

Analysis of a physiotherapy program in a group of patients with multiple sclerosis.

Análise de um programa de fisioterapia em grupo de pacientes com Esclerose Múltipla.

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Abstract

Introduction: Multiple sclerosis (MS) is a progressive disease that affects a population usually under 40 years of age. These people used to be advised to reduce their level of physical activity to reduce the risk of new outbreaks. On the other hand, groups of people with MS have been involved in therapeutic physical activity programs and achieved similar benefits to those obtained by healthy people. **Objective:** The aim of this study was to characterize the physical therapy procedures and analyze the efficiency of physiotherapy group in these individuals. **Method:** Participated in this quasi-experimental study, 04 participants (37.2±6 years, 7±3 years of injury, 22.8±3 kg/m²) with MS attending physiotherapy group in the CEAFIR FCT/UNESP. To characterize the functional capacity and motor skills of the Berg Balance Scale (BBS) and Six-minute walk test (6MWT) were used, the perceived quality of life was assessed by SF-36. The evaluations took place before starting the exercise protocol group and after 18 sessions. 18 sessions were filmed for description of physical therapy procedures used during physical therapy sessions in groups. For statistical analysis, GraphPad Prism 5 program (GraphPad Software Inc., San Diego, CA, USA) was used. Data normality was assessed using the Shapiro Wilk test and comparison of data was performed by paired t test ($p < 0.05$). **Results:** There was a significant difference in body balance and functional ability of participants by BBS and by the 6MWT, respectively, in the comparison between the first assessment and the second assessment ($p = 0.01$). There was no significant difference when comparing the hemodynamic parameters during the 6MWT and the perception of HRQoL compared between the two assessments ($p > 0.05$). **Conclusion:** The physiotherapy program group for ME proved effective in improving and maintaining body balance and functional capacity of these participants.

Keywords: Multiple Sclerosis. Physical Therapy. Motor Activity.

Resumo

Introdução: A Esclerose Múltipla (EM) é uma doença progressiva, que acomete uma população geralmente com idade inferior aos 40 anos. Durante certo tempo, essas pessoas eram orientadas a reduzir seu nível de atividade física para diminuir o risco de novos surtos. Contrariamente a isso, grupos de pessoas com EM têm se envolvido em programas de atividade física terapêutica e alcançado benefícios similares àqueles obtidos por pessoas saudáveis. **Objetivo:** O objetivo deste estudo foi caracterizar as condutas fisioterapêuticas e analisar a eficiência da fisioterapia em grupo nesses indivíduos. **Método:** Participaram desse estudo quasi-experimental 04 participantes (37,2±6 anos; 7±3 anos de lesão; 22,8±3 kg/m²) com EM que freqüentam a fisioterapia em grupo do CEAFIR da FCT/UNESP. Para caracterização das habilidades motoras e capacidade funcional foram utilizadas a Escala de Equilíbrio de Berg (EEB) e Teste de Caminhada de Seis minutos (TC₆); a percepção de qualidade de vida foi avaliada pelo questionário SF-36. As avaliações aconteceram antes de iniciar o protocolo de exercícios em grupo e após 18 sessões. Foram filmadas 18 sessões para descrição das condutas fisioterapêuticas utilizadas durante as sessões de fisioterapia em grupo. Para a análise estatística foi utilizado o programa GraphPad Prism 5 (GraphPad Software Inc., San Diego, CA, EUA). A normalidade dos dados foi feita pelo teste de Shapiro Wilk e a comparação dos dados foi feita pelo teste t pareado ($p < 0.05$). **Resultados:** Houve uma diferença significativa no equilíbrio corporal e capacidade funcional dos participantes pela EEB e pelo TC₆, respectivamente, na comparação entre a primeira avaliação e a segunda avaliação ($p = 0.01$). Não houve diferença significativa na comparação entre os parâmetros hemodinâmicos durante o TC₆ e na percepção de QVRS comparação entre as duas avaliações ($p > 0.05$). **Conclusão:** O programa de fisioterapia em grupo para EM se mostrou eficiente na melhora e manutenção do equilíbrio corporal e capacidade funcional desses participantes.

Palavras-chave: Esclerose múltipla. Fisioterapia. Atividade Física.

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INTRODUCTION

Multiple sclerosis (MS) is a progressive disease that affects young adults, usually under 40 years of age. According to statistics from the Ministerio da Saude, the number of cases in the city of Sao Paulo increased five-fold from 2002 to 2009 and currently there are 15 cases per 100 000 inhabitants. Throughout Brazil, there are about 24,000 people with the disease and, in the United States, the incidence is much higher, reaching 200 people per 100 000 inhabitants.⁽¹⁾

The progression of MS is characterized by the occurrence of relapses, defined as the appearance of new symptoms or worsening of pre sudden deficits, which has more than 24 hours duration. Signs and symptoms vary in character intensity and duration, progression and transition.⁽²⁾ The major motor signs of MS include muscle contractures, gait disturbance, fatigue, balance deficits, nystagmus, intention tremor, difficulty in swallowing and breathing.⁽³⁾ In addition to these, fatigue is one of the most frequent manifestations of MS and can be very limiting.⁽⁴⁾

For a time, individuals with MS were advised to reduce their level of physical activity. This approach aimed to conserve energy in order to monitor fatigue and reduce the risk of exacerbation of the symptoms of the disease. The adoption of a sedentary lifestyle reflected in an increased risk for heart disease and decreased functional capacity of these individuals.⁽⁵⁾ Contrary to this, in recent years, groups of people with MS have been involved in programs with exercise and achieved benefits perception of disease-related symptoms and execution of activities of daily living.⁽⁶⁻⁹⁾

Within this new landscape, the guidelines for young adults with MS who have mild to moderate disabilities were created. According to these guidelines, individuals with MS need at least 30 minutes of moderate intensity aerobic activity and strength training exercises for the major muscle groups twice a week. Meet these parameters can be active to reduce fatigue, improve mobility and elements of health-related quality of life (HRQOL).⁽¹⁰⁾

Among the various treatments, the practice of group therapy has shown a strong growth in our reality, revealing a multiplicity of interventions in various contexts and a growing acceptance among professionals and the participants themselves.⁽¹¹⁾

Whereas there are many studies describing specific therapeutic exercise protocols for individuals with MS a model of physiotherapy group was created, which occurs twice a week in the Centro de Estudos e Atendimento em Fisioterapia e Reabilitação da Pesquisa (CEAFIR) da Faculdade de Ciências e Tecnologia da Universidade Estadual Paulista (FCT/UNESP). Given this, this study aimed to characterize the approach taken in this model and analyze their results, fostering physical therapy practice.

METHODS

Sample

Were included in this quasi-experimental study four (04) individuals with a diagnosis of MS and ability to ambulate or not using accessories that assist the march, who attend physiotherapy in the CEAFIR group. Participants were notified in advance about the objectives and procedures of the research and from reading, understanding and signing an informed consent, were included in this study. The project was submitted and approved by the Research Ethics Committee of FCT/UNESP (CAAE: 20628713.9.0000.5402).

Group Physiotherapy

The program Physical Therapy Group in this study was based on the Guidelines for MS, which recommends 55 minutes of exercise twice a week arranged in 12 repetitions each, with rest time of 30 seconds between sets.⁽¹⁰⁾ Stretches muscle were also used in a single repetition of 10 seconds for each muscle group worked. Sessions were started in the sitting position where performed stretching in sternocleidomastoid muscles, triceps, biceps, flexors and extensors of the wrist and fingers, then the orthostatic performs stretching the quadriceps femoris, iliopsoas, and soleus gastrocnemio, spine extensors and spine flexors. After the stretching still seated himself initiated active exercises of flexion, extension, abduction, internal and external rotation and shoulder flexion, elbow extension using sticks, hula hoops and weights 0.5 kg. Still seated exercises performed active knee extension and flexion of the hips, with a 0.5 kg ankle weight on the ankle region. Was then initiated the exercises in the standing position active exercises of abduction and hip adduction, hip extension and plantar flexion. After these exercises, the participants took part in a circuit of balance in a corridor of 30 meters with obstacles of varying difficulty using hula hoops, sensory mats, rugs, stairs/ramp and trampoline. Each participant walked through the circuit twice. Before the end of the session was held in the relaxation sitting position. The participant was instructed to breathe in a more concentrated form in the diaphragm.

Evaluation protocol

For evaluation of motor skills and functional capacity of the Berg Balance Scale (BBS) and Six-minute walk test (6MWT) were used; perception of quality of life was assessed using the SF-36. Evaluations were performed before starting the exercise protocol group and after 18 sessions of physiotherapy group.

The BBS measures 14 items, aspects of static and dynamic balance that receive a score from 0 to 4 based on the ability to achieve the requirements in this test. The score 0 is the inability to complete an item and the

score 4 is the ability to complete the task independently and efficiently. The score ranges from 0 to 56 points.⁽¹²⁾

The 6MWT was performed in a corridor 30 meters long in an air-conditioned environment. Before starting the test are checked vital signs: heart rate (HR), respiratory rate (RR), blood pressure (BP), peripheral oxygen saturation (SpO₂) and the Borg Scale of Perceived Exertion modified. In the third minute the participant walks the runway are measured by pulse oximetry, HR and SpO₂. At the end of six minutes with the participant still in the upright position, are measured the same initial parameters and how many meters are verified participant-traveled at this time.^(13,14)

The SF-36 is a generic instrument for assessing quality of life, which has 36 items that measure eight dimensions of health: physical functioning (10 items), role-physical (4 items), bodily pain (2 items) general health (5 items), vitality (4 items), social functioning (two items), role emotional (three items) and mental health (5 items). The score ranges 0-100, 100 being the best perceived quality of life. In this study, the questionnaire was self-administered.

To analyze the physical therapy group, 18 sessions using a digital camera to study the pictures, description of stages and physical therapy procedures used during the sessions were filmed. In this analysis stages of the session, the exercises used, the number and the runtime of each exercise, the body segments used during the exercises and the number of exercises performed in each therapy were evaluated. The sessions took place twice a week lasting 55 minutes session.

Statistical Analysis

Statistical analysis was performed using GraphPad Prism 5 (GraphPad Software Inc., San Diego, CA, USA). The normality of data was done by the Shapiro-Wilk test and comparison of data was performed by paired t test (p <0.05).

RESULTS

The characterization of participants was accomplished through the collection of anthropometric data be-

fore the start of group physiotherapy sessions, these are presented in Table 01.

The results obtained before and after 18 sessions of group physiotherapy for BBS and 6MWT are presented in Table 02. Both the BBS and the 6MWT presented a significant difference when comparing the first and second evaluation (p <0.05). The values of hemodynamic parameters evaluated before and after the 6MWT showed no statistical differences in between them (Table 03), the same as the values of the perceived quality of life (Table 04).

The analysis of the filming of the sessions is shown in Table 05. The sessions were initiated in the sitting position where it was in active stretches and exercises for upper and lower limbs. Then the exercises in the standing position were performed, and in that position all the exercises were to the lower limbs. After completion of the exercises for the lower limbs, patients should undergo a circuit mounted on a corridor of 30 meters with obstacles of varying difficulty. Each participant walked through the circuit twice. Before the end of the session

Table 01. Anthropometric data of the subjects evaluated.

Subjects	Age (years)	Injury time (years)	BMI (kg/m ²)
1	48	3	21.3
2	39	12	23.5
3	32	8	20.2
4	31	4	20.9
Mean±sd	37.2±6	7±3	22.8±3

Table 02. Results obtained before (01) and after (02) 18 sessions of physiotherapy group for the Berg Balance Scale (BBS) and six-minute walk test (6MWT).

Subjects	BBS 01	BBS 02	TC6 01	TC6 02
1	53	55	174	387
2	45	56	184	300
3	53	53	325	326
4	52	54	242	467
Mean ± sd	51±3	54±1*	197±25	370±64*

* Statistically significant difference when comparing the evaluation before (01) and after (02) (p ≤ 0.05).

Table 03. Values of hemodynamic parameters obtained before (01) and after (02) 18 group physiotherapy sessions in the six minute walk test (6MWT).

Parameters Hemodinamics	Evaluation 01				Evaluation 02			
	Initial	3'	Final	Rest	Initial	3'	Final	Rest
SBP (mmHg)	100±20	-	130±20	110±20	110±20	-	130±15	120±10
DBP (mmHg)	72±15	-	85±10	70±10	70±10	-	80±10	75±10
HR (bpm)	79±9	106±8	115±5	96±1	85±7	109±9	112±7	98±1
SpO ₂ (%)	99±1	96±2	95±3	97±1	98±1	97±1	95±2	96±1
RR (rpm)	12±2	-	16±2	14±1	14±2	-	18±2	16±1
Borg Dyspnea	5±2	-	6±3	4±1	4±2	-	5±3	3±1
Borg lower limbs	16±3	-	19±2	15±3	16±5	-	17±2	16±3

* Systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), peripheral oxygen saturation (SpO₂), respiratory rate (RR) and modified borg scale (dyspnea e Lower limbs).

the patient was instructed to come back to perform a seated position muscular relaxation.

DISCUSSION

The balance and functional capacity of the assessed participants improved after 18 sessions of physiotherapy group, according to assessments by the Berg Balance Scale (BBS) and Six Minute Walk Test (6MWT), respectively. The perception of quality of life in all domains of the SF-36 increased after 18 sessions of physiotherapy group, however no significant difference was observed in the analyzed period.

Rodrigues et al.⁽¹⁵⁾ also found evidence that physiotherapy treatment helps in maintaining body balance, when compared evaluation according to BBS before and after 15 training sessions that function in participants with MS. Another study evaluated 04 individuals with MS before and after 30 sessions of physical therapy and found a significant improvement in static and dynamic balance and gait performance.⁽¹⁶⁾ These findings reinforce our study and demonstrates the importance of physiotherapy group treatment in maintaining the balance body in individuals with MS.

Our findings found no significant difference when comparing the hemodynamic parameters measured during the 6MWT before and after 18 sessions of physiotherapy group, but significantly increased the distance walked during the 6MWT after 18 sessions of physiotherapy group and therefore we can infer that this increase in distance traveled can positively influence functional capacity.

Carter et al.⁽¹⁷⁾ also found a good functional motor response in individuals with MS undergoing resistance exercise performed three times a week for 10 weeks, as well as an improvement in the perception of fatigue of these individuals. In the study by Snook et al.⁽¹⁸⁾ MS patients remained with an accelerometer for 07 days revealing a lower threshold of fatigue in patients with lower levels of physical activity compared to physically active individuals. Another study also suggested that efficiency in the execution of the exercise in this population, is closely linked with the perception of disease symptoms.⁽¹⁹⁾ The study by White et al.⁽⁹⁾ evaluated the

effect of eight weeks of a program of progressive resistance training for the lower limbs. Participants showed significant improvements in isometric strength of the quadriceps and plantar flexor muscles, beyond the improvement in performance in the execution while ascending and descending the ladder test and reduction in self-reported fatigue with a trend towards reduced disability and improved march. Romberg et al.⁽⁸⁾ studied the impact of 23 weeks of resistance training with elastic bands and aerobic exercise in 95 individuals with MS. Significant improvements in walking tests were observed, as well as improvement in muscular resistance in the upper limbs. The results presented in this work linked those found in our study emphasize the importance of physiotherapy in maintaining the functional capacity of individuals with MS.

Besides the change in motor functions, individuals with MS may show changes in emotional, social and cognitive aspects, which significantly affects their perception of QoL. The health and welfare of these individuals may be strongly impacted by the disease and/or side effects of medications with significant interference in QOL. The study by Morales et al.⁽²⁰⁾ studied the perception of HRQoL using the SF-36 questionnaire and it was observed that participants with MS had significantly lower scores in all domains and components studied when compared with healthy individuals. Ford et al.⁽²¹⁾ stud-

Table 05. Representation of the results found in the analysis of the filming of the exercises performed during physiotherapy group.

Description	Duration (minuts)	Number of exercises
Seated Position	24±1	19±1
Stretches of the UL and neck	3±1	5±1
Stretches of LL	2±1	3±1
Active UL exercises	14±2	6±1
Active LL exercises	3±1	2±0,5
Relaxation	2±0.4	3±1
Standing position	18±1	7±1
Stretches of LL	3±1	3±1
Active LL exercises	9±3	4±1
Circuit	6±1	-

* UL = upper limbs; LL = lower limbs.

Table 04. Results obtained in the evaluation of the perceived quality of life in each domain of the SF-36, before the start of physiotherapy group (01) and after 18 sessions (02).

Domain	Mean±sd 01	Median 01	Percentile 01	Mean±sd 02	Median 02	Percentile 02	p
PF	29±15.6	35	[12.5-45.5]	36±6	35	[30-42.5]	0.75
RP	30±32	25	[0-62.5]	50±17.7	50	[37.5-62.5]	0.32
Pain	30±19	41	[10-46]	45.2±21.5	51	[25.5-62]	0.23
GH	45±29	35	[21-74.5]	51.6±22	52	[33.5-69.5]	0.67
VT	27±29	30	[0-52.5]	49±28	60	[25-67.5]	0.33
SF	50±15	50	[37.5-62.5]	60±16	62.5	[43.8-75]	0.38
RE	46.4±44.6	66	[0-83]	72.8±15.2	66	[66-83]	0.4

* Physical Functioning (PF), Role-Physical (RP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE).

ied the characteristics of the disease and HRQoL using the SF-36 in a population of 206 individuals with MS and found a better perception of HRQoL in individuals in old age compared to younger individuals.

In another study with 04 individuals with age range of 33-53 years have also found no significant differences in HRQoL after 30 sessions of physical therapy.⁽¹⁶⁾ Our results also showed no significant differences in HRQoL, but there was an increase in the values of domains of the SF36, which may indicate a more studied to be an important clinical change. Both studies may not have found a significant difference in HRQoL due to the age range of participants, as all young adults were evaluated, and the perception of the limitation of the disease is differentiated compared to an older population. A young population, perception about the dysfunctions of MS can affect the development of social activities, acting starkly on HRQoL.

The practice of physiotherapy in group shows a marked increase in our reality. Ropollo et al.⁽²²⁾ had a group of 35 women with MS to a combined aerobic training and strength exercises for 12 weeks and found evidence that physical activity benefits the perception of fatigue, depression, social activity and quali-

ty of life. The physiotherapy program in a group of this study took into account work that had grounding in EM guidelines, which recommends physical exercise twice a week, lasting 30-60 minutes with exercises done for upper and lower limbs on one or two sets of 10 reps to 15 reps.^(10,23)

In the protocol of physiotherapy group, the time of exercise in the sitting position was superior to the standing position, because individuals with MS fadigate rapidly during the execution of the exercises. MS being a neurodegenerative disease, is necessary for the patient to work all body segments, however, should not require excessive energy demand in these patients, not to accelerate the degenerative process. This proposal physiotherapy showed improvement in balance and functional ability of the participants.

CONCLUSION

The group physiotherapy program for MS held at the FCT-UNESP proved effective in improving and maintaining body balance and functional ability of participants and positively influence the perception of these HRQL individuals.

REFERENCES

1. Lopes KN, Nogueira LAC, Nóbrega FR, Alvarena-Filho H, Alvarenga RMP. Limitação funcional, fadiga e qualidade de vida na forma progressiva primária da Esclerose Múltipla Rev Neurocienc 2010;18(1):13-17.
2. World Health Organization. The World Health Organization Quality Of Life Assessment (WHOQOL): position paper from the World Health Organization. Soc Sci Med. 2010;41:403-9.
3. Poser CM, Paty DM, Scheinenberg L. New diagnosis criteria for multiple sclerosis: guidelines for research protocols. Ann Neurol, 1983;13:227-31.
4. Mendes MF, Tilbery CP, Felipe E. Fadiga e esclerose múltipla – estudo preliminar de 15 casos através de escalas de auto-avaliação. Arq Neuropsiquiatr. 2000;58(2):467-70.
5. Kuspinar A, Anderson RE, Teng SY, Asano M, Mayo NE. Predicting Exercise Capacity Through Submaximal Fitness Tests in Persons With Multiple Sclerosis. Arch of Phys Med Rehabil. 2010;91(9):1410-7.
6. Debolt LS, Mccubbin JA. The effect of home-based resistance exercise on balance, power, and mobility in adults with multiple sclerosis. Arch Phys Med Rehabil. 2004;85(2):290-7.
7. Oken BS, Kishiyama S, Zajdel D, Bourdette D, Carlsen J, Haas M, et al. Randomized controlled trial of yoga and exercise in multiple sclerosis. Neurol. 2004;62(11):2058-64.
8. Romberg A, Virtanen A, Ruutinen J, Aunola S, Karppi SL, Vaara M, et al. Effects of a 6-month exercise program on patients with multiple sclerosis: a randomized study. Neurol. 2004; 63(11):2034-8.
9. White LJ, McCoy SC, Castellano V, Gutierrez G, Steven JE, Walter G, et al. Resistance training improves strength and functional capacity in persons with multiple sclerosis. Multiple Sclerosis 2004; 10: 668-674.
10. Latimer-Cheung AM, Martina AMG, Hicks AL, Motl RW, Pilutti LA, Duggan M, et al. Development of Evidence-Informed Physical Activity Guidelines for Adults With Multiple Sclerosis. Archives of Physical Medicine and Rehabilitation. 2013; 94(9):1829-1836. <http://dx.doi.org/10.1016/j.apmr.2013.05.015>
11. Carvalho AC, Vanderlei LCM, Bofi TC, Pereira JDAS, Nawa VA. Projeto Hemiplegia – Um modelo de fisioterapia em grupo para hemiplégicos crônicos. Arq Ciênc Saúde. 2007; 14(3):161-8.
12. Berg KO, Wood-Dauphée S, Willians JI. The balance scale: reability assessment with elderly residents and patients with an acute stroke. Scand J Rehab Med. 1995;10(4):27-36.
13. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002; 166(1):111-7.

14. Campolina AG, Bortoluzzo AB, Ferraz MB, Ciconelli RS. Tradução para a língua portuguesa e validação do questionário genérico de avaliação de qualidade de vida SF-36 (Brasil SF-36). *Rev. Bras. Reumatol.* 1999; 39(3):143-150.
15. Rodrigues IF, Nielson MBP, Marinho AR. Avaliação da fisioterapia sobre o equilíbrio e a qualidade de vida em participantes com esclerose múltipla. *Rev Neurocienc.* 2008;16 (4):269-74.
16. Pereira GC, Vasconcellos THF, Ferreira CMR, Teixeira DG. Combinações de Técnicas de Fisioterapia no Tratamento de Pacientes com Esclerose Múltipla: Série de Casos. *Rev Neurocienc.* 2012; 1-11.
17. Carter AM, Daley AJ, Kesterton SW, Woodroffe NM, Saxton JM, Sharrack B. Pragmatic exercise intervention in people with mild to moderate multiple sclerosis: A randomised controlled feasibility study. *Contemporary Clinical Trials.* 2013; 35(2):40-7. doi: 10.1016/j.cct.2013.04.003.
18. Saxton JM, Carter A, Daley AJ, Snowdon N, Woodroffe MN, Petty J, et al. Pragmatic exercise intervention for people with multiple sclerosis (ExIMS Trial): Study protocol for a randomised controlled trial. *Contemporary Clinical Trials.* 2013; 34(2):205-211. doi.org/10.1016/j.cct.2012.10.011
19. Snook EM, Motl RW. Physical Activity Behaviors in Individuals with Multiple Sclerosis: Roles of Overall and Specific Symptoms, and Self-Efficacy. *Journal of Pain and Symptom Management.* 2008; 36(1):46-53. doi: 10.1016/j.jpainsymman.2007.09.007.
20. Morales RR, Morales NMO, Rocha FCG, Fenelon SB, Pinto RMC, Silva CHM. Qualidade de vida em portadores de esclerose múltipla. *Arq Neuropsiquiatr* 2007; 65(2-B):454-460. doi.org/10.1590/S0004-282X2007000300018.
21. Ford HL, Gerry E, Johnson MH, Tennant A. Health status and quality of life of people with multiple sclerosis. *Disabil Rehabil.* 2001;23(12):516-21.
22. Ropollo M, Mulasso A, Gollin M, Bertolloto A, Ciairano S. The role of fatigue in the associations between exercise and psychological health in Multiple Sclerosis: Direct and indirect effects. *Mental Health and Physical Activity.* 2012; 6(2):87-94. doi.org/10.1016/j.mhpa.2013.05.002
23. Motl RW, Pillut LA, Sandroff BM, Klaren R, Balantrapu S, McAuley E, et al. Rationale and design of a randomized controlled, clinical trial investigating a comprehensive exercise stimulus for improving mobility disability outcomes in persons with multiple sclerosis. *Contemporary Clinical Trials.* 2013; 35(1):151-8. <http://dx.doi.org/10.1016/j.cct.2013.03.005>