed along with the limitations of the research.

The overall aim of this thesis was to evaluate the effectiveness of two different physiotherapy interventions and yoga for use in a community setting by Multiple Sclerosis Ireland. In addition to this, this thesis aimed to add to the limited knowledge base, highlighted in the literature review in Chapter 2, surrounding the treatment of PwMS with moderate to severe gait impairment. The specific objectives of the intervention study were to:

1. To evaluate the immediate and follow up effects of two types of physiotherapy interventions (group and individual) and yoga on PwMS who mobilise with at least bilateral assistance.

2. To compare the effectiveness of these interventions in order to establish the most effective treatment option for this population of PwMS.

3. To explore signs and symptoms of MS that may be associated with the outcome of the above interventions.
8.2 Effect of Interventions

The findings of the literature review evaluating interventions used in PwMS with moderate to severe mobility impairment revealed that we don’t know specific outcomes for this population or how this specific group of PwMS respond to treatment. A multitude of interventions were used and it remains unknown which is optimal for use in clinical practice.

Previous studies grouped PwMS with varying levels of mobility together and it remained unclear which interventions were more effective for participants with more severe mobility impairment (EDSS > 6 or GNDS mobility component score of 3 or 4). This study aimed to address this by including only participants with a GNDS mobility component score of 3 or 4 (equivalent to EDSS >6) therefore, making the results specific to this population of PwMS. This is the first known randomised controlled trial specifically for PwMS with moderate to severe mobility impairment.

Physiotherapy was one of the treatment options evaluated in this population of PwMS. A survey of PwMS in Ireland revealed that physiotherapy was the service they required the most and was not readily available to them (Coote et al., 2010). This information was used to devise a group physiotherapy treatment aimed at improving balance and strength in order to begin to evaluate the effect of physiotherapy intervention on this population of PwMS. Overall, this group intervention showed the greatest improvements.

The results of the study (Chapter 7) highlight the appropriateness, suitability and relevance of the content of the group physiotherapy intervention for this population of PwMS. Participants reported walking/mobility (n=49), balance (n=41), fatigue (n=36) and weakness (n=34) as the top four most commonly reported problems. The results showed that group physiotherapy improved three out of four of the participants’ main problems.
One of the main limitations of this study is that several groups were not treated with the interventions they were originally allocated to. It is evident from the results (Chapter 7) that there were smaller numbers in the yoga (n=13) and control groups (n=15) compared with both group and individual physiotherapy interventions (n=48 and n=36 respectively). Following further exploration it was revealed that, interestingly, groups of participants lobbied the regional offices on hearing they were allocated to the yoga or control groups. These participants were subsequently randomly allocated to group or individual physiotherapy interventions.

The second limitation is that the groups were not similar at baseline. The control group were different to the treatment groups at baseline in two ways. They were significantly younger, 49 compared with 57, 58, 52 (p=0.029), and they had a significantly shorter time since diagnosis than the other participants, 10 years compared with 18, 13, 15 (p=0.002). This may have affected the results and partly explain the unexpected improvements observed in the control group as this cohort of participants may not be representative of this population of MS in general. The yoga group reported a significantly lower impact of fatigue (p=0.034) at baseline compared to the other groups. These limitations introduce a high level of selection bias in this study (Cochrane Handbook for Systematic Reviews of Interventions,(Higgins and Green, 2008) and must be considered in the interpretation of the results.

The effect of the interventions varied according to each outcome measure. The main findings of each outcome measure will be discussed individually.
8.2.2 Physical Impact of MS

The physical impact of MS was measured using the Multiple Sclerosis Impact Scale – 29v2. A higher score on this scale indicates a greater impact of MS on a person’s physical functioning. This was selected as the primary outcome measure for this study because it measures at the level of participation (recommended by the WHO - ICF 2001) and because of its prominent psychometric properties.

To the best of our knowledge the current study is the first to evaluate the effect of specific physiotherapy interventions on participation using the MSIS-29v2 component scores in a sample of PwMS with an EDSS of 6.5 and above only. This means that direct comparisons with other studies results cannot be made.

The improvements seen in both group and individual physiotherapy were statistically significant (p= 0.004 and 0.012 respectively). The score on the MSIS-29v2 physical component decreased for the control group, suggesting a decrease in the physical impact of MS, and increased for the yoga group suggesting an increase in the physical impact of MS. These changes were not statistically significant. Unexpectedly, the change observed in the control group mirrored that of the physiotherapy intervention groups. The impact of MS was reduced in similar magnitude (mean change of 5) to the physiotherapy interventions indicating that there was no significant difference in HRQoL scores between the physiotherapy interventions and the control group. As the methodology states participants in the control group received their treatment of choice after the week 12 assessments. This may have affected the self report outcome measures as they may have felt positive about receiving their preferred intervention in the future. This may also reflect a possible placebo effect of having two one hour individual assessments with a physiotherapist. Another reason for this may be the small numbers of participants in the control group and the issues surrounding randomisation. The control group of PwMS may not be truly representative of the general population of PwMS with moderate to severe mobility impairment as they were younger and more recently diagnosed.
The mean changes observed for group physiotherapy and one to one physiotherapy were, 4.54 and 4.52 respectively and as previously mentioned these were both statistically significant changes. The previous effect of physiotherapy interventions on Quality of Life is unclear. Only one out of five previous studies that evaluated physiotherapy interventions in a mixed mobility cohort of PwMS used a QoL outcome measure. Rasova et al (2006) used the Multiple Sclerosis Quality of Life (MSQoL) scale when comparing neurophysiologically based physiotherapy, bicycle ergometry, a combination of both and a control group. Similarly to the current study Quality of life improved statistically in the physiotherapy based intervention groups. That study, however, included participants of varying levels of mobility (EDSS 0 – 6.5).

The minimal clinically important change for the physical component of the MSIS-29 v1 was established as 9 in PwMS with an EDSS between 5.5 and 8.5 (Costelloe et al., 2007). This is greater than the change scores observed in the current study but these values were obtained using version one of the MSIS-29 and by comparing change scores to the change scores on the EDSS, which has been shown to lack sensitivity to change. The maximum score on the physical component of the MSIS-29v1 is greater than the maximum score for the same component in version two. In theory, the changes needed to be clinically significant should be lower for the MSIS-29v2 but this has yet to be established.

Giesser et al (2007) used version 1 of the scale when evaluating the effect of treadmill training using body weighted support on only participants with an EDSS > 6.5. They used a total score and not the recommended physical and psychological component scores and found small improvements in three out of the four participants.

There was no statistically significant change observed in the yoga group. The mean score was reduced at week 12 suggesting an increase in the physical impact of MS. This is in contrast to the findings of previous studies. Oken et al (2004) used the generic SF-36 when evaluating the effect of yoga in PwMS significant improvements were observed on this measure. The mean age of the participants in the yoga group in the study by Oken et al (2004) was 48, whereas, the mean age of
the participants in the yoga group in the current study was 58. The mobility levels of the participants in that study (PwMS who used walking aids and those that did not) also differed from the participants in this study (PwMS who used bilateral assistance to walk).

Ahmadi et al (2010) found that QoL, as measured on the Multiple Sclerosis Quality of Life-54 questionnaire, significantly improved following a yoga intervention in PwMS with an EDSS score between 1 and 4. These conflicting results could be due to methodological differences, different content of the yoga interventions and small sample sizes. Another possible reason for these differing results is that the EDSS scores of the participants in this study were much higher than previous studies and that yoga may not be effective for more disabled PwMS. The results also suggest that yoga may be more beneficial for PwMS who are more mobile and that further research is needed to establish the effect of yoga on PwMS with an EDSS score of greater than 6.

8.2.3 Psychological Impact of MS

The psychological component of the MSIS29v2 score was reduced significantly for group physiotherapy suggesting a decrease in the psychological impact of MS. This was not the case for individual physiotherapy or yoga. A possible reason for this could be the potential psychological benefits and social interaction involved with exercising in a group. The absolute change was highest for group physiotherapy with a decrease of 3 between weeks 1 and 12. The median change scores observed for the control group and individual physiotherapy were 2 and 1 respectively, whereas, the yoga group increased their scores by 1.

Qualitative results from the pilot study (Chapter 5) highlighted the importance of exercising in a group and this may have resulted in the significant change in scores in the group physiotherapy. The absolute change observed for group physiotherapy and the control group were similar but did not reach statistical significance for the control group. This may have been due to the smaller numbers of participants in the control group which may have increased the risk of Type II error. Participants in the
pilot study acknowledged the understanding felt between other PwMS who had similar mobility impairment and experiences:

“We all understand each other, because we’re all in the same boat”

Another qualitative study evaluated the effect of exercising in a group for PwMS who have less mobility impairment (EDSS ≤6). Focus groups were conducted and participants (n=14) discussed the psychological benefits of this type of exercise. These included feelings of empowerment, confidence, hope and motivation (Clarke and Coote, 2010).

The MSIS-29v2 was not used in other studies evaluating physiotherapy in PwMS so direct comparisons cannot be made with the findings of these studies. One study (Rasova et al., 2006) found that there was an improvement in depression on the Beck Inventory Scale following a physiotherapy intervention. The possible placebo effect observed in the control group for the physical component score of the MSIS-29v2 was also apparent from the results regarding the psychological impact of MS. Participants may have felt more confident by knowing they were about to receive their preferred intervention. Confidence is assessed as part of the psychological component of the MSIS-29v2.

As previously mentioned the MSIS-29v2 was chosen as the primary outcome measure for this study due to its high psychometric properties and because it assesses at the level of participation. On reflection, and following the analysis of the results, the effect of physiotherapy interventions on QoL in this cohort of PwMS still remains inconclusive. This measure may not capture the variables that affect quality of life in a sample of PwMS with more severe limitations. Future research should consider the qualitative evaluation of exercise interventions in order to gain a true reflection of the impact of these interventions on QoL and consider using these qualitative findings to develop an outcome measure that assesses participation in PwMS with moderate to severe limitations.
8.2.4 Fatigue

Fatigue was assessed using the MFIS. An increase in score on this scale indicates an increase in the impact of fatigue, whereas, a decrease in score indicates that the impact of MS is reduced. The findings of the MFIS echo the findings of the other self report measure, the MSIS-29v2. There were similar improvements observed between weeks 1 and 12 for both physiotherapy interventions and the control group suggesting a placebo effect. These improvements were statistically significant for both physiotherapy interventions. There was a trend for worsening of the impact of fatigue observed in the yoga group.

The exact cause and mechanisms of fatigue experienced by PwMS remain unclear making it difficult to comprehensively explain the improvements observed. Fatigue in MS has been shown to be multidimensional and more complex than the fatigue experienced in other neurological conditions such as Parkinson’s Disease (Smith and Hale, 2007). This contributes to the complexity of the measurement, treatment and understanding of fatigue in MS.

Similarly to the results for HR-QoL, the impact of fatigue was reduced for the control group at week 12 (mean change of 6.3). This, as previously mentioned may have been due to the placebo effect of having two assessments with a chartered physiotherapist. A recent study (Dodd et al., 2011) addressed the impact of social interaction on the effect of treatment by comparing group progressive resistance training (PRT) with a control group who attended a social interaction class to counteract the social aspects and increased attention of exercising in a group. Interestingly, participants in the control group in that study also decreased their impact of fatigue (as measured by the MFIS) by 4.8 points. There was no significant treatment effect for fatigue in this study indicating the importance of social interaction and the possible placebo effect associated with this. This effect needs to be addressed as a confounding factor in future studies.
The effect of physiotherapy interventions on fatigue in this population of PwMS has not been established. There is, however, evidence pertaining to the effect of exercise interventions in a more mobile population of PwMS (EDSS<6). Aerobic exercise has been shown to reduce the impact of fatigue (measured using the MFIS) for this population of PwMS (McCullagh et al., 2008, White et al., 2004). The improvements in these studies may be explained by the aerobic content of the interventions. Inactivity has been associated with increased fatigue in healthy populations (Berlin et al., 2006) and research suggests that PwMS are less physically active than healthy populations (Motl et al., 2005). Improving their overall fitness through aerobic training may reduce fatigue in this population. A recent review (Andreasen et al., 2011) on the effect of exercise therapy on PwMS highlighted that the majority of studies that included PwMS with fatigue demonstrated positive results. The studies, however, did not evaluate fatigue as the primary outcome and further research is needed to establish the optimal exercise modalities and parameters for the treatment of MS fatigue.

Because there was no aerobic element to the interventions used in this study the reasons why fatigue might have improved are different. A recent study by (O'Dwyer and Coote, 2010) revealed that PwMS use more energy to complete activities of daily living. The content of the intervention used in this study aimed to improve the strength and quality of functional movements (for example stepping and transfers), this may have led to more efficient movement patterns, decreased energy expenditure and decreased fatigue. Other possible mechanisms for the reduction in the impact of fatigue in the current study include the repetitive nature of the exercises which may have improved plasticity and axonal regeneration and increased strength and hence reduced muscle fatigue locally. The improvements seen in the control group in this study mirrored those in the physiotherapy intervention groups, therefore, it is more likely that the improvements observed for fatigue may be explained by the social interaction with a physiotherapist as the control group did not undertake repetitive exercise. As previously mentioned this needs to be corroborated in future studies using a larger, matched control group.
Similarly to the current study, Rasova et al (2006) showed statistically significant improvements in the total score of the MFIS. The magnitude of the mean change in that study (8.27 for physiotherapy) was greater than that seen in the current study (5.14 and 7.7 for group physiotherapy and individual physiotherapy respectively). This may be explained by the differences in frequency of the intervention delivery (twice weekly versus once weekly), content of the interventions (aerobic component versus no aerobic component) and differences in levels of mobility of the participants.

Unlike the results of this study, yoga has been shown to reduce the impact of fatigue as measured using the MFIS (Velikonja et al., 2010). Similarly to the findings for fatigue, the yoga group did not improve in the other self report measure (MSIS-29v2). This could be due to the different methodologies used or the differences in the cohorts involved as previously mentioned. It also has to be taken into account that the score at baseline for the yoga group in the current study was significantly lower at 30.4 (indicating a lower impact of fatigue) than the intervention and control groups. A cut off score of 38 on the MFIS has been shown to represent clinically significant fatigue in PwMS (Flachenecker et al., 2002). The mean score of 30.4 observed in the yoga group is below this cut of score indicating the absence of clinically relevant fatigue in this group which may explain why no relevant improvements were observed despite the inclusion of relaxation, meditation and breathing exercises as part of the yoga intervention. The baseline score in the study by Velikonja et al (2010) was higher at 46 suggesting that the impact of fatigue was greater for these participants; therefore, they may have had more potential to improve.

8.2.5 Balance

The results of this research suggest a significant treatment effect for balance. Both physiotherapy interventions and yoga led to statistically significant improvements that were not seen in the control group.
The Berg Balance Scale was used to assess balance. The scale is measured from 0 – 56 and the higher the score the greater the participants performance. This scale has been used in other MS studies (Cattaneo et al, 2007b, Giesser et al 2007, Smedal et al 2006, Lord et al 1998,) and it is also widely used to evaluate the effect of treatments in other populations e.g. stroke rehabilitation, elderly falls rehabilitation and vestibular rehabilitation.

The available evidence for the effect of specific physiotherapy interventions on balance in PwMS is mainly positive. Three studies evaluating physiotherapy showed improvements of on the BBS similar to the results of the current study (Cattaneo et al, 2007b, Smedal et al 2006, Lord et al 1998). Cattaneo et al (2007b) found that balance rehabilitation using motor and sensory strategies was more effective that balance rehabilitation using motor strategies alone (mean change of 6.7 and 4.8 respectively). The mean changes observed for group physiotherapy, individual physiotherapy and yoga were, 5.7, 3.7 and 5.3 respectively. The exact content of the interventions used in those studies is not revealed making comparisons with the current study difficult. It must also be noted that the participants in that study (Cattaneo et al., 2007b) had greater baseline scores (43, 44, 41 for each treatment group respectively) than the participants in this study (28, 30 and 23 for the intervention groups) which may have contributed to the slightly lower change scores observed in this study.

The specific balance exercises included in the content of the group physiotherapy intervention were expected to improve balance. As previously mentioned improvements were also observed in the yoga group. This may be due to the content of the yoga intervention which included the holding of static poses aimed at improving trunk control, which has been shown to affect balance in PwMS (Cameron and Lord, 2010).

The minimal clinical important difference (MCID) on the BBS has not been established for PwMS but there is a value available for the stroke population. Stevenson et al 2001 found that a change of ±6 is observed then one can be 90% confident of genuine change in stroke, another neurological condition where balance deficits are common. The mean change seen for group physiotherapy
approached this and for individual physiotherapy it was lower (5.71 and 3.68 respectively). There is a need to calculate the MCID on the BBS for PwMS with moderate to severe mobility limitations.

A small study of four participants with no control comparison by Giesser et al (2007) was the only known study to use the BBS specifically for PwMS with an EDSS score of > 6.0. The effect of body weighted support on a treadmill showed improvements of more than six in two participants, less than six in one and no improvement was seen in the final participant. The results of that study cannot be extrapolated to a larger population of PwMS with an EDSS > 6 due to the small sample size and lack of a control comparison. The current study aimed to address this by including a control group comparison and is the biggest to date evaluating balance specifically in a population of PwMS with an EDSS score of > 6.0.

Only one previous study assessed the effect of yoga on balance in PwMS (Ahmadi et al., 2010). They also used the BBS and showed that there was a statistically significant improvement following yoga that was not seen in the control group. Direct comparisons cannot be made with this and the current research, however, as the participants in that study were more ambulatory (EDSS ≤ 6) and their baseline scores were greater (46 compared to 22 in the current study). The results of the current research, in conjunction with, the above study’s results suggest that yoga may improve balance in PwMS with different levels of mobility.

It is evident that there are differences between the self report and objective outcome measures in the yoga group. Objectively, they improved (significant increase in BBS scores) but they did not feel it reduced the physical or psychological impact of MS as measured on the MSIS-29v2. It is known that a number of groups of participants rebelled against participating in yoga and, therefore, preference for interventions may have had an influence on the subjective self report scores.

The literature surrounding balance abnormalities in MS suggests that PwMS have delayed postural responses, have difficulty maintaining upright positioning and slowed movement towards their limits of stability (Cameron et al., 2008). A study looking at the clinical aspects of standing balance in MS (Frzovic et al., 2000)
found that when the base of support was reduced e.g. tandem stance, single leg stance and stepping, PwMS performed less well than healthy controls and were less able to maintain standing balance. Cameron et al (2008) found that the decreased speed of the postural responses correlated with the decreased speed of somatosensory conduction in the spinal cord. It has also been shown that central integration deficits add to balance impairment in PwMS (Hamilton et al., 2009). These findings could explain why a greater improvement was seen for an intervention using sensory strategies (Cattaneo et al 2007b) than in the current study as there was no sensory component to the intervention used. The sensory strategies used involved performing motor tasks in different perceptual contexts. This was done by performing the exercises with eyes closed, with the use of foam pads under the feet and with the use of modified lenses. The importance of sensory function to balance rehabilitation is also evident from the results of the post hoc analysis (Chapter 7). Sensation was one of the only clinical variables that significantly influenced balance scores on the BBS at week 12.

As described previously in Chapter 6 of this document there is a high prevalence of falls in PwMS. The exact cause of falls in this population is unknown but balance impairment, both subjectively reported and scored on the BBS, has been shown to be a risk factor (Cattaneo et al., 2002, Finlayson and Peterson, 2006, Nilsagard et al., 2009). The improvement in balance scores observed in the current study could explain the decrease in the number of falls reported and the number of people who fell between week 1 and week 12 and this will be explored further in Chapter 9.

8.2.6 Walking Distance

The results of the 6MWT were difficult to interpret because the data was not normally distributed and a large range of scores was observed. While this research only included participants with a Guy’s Neurological Disability Scale component of 3 or 4 there was a still a great amount of variability in distance walked, with some participants walking less than 10 metres and some walking more than 200 metres. The American Thoracic Society Guidelines (Enright, 2003) recommended not to
use a treadmill or a circular track and to standardise when assessing distance as the primary variable of the 6MWT. Taking these guidelines into consideration, it was decided that a 10 metre walkway with a chair at each end would be used. This distance was deemed feasible in the community settings (hotels, leisure centres, etc.). The chairs were available if rest periods were required.

A statistically significant improvement was only observed for individual physiotherapy but the largest median change was observed for group physiotherapy (20.2 metres). There was no improvement for the yoga or control groups. Rest periods were documented in 59% of the tests and there was no difference between the numbers of rests in each of the groups.

Wide variability of distances walked in six minutes has been acknowledged within each of the EDSS levels (Bethoux and Bennett, 2011). This means that patients with higher levels of disability walked greater distances because of the walking aid used. Other factors may have also affected the variability of the distances walked such as environmental factors and fatigue. The normal variability of other walking tests such as the timed 25ft walk test is 20% (Kragt et al., 2006). The normal variability of the 6MWT is difficult to establish due to the heterogeneous walking ability of PwMS even when they are placed in subgroups according to their mobility level. The percentage improvements observed for the group and individual physiotherapy interventions were 20.1% and 19.4% which is similar in magnitude to the normal variability observed in walking tests. Further research need to be conducted evaluating the variability of walking tests specifically for PwMS with more severe mobility impairment.

Paltamaa et al (2005) established 85 metres as a clinically significant improvement for the 6MWT. However, this value was obtained using participants who were more ambulatory (EDSS between 1 and 6) than the participants in the current study. Research evaluating walking tests in PwMS predominantly involves participants with an EDSS of less than 6.5. Gijbels et al (2010) found that the average distance walked over 6 minutes for twenty one participants with moderate MS (EDSS 4.5 – 6.5) was 281m ±121. Another study (Goldman et al., 2008) defined having the same EDSS score (4.5 – 6.5) as severe MS and found that the average distance
walked over 6 minutes was 379m ±76.3. Those scores were of greater magnitude than the median baseline scores for the current research, where participants had an EDSS score ≥ 6.5. The median baseline scores were 101m (39.5), 83.75m (39.88), 70m (30) and 83.5 (44) for group physiotherapy, individual physiotherapy, yoga and the control group respectively indicating a decreased walking capacity for the participants in this study compared to other literature.

There is no MCID for the 6MWT specifically for this population of PwMS. Savci et al 2005 showed that limitations of activities of daily living were associated with a lower distance walked on the 6MWT. Increasing walking capacity may increase day to day functioning for PwMS. It is possible that the degree of change meaningful to patients with greater disability would be considerably less than the 85m suggested by Paltamaa et al (2005).

The yoga group’s median walking distance was actually reduced at week 12. The lack of improvement observed here may be explained by the specificity of training principle because the intervention consisted of relaxation, stretching and static poses and not exercises specifically aimed at improving walking. The content of the group physiotherapy intervention contained elements of gait including stepping and single leg weight bearing which may explain the translations to function observed for this group. Balance impairment has also been shown to negatively affect walking (Cameron and Lord, 2010). Improving balance through the completion of balance exercises may have improved participants’ walking capacity.

Previous studies evaluating the effect of physiotherapy and other interventions on walking ability used a multitude of different outcomes of gait such as the GAITrite (Smedal et al., 2006) the Rivermead mobility index (Wiles et al., 2002, Lord et al., 1998, Van den Berg et al., 2004) 10 metre timed walk (Giesser et al., 2007, Lord et al., 1998). This makes comparisons between with the findings of these studies and the current studies difficult to establish. These studies also contain a mixed cohort of PwMS with varying levels of mobility different to the participants in the current study, therefore, it is impossible to determine the effect of the interventions of the participants with increased levels of mobility impairment.
A study by Gijbels et al (2010) found that the 6MWT was the most effective at predicting habitual walking over other walking capacity tests in both mild and moderate MS subgroups (Timed up and Go, Timed 25-Foot Walk and the 2 Minute Walk Test) and this supports its use in this study. However, as previously highlighted, the average baseline walking distance reported for the moderate MS subgroup in that study was 284 metres. This was significantly higher than the baseline values observed in this study (101, 83.75, 70 and 83.5 for group physiotherapy, individual physiotherapy, yoga group and control group respectively). This suggests that in a more severely disabled population the 6MWT may not reflect or capture improvements in walking capacity.

Further research is needed into which measure of walking ability is optimal for use in PwMS with moderate to severe mobility limitations. A recent study (Gijbels et al., 2011) compared the 2MWT and the 6MWT in 40 PwMS with varying levels of mobility (EDSS 1 – 6.5) and found that the 2MWT may be a practical replacement for the 6MWT in clinical practice but further research is required to assess the sensitivity to change of these measures following intervention.

The content of the interventions may have also had an effect on the conflicting results observed. Walking was not practiced as part of the interventions, therefore, can direct translation to improvements in walking be expected if the specific task was not trained.

Walking is a multifaceted physical function that necessitates the incorporation of locomotion with motor control, musculoskeletal function, sensory input, balance and posture. Therefore, the relationship between mobility, balance and strength is complex and improvements in walking may be due to a number of factors. There is evidence to suggest that PwMS have decreased muscle strength compared to people without impairment. Lambert et al (2001) revealed that PwMS demonstrated up to 26% less muscle power than healthy controls and experienced muscle fatigue approximately 10% more quickly with repetitive contractions. Maximal voluntary contraction (MVC) in 16 PwMS was shown to be 27% lower than those of 18 healthy controls in another study by NG et al (2004). This decrease in strength has been shown to correlate with walking in PwMS. In 20 PwMS reduced quadriceps
and hamstring strength significantly correlated with gait speed and postural sway with eyes closed (Yahia et al., 2011). Motor function changes were also shown to be associated with impaired ambulation, as measured on the 25ft walk test. This evidence suggests that the mechanism of improvements observed for balance and walking in the current study may be explained by improvements in muscle strength due to the strengthening components of the physiotherapy interventions. This relationship cannot be explored in this study due to the lack of an appropriate measure of muscle strength.
8.3 Group Therapy Vs Individual Therapy

There were no statistically significant differences between group and individual physiotherapy interventions for any of the above outcome measures. This suggests that treating PwMS who have moderate to severe mobility impairment in a group with balance and strengthening exercises can be as effective as individualised treatment.

Group therapy is a commonly used by physiotherapists in the treatment of elderly fallers and has been shown to have positive effects. The benefits of the group setup include motivation and social support (Barnett et al., 2003, Lord et al., 2003). A recent study by Learmonth et al (2011) evaluated exercise in the form of group therapy in 16 people with moderate MS. To be included in the study participants had to have an EDSS score of between 5 and 6.5 and the mean score of the participants was 5.98 (±0.43). A leisure club based exercise class with aerobic, strengthening and balance exercises was compared to a control group told not to change their normal routine. Unlike the results in the current study, there was no significant group/time interaction for balance (also measured using the BBS). There were no statistically significant differences between the group exercise class and the usual care group for any of the outcomes evaluated (Timed 25ft walk, Timed up and Go, 6MWT), however, large effect sizes were observed suggesting that the study may have been underpowered. Although the study by Learmonth et al (2011) evaluated the effects of group therapy on moderately affected PwMS it did not compare the effects of group therapy to individual therapy which is one of the main novelties of this current research.

No other study to date has compared the effect of group and individual therapy in PwMS. This has been done in other populations and the results were comparable to the findings of this study. Circuit class therapy was found to be just as effective as individual physiotherapy for inpatient stroke rehabilitation (English et al., 2007). There were no statistically significant differences between group and individual interventions for rehabilitation following joint replacement surgery (Coulter et al., 2009). Individual and group treatment for female urinary incontinence appeared to
be equally beneficial in a study by Camargo et al (2009), despite the sensitive nature of the issue of incontinence.

The results suggest that group physiotherapy had a significant effect of reducing the psychological impact of MS, an important change at participation level that was not seen with individual physiotherapy treatment. There was a trend for improvement observed in the control group but due to the small numbers in this group there may have been a risk of Type II error, therefore, with increased numbers the change observed may have reached significance. When considering the person as a whole and the WHO ICF framework recommendations this data supports group treatment over individual treatment, however this needs to be evaluated against a larger, similar control group.

Along with the benefits observed on the individual outcome measures for participants, group therapy may have benefits for health care providers. It is less resource intensive allowing more people to be treated in a shorter space of time and this may be more cost effective than individual treatment sessions. A study currently being undertaken in Ireland (Hurley et al., 2009) is comparing the cost of a group exercise class and usual individualised physiotherapy in a cohort of people with chronic low back pain. Group therapy may be more beneficial for both PwMS and the health service providers responsible for their care but further research is needed to evaluate the cost-effectiveness of group treatment and to compare the efficacy of group treatment to a larger, similar control group.

8.4 Twenty Four Week Follow up

The analysis of follow up data was performed only using participants that were present for all three assessments. This meant that due to drop outs there was a decrease in the number of participants included in the analysis and, therefore, there may be issues with Type II error due to reduced sample size.
The main findings of the follow up analysis revealed that the improvements observed for the physiotherapy interventions had decreased at 24 weeks but they did not return to their baseline values. None of the changes between week 12 and week 24 were statistically significant. There was a trend for improvement observed in the yoga group for all outcome measures between week 12 and week 24.

There were only nine participants included in the yoga group for this analysis and on further examination it was revealed that following the completion of the yoga programme five out of the nine participants had taken part in some form of physiotherapy and this may have caused the changes observed within this time. Participants did not receive this physiotherapy treatment as part of the Getting the Balance Right project but sought it privately. This highlights the perceived need for physiotherapy in this population. Subjectively participants did not improve following the yoga intervention but when this intervention was completed and participants started physiotherapy treatment their subjective scores improved. The importance of patient preference is again evident here.

Surprisingly there was a lack of analysis of results at follow up in the previous intervention studies that included PwMS with varying levels of mobility. There was no previous evidence to suggest whether benefits would be maintained or not. The follow up assessment was conducted three months after the completion of the intervention period in this study. Multiple Sclerosis is a chronic and progressive condition and the maintenance and evaluation of improvements at follow up is of the utmost importance to PwMS and clinicians responsible for the treatment of that person.

There is conflicting evidence surrounding the effect of interventions at follow up in PwMS with and EDSS of >6. Dalgas et al (2010) evaluated the effects of 12 weeks of lower extremity progressive resistance in 31 PwMS. They found no significant deterioration at 12 week follow up for fatigue, strength, QoL, functional outcomes or mood compared with results immediately after the intervention. In contrast to this, McCullagh et al (2008) found that following a three month aerobic intervention the positive results observed for fatigue, function and HRQoL were not maintained at six month follow up but similarly to the current study scores did not
return to baseline values. The differences observed here may be explained by the
different content of the interventions and the activity levels of participants between
cessation of the intervention and follow up assessment. Group therapy has been
shown to be beneficial in PwMS and can provide motivational and peer support
(Clarke and Coote, 2010). The rolling out of group exercise classes may facilitate
the maintenance of improvements and increase physical activity in PwMS that use
bilateral assistance. Further trials need to address the long term effects of
rehabilitation (three months and longer) in PwMS with all levels of mobility.
8.6 Factors that affect outcome

The results of the current study for group physiotherapy show that the majority of participants improved, however, variability in point estimates showed that there were some participants who did not improve. These participants may have had other symptoms and impairments that required different treatment to the prescribed intervention provided and this may have influenced the outcome.

A post hoc analysis was performed with the aim of revealing specific signs and symptoms that may influence outcome. This has not previously been conducted in a population of PwMS, therefore, it was an exploratory data analysis.

Multiple regression analysis was performed using the outcome score (Week 12) on the physical component of the MSIS-29v2 as the dependent variable. Because of the disparity between the results for the subjective and objective measures a second analysis was conducted using the outcome scores for the BBS as the dependent variables.

The literature review in Chapter 3 of this document identified possible demographic and clinical factors that may influence outcome. The only variable that contributed significantly to the outcome score on the physical component of the MSIS-29v2 was the baseline score on the same measure. BBS scores at baseline and sensation (normal/impaired) significantly contributed to the BBS scores at outcome, indicating that better balance scores and normal sensation are associated with a better score at outcome on the BBS. This highlights the need to assess sensation when physical interventions to improve balance are being evaluated in both clinical and research settings. This, combined with the findings of Cattaneo et al (2007b), greater improvements observed for balance retraining aimed at motor and sensory strategies than for balance retraining aimed at motor strategies, suggests that future research and practice needs to address sensory strategies in balance rehabilitation.

Factors identified from the natural history studies in Chapter 3 did not appear to influence the outcome of the interventions. This may be due to the fact that once an
EDSS score of 7 is reached or a relapsing course develops into a progressive course there is no difference in age or duration of the disease. Further exploration is required into the influence of specific symptoms on outcome in a larger sample of PwMS with moderate to severe mobility limitations.

The poor explanation of variance observed in the dependent variables due to the signs and symptoms included could imply that there may be other variables that influence a positive outcome that were not assessed in this trial. This analysis is limited by the absence of an appropriate measure of strength which may have also influenced outcome. There are a multitude of other factors which may have explained the variance seen for the MSIS-29v2 data. These include the settings used in the study, which varied from community halls to hotel gyms, the level of clinical experience of the deliver, patient preference and the individual motivation of each participant. The results show that 37% of the variance in the MSIS-29v2 was accounted for using the variables in the regression model. This suggests that this study did not capture all of the factors that were important to participants and influenced their HRQoL.

This analysis was performed as a post hoc, exploratory analysis to address an additional aim of this thesis. The study was not designed to address this analysis and the sample size required for this type of analysis was not established prior to commencement of the trial. The method of assessment for certain variables such as the MAS for tone may have also affected the results as this measure has questionable psychometric properties. Future studies need to evaluate the effect of clinical, demographic and environmental factors on the outcome of physiotherapy interventions in PwMS with moderate to severe mobility limitations with appropriate methodological considerations and larger sample sizes.
8.7 Methodological Issues and Limitations

A literature review was conducted to evaluate the effectiveness of physiotherapy and exercise interventions in PwMS with moderate to severe mobility impairments (Chapter 2). Methodological weaknesses of the included trials were assessed and analysed using the Cochrane Handbook for Systematic Reviewers. The methodology of the current study aimed to address these limitations and decrease the risk of bias by having a control group, a follow up assessment, appropriate randomisation, a larger sample size and reproducible interventions. However, as this was a community based study, some of the protocol was not adhered to and some methodological issues arose. The limitations of the current study will be described according to the four types of bias identified in the literature review, selection bias, performance bias, attrition bias and detection bias. These limitations reflect the challenges associated with research outside laboratory or hospital settings, with people with greater levels of disability than previous studies and. They also reflect the reality of conducting research in conjunction with a charity (MSI).

Selection Bias

If the randomisation procedure was properly adhered to there would have been equal numbers in the three intervention groups and the control group. The purpose of randomisation is to ensure that comparison groups are similar at baseline. This was not the case as there were a greater number of participants in the physiotherapy intervention than there was in the yoga and control groups. At baseline, the control group were significantly younger and had a shorter time since diagnosis and the yoga group had a significantly greater impact of fatigue. These differences between groups could have been caused by the insufficient randomisation procedure and increased the risk of selection bias in this study. The results for the yoga group need to be interpreted with caution as previously mentioned further evaluation of yoga in this population of MS with a larger sample size is needed. The control group in this study may not have been representative of this population of PwMS due to the small number of participants. To avoid this in future trials, persons involved in the
randomisation procedure should be appropriately trained and should be advised of the significance of strict adherence to the protocol.

Information letters were sent to interested candidates and this may have resulted in responses from participants who were more willing or motivated to take part in an exercise intervention trial. This makes it difficult to conclude if the cohort that consented to take part was a typical representation of this population of PwMS in Ireland.

Performance Bias

To limit the risk of performance bias the duration of all three interventions (group physiotherapy, individual physiotherapy and yoga) had a standardised duration of one hour a week for ten weeks. The results of this study suggest that group physiotherapy is as effective as individual treatment for PwMS who mobilise with bilateral assistance but there are a number of factors that need to be taken into account before the generalisation of this result. Training days were provided for physiotherapists involved to standardise the group physiotherapy intervention, however, this may have contaminated the individual physiotherapy treatments. The results revealed that the majority of physiotherapists delivering individual treatment used aspects of the group therapy protocol, therefore, group and individual interventions were similar. This may be explained by the level of clinical expertise of the physiotherapists involved and it is a possibility that physiotherapists in the community setting are not adequately experienced in the treatment of PwMS and because of this adhered to the specified protocol. The results of this study may have been different if therapists involved in the individual intervention groups had not attended the training days and had were experienced and specialised in the treatment of PwMS.

Attrition Bias

Reasons for all dropouts were documented in this study to minimise the risk of attrition bias. There were, however, unknown reasons for six (17%) of dropouts. The overall attrition at week 12 was 22%. Attrition rates in other physiotherapy
studies varied greatly 24%, 13%, 15% and 7% (Cattaneo et al., 2007b, Lord et al., 1998, Rasova et al., 2006 and Wiles et al., 2002 respectively). These differences may be explained by the variety of settings (home versus hospital), sample sizes and interventions used.

Detection Bias

In this study the assessors of the interventions were blinded to the aspects of the interventions delivered. It was, however, impossible to blind participants to the interventions used. Blinding of participants in non pharmacological studies is notoriously difficult and the possibility of a ‘placebo’ effect is evident in this study. The importance of patient preference was previously highlighted as a potential explanation for the results observed for the self report outcome measures in this study. Patient preference was not established at the commencement of this trial but future studies need to account for this at baseline in order to assess the effect of preference on the effect of treatment. The CONSORT guidelines for reporting of intervention trials recommend the assessment of patient preference (Boutron et al., 2008).

No reliable measure of strength was available for analysis. Hand held dynamometry was used to assess strength but a subsequent analysis of its between rater reliability showed that it was highly unreliable and had large standard error values (Toomey and Coote, 2009). This is a limitation of the current study because there was a strength component to the group physiotherapy intervention and any potential improvement/deterioration in strength could not be evaluated. There are also some other factors pertaining to the increased risk of detection bias in this study. The MSIS-29v2 has not been used in other studies and the threshold for clinically meaningful change is not available, therefore, it remains unknown if the change observed for the physiotherapy intervention groups and the control group is enough to suggest real change in HR-QoL. It is also possible that the 6MWT may not have been a suitable outcome measure for all the participants in this study due to the great variability in the distances walked over the six minute period. It is possible that a qualitative outcome measure such as the Multiple Sclerosis Walking Scale-12
(Hobart et al., 2003) may have provided additional more relevant information. Future research needs to address the consensus surrounding the use of walking tests in PwMS with severe mobility limitations. This methodology did not provide any qualitative data. Qualitative analysis may have provided more information on the reasons why group therapy was more effective for some participants than others.

The limitations highlighted here are indicative of the challenges of conducting a multi-centred, community based trial in conjunction with a charity (MSI). This trial does, however, provide important recommendations for the use of these interventions for PwMS and for future research in this area and service delivery. These will be addressed in more detail in Chapter 10 of this document.
Chapter 9 - Falls in People with Multiple Sclerosis

9.0 Introduction

As seen in the Chapter 7 balance improved in the three intervention groups (group physiotherapy, individual physiotherapy and yoga). This was particularly evident in the participants who received group physiotherapy. Improving balance has been shown to decrease the incidence of falls in an elderly population (Marigold et al., 2005) and in one study of PwMS (Cattaneo et al., 2007b). As part of each assessment (Week 1, Week 12 and Week 24) in the current study participants were asked if they had fallen in the previous three months. Because of the interesting findings related to balance, a secondary analysis of the falls and balance data was conducted and this is presented in this chapter.

This study will firstly review the literature surrounding the prevalence, risk factors and interventions for falls reduction, and will then present the findings of this study in each of those three areas.

1. Prevalence of falls
2. Risk factors associated with falling
3. The effect of the interventions used to prevent falls
9.1 Falls in PwMS - Background

A fall can be defined as ‘an unexpected contact of any part of the body with the ground’ (Nilsagard et al., 2009). Falls have many negative consequences and significant cost implications for both the person who falls and the health service that is involved in the care of that person. Falls can lead to activity curtailment, decreased social participation, injury and an increased fear of falling (Peterson et al, 2007). It has been well established that activity in the form of regular aerobic or strengthening exercise can have positive effects on both disease symptoms and fitness levels in more ambulatory PwMS (Rietberg et al., 2004). Activity curtailment and inactivity can increase the risk of developing cardiovascular disease, diabetes, obesity and osteoporosis. Deconditioning due to inactivity in PwMS can also increase levels of fatigue which may increase the extent of other symptoms (Krupp and Christodolou, 2001).

Many of the symptoms that PwMS experience can contribute to an increased likelihood of a fall. Balance impairment is one of the most commonly reported symptoms in PwMS (Bakshi, 2003, Finlayson and Peterson, 2006) and was among the top three problems reported by 36 (32.4%) participants in the current study (Chapter 7, Figure 10). This, along with other symptoms such as visual disturbance, sensory and gait impairment and fatigue challenges their ability to mobilise safely in their home or community. PwMS have been shown to perform poorly on standing balance tests compared to controls (Frzovic et al., 2000) and balance performance was impaired in both relapsing and progressive forms of the disease (Soyeur et al., 2006). Adequate balance relies on the combination of input from visual, somatosensory and vestibular input and a deficit in any of these inputs may lead to insufficient motor responses (Shumway-Cook and Woollacott, 2001), which are often observed in PwMS.
9.1.1 Prevalence

Several studies have explored the prevalence of falls in PwMS. The main results from these studies can be seen in Table. It can be seen that the prevalence of falls is greater that fifty percent in each of the studies. Prevalence rates range from 50% to as high as 63%.

Table 33 Studies evaluating prevalence of falls in PwMS

<table>
<thead>
<tr>
<th>Author</th>
<th>Subjects</th>
<th>Prevalence</th>
<th>Time period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nilsagard et al (2009)</td>
<td>n=76 (25 – 71 yrs) EDSS range 3.5 - 6.0</td>
<td>63%</td>
<td>past 3 months</td>
</tr>
<tr>
<td>Peterson et al (2008)</td>
<td>n=354 (&gt;55 yrs) 73% used a mobility aid (Stick or rollator)</td>
<td>50%</td>
<td>past 6 months</td>
</tr>
<tr>
<td>Peterson et al (2007)</td>
<td>n=1064 (45 – 90 yrs) 60% used a walking aid (Stick or rollator)</td>
<td>52.80%</td>
<td>past 6 months</td>
</tr>
<tr>
<td>Finlayson and Peterson (2006)</td>
<td>n=1089 (45 – 90 yrs) all levels of mobility</td>
<td>52.20%</td>
<td>past 6 months</td>
</tr>
<tr>
<td>Cattaneo et al (2002)</td>
<td>n=50 (25 – 65 yrs) 91% used a walking stick</td>
<td>54%</td>
<td>past 2 months</td>
</tr>
</tbody>
</table>

EDSS Expanded Disability Scale Score

Only one study collected data prospectively over a 3 month period (Nilsagard et al 2009). Participants were asked to record the amount of falls and near falls they experienced as they happened. Sixty three percent of participants reported at least one fall, of these fallers 66% reported falling twice or more and 23% reported falling ten times or more. The prevalence of falls recorded in this study using prospective data collection was slightly higher than those recorded in the studies using retrospective data collection.
Three studies (two with the same methodology) used a 6 month time frame (Peterson et al., 2007a, Finlayson and Peterson, 2006, Peterson et al., 2007b) prior to questioning and participants reported very similar rates of falls (50%, 52.8% and 52.2%). As well as incidence of falls, fear of falling was present in 63.5% of a sample of over 1000 PwMS and of these participants 82.6% curtailed their activity levels (Peterson et al., 2007b). Over half of the falls reported in one study (Peterson et al., 2007a) caused an injury and 23% required medical attention.

9.1.2 Risk Factors

As previously mentioned many of the symptoms of MS may contribute to an increased likelihood of falls. In order to develop effective falls prevention programmes for PwMS the factors that are associated with falls in this population need to be identified. Three studies have examined the possible risk factors associated with falls in PwMS. Different methodologies were used to establish these risk factors. One was a longitudinal study (Nilsagard et al., 2009) and two used a cross sectional design (Cattaneo et al., 2002, Finlayson and Peterson, 2006). Logistic regression analysis formed the basis for each of the statistical analyses performed.

The variables investigated as possible risk factors in these studies were a mix of subjective self report measures and objective performance based measures. Objective measures used as possible risk factors and predictors of falls included; the Berg Balance Scale, Timed up and Go Test, the Modified Ashworth Scale (MAS), the Four Square step test, Equiscale test, Motricity Index, Rivermead Mobility Index, and the Hauser Ambulation Index.

The use of a walking aid or mobility device was identified in all three studies as a risk factor for falling (Cattaneo et al., 2002, Finlayson and Peterson, 2006, Nilsagard et al., 2009). This is particularly relevant to the participants in this study, who all used at least a bilateral aid to walk outside. Being male and having impaired balance and mobility were the second most common risk factors
identified. Other reported risk factors included, fatigue, problems concentrating, incontinence of the bladder, heat sensitivity and reduced muscular endurance.

The results show that the risk factors identified varied across the studies and a wide range of factors are associated with an increased likelihood of falling. This could be due to the different methodologies used, the variability in sample sizes and participants, and the different time frames assessed.

### 9.1.3 Treatment to reduce falls

Despite the high prevalence of falls reported in PwMS there is a limited amount of evidence surrounding fall prevention interventions. Several studies used interventions that address balance limitations but did not use any falls related outcome measures.

One study by Cattaneo et al (2007b) reported the number of falls reported before and after three different interventions (balance rehabilitation to improve motor strategies, balance rehabilitation to improve motor and sensory strategies and conventional therapy) as a primary outcome. The results showed that there was a significant decline in the number of falls reported before and after all three interventions. A recent pilot study by Prosperini et al (2010) aimed to improve balance and reduce falls risk using a novel approach of visuo-proproceptive feedback training. They found that the training led to more accurate postural strategies and that this may decrease risk of falling. These results need to be interpreted with caution as this was a pilot study with methodological limitations.

Along with these single intervention studies a multiple intervention study was conducted that aimed to increase knowledge of fall risk factors and modify behaviours to reduce the risk of falls in a sample of thirty PwMS (Finlayson et al., 2009). The results showed that participants were able to increase their knowledge of falls risk factors and modify their behaviour, for example, having an emergency plan in the event of a fall, planning activities of daily living, avoiding certain activities and checking walking aids to reduce the risk of falling.
9.2 Methodology

9.2.1 Aim and objectives

The overall aim of this secondary analysis was to gain more information about falls in this particular cohort of PwMS. The specific objectives were:

1. To establish the prevalence of falls over a three month period for this cohort of PwMS.

2. To explore the risk factors associated with the increased likelihood of reporting a fall at baseline in this cohort.

3. To assess the effect of having group physiotherapy, individual physiotherapy or yoga on the number of falls reported.

9.2.2 Data collection

The data on number of falls reported was collected retrospectively. As part of the current study participants were asked at week 1 and week 12 if they had experienced a fall in the previous three months and if so, how many.

9.2.3 Statistical Analysis

Descriptive statistics were calculated to describe the incidence of one or more falls in the three month period prior to commencement of study period. In order to assess the effect of the intervention on the proportion of fallers (people who reported one or more falls) McNemar’s test was used to analyse the data. This was considered the appropriate statistical analysis due to the within subject design, the binary variables involved and due to the abnormal distribution of the data.
The possible risk factors associated with an increased likelihood of reporting a fall were identified by exploring the available literature on falls in PwMS and by assessing which potential variables differed significantly between fallers and non fallers.

In order to assess any significant differences between fallers and non fallers for the potential risk factors independent t-tests were used for continuous data that was normally distributed, Mann Whitney U tests were performed on data that was abnormally distributed and chi squared tests for independence were used for categorical data.

A logistic regression analysis was used to identify which of these possible risk factors were most associated with the likelihood of reporting a fall. The dependent variable for this analysis was the participants’ response to the question, ‘Have you had a fall in the last 3 months?’ The response to this was either yes or no. Due to the dichotomous nature of the responses logistic regression was used to analyse the data. The independent variables were entered into the model and odds ratios were used to describe the strength of the association between these variables and the fallers and non fallers, e.g. how much more likely it is that someone who has a certain trait will have reported falls in the last 3 months compared to someone who does not have that trait.
9.3 Results

This section will present the findings of the secondary analysis according to the objectives in the following order, prevalence, risk factors and effect of treatment.

9.3.1 Prevalence

For the participants involved (n=111) the prevalence of falls reported in the last three months was 50.5%. Of these 22.3% reported 3 or more falls in the same period. The total number of falls reported was 163 for all participants, an average of almost three falls per participant who reported falling.

9.3.2 Risk factors

Statistical differences between fallers and non-fallers at baseline for the total cohort were found for 3 of the outcome measures. Fallers had a higher physical and psychological impact of MS than non fallers as measured on the MSIS – 29 v2 and this was statistically significant (Table 34). It is also evident that fallers scored on average 11 points more in the Modified Fatigue Impact Scale indicating a higher impact of fatigue that was statistically significant.
Table 34 Characteristics of fallers and non fallers

<table>
<thead>
<tr>
<th></th>
<th>Fallers (n=56)</th>
<th>Non Fallers (n=55)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>55.6 (±10.4)</td>
<td>54.7 (±11.1)</td>
<td>0.586</td>
</tr>
<tr>
<td><strong>Gender m/f</strong></td>
<td>17/38</td>
<td>23/32</td>
<td>0.116</td>
</tr>
<tr>
<td><strong>GNDS mobility score 3/4</strong></td>
<td>33/23</td>
<td>33/21</td>
<td>0.858</td>
</tr>
<tr>
<td><strong>Time since diagnosis</strong></td>
<td>16.6 (±5)</td>
<td>14.1 (±3)</td>
<td>0.561</td>
</tr>
<tr>
<td><strong>LL Sensation normal/abnormal</strong></td>
<td>27/25</td>
<td>31/23</td>
<td>0.452</td>
</tr>
<tr>
<td><strong>Proprioception normal/abnormal</strong></td>
<td>34/20</td>
<td>37/15</td>
<td>0.551</td>
</tr>
</tbody>
</table>

*Outcome Measures*

<table>
<thead>
<tr>
<th></th>
<th>Fallers (n=56)</th>
<th>Non Fallers (n=55)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MSIS29v2-physical</strong></td>
<td>54 (±9.5)</td>
<td>50.3 (±10.8)</td>
<td>0.048*</td>
</tr>
<tr>
<td><strong>MSIS29v2-psychological</strong></td>
<td>19.5 (5.5)</td>
<td>15 (4)</td>
<td>0.001*</td>
</tr>
<tr>
<td><strong>Berg Balance Scale</strong></td>
<td>28.2 (±10)</td>
<td>29.5 (±11)</td>
<td>0.879</td>
</tr>
<tr>
<td><strong>6MWT Distance</strong></td>
<td>78 (41.5)</td>
<td>92.5 (49.5)</td>
<td>0.174</td>
</tr>
<tr>
<td><strong>MFIS</strong></td>
<td>46.7 (±14.1)</td>
<td>38 (±16.9)</td>
<td>0.002*</td>
</tr>
</tbody>
</table>

*Statistically significant

GNDS Guy’s Neurological Disability Scale, LL Lower Limb, MSIS-29v2 Multiple Sclerosis Impact Scale 29 version 2, 6MWT Six minute walk test, MFIS Modified Fatigue Impact Scale.
Data was assessed for multicollinearity. This was done to assess if any of the independent variables had high intercorrelations which may have affected the outcome of the results. This was not the case. The data met the assumptions for logistic regression.

Direct logistic regression analysis was performed to assess the impact of a number of variables on the likelihood that participants would report experiencing a fall in the previous three months. The model contained nine independent variables. The results for each variable can be seen in Table 35. The overall model containing all factors was statistically significant $\chi^2 (9, n=111) =16.25, p=0.039$, indicating that the model was able to distinguish between participants who reported falling and those that did not. The model as a whole explained between 16.6% (Cox and Snell $R^2$) and 22.1% (Nagelkerke $R^2$) of the falls status and correctly classified 63.6% of cases. As shown in table one only one of the independent variables made a unique statistically significant contribution to the model. This was score on the Multiple Sclerosis Impact Scale v2 psychological component at baseline, OR = 1.12, $p = 0.015$. 
Table 35  Logistic regression results predicting likelihood of falling

<table>
<thead>
<tr>
<th></th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>OR</th>
<th>95% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.01</td>
<td>0.02</td>
<td>0.244</td>
<td>1</td>
<td>0.621</td>
<td>0.01</td>
<td>(0.969, 1.053)</td>
</tr>
<tr>
<td>Sex</td>
<td>-0.069</td>
<td>0.482</td>
<td>3.254</td>
<td>1</td>
<td>0.071</td>
<td>0.42</td>
<td>(0.163, 1.078)</td>
</tr>
<tr>
<td>GNDS mobility score 3 / 4</td>
<td>0.043</td>
<td>0.367</td>
<td>0.373</td>
<td>1</td>
<td>0.83</td>
<td>1.003</td>
<td>(0.919, 1.026)</td>
</tr>
<tr>
<td>LL Sensation</td>
<td>-0.08</td>
<td>0.454</td>
<td>0.031</td>
<td>1</td>
<td>0.861</td>
<td>0.924</td>
<td>(0.379, 2.248)</td>
</tr>
<tr>
<td>Proprioception</td>
<td>0.112</td>
<td>0.517</td>
<td>0.047</td>
<td>1</td>
<td>0.829</td>
<td>1.118</td>
<td>(0.406, 3.080)</td>
</tr>
<tr>
<td>MSIS29 physical</td>
<td>-0.001</td>
<td>0.049</td>
<td>0.002</td>
<td>1</td>
<td>0.963</td>
<td>0.999</td>
<td>(0.948, 1.052)</td>
</tr>
<tr>
<td>MSIS29 psychological</td>
<td>0.106</td>
<td>0.062</td>
<td>2.94</td>
<td>1</td>
<td>0.05</td>
<td>1.12</td>
<td>(0.985, 1.225)</td>
</tr>
<tr>
<td>Berg Balance Scale</td>
<td>-0.006</td>
<td>0.022</td>
<td>0.088</td>
<td>1</td>
<td>0.77</td>
<td>0.99</td>
<td>(0.954, 1.037)</td>
</tr>
<tr>
<td>MFIStotal</td>
<td>0.027</td>
<td>0.019</td>
<td>2.058</td>
<td>1</td>
<td>0.15</td>
<td>1.02</td>
<td>(0.99, 1.065)</td>
</tr>
</tbody>
</table>

9.3.3 Effect of intervention

Along with the improvement in balance scores on the BBS the risk of falls was also reduced. The interpretation of falls risk as measured on the BBS is divided into three categories of risk, low (scores of >40) medium (scores between 21 and 40) and high (scores of <20) (Wood-Dauphinee et al., 1997). Riddle and Scott (1999) also suggested a cut off score of 40/56 to identify falls risk. Twenty five percent of group physiotherapy participants and almost fourteen percent of individual physiotherapy participants crossed the threshold from having a moderate risk of falls to having a low risk of falls.
The number of fallers before and after each of the interventions and the control group can be seen in Table 36. The number of fallers after the intervention was reduced for each of the four groups. The reduction in the number of fallers from 28 before to 11 after group physiotherapy was statistically significant (p=0.005). There was a statistically significant reduction in the number of falls reported before and after group physiotherapy (p=0.001). The reduction in the number of falls approached significance for individual physiotherapy and yoga. There was a trend towards a reduction in the number of falls reported in the control group.
Table 36 Number of fallers, falls and p values for group physiotherapy, 1:1 physiotherapy, yoga and the control group

<table>
<thead>
<tr>
<th>Group</th>
<th>Fallers Pre Intervention (%)</th>
<th>Fallers Post Intervention (%)</th>
<th>p value (McNemars)</th>
<th>Total number of falls pre</th>
<th>Total number of falls post</th>
<th>p value (Wilcoxon Signed Rank test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group Physiotherapy(n=48)</td>
<td>28(58.3)</td>
<td>11(22.9)</td>
<td>0.005*</td>
<td>63</td>
<td>25</td>
<td>0.001*</td>
</tr>
<tr>
<td>1:1 Physiotherapy(n=35)</td>
<td>16(45.7)</td>
<td>9(25.7)</td>
<td>0.118</td>
<td>61</td>
<td>21</td>
<td>0.088</td>
</tr>
<tr>
<td>Yoga (n=13)</td>
<td>7(53.8)</td>
<td>3(23.1)</td>
<td>0.125</td>
<td>25</td>
<td>8</td>
<td>0.091</td>
</tr>
<tr>
<td>Control (n=15)</td>
<td>5(33.3)</td>
<td>2(13.3)</td>
<td>0.375</td>
<td>14</td>
<td>2</td>
<td>0.131</td>
</tr>
</tbody>
</table>

*Statistically significant
9.4 Discussion

9.4.1 Prevalence

The findings of this analysis revealed that 50.5% of participants reported a fall in the previous three months. This prevalence rate is consistent with those previously reported, 54%, 52.2%, 52.8% and 50%, (Peterson et al., 2007a, Cattaneo et al., 2002, Finlayson and Peterson, 2006, Peterson et al., 2007b) despite the variation in time periods used (2 -6 months). These studies used self report retrospective data collection similar to this study.

A higher prevalence of falls was described in a study by Nilsagard et al (2009) (63%). This may be explained by the method of data collection used. The number of falls reported was collected prospectively and the study was conducted over a nine month period compared to three months in the current study.

A systematic review of methods of measuring falls in fall prevention trials recommended prospectively collecting falls data in order to accurately assess falls frequency (Gillespie et al., 2009). PwMS commonly experience memory or cognitive difficulties. It has been reported that 45 – 60 % of PwMS experience cognitive impairment (Strober et al., 2009). This may affect their ability to accurately recall the number of falls they have previously experienced (Ganz et al., 2005). Future studies should aim to prospectively collect falls data using a diary based recording system

The prevalence of falls in community dwelling adults over the age of sixty five is 30% (Hausdorf et al., 2001) and this rises to 50% in people over the age of seventy (Bergland and Wyller, 2004). The findings of the current research and other studies suggest that the rate of falls is higher in PwMS than it is in community dwelling older adults. The higher prevalence rate of 63% observed for PwMS is similar to the prevalence of falls observed in Parkinson’s Disease which was reported as 68% in a prospective study by Wood et al (2002).
9.4.2 Risk Factors for falls

Preliminary analysis of the difference between fallers and non fallers indicated that fallers had significantly higher scores on the MFIS (indicating a greater impact of fatigue), and on both the physical and psychological components of the MSIS-29v2 (indicating a greater physical and psychological impact of MS) than non fallers. It is difficult to establish whether these self report measures are increased because of falls, or whether the increase in fatigue may be responsible for falls. The link between fatigue and falls warrants further investigation.

The logistic regression analysis was exploratory and aimed to establish any possible risk factors associated with the likelihood of reporting a fall in a three month period. Unlike other studies that have previously evaluated the risk factors for falling in this population, only one variable was significantly associated with the increased likelihood of a fall and this was a higher score on the psychological component of the MSIS29v2. This could be due to the smaller sample size in the current study or the differences in the measurement of the variables and the time frames used. The current study included only participants who used at least bilateral assistance to mobilise outdoors, whereas, previous studies included participants with varying levels of mobility.

Interestingly, scores on the BBS were not predictive of falls in the current population. This is in contrast to previous studies (Nilsagard et al., 2009 and Cattaneo et al., 2002) which found that scores on the BBS and another objective measure, the Equiscale Test, significantly contributed to the increased likelihood of reporting falls. This may be explained by the differences in populations used. Participants who reported a fall in the current study had a mean score of 28.2 (±10) on the BBS at baseline, whereas, the median scores of fallers was 48 in Nilsagard’s study. This may indicate that as balance impairment increases the association of objective balance scores with falls decreases and different factors may be associated with an increased likelihood of falling in PwMS who have more severe mobility limitations.
The effect of the psychological involvement impact of MS on falls has not been established previously. One study (Finlayson and Peterson, 2006) found that a fear of falling was a risk factor for falls in PwMS. The psychological component of the MSIS29v2 measures the overall impact of factors such as confidence, depression, and anxiety among others. The association of the psychological component of the MSIS29v2 may have captured the effect of fear of falling on falls in this cohort. The effect of psychological factors on falls and vice versa in PwMS needs to be addressed in future research in this area.

There was a lack of risk factors found to be associated with the increased likelihood of a fall in this study, however, a multitude of risk factors have been previously identified in the literature surrounding PwMS. This highlights the complexity and multi-factorial nature of falls in this population. The most commonly reported risk factors are factors clinicians and researchers can assess in the treatment and evaluation of falls intervention programmes such as the use/correct use of a walking aid and balance impairment. Because of the multi-factorial nature of falls in this population the effect of multidisciplinary falls prevention interventions may prove beneficial and needs to be researched in the future.
9.4.3 Effect of intervention on falls

A recent study (Matsuda et al., 2011) highlighted the fact that despite the high prevalence of falls reported in PwMS there was a lack of communication with health care professionals surrounding these falls. Only half of the two hundred and sixty five participants that reported falling spoke to a health care professional about their fall/falls. It was, however, reported that over 90 % of the participants reported that the health care professional involved recommended one or more fall-prevention strategies.

Despite the high prevalence of falls in this PwMS and the frequent use of falls prevention strategies among clinicians when treating PwMS there is a lack of evidence surrounding falls prevention for this population.

Falls and falls prevention programmes have been extensively researched in the elderly. A recent Cochrane review (Gillespie and Handall, 2009) has been conducted containing 111 articles on interventions aimed at reducing falls in the elderly. The effectiveness of these programmes has been well established in decreasing the number of falls and falls risk. Thirty one of these studies evaluated the effects of multi-factorial interventions. Participants in these studies received a combination of interventions usually as part of a multidisciplinary input. These interventions, overall, were effective in reducing rate of falls. Group exercise, in the form of balance and strengthening exercises, was the most commonly used treatment. The results showed a reduction in falls in an elderly population and also in a population at risk of falls.

The findings of the current research suggest that group physiotherapy in the form of a circuit style balance and strengthening class significantly reduces the number of fallers and falls reported. There was a reduction in falls observed for individual physiotherapy and yoga and these approached statistical significance. As previously mentioned only one previous study has used number of falls reported as an outcome measure before and after balance training in PwMS. Cattaneo et al (2007) reported similar reductions in number of fallers before and after two types of balance training programmes and conventional therapy. The number of falls in that study
was reduced by 42 and 45% in the balance training groups and in this study the number of falls was reduced by 39 and 34% for group and individual physiotherapy respectively. The balance and strength based intervention used in the current study was based on fall prevention literature in the elderly. The reasons for this was because these programmes have been shown to be successful in improving balance and reducing falls (Gillespie and Handall, 2009) and older adults and PwMS both experience symptoms that contribute to a decrease in balance control, such as visual and sensory impairment and decreased strength and coordination. There was also a trend towards a reduction in the number of falls in the control group and this may have reached significance if the number of participants in the control group was increased.

It is evident from previous literature that there is a large prevalence of falls and risk of falls in PwMS. Falls may lead to physical injuries and hospitalisation and recent research has highlighted that the risk of a hip fracture in PwMS was almost three times greater for PwMS than for control participants (Bazelier et al., 2011). That study had a large sample size (5565 PwMS and 33,360 control participants) and found that bone mineral density (BMD) was significantly lower at baseline for PwMS and the risk of an osteoporotic fracture was one and a half times greater for PwMS than for control participants. Many factors associated with MS contribute to changes in BMD. These include the use of oral or intravenous corticosteroids for the treatment of relapses and low levels of activity or mobility. The results of this study suggest that a group physiotherapy programme including balance and strengthening exercises may decrease the incidence of falls and, therefore, may decrease the risk of physical injuries such as fractures in PwMS.

As previously mentioned the score on the psychological component MSIS-29v2 was the only significant variable associated with the increased likelihood of reporting a fall. Previous qualitative literature has highlighted the psychological benefits for PwMS of exercising in a group (Clarke and Coote, 2010). These included the feelings of empowerment, confidence, hope and motivation. The effect of the group intervention on these psychological factors may have contributed to the statistically significant reduction in falls observed for group physiotherapy.
One of the limitations of this analysis was that it was performed secondary to the main study outcomes and was not the primary aim of this study. Due to this all of the variables that may have influenced falls were not considered at baseline and falls data was collected retrospectively which may not be the most effective method of data collection on this population. The small number in the yoga group does not adequately address the effect of yoga on falls in this cohort of PwMS. The lack of a reliable measure of strength is also a limitation to this analysis as the relationship between falls, balance and strength could not be explored.

9.5 Conclusions

There is a high prevalence of falls in PwMS. The prevalence reported in this study of PwMS who mobilise with at least bilateral assistance is similar to those observed in international studies, despite the fact that this population was more disabled than those in the other studies.

There is a lack of evidence surrounding interventions for fall prevention in PwMS. Future research needs to address this by evaluating single and multi disciplinary interventions and comparing them to matched control groups.

Group physiotherapy in the form of a circuit style balance and strengthening programme significantly decreased the number of fallers and the number of falls reported, suggesting this may be an effective treatment option for PwMS who are at risk of falls and may decrease the cost related burden of falls on health service providers. The reduction in the number of falls before and after individual physiotherapy and yoga approached significance. There were smaller numbers of participants in the yoga and control groups, therefore, this may have increased the possibility of Type II error.

Future research into the efficacy of fall prevention programmes needs to use consistent prospective measures of falls reporting to allow for more reliable comparisons to be made. The evaluation of risk factors associated with falls in
future research also needs to be more consistent in terms of sample size and population, time periods and measurement of variables. The effect of psychological factors on falls in PwMS also needs to be explored further in future research.
Chapter 10 Conclusion

10.0 Introduction

This concluding chapter will summarise the main findings of this thesis and highlight the implications for clinical practice and future research in the area.

10.1 Summary of main findings

The findings of the literature review (Chapter 2) suggested that a multitude of interventions can be effective in the treatment of PwMS with moderate to severe mobility impairment. These studies, however, included participants of varying levels of mobility impairment and the optimal intervention for PwMS with more severe mobility limitations remained unclear. The current research aimed to address this by including specifically PwMS who mobilise with at least bilateral assistance (GNDS score 3 or 4).

This study was the first known randomised controlled trial with participants stratified according to their mobility level. This research is also novel in other ways as it is the first study comparing group physiotherapy to individual physiotherapy in a population of PwMS. It is the first known study evaluating a physiotherapy intervention to assess the maintenance effect of treatment by assessing at 3 month follow up. It is also the first study to explore the influence of a set of variables on outcome at participation and impairment level.

The results of the main study showed that there was a significant treatment effect for balance for group physiotherapy, individual physiotherapy and yoga. The intervention groups all improved significantly, whereas, the control group demonstrated a trend for deterioration.
Similar decreases in scores were observed for both group physiotherapy and individual physiotherapy on the subjective, self report outcome measures. A decrease in score on the MSIS29v2 and the MFIS indicates a decrease in the physical and psychological impact of MS and a decrease in the impact of fatigue. Unexpectedly, improvements of similar magnitude were observed for the control group on these subjective measures. In contrast, the yoga group showed an increase in the impact of MS and fatigue. This brings into question the placebo effect of contact with a physiotherapist for two assessments and the role of patient preference in assessing the outcome of interventions.

There was large variability observed for distances recorded on the 6MWT. The distance walked in six minutes increased for both physiotherapy interventions, whereas, there was a decrease in the distance walked for the yoga group. There was no statistical change observed in the control group.

Overall, the most statistically significant and clinically relevant improvements were detected for group physiotherapy. The top four most commonly reported problems in this cohort of PwMS were mobility/walking, balance, fatigue and weakness. The implementation of community based physiotherapy interventions showed improvements for the first three of these problems. The effect of the interventions on strength is not known due to the lack of a reliable measure of strength.

The results of the follow up analysis revealed that the improvements observed for group physiotherapy and individual physiotherapy were not maintained at week 24. Their scores, however, did not return to baseline. The yoga group showed a trend for improvement between week 12 and week 24. On further examination it was revealed that over half of the participants had started some form of physiotherapy within that period.

A post hoc analysis explored the influence of specific variables on outcome at participation and impairment level. The physical component score of the MSIS-29v2 at week 12 was initially chosen as the dependent variable but due to the disparity of the results observed between the subjective and objective outcome measures the influence of the variables on BBS scores at outcome was also
explored. The results revealed that no impairment or demographic variables significantly contributed to outcome on the physical component of the MSIS-29v2 except the baseline scores on that measure. Sensation and baseline BBS significantly influenced scores on the BBS at outcome.

Recent literature focusing on falls in PwMS highlighted that there is a high prevalence of falls in his population. Despite this high prevalence ($\geq 50\%$) there is a lack of studies evaluating the effects of fall prevention interventions in PwMS. The results of the analysis of falls in this thesis revealed a similar, high prevalence of falls. The group intervention resulted in a significant reduction in the number of fallers and falls reported. Lower scores on the psychological component of the MSIS-29v2 were associated with an increased likelihood of reporting a fall in the previous three months.

Multiple Sclerosis Ireland frequently provides yoga as a treatment option for its members. It is clear from this research that PwMS with moderate to severe mobility impairment do not want to partake in yoga and, although, objective improvements were observed for balance, participants in the yoga group subjectively reported a worsening in the physical and psychological impact of MS and in the impact of fatigue. This research highlights the importance of patient preference and demonstrates the importance of the role of the physiotherapist in the treatment of PwMS with increased disability as perceived by the PwMS themselves.

Balance impairment is a common and debilitating symptom for PwMS and was the second most commonly reported problem for the participants in this study. It has been shown to be a risk factor for falls and may lead to a decrease in physical activity. Group physiotherapy, individual physiotherapy and yoga were effective in improving balance for PwMS who use bilateral aid to walk.

The positive results observed for balance were not maintained at follow up. As multiple sclerosis is a chronic progressive disease of which there is presently no cure minimising disability and the impact of MS is an important goal of any intervention. The maintenance of these improvements is also of utmost importance and this research suggests that participants should be reassessed three months
following the cessation of an intervention and that the rollout of regular group interventions may play an important role in minimising physical disability for this population of PwMS.

### 10.2 Implications for Clinical Practice

The findings of this thesis have important clinical implications for physiotherapists and health service providers responsible for the management of PwMS with moderate to severe mobility impairment. The current transition of health care provision from the acute services to a primary care model makes this research timely and appropriate.

Group physiotherapy, in the form of balance and strength exercises, may provide a less costly and equally effective alternative to the traditional approach of individual physiotherapy. Physiotherapists should consider treating PwMS who mobilise with bilateral assistance in a group if they are aiming to improve balance, HRQoL, fatigue and decrease falls. Transport was provided for participants by MSI as part of the GTBR project so there was no monetary cost for participants or time costs for family members. Physiotherapists should consider the cost of transport or participants when implementing group therapy as transport issues have been shown to be a barrier to exercise for PwMS (Garrett and Coote, 2008).

The results of this research highlight the importance of the role of the physiotherapist as perceived by this population of PwMS. Participants in the control group felt more positive about the impact of their MS after two assessments with a physiotherapist and knowing that they were about to receive physiotherapy. Participants in yoga chose to have physiotherapy outside of the study and did not perceive a reduction in impact of MS and fatigue despite yoga bringing about a positive effect on balance. Unlike, more ambulatory PwMS (Strand A participants in the GTBR project), who benefited from physical interventions led by fitness and yoga instructors, it appears that PwMS with moderate to severe mobility value the
input of a physiotherapist. Service providers such as MS Ireland and primary care teams should take this into account when implementing interventions for this population.

Clinicians evaluating these types of programmes should reassess patients three months after cessation of the intervention. Improvements do not seem to be maintained at this point but have not returned to baseline. The rollout of group intervention may be appropriate to facilitate maintenance of improvements and activity levels.

The presence of abnormal sensation may influence the outcome of a balance rehabilitation programme. Physiotherapists should assess sensation prior to commencing such a programme and consider the use of sensory strategies in conjunction with physical balance exercises.

Clinicians addressing falls prevention in this population of MS need to consider the multifactorial cause of falls. Psychological factors should be taken into account in conjunction with the physical impairments that are assessed in clinical practice. When assessing falls in this population clinicians should record the number of falls prospectively, for example, using patient reported falls diary. The reduction in falls observed after the physiotherapy intervention has important implications for both the PwMS and the health service responsible for their care in terms of cost reduction through injury prevention. Group physiotherapy, in the form of balance and strengthening exercises, has a role in the prevention of falls in this population of PwMS.

10.3 Implications for Future Research

The results of this thesis have highlighted priorities for future research.

Although every effort was made to address the methodological weaknesses of the previous studies addressed in the literature review (Chapter 2) some methodological issues arose and these need to be focused on in future research. The limitations of
this study reflect the challenges of research in the community. Future trials should continue to move beyond the structure of hospital and research labs and out into the community where greater research challenges exist. Further comparisons need to be made between the physiotherapy interventions and a larger matched control group. Future evaluation of physiotherapy interventions should include a reliable assessment of strength. This will allow the effect of the interventions on strength to be evaluated and also allow for the exploration of the relationship between strength, balance and falls in this population of PwMS.

The effect of yoga specifically on PwMS with moderate to severe mobility impairment needs to be evaluated further. The results of this study suggest that yoga may not be a suitable treatment option for this population of PwMS. This needs to be corroborated in studies using larger sample sizes and compared to a control group with similar baseline characteristics.

Future studies evaluating the effect of balance interventions on PwMS should incorporate sensory strategies in the content of the programmes. The intervention in this study only focused on motor strategies. Future studies should design interventions using exercises that stimulate the sensory system such as performing tasks with eyes closed, on uneven surfaces or moving platform or using altered visual feedback as sensation was found to be a significant predictor for Berg Balance Scale scores at outcome.

The use of outcome measures needs to be more consistent in future studies to allow for comparisons between different interventions. Consensus needs to be reached on a measure of walking ability for PwMS with moderate to severe mobility impairment. This is important due to the large variability observed on walking tests and the heterogeneity of walking ability even among subgroups of PwMS. A shorter walking test may be sufficient for some of the participants in this study but future research needs to focus on consistent classification of moderate and severe mobility impairment and needs to address which walking test is the most appropriate for evaluating walking ability in these different subgroups of PwMS.
Future research should assess the overall cost differences between group therapy and individual therapy. A cost analysis should be performed looking at the monetary costs such as renting a facility for group interventions and transport as well as time costs for physiotherapists in terms of planning groups and number of patients treated.

The variables used in the post hoc analysis did not adequately explain the variance at outcome for impact of MS. Future studies need to address other variables that may influence the outcome of a physiotherapy intervention on participation, such as, experience of the therapist, setting and other physical symptoms commonly reported in PwMS such as incontinence.

Future research evaluating falls prevention in this population of PwMS should assess the efficacy of a multi disciplinary treatment approach that addresses the psychological, physical and cognitive factors associated with falls. Finlayson et al, (2009) evaluated an education falls risk management programme, future research should explore the effects of interventions combining elements of physiotherapy and occupational therapy. The ability of the BBS to predict or identify fallers in this population needs to be evaluated as there was no significant difference in scores on the BBS between PwMS who reported falling in the last three months and those that did not.

The current evidence base for the treatment of PwMS with moderate to severe mobility impairment is limited. This study adds to that evidence base but further studies are needed using consistent outcome measures to allow for comparisons and targeted treatments to establish which interventions are optimal.
References


PETE RSON, E., CHO, C., VON KOCH, L. & FINLAYSSON, M. (2007a) Injurious fall among middle aged and older adults with MS. Archive of Physical and Medical Rehabilitation, 89, 1031-1037.


Appendices
APPENDIX A – PUBLICATIONS AND CONFERENCE PRESENTATIONS

Peer Reviewed Publications


Conference Presentations

Hogan, N., Garrett, M., Larkin, A., Saunders, J., Coote, S. “Comparing the effects of group and individual physiotherapy on fatigue and Health Related QoL in people with MS”. Poster presentation. Awarded prize of best Rehabilitation in MS (RIMS) poster, European Congress of Treatment and Research in Multiple Sclerosis (ECTRIMS), Sweden, October 2010.

Hogan, N., Garrett, M., Larkin, A., Saunders, J., Coote, S. “The Effects of group and individual physiotherapy on falls in people with MS”. Platform presentation and travel award, European Congress of Treatment and Research in Multiple Sclerosis (ECTRIMS), Sweden, October 2010.


APPENDIX B – MULTIPLE SCLEROSIS IMPACT SCALE VERSION 2

<table>
<thead>
<tr>
<th>MS Impact Scale version 2 (MSIS-29v2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The following questions ask for your views about the impact of MS on your day-to-day life during the past two weeks.</td>
</tr>
<tr>
<td>For each statement, please circle the one number that best describes your situation.</td>
</tr>
<tr>
<td>Please answer all questions.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In the past two weeks, how much has your MS limited your ability to ...</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do physically demanding tasks?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>2. Grip things tightly (e.g. turning on taps)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>3. Carry things?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In the past two weeks, how much have you been bothered by ...</th>
<th>Not at all</th>
<th>A little</th>
<th>Moderately</th>
<th>Extremely</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Problems with your balance?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>5. Difficulties moving about indoors?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>6. Being clumsy?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>7. Stiffness?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>8. Heavy arms and/or legs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>9. Tremor of your arms or legs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>10. Spasms in your limbs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>11. Your body not doing what you want it to do?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>12. Having to depend on others to do things for you?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>13.</td>
<td>Limitations in your social and leisure activities at home?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>14.</td>
<td>Being stuck at home more than you would like to be?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>15.</td>
<td>Difficulties using your hands in everyday tasks?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>16.</td>
<td>Having to cut down the amount of time you spent on work or other daily activities?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>17.</td>
<td>Problems using transport (e.g. car, bus, train, taxi, etc.)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>18.</td>
<td>Taking longer to do things?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>19.</td>
<td>Difficulty doing things spontaneously (e.g. going out on the spur of the moment)?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>20.</td>
<td>Needing to go to the toilet urgently?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>21.</td>
<td>Feeling unwell?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>22.</td>
<td>Problems sleeping?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>23.</td>
<td>Feeling mentally fatigued?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>24.</td>
<td>Worries related to your MS?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>25.</td>
<td>Feeling anxious or tense?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>26.</td>
<td>Feeling irritable, impatient, or short-tempered?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>27.</td>
<td>Problems concentrating?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>28.</td>
<td>Lack of confidence?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>29.</td>
<td>Feeling depressed?</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>
APPENDIX C – MODIFIED FATIGUE IMPACT SCALE

Modified Fatigue Impact Scale (MFIS)

Fatigue is a feeling of physical tiredness and lack of energy that many people experience from time to time. But people who have medical conditions like MS experience stronger feelings of fatigue more often and with greater impact than others.

Following is a list of statements that describe the effects of fatigue. Please read each statement carefully, then circle the one number that best indicates how often fatigue has affected you in this way during the past 4 weeks. Please answer every question. If you are not sure which answer to select, choose the one answer that comes closest to describing you.

Name: __________________________ Date: __________________________

Because of my fatigue during the past 4 weeks I have...

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
<th>Never</th>
<th>Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>been less alert</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>had difficulty paying attention for long periods of time</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>been unable to think clearly</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>been clumsy and uncoordinated</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>been forgetful</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>had to pace myself in my physical activities</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>been less motivated to do anything that requires physical effort</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>been less motivated to participate in social activities</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>been limited in my ability to do things away from home</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>trouble maintaining physical effort for long periods</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>had difficulty making decisions</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>been less motivated to do anything that requires thinking</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>been feeling as though my muscles are weak</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>been physically uncomfortable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>had trouble finishing tasks that require thinking</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>had difficulty organizing my thoughts when doing things at home/work</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>been less able to complete tasks that require physical effort</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>been thinking more slowly</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>had trouble concentrating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>limited my physical activities</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>needed to rest more often or for longer periods</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX D - BERG BALANCE SCALE

Name: ___________________________ Date: _________________

Location: ___________________________ Rater: ___________________

<table>
<thead>
<tr>
<th>ITEM DESCRIPTION</th>
<th>SCORE (0-4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting to standing</td>
<td>________</td>
</tr>
<tr>
<td>Standing unsupported</td>
<td>________</td>
</tr>
<tr>
<td>Sitting unsupported</td>
<td>________</td>
</tr>
<tr>
<td>Standing to sitting</td>
<td>________</td>
</tr>
<tr>
<td>Transfers</td>
<td>________</td>
</tr>
<tr>
<td>Standing with eyes closed</td>
<td>________</td>
</tr>
<tr>
<td>Standing with feet together</td>
<td>________</td>
</tr>
<tr>
<td>Reaching forward with outstretched arm</td>
<td>________</td>
</tr>
<tr>
<td>Retrieving object from floor</td>
<td>________</td>
</tr>
<tr>
<td>Turning to look behind</td>
<td>________</td>
</tr>
<tr>
<td>Turning 360 degrees</td>
<td>________</td>
</tr>
<tr>
<td>Placing alternate foot on stool</td>
<td>________</td>
</tr>
<tr>
<td>Standing with one foot in front</td>
<td>________</td>
</tr>
<tr>
<td>Standing on one foot</td>
<td>________</td>
</tr>
</tbody>
</table>

Total  ________

GENERAL INSTRUCTIONS

Please document each task and/or give instructions as written. When scoring, please record the lowest response category that applies for each item.

In most items, the subject is asked to maintain a given position for a specific time. Progressively more points are deducted if:

- the time or distance requirements are not met
- the subject’s performance warrants supervision
- the subject touches an external support or receives assistance from the examiner
Subject should understand that they must maintain their balance while attempting the tasks. The choices of which leg to stand on or how far to reach are left to the subject. Poor judgment will adversely influence the performance and the scoring.

Equipment required for testing is a stopwatch or watch with a second hand, and a ruler or other indicator of 2, 5, and 10 inches. Chairs used during testing should be a reasonable height. Either a step or a stool of average step height may be used for item #12.

SITTING TO STANDING
INSTRUCTIONS: Please stand up. Try not to use your hand for support.
( ) 4 able to stand without using hands and stabilize independently
( ) 3 able to stand independently using hands
( ) 2 able to stand using hands after several tries
( ) 1 needs minimal aid to stand or stabilize
( ) 0 needs moderate or maximal assist to stand

STANDING UNSUPPORTED
INSTRUCTIONS: Please stand for two minutes without holding on.
( ) 4 able to stand safely for 2 minutes
( ) 3 able to stand 2 minutes with supervision
( ) 2 able to stand 30 seconds unsupported
( ) 1 needs several tries to stand 30 seconds unsupported
( ) 0 unable to stand 30 seconds unsupported

If a subject is able to stand 2 minutes unsupported, score full points for sitting unsupported. Proceed to item #4.

SITTING WITH BACK UNSUPPORTED BUT FEET SUPPORTED ON FLOOR OR ON A STOOL
INSTRUCTIONS: Please sit with arms folded for 2 minutes.
( ) 4 able to sit safely and securely for 2 minutes
( ) 3 able to sit 2 minutes under supervision
( ) 2 able to sit 30 seconds
( ) 1 able to sit 10 seconds
( ) 0 unable to sit without support 10 seconds

STANDING TO SITTING
INSTRUCTIONS: Please sit down.
( ) 4 sits safely with minimal use of hands
( ) 3 controls descent by using hands
( ) 2 uses back of legs against chair to control descent
( ) 1 sits independently but has uncontrolled descent
( ) 0 needs assist to sit

TRANSFERS
INSTRUCTIONS: Arrange chair(s) for pivot transfer. Ask subject to transfer one way toward a seat with armrests and one way toward a seat without armrests. You may use two chairs (one with and one without armrests) or a bed and a chair.
( ) 4 able to transfer safely with minor use of hands
( ) 3 able to transfer safely definite need of hands
( ) 2 able to transfer with verbal cuing and/or supervision
( ) 1 needs one person to assist
( ) 0 needs two people to assist or supervise to be safe

STANDING UNSUPPORTED WITH EYES CLOSED
INSTRUCTIONS: Please close your eyes and stand still for 10 seconds.
( ) 4 able to stand 10 seconds safely
( ) 3 able to stand 10 seconds with supervision
( ) 2 able to stand 3 seconds
( ) 1 unable to keep eyes closed 3 seconds but stays safely
( ) 0 needs help to keep from falling
STANDING UNSUPPORTED WITH FEET TOGETHER
INSTRUCTIONS: Place your feet together and stand without holding on.

( ) 4 able to place feet together independently and stand 1 minute safely
( ) 3 able to place feet together independently and stand 1 minute with supervision
( ) 2 able to place feet together independently but unable to hold for 30 seconds
( ) 1 needs help to attain position but able to stand 15 seconds feet together
( ) 0 needs help to attain position and unable to hold for 15 seconds

REACHING FORWARD WITH OUTSTRETCHED ARM WHILE STANDING
INSTRUCTIONS: Lift arm to 90 degrees. Stretch out your fingers and reach forward as far as you can. (Examiner places a ruler at the end of fingertips when arm is at 90 degrees. Fingers should not touch the ruler while reaching forward. The recorded measure is the distance forward that the fingers reach while the subject is in the most forward lean position. When possible, ask subject to use both arms when reaching to avoid rotation of the trunk.)

( ) 4 can reach forward confidently 25 cm (10 inches)
( ) 3 can reach forward 12 cm (5 inches)
( ) 2 can reach forward 5 cm (2 inches)
( ) 1 reaches forward but needs supervision
( ) 0 loses balance while trying/requires external support

PICK UP OBJECT FROM THE FLOOR FROM A STANDING POSITION
INSTRUCTIONS: Pick up the shoe/slipper, which is place in front of your feet.

( ) 4 able to pick up slipper safely and easily
( ) 3 able to pick up slipper but needs supervision
( ) 2 unable to pick up but reaches 2-5 cm (1-2 inches) from slipper and keeps balance independently
( ) 1 unable to pick up and needs supervision while trying
( ) 0 unable to try/needs assist to keep from losing balance or falling
TURNING TO LOOK BEHIND OVER LEFT AND RIGHT SHOULDERS WHILE STANDING

INSTRUCTIONS: Turn to look directly behind you over toward the left shoulder. Repeat to the right. Examiner may pick an object to look at directly behind the subject to encourage a better twist turn.

(    ) 4  looks behind from both sides and weight shifts well
(    ) 3  looks behind one side only other side shows less weight shift
(    ) 2  turns sideways only but maintains balance
(    ) 1  needs supervision when turning
(    ) 0  needs assist to keep from losing balance or falling

TURN 360 DEGREES

INSTRUCTIONS: Turn completely around in a full circle. Pause. Then turn a full circle in the other direction.

(    ) 4  able to turn 360 degrees safely in 4 seconds or less
(    ) 3  able to turn 360 degrees safely one side only 4 seconds or less
(    ) 2  able to turn 360 degrees safely but slowly
(    ) 1  needs close supervision or verbal cuing
(    ) 0  needs assistance while turning

PLACE ALTERNATE FOOT ON STEP OR STOOL WHILE STANDING UNSUPPORTED

INSTRUCTIONS: Place each foot alternately on the step/stool. Continue until each foot has touch the step/stool four times.

(    ) 4  able to stand independently and safely and complete 8 steps in 20 seconds
(    ) 3  able to stand independently and complete 8 steps in > 20 seconds
(    ) 2  able to complete 4 steps without aid with supervision
(    ) 1  able to complete > 2 steps needs minimal assist
(    ) 0  needs assistance to keep from falling/unable to try

STANDING UNSUPPORTED ONE FOOT IN FRONT

INSTRUCTIONS: (DEMONSTRATE TO SUBJECT) Place one foot directly in front of the other. If you feel that you cannot place your foot directly in front, try to step far enough ahead that the heel of your forward foot is ahead of the toes of the
other foot. (To score 3 points, the length of the step should exceed the length of the other foot and the width of the stance should approximate the subject’s normal stride width.)

(    ) 4 able to place foot tandem independently and hold 30 seconds
(    ) 3 able to place foot ahead independently and hold 30 seconds
(    ) 2 able to take small step independently and hold 30 seconds
(    ) 1 needs help to step but can hold 15 seconds
(    ) 0 loses balance while stepping or standing

STANDING ON ONE LEG
INSTRUCTIONS: Stand on one leg as long as you can without holding on.

(    ) 4 able to lift leg independently and hold > 10 seconds
(    ) 3 able to lift leg independently and hold 5-10 seconds
(    ) 2 able to lift leg independently and hold ≥ 3 seconds
(    ) 1 tries to lift leg unable to hold 3 seconds but remains standing independently.
(    ) 0 unable to try of needs assist to prevent fall
Participant Information Sheet

**Title:** Exercise to improve balance and mobility in people with multiple sclerosis. A Pilot Study

**Introduction**

Evidence has shown many benefits to exercise in people with MS. The aim of this study is to test the feasibility and suitability of outcome measures for use in a larger study and to gain preliminary data on differences between physiotherapy interventions.

**Procedures**

A weekly balance exercise programme will take place in Limerick/Galway/Wexford. A week before and a week after the programme you will be assessed. This will involve a test of your balance. Fatigue and quality of life will be assessed using two questionnaires and walking distance over 2 minutes will also be assessed. A discussion about the benefits and disadvantages of the exercise programme will also be held for approximately 45 minutes.

**Benefits**

Research has shown that a people with moderate MS participating in a balance exercise programme can benefit from improvements in strength, fitness, fatigue and walking ability.
Risks

The risks of participating in this study are not greater than those in standard physiotherapy intervention or regular exercising in the community. Previously it was thought that exercise could exacerbate symptoms or relapses. However current research shows this is not the case.

Exclusion from Participation

You will need to have a definite diagnosis of MS and need to be using at least two sticks when walking outdoors to be included in the study. If permission to exercise has not been obtained from your GP you will excluded from this study.

Confidentiality

We will not disclose any information that can be identified with you nor connect your name to any information we present. All information will be confidential within the research team. Your participation is completely voluntary and you may withdraw at any time.

Compensation

There will be no compensation for participation in this study

Voluntary Participation & Stopping the Study

You're participation in this study is entirely voluntary and you are free to withdraw from the project at any stage without giving any reason

Permission
With your consent permission will be sought from your General Practitioner regarding your eligibility to participate.

**Complaints Procedure**

The procedures in this study have been subject to review and approval by the Mid-Western Ethics Committee. If you have any concerns or complaints about this study and wish to contact someone independent, you may contact The Chairperson of the Mid-Western Ethics Committee.

The Chairperson
Scientific Research Ethics Committee
Limerick Regional Hospital,
Dooradoyle,
Limerick.

**Further Information**
If you have any questions regarding the study feel free to contact Dr Susan Coote 061 234278, email: susan.coote@ul.ie or Neasa Hogan 0876333113, email: neasa.hogan@ul.ie

PARTICIPANT CONSENT FORM

Please read the following questions and tick the appropriate Yes or No box. Please sign the bottom of the page if you consent to participate in this study.

<table>
<thead>
<tr>
<th>I have read and understood the information leaflet</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>I know that my participation is voluntary and that I can withdraw from the project at any stage without giving any reason</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I agree to permit contact with my GP regarding my participation in this study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I agree to notify the Investigator of any side effects arising during the study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I agree to participate in this study</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SIGNATURE       BLOCK CAPITALS       DATE

Participant: ___________________  _______________   ________

Investigator: _________________  _______________  ________

Witness: _________________  _______________  ________
APPENDIX G – DYNAMIC GAIT INDEX

Grading: Mark the lowest category which applies. Total individual scores (24 possible).

1. Gait Level Surface ______
   Instructions: Walk at your normal speed from here to the next mark (20').
   Grading: Mark the lowest category that applies.
   
   (3) Normal: Walks 20', no assistive devices, good speed, no evidence for imbalance, normal gait pattern.
   (2) Mild impairment: Walks 20', uses assistive devices, slower speed, mild gait deviations.
   (1) Moderate impairment: Walks 20', slow speed, abnormal gait pattern, evidence for imbalance.
   (0) Severe impairment: Cannot walk 20' without assistance, severe gait deviations, or imbalance.

2. Change in gait speed ______
   Instructions: Begin walking at your normal pace (for 5'), when I tell you "go," walk as fast as you can (for 5'). When I tell you "slow," walk as slowly as you can (for 5').
   
   (3) Normal: Able to smoothly change walking speed without loss of balance or gait deviation. Shows a significant difference in walking speeds between normal, fast, and slow speeds.
   (2) Mild impairment: Able to change speed but demonstrates mild gait deviations, or no gait deviations but unable to achieve a significant change in velocity, or uses and assistive device.
   (1) Moderate impairment: Makes only minor adjustments to walking speed, or accomplishes a change in speed with significant gait deviations, or changes speed but has significant gait deviations, or changes speed but loses balance but is able to recover and continue walking.
   (0) Severe impairment: Cannot change speeds, or loses balance and has to reach for wall or be caught.

3. Gait with horizontal head turns ______
   Instructions: Begin walking at your normal pace. When I tell you to "look right," keep walking straight, but turn your head to the right. Keep looking to the right until I tell you "look left," then keep walking straight and turn your head to the left.
Keep your head to the left until I tell you, "look straight," then keep walking straight but return your head to the center.

(3) Normal: Performs head turns smoothly with no change in gait.
(2) Mild impairment: Performs head turns smoothly with slight change in gait velocity (i.e., minor disruption to smooth gait path or uses walking aid).
(1) Moderate impairment: Performs head turns with moderate change in gait velocity, slows down, staggers but recovers, can continue to walk.
(0) Severe impairment: Performs task with severe disruptions of gait (i.e., staggers outside 15° path, loses balance, stops, reaches for wall).

4. Gait with vertical head turns ______
Instructions: Begin walking at your normal pace. When I tell you to "look up," keep walking straight, but tip your head and look up. Keep looking up until I tell you "look down," then keep walking straight and turn your head down. Keep looking down until I tell you, "look straight," then keep walking straight but return your head to the center.

(3) Normal: Performs head turns with no change in gait.
(2) Mild impairment: Performs task with slight change in gait velocity (i.e., minor disruption to smooth gait path or uses walking aid).
(1) Moderate impairment: Performs tasks with moderate change in gait velocity, slows down, staggers but recovers, can continue to walk.
(0) Severe impairment: Performs task with severe disruption or gait (i.e., staggers outside 15° path, loses balance, stops reaches for wall).

5. Gait and pivot turn ______
Instructions: Begin walking at your normal pace. When I tell you to "stop and turn," turn as quickly as you can to face the opposite direction and stop.

(3) Normal: Pivot and turns safely within 3 seconds and stops quickly with no loss of balance.
(2) Mild impairment: Pivot turns safely in >3 seconds and stops with no loss of balance.
(1) Moderate impairment: Turns slowly, requires verbal cueing, requires several small steps to catch balance following turn and stop.
(0) Severe impairment: Cannot turn safely, requires assistance to turn and stop.
6. Step over obstacle ______

Instructions: Begin walking at your normal speed. When you come to the shoe box, step over it, not around it, and keep walking.

(3) Normal: Able to step over box without changing gait speed; no evidence for imbalance.
(2) Mild impairment: Able to step over box, but must slow down and adjust steps to clear box safely.
(1) Moderate impairment: Able to step over box but must stop, then step over. May require verbal cueing.
(0) Severe impairment: Cannot perform without assistance.

7. Step around obstacles ______

Instructions: Begin walking at your normal speed. When you come to the first cone (about 6' away), walk around the right side of it. When you come to the second cone (6' past first cone), walk around it to the left.

(3) Normal: Able to walk around cones safely without changing gait speed; no evidence of imbalance.
(2) Mild impairment: Able to step around both cones, but must slow down and adjust steps to clear cones.
(1) Moderate impairment: Able to clear cones but must significantly slow speed to accomplish task, or requires verbal cueing.
(0) Severe impairment: Unable to clear cones, walks into one or both cones, or requires physical assistance.

8. Stairs ______

Instructions: Walk up these stairs as you would at home (i.e., using the rail if necessary). At the top, turn around and walk down.

(3) Normal: Alternating feet, no rail.
(2) Mild impairment: Alternating feet, must use rail.
(1) Moderate impairment: Two feet to stair, must use rail.
(0) Severe impairment: Cannot perform safely.
First I want to give you some information about the project which has 2 parts to it. The first part is that we are organising Physiotherapy classes and treatments; the second part is that we’re hoping to measure as many people as possible and use the results for a research study to show that these classes are beneficial and should be continued. Today we need to get some information from you and to check that you can take part, then we will send you out an information leaflet and consent form, then when you send that back and we have all the paperwork is in order we will be able to give you a date to be assessed by a Chartered Physiotherapist.

**PART 1 – CONTACT INFORMATION**

Name of participant______________________________________________________

Name of person giving information (where applicable)
__________________________

Address of participant:
___________________________________________________

Phone:_________________________________________________________________

We want to let your GP know that you’ll be taking part in the study, and have their contact details in case there is a problem at any time is that OK with you?

YES □  NO □

What is your GP’s
Name__________________________________________________

GP’s Address:
___________________________________________________________________
___________________________________________________________________

Do you see a neurologist? Who do you see and where?
_______________________________________________________________

Are you a member of the MS Society? YES □ NO □

IF NO – You don’t need to be a member to be part of the project, but if you would like to join at any time just let us know

PART 2 – MOBILITY LEVEL

Do you have any problems walking? YES □ NO □
IF NO SCORE & MOVE ON TO PART 3

Do you use a walking aid? YES □ NO □
IF NO SCORE & MOVE ON TO PART 3

How do you usually get around outdoors? ________________________________
IF USE A WHEELCHAIR ASK -

Can you stand and walk a few steps with help? YES □ NO □

MOBILITY SCORE
Walking is not affected 0
Walking is affected, but walks independently (without aid) 1
Usually uses unilateral support (stick, single crutch, or one arm) to walk outdoors 2
Usually uses bilateral support (two sticks or crutches, frame, or two arms) to walk outdoors 3
Usually uses wheelchair to travel outdoors, but able to stand and walk a few steps with or without help 4
Restricted to wheelchair, unable to stand and walk a few steps even with help 5
Unknown X

*SCORE 0, 1, 2 – Strand A,*
*SCORE 3, 4 – Strand B,*
*SCORE 5 – Strand C*

**PART 3 – EXCLUSION CRITERIA**

I need to ask you another few questions to check that it’s OK for you to take part:

Have you had steroid treatment in the last 3 months? YES □ NO □

Are you currently having any worsening of symptoms or a relapse? YES □ NO □

*WHERE APPLICABLE:*

Are you pregnant? YES □ NO □

**IF YES TO ANY OF QUESTIONS ABOVE:**

Because you have been on steroids recently, we need you to wait until 3 months after that before you take part. We will get all of the paperwork sorted, then once the 3 months is up we will get back to you with a date

DATE FOR RE-CONTACTING ____________________
Because you are having a worsening of symptoms at the moment you can’t take part in the research part of the project, but we can arrange for you to have Physio treatment, would you like us to do that?

YES □ NO □

Unfortunately if you’re pregnant you won’t be able to take part in the study and you should check with your GP to see if you should be having Physio or exercise classes at the moment.

IF NO TO ALL ABOVE QUESTIONS:
Great, it looks like you’ll be able to take part in the project. We’re going to send you an information leaflet to make sure that you have all the information you need about the project, and a consent form which I need you to fill out and send back to me. Then once we have those we’ll send you a date to be assessed. If you have any more questions after you get the information leaflet let us know and we can hopefully answer them for you.

Have you any specific transport needs? do we need to arrange transport for you to get to the classes?

YES □ NO □

Do you need us to arrange childcare or anything to allow you to attend?

YES □ NO □

NOTES
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
___________________________________________________________________
The aim of the Getting the Balance Right project is to give people with MS physiotherapy and exercise programmes and to do research to see what the benefit is. The MS Society will organize the treatments and the Physiotherapy Department at University of Limerick will test the outcomes of these treatments.

Studies have shown many benefits to exercise for people with MS. Because we do not know which treatment is best or whether one on one physiotherapy is better than group physiotherapy this study will put people into different treatment groups and compare them. Which group they are in is chosen as if ‘by the toss of a coin’.

What will I have to do?

You will receive a treatment for approximately one hour a week for ten weeks

The treatments that you may receive are:

1. Group exercise led by a physiotherapist

2. One on one treatment by a physiotherapist

3. Group Yoga

The toss of the coin may mean you are allocated to a group that will not receive a treatment for the moment (a control group), but you will have a treatment in three months time.

A week before, a week after, and twelve weeks after the classes you will be assessed by a chartered physiotherapist who will ask you questions about your general health, look at your balance, strength, walking and give you a questionnaire about fatigue and also one for quality of life. This will take approximately 1 hour 15 minutes. S/he will not know which group you were
assigned to.

Requirements to take part

You have already been asked some questions regarding your suitability to take part. However, you will also be assessed by a Chartered Physiotherapist who will decide if there are any other reasons that you may not be suited to this exercise.

Benefits and Risks

You may have improvements in strength, balance, disability, walking, fatigue, and some people can experience improved mood. The risks of participating in this study are not over those in standard physiotherapy intervention or regular exercising in the community. Your Doctor (GP) will be notified of your participation.

Confidentiality

All information will be confidential within the research team. We will not disclose any information that can be identified with you nor connect your name to any information we present. The results will be published and presented where relevant without you being identified.

Voluntary participation

Your participation is completely voluntary and you may withdraw at any time. There will be no remuneration for participation in this study. If taking part in this research study harms you, there are no special compensation arrangements. If you are harmed due to someone’s negligence, then you may have grounds for a legal action.

If you have questions regarding the study please feel free to contact Susan, Neasa, Maria or Marie on 061 234278

Thank you for considering taking part in this study
GETTING THE BALANCE RIGHT
Participant Consent Form

Please read the following questions and tick the appropriate Yes or No box. Please sign the bottom of the page if you consent to participate in this study.

Participant Name: ___________________________

| I have read and understand the information sheet. | YES | NO |
| Someone has read the information sheet to me and I understand about the study | YES | NO |
| I am authorised to make decisions on behalf of the above person and I have read and understand the information leaflet | YES | NO |

*Please tick one of the above options*

<p>| I agree to be assessed by a chartered physiotherapist and for my data to be used for the research project | YES | NO |
| I understand that I might have one of three treatments, or a three month wait before being treated, and I agree to this | YES | NO |
| I know that my participation is voluntary and that I can withdraw from the project at any stage without giving any reason | YES | NO |
| I agree that my GP will be notified of my participation in this study | YES | NO |
| I agree to notify the Investigator of any side effects arising during the study. | YES | NO |
| I agree to be treated as part of the Getting the Balance Right Project | YES | NO |</p>
<table>
<thead>
<tr>
<th>Name of Participant (in block letters)</th>
<th>Date</th>
<th>Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name of Decision Maker (Where applicable)</td>
<td>Date</td>
<td>Signature</td>
</tr>
<tr>
<td>Researcher</td>
<td>Date</td>
<td>Signature</td>
</tr>
</tbody>
</table>
APPENDIX K – LETTER TO GENERAL PRACTICIONER

Physiotherapy
Department
University of Limerick
Castletroy
Limerick

Date: _______________________

Dear Dr _____________________

The “Getting the Balance Right” project is a collaboration between Multiple Sclerosis Ireland and the Physiotherapy Department at the University of Limerick, funded through Tesco Charity of the year and the Pobal, Dormant Accounts flagship projects fund.

The broad aim of the project is to deliver physiotherapy and exercise programmes for people with Multiple Sclerosis and to formally evaluate the outcome of these through a series of randomised controlled trials.

Your patient _________________________________ has expressed an interest in participating and has been stratified to strand _______, the information leaflet for that strand of the study is attached for your information.

All patients will be assessed by a chartered physiotherapist to establish their suitability for the programme. No adverse effects are anticipated as all interventions are either standard physiotherapy practice or currently in use by the MS Society.

If you have any questions or concerns please feel free to contact us at susan.coote@ul.ie or 061 234 278

______________________
Dr Susan Coote, MISCP
APPENDIX L – GUYS NEUROLOGICAL DISABILITY SCALE COMPONENT

**MOBILITY SCORE**

0 Walking is not affected

1 Walking is affected, but walks independently (without aid)

2 Usually uses unilateral support (stick, single crutch, or one arm) to walk outdoors

3 Usually uses bilateral support (two sticks or crutches, frame, or two arms) to walk outdoors

4 Usually uses wheelchair to travel outdoors, but able to stand and walk a few steps with or without help

5 Restricted to wheelchair, unable to stand and walk a few steps even with help
APPENDIX M – LETTER TO DELIVERERS

Dear Physiotherapist

Thank you for agreeing to participate in the “Getting the Balance Right” programme. The following Intervention pack includes some details in order for the research part of the project to be completed.

To get all the data needed for the outcome measures the Resting Heart Rate for each individual is required at week 1 and week 10 of the intervention.

The participants have been advised how to do this in a standard way during assessment and should have calculated this by the first week of the class. However, this must be documented by you at week 1 in the sheet provided. Remind the participants to get their new resting Heart Rate in week 9 and document it again when they come back in week 10.

Standardised instructions in how to get Resting Heart Rate and a sheet for documenting the same are included in this pack. A reminder sheet containing the exercises for the circuit class is also provided including examples of possible progressions for the exercises.

Additionally, in order to reproduce this study and to write up the report. It is essential that we know what the participants are doing. For one on one physiotherapy exact treatments must be recorded. Individual physiotherapy notes must also be recorded for the group intervention. Forms for this are included in the pack.

Finally, a sheet for attendance/deviations from normal is also provided. Please tick if the participant attended and document if there was any deviations from the prescribed class.

If you have any questions, please do not hesitate to contact the research team in the University of Limerick or the MS Society.
Kind Regards,

Neasa Hogan, MScP

Chartered Physiotherapist
Department of Physiotherapy
Health Sciences Building
University of Limerick
Limerick
Ireland

Phone: + 353 61 233768
Mob: + 353 87 6333113
APPENDIX N – GROUP PHYSIOTHERAPY CLASS

Strand B Physiotherapy led balance and strength exercises

The following exercises should be completed at each class:
All exercises should be explained and demonstrated on week 1

1. Sit to Stand       2. Squat       3. Calf Raises


Progressions of each exercise:

Sit to Stand
Hand positioning- may initially need to use hands to rise from chair, then hands by side, then hands across chest.
Seat height- may initially require a higher seat height which can be lowered to increase intensity of exercise.
Weights- Hand held weights can be given to participants who need further progression
To be performed in sets of 12. Increase amount of sets as participants ability increases.

Squat
Support- may initially need bilateral support, decrease to unilateral and none as participant is able.
Repetitions- to be performed in sets of 12 and number of sets increased as participant progresses.
Weights- may be given to participants who are able to complete three sets of 10 reps with no support

Calf Raises
Support- may initially need bilateral support, this can be decreased as
participant progresses to unilateral support to independent calf raises.

Repetitions- to be completed in sets of 12, to be increased as participant progresses

Base of Support- if participant is able they may perform single leg calf raises

**Step ups**

Participant should be within parallel bars for this exercise

Support- participant may start off with bilateral support, then decreasing to unilateral then to none

Steps- initially participant will step on to step, then on to step and over, then on to step over and backwards

Step height- when participant is comfortable with all directions of stepping step height may be increased

**Side Stepping**

Participant should be using parallel bars for this exercise

Support- participant may start off with bilateral support, then decreasing to unilateral then to none

Number of steps- initially participant may take only one step in each direction, this should be increased as participants’ ability increases.

**Tandem Stepping/Walking**

Participant should be within parallel bars for this exercise

Support- participants may start off with bilateral support, then decreasing to unilateral then to none

Stepping- participants may initially just place one foot in front of the other and hold this position

Number of steps- the number of steps can then be increased

Crossover- participant may become competent at stepping one foot in front of the other this can be progressed to one foot crossing over the other.

**Please Note:**

Some participants may not need all the above progressions. Progression should be based on participants’ ability to perform the
exercise.

Equipment needed:
Parallel bars
Chairs
Step
Stopwatch
APPENDIX O – BASELINE ASSESSMENT FORM

Baseline Participant Assessment Sheet

Participant Code:

GNDS score:

Date:

Section 1

Sex: __________

DOB: __________

Type of MS: __________

Length of time since first symptoms: __________

Length of time since diagnosis: __________

Number of hospital admissions for MS this year: __________

Number of steroid treatments this year: __________

Most recent Relapse: __________

Medications: Dose and frequency
(e.g. anti spasmodic, disease modifying, analgesics, steroids)

Ask patient to bring in list if can’t remember)
Current problem(s) relating to MS?

(If pain reported get overall Verbal Numeric Rating Scale (VNRS) score)

Medical history (current and previous):

Have you been ill recently?

Probes
  o Other medical conditions (Special questions, red flags)
  o Previous Injury
  o Any chest pain or breathlessness?
  o Family Hx of heart problems
  o Vision
  o Continence
  o Pain
History of falls? __________

If yes, frequency in the last three months __________

Dizziness? Unsteadiness?

Section 2

Activities in the last year?

Physiotherapy:

Details:

Exercise class (es):

Details of class (FITT):

Rehabilitation:

Details:
Current activities

Details of exercise (Frequency, Intensity, Type, Duration):

Are you currently receiving any other treatment? (For example physiotherapy, exercise, complimentary and alternative treatment)

Soc Hx

Type of residence? Rural/urban? Assisted living? ______________

Employment status: ______________

Assistance at home (type):

Hours of help daily:
Section 3

Co-ordination (affected arm)

Finger to nose test
  Normal speed
  Normal accuracy
  Tremor yes/no

ROM
Ankle DF  R    L

Sensory Assessment

Describe:
Light touch VNRS  0 no sensation at all
                  10 full sensation

Location        1. Dorsum of the foot
                2. Lateral Calf
                3. Medial Knee
                4. Middle fibres of Deltoid
                5. Lateral forearm
                6. Lateral Posterior aspect of the hand
Do you have any difficulties in feeling temperature with your hands or feet?

**Proprioception**

Normal/Abnormal

Big Toe  R)   L)

PIP Index Finger  R)   L)

Note: any impairment in range or strength

**Section 4**

**Tone/Spasticity**

**Modified Ashworth Scale, Rate 0 to 5**

Elbow and Knee

(most impaired side)

Note: any impairment of range

0 = No increase in Muscle Tone

1 = Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension

2 = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM (range of movement).
3 = Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the reminder (less than half) of the ROM (range of movement).

4 = Considerable increase in muscle tone passive, movement difficult.

5 = Affected part(s) rigid in flexion or extension.

Additional Notes:

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________

Resting Heart Rate
APPENDIX P – FOLLOW UP ASSESSMENT FORM

Follow up Participant Assessment Sheet

Participant Code:

GNDS score:

Date:

In addition to repeating the outcome measures, the participant should be asked if there has been a change in any of the following:

- Medications: Dose and frequency (anti spasmodic, disease modifying, analgesics, steroids)

- Current problem(s) relating to MS?

(If pain reported get overall Verbal Numeric Rating Scale (VNRS) score)

- Have you been ill since entering into this programme? (nb relapse / falls)

Describe details:
Current exercise activities?
(remember Frequency, Intensity, Type, Duration)

Hours of home help/ assistance?

Have you had any change in employment status?

Have you received any other physiotherapy since starting this programme?
Additional notes (anything else the participant would like to report):

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
APPENDIX Q – STANDARDISED DOCUMENTATION

Resting Heart Rate

During Assessment, participants were asked to get their Resting Heart Rate (RHR). Please document this below in weeks 1 and 10.

Calculating Resting Heart Rate

- Ask participant to feel the carotid pulse in their neck.
- On feeling the pulse count for 30 seconds
- Start counting beats at zero
- This must be done first thing in the morning on waking (i.e. before getting out of bed)

Alternatives: If participant has problems feeling their own pulse you can Send them home with a heart rate monitor to get their morning heart rate, get them to lie still for a half an hour in the class venue and count the beats yourself using the same guidelines as above or with a heart rate monitor.

Documentation of RHR Weeks 1 and 10

<table>
<thead>
<tr>
<th>Participant code</th>
<th>Baseline Resting Heart Rate (Week 1)</th>
<th>Follow up Resting Heart Rate (Week12)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Participant Performance Sheet

To be given to participants at the start of each class and filled out by them during the class. To be taken back at the end of each class.

Name:

<table>
<thead>
<tr>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reps</td>
<td>Sets</td>
<td>Reps</td>
<td>Sets</td>
<td>Reps</td>
</tr>
<tr>
<td>Sit to Stand</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calf Raises</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
<th>Week 9</th>
<th>Week 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reps</td>
<td>Sets</td>
<td>Reps</td>
<td>Sets</td>
<td>Reps</td>
</tr>
<tr>
<td>Sit to Stand</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Calf Raises</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Please document one sheet for every participant.

**Weekly attendance sheet/deviations from Normal**

Participant Name: __________________________

<table>
<thead>
<tr>
<th>Week</th>
<th>Attended (please tick)</th>
<th>Deviations from prescribed class (please comment)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Please Document individual physiotherapy notes every week. 8 sheets required in total. Please keep a copy of these for the MS Society

Participant Name:

Week 1:

Week 2:

Week 3:

Week 4:
Week 5:

Week 6:

Week 7:

Week 8:
Week 9:

Week 10: