Assessment of Activity Pacing in Relation to Physical Activity and Health-Related Quality of Life in Adults with Multiple Sclerosis:

A Foundation for Further Intervention Development

Ulric S. Abonie, PhD; Bregje L. Seves, MSc; Femke Hoekstra, PhD; Trynke Hoekstra, PhD; Lucas H.V. van der Woude, PhD; Rienk Dekker, PhD; Florentina J. Hettinga, PhD

From the Department of Physiotherapy and Rehabilitation Sciences, University of Health and Allied Sciences, Ho, Ghana (USA); School of Sport, Rehabilitation, and Exercise Science, University of Essex, Colchester, UK (USA); Center for Human Movement Sciences (BLS, FH, TH, LHVvdW) and Department of Rehabilitation (FH, LHVvdW, RD), University of Groningen, University Medical Center Groningen, Groningen, the Netherlands; Department of Health Sciences and Amsterdam Public Health Institute, Vrije Universiteit Amsterdam, Amsterdam, the Netherlands (TH); and Department of Sport, Exercise, and Rehabilitation, Northumbria University, Newcastle upon Tyne, UK (FJH). Correspondence: Florentina J. Hettinga, PhD, Department of Sport, Exercise, and Rehabilitation, University of Northumbria, Northumberland Building, College Lane, Newcastle upon Tyne, NE1 8SG, United Kingdom; e-mail: florentina.hettinga@northumbria.ac.uk.

Running head: Activity Pacing in Persons with MS

DOI: 10.7224/1537-2073.2020-047

© 2021 Consortium of Multiple Sclerosis Centers.
Practice Points

- There is no clear behavioral strategy to improve physical activity (PA) while managing fatigue in persons with MS when no interventions are offered. This study underscores the need to develop and design interventions to help improve engagement in PA and manage fatigue symptoms in persons with MS.

- Persons with MS could benefit from guidance on the optimal use of activity pacing strategies to manage MS symptoms and improve PA levels. The present study provides the foundation for further intervention development.
Abstract

**Background:** Activity pacing is a behavioral strategy for coping with fatigue, optimizing physical activity (PA) levels, and achieving a paced approach to lifestyle and sustainable self-regulated exercise practice to optimize health and well-being. Yet little is known about how activity pacing affects PA and health-related quality of life (HRQOL) while controlling for fatigue and demographic characteristics over time in adults with multiple sclerosis (MS). This study examined the natural use of activity pacing and how it is associated with PA and HRQOL over time in adults with MS.

**Methods:** Sixty-eight adults with MS (mean ± SD age, 45.2 ± 10.9 years) completed questionnaires on their activity pacing, fatigue, PA, and HRQOL 14, 33, and 52 weeks after rehabilitation. Associations between the variables were examined using multilevel models.

**Results:** No associations were found between activity pacing and PA ($\beta = -0.01, P = .89$) or between activity pacing and HRQOL ($\beta = -0.15, P = .09$).

**Conclusions:** This study provides an initial understanding of how activity pacing relates to PA and HRQOL in people with MS over time and indicates that there is no clear strategy among adults with MS that is successful in improving PA and HRQOL in the short- or long-term. Persons with MS may benefit from goal-directed activity pacing interventions to improve longitudinal engagement in PA, and the present study provides a foundation for further intervention development. *Int J MS Care.*
It is a well-known principle that regular physical activity (PA) can improve physiological performance and psychological well-being; however, although compelling evidence exists for its efficacy in healthy individuals, engaging in an active lifestyle is often challenging for people with chronic conditions. Fatigue symptoms can significantly impede engagement in PA and, consequently, health-related quality of life (HRQOL) in people with multiple sclerosis (MS). The experience of fatigue symptoms can lead to cycles of overactivity followed by prolonged periods of fatigue-induced inactivity. Consequently, adequate management of fatigue is most important when organizing PA for people with heightened fatigue sensation.

Instruction in activity pacing is believed to help manage symptoms and has been widely used in pain management. Activity pacing involves splitting one’s daily activities into small, manageable pieces to minimize the influence of fatigue-related symptoms, and allow steady progressive upturns in activity. The activity pacing aims to disentangle fatigue experience from PA behavior and to offset the overactivity-underactivity pattern where excessive activity can result in symptom worsening that necessitates a prolonged period of inactivity or rest as a means to recover. The concept of activity pacing hypothesizes that by perceiving an increase in PA without worsening of fatigue symptoms, persons are more likely to feel in control and focus less on their fatigue sensation, which can in turn result in beneficial effects on fatigue symptoms and activity participation.

The few studies on natural use of activity pacing (the activity pacing persons enact in their daily routine without undergoing an explicitly taught activity pacing program) has produced varying outcomes. In some studies, pacing was associated with low PA levels and other poor health indicators, and in other studies the opposite or no association was found. The cross-sectional nature of these studies limits us to exploring what happens to fatigue symptoms,
PA, and HRQOL when a person engages in activity pacing over time. For example, do persons engage in more pacing to reduce the influence of fatigue symptoms on activity and thereby optimize their PA and HRQOL?\textsuperscript{7,14} Studies that examine how activity pacing relates to PA and well-being in the context of fatigue experience and perceived risk of overactivity over time are thus needed to inform and guide treatment efforts (establish the need for and influence the design of activity pacing interventions).

This study examined longitudinal associations among activity pacing, PA, and HRQOL in adults with MS 1 year after rehabilitation, with fatigue and perceived risk of overactivity as confounders. Because activity pacing could be a successful strategy to lessen the influence of symptoms on activity and progressively increase activity without worsening of symptoms,\textsuperscript{15} we hypothesized that pacing engagement would be associated with high levels of PA and HRQOL over time. We also hypothesized that pacing engagement would moderate the associations between fatigue and PA and between fatigue and HRQOL over time—specifically, over time people who engage in activity pacing would display weaker associations between fatigue and PA, to reflect independence of PA and fatigue, compared with people who engage in overactive behavior.

**Methods**

**Design**

This is an analysis of data from a larger longitudinal multicenter study in the Netherlands (Rehabilitation, Sports, and Active lifestyle [ReSpAct]) to evaluate the nationwide...
implementation of an active lifestyle program—Rehabilitation, Sports, and Exercise—among persons with a wide range of chronic diseases and/or physical disabilities in Dutch rehabilitation. Data from 14-, 33-, and 52-week follow-up assessments of persons with MS selected from the ReSpAct data set were used for these analyses. Ethical approval for this study was obtained from the Center for Human Movement Sciences of the University Medical Center Groningen and at participating institutions.

Participants

Participants were recruited from 18 rehabilitation centers and hospitals in the Netherlands. Participant recruitment was from May 2013 to August 2015. Participants were recruited on referral to the participating rehabilitation institutions across the Netherlands. Potential participants received information on study rationale and procedures, had questions answered, and were checked for the inclusion criteria. Participants were included if they were 18 years or older, had a diagnosis of MS and received inpatient or outpatient rehabilitation care or treatment based on medicine consultation at one of the participating rehabilitation centers or hospitals, and participated in the Rehabilitation, Sports, and Exercise program. Participants were excluded from the study if they were not able to complete the questionnaires, even with help, or participated in another PA stimulation program. Written informed consent was obtained from eligible and willing participants.

Procedure
Enrolled participants were assessed through standardized measurements after rehabilitation. At each assessment point (14, 33, and 52 weeks), the measurement consisted of filling out a set of questionnaires on paper or digitally. Participants filled out an adapted version of the Short Questionnaire to Assess Health-Enhancing Physical Activity (SQUASH). Participants also completed the Activity Pacing and Risk of Overactivity Questionnaire, the Fatigue Severity Scale, and the RAND 12-item Health Survey (RAND-12) to assess their engagement in activity pacing and risk of overactivity, fatigue, and HRQOL, respectively.

Measures

Background demographic characteristics included age, sex, and body mass index (BMI; calculated as weight in kilograms divided by height in meters squared).

Engagement in Activity Pacing

The engagement in pacing decisions subscale of the newly developed Activity Pacing and Risk of Overactivity Questionnaire was used to assess engagement in pacing, as done in the study by Abonie et al. The questionnaire was used to evaluate how and based on which aspects participants modify their activity pacing behavior over the day, and it provided insight into engagement in activity pacing and perceived risk of overactivity in daily life. The participants scored the seven items of the questionnaire on a scale from 1 to 5 (1, never; 2, rarely; 3, sometimes; 4, often; 5, very often). This generated two subscale scores (engagement in pacing score and perceived risk of overactivity score) that ranged from 1 to 5.
Physical Activity

Physical activity was assessed with an adapted version of the SQUASH.\textsuperscript{17} The SQUASH is a self-reported recall questionnaire used to assess the daily PA of healthy adults based on an average week in the past month. The SQUASH was adapted to make it applicable for people with a chronic disease or physical disability. Within the domains commuting activities, leisure-time activities, and sports activities, the items wheelchair riding and hand cycling were added. In addition, the item tennis was modified to (wheelchair) tennis. Last, self-reported intensity was categorized as light, moderate, and vigorous instead of as slow, moderate, and fast. Total minutes of PA per week was calculated by multiplying frequency (days per week) and duration (minutes per day) for each activity.\textsuperscript{17} The original SQUASH has demonstrated good test-retest reliability and internal consistency and moderate concurrent validity in ordering participants according to their level of PA.\textsuperscript{20,21} The adapted SQUASH has good test-retest reliability.\textsuperscript{17}

Health-Related Quality of Life

Health-related quality of life was assessed using the RAND-12 (version 1.0),\textsuperscript{19} a validated and reliable questionnaire.\textsuperscript{22} The RAND-12 assesses seven health domains: general health, physical functioning, role limitations due to physical health problems, bodily pain, role limitations due to emotional problems, vitality/mental health, and social functioning. The RAND-12 was scored using the recommended scoring algorithm for calculating global health.\textsuperscript{23}
which represents all domains of HRQOL. The score ranged from 18 to 62, with a higher score indicating better HRQOL.

Fatigue

Fatigue was measured using the Fatigue Severity Scale.\textsuperscript{18} The scale has been proved to be a valid and reliable measure to determine the impact of fatigue and to detect change over time in persons with MS.\textsuperscript{24} The scale includes nine questions, scored on a scale from 1 to 7 (1, completely disagree; 7, completely agree). The items were averaged to calculate the fatigue severity total mean score, ranging from 1 (no fatigue) to 7 (very severe fatigue), with a score of 4 or greater indicating severe fatigue.\textsuperscript{18,25}

Statistical Analysis

Descriptive statistics were calculated for participants’ age, sex, BMI, engagement in activity pacing, perceived risk of overactivity, fatigue, PA, and HRQOL using SPSS Statistics, version 24 (IBM Corp).\textsuperscript{26} Multilevel analyses were performed to determine how engagement in activity pacing was related to PA and HRQOL after rehabilitation by using MLwiN statistical software.\textsuperscript{27} The multilevel analyses created models of PA and HRQOL, with engagement in pacing as the independent variable. A two-level model was used in which repeated measures within individuals (level 1) were clustered within individuals (level 2). The models included sex, age, and BMI as covariates and perceived risk of overactivity and fatigue as confounders. These variables were included in the models based on them being general demographic variables of
interest in studies on PA behavior and fatigue and on known associations with perceived fatigability and PA behavior. All variables in the multilevel model were standardized. Random intercepts were considered, thus allowing a unique intercept for each individual. Because we expect variation in PA and HRQOL between individuals, random slopes were entered into the model to properly account for correlations among repeated measures within individuals. The variables were entered separately into the initial model. In model 1, age, sex, BMI, and fatigue were entered. In model 2, perceived risk of overactivity and engagement in activity pacing were entered. In the final model, age, sex, BMI, fatigue, perceived risk of overactivity, engagement in activity pacing, and interaction terms of fatigue with engagement in activity pacing and perceived risk of overactivity were included. During each step, goodness of fit was evaluated by comparing the –2*Log Likelihood (IGLS deviance) of the previous model with the most recent model. A \( P < .05 \) was regarded as statistically significant.

Results

A total of 68 adults with MS were included in this study. Descriptive statistics of the study sample and outcome measures at each assessment point after rehabilitation are presented in Tables 1 and 2, respectively. Results indicate that the sample was on average overweight according to BMI scores (BMI ≥ 25), had a mean ± SD age of 45.2 ± 10.9 years, and was 22% male.

Engagement in Activity Pacing and PA
Results of the multilevel analysis of activity pacing association with PA while controlling for demographic variables (age, sex, and BMI) and perceived risk of overactivity and fatigue as confounders are presented in Table S1, which is published in the online version of this article at ijmsc.org. Engagement in activity pacing was not associated with long-term PA ($\beta = -0.01, P = .89$).

Testing of interaction effects showed that perceived risk of overactivity moderated the association between fatigue and PA ($\beta = -0.19, P = .02$). In other words, perceived risk of overactivity predicted the association between fatigue and PA. This finding suggests that for those who are at risk of overactivity, there is a negative association between fatigue and PA. Age, sex, and BMI were not significantly related to PA ($P > .05$).

**Engagement in Activity Pacing and HRQOL**

Results of the multilevel analysis of activity pacing association with HRQOL while controlling for demographic variables and perceived risk of overactivity and fatigue as confounders are presented in Table S2. Engagement in activity pacing was not associated with HRQOL ($\beta = -0.15, P = .09$). However, fatigue was negatively related to HRQOL ($\beta = -0.33, P < .001$). In addition, age was significantly related to higher HRQOL ($\beta = 0.27, P = .004$) and BMI was significantly related to lower HRQOL ($\beta = -0.32, P < .001$).

Testing of interaction effects showed that perceived risk of overactivity moderated the association between fatigue and HRQOL ($\beta = -0.13, P = .04$). This finding suggests that for those who are at risk of overactivity, there is a negative association between fatigue and HRQOL.
Discussion

In this study we investigated how self-reported activity pacing relates to PA and HRQOL over time (52 weeks after rehabilitation) while controlling for demographic characteristics, fatigue, and perceived risk of overactivity in adults with MS. The study sample reported severe fatigue complaints similar to in studies evaluating fatigue in MS populations. We found no associations between engagement in activity pacing and self-reported PA or between activity pacing and HRQOL. Conversely, we found that fatigue was significantly associated with HRQOL. Specifically, fatigue was significantly associated with low HRQOL. This finding was in accordance with the literature that fatigue contributes to low HRQOL. It thus seems that without targeted activity pacing interventions, engagement in activity pacing does not result in improvement in PA behavior and HRQOL. The study outcome thus suggests that people with MS may benefit from an intervention in the form of guidance on optimal use of activity pacing to achieve a paced approach to lifestyle and sustainable self-regulated exercise, and to help dissociate PA behavior from fatigue symptoms.

Despite activity pacing being a greatly recommended adaptation strategy in chronic pain, it is underresearched, with very few works on it in fatigue management in the MS population. Studies that examined associations between activity pacing, PA, and HRQOL in people with MS are scarce. Activity pacing could be a valuable approach in fatigue management, and examining how people with MS naturally pace their activities in daily life is essential to better understand how to guide and improve treatment efforts for this population.
Testing of interaction effects in this study allows us to examine some key assumptions about activity pacing effects on a momentary basis. For instance, there is an assumption that when people experience instants of high fatigue sensations, their PA behavior will be affected. However, activity pacing is a potential adaptive strategy to modify the expected association between fatigue and PA behavior. In other words, activity pacing could help dissociate PA behavior from fatigue symptoms. To our knowledge, this is the first known study testing whether activity pacing moderates the association between PA and fatigue in adults with MS. We hypothesized that people who most frequently report activity pacing engagement would demonstrate the weakest associations between fatigue symptoms and PA, and people who most frequently report overactive behavior would have the strongest associations between symptoms and activity. We found that activity pacing did not significantly moderate the association between fatigue and PA. Also, it thus seems that without interventions targeting activity pacing behavior, the natural use of activity pacing does not result in a positive effect on fatigue, PA, or quality of life. This finding was contrary to that reported by Murphy et al in their study evaluating how pacing related to fatigue and PA in people with symptomatic knee and hip osteoarthritis.

Conversely, perceived risk of overactivity moderated the associations between fatigue and PA and between fatigue and HRQOL. For those who frequently reported perceived risk of overactivity, there were negative associations between fatigue and PA and between fatigue and HRQOL. These findings suggest that those who experience decreases in PA and HRQOL with increased fatigue are more likely to be engaging in overactive behavior (too many or prolonged periods of activities, resulting in high fatigue sensation and subsequent prolonged inactive periods) than those who either do not experience a relationship between fatigue and HRQOL or...
experience increases in HRQOL in the context of higher fatigue. However, note that we cannot
determine from these data whether perceived risk of overactivity causes a stronger association
between fatigue and PA or whether the strong association between fatigue and PA evokes
overactive behavior. Equally, we cannot determine from these data whether perceived risk of
overactivity causes a stronger association between fatigue and HRQOL or whether the strong
association between fatigue and HRQOL evokes overactive behavior.

Taken together, the findings for the moderating effect of activity pacing and perceived
risk of overactivity on the fatigue-PA relationship indicate that the natural use of activity pacing
may be impelled by complex coping strategies. It is likely that persons with MS engage in more
complex behavioral strategies in the context of the fatigue-activity association. In other words,
people with MS may not be only a “pacer,” an “overactive,” or an “avoider,” and the choice of a
coping strategy may be contingent on the exact state one may be in. For example, people may be
overactive when their fatigue sensation is low and may pace their activities when their fatigue
sensation is high. Similarly, people may be pacing their activities when fatigue sensations are
low and avoiding activities when fatigue sensations are high. This points to an important idea
that activity pacing may possibly be seen as an adaptive or maladaptive behavior contingent on
whether people are using it to optimize their daily activities or to avoid activities.

The findings of the present study as well as the lack of associations between activity
pacing and PA and fatigue found in our previous cross-sectional exploratory study indicate that
when no interventions are introduced there is no distinct approach that is effective in improving
PA and HRQOL in both the short and long term in persons with MS. Thus, persons with MS
might benefit from guidance or advice in the form of optimal use of activity pacing to promote
longitudinal engagement in PA. This highlights the need for the development and design of goal-
directed interventions incorporating activity pacing to stimulate a physically active lifestyle in people with MS.

To help do this, more research that focuses on moment-to-moment dynamic associations among activity pacing, changes in fatigue, and actual PA behavior is needed. This research would help provide a better understanding of the associations between natural use of activity pacing and PA behavior and would help guide treatment efforts for persons with MS. Despite the feasibility and easy use of questionnaires to assess PA, self-reported measures are susceptible to bias. The use of a self-report measure to assess activity level in this study is a limitation. Therefore, additional real-time PA measures are recommended in future studies. In addition, the lack of information on participants’ MS type, MS-specific fatigue, and disease severity in this study limits the ability to draw firm conclusions. Note that participants received rehabilitation treatment as part of the larger multicenter study, and we cannot exclude that centers incorporated advice on activity pacing separately. However, a structured PA management (eg, activity pacing) program was not included in the multicenter study, and we believe this has not had an effect on the findings of the present study.

A strength of this study is the novel and long-term approach to explore the longitudinal associations between engagement in activity pacing and PA and quality of life using multilevel modeling. This could provide important input for the development of future interventions that will affect the PA behavior of persons with MS. Examination of the influence of engagement in activity pacing on the associations between fatigue and PA and between fatigue and quality of life provide novel insights into the complex interplay between fatigue and activity behavior. This is the first known study to explore long-term associations between activity pacing and PA and quality of life in persons with MS. The unique data set spanning three measurement points of
activity pacing behavior, PA, HRQOL, and fatigue in persons with MS over a 1-year period is a strength of the study.

Conclusions

This study examined the associations between activity pacing and PA and HRQOL while controlling for demographic characteristics, fatigue, and perceived risk of overactivity 1 year after rehabilitation in a sample of adults with MS. The results provide an initial understanding of how activity pacing relates to PA and HRQOL in people with MS over time. Activity pacing seems not be used successfully by persons with MS when no interventions are offered. There is, thus, a need to explore activity pacing interventions for persons with MS. We found that high fatigue was related to low HRQOL. Furthermore, we found that perceived risk of overactivity moderated the associations between fatigue and PA and between fatigue and HRQOL. Persons with MS exhibiting a high perceived risk of overactivity and reduced PA and HRQOL in the context of high fatigue could benefit from an intervention in the form of instruction in activity pacing to adequately manage their fatigue and improve their PA. The present study provides the foundation for further intervention development.

Acknowledgments: The authors thank all the participants for their contribution to the ReSpAct study and the following organizations for their support in the ReSpAct study: Adelante zorggroep, Bethesda Ziekenhuis, De Trappenberg, De Vogellanden, Maasstad Ziekenhuis, Medisch Centrum Alkmaar, Militair Revalidatiecentrum Aardenburg, Revalidatiecentrum
Leijpark, Revalidatiecentrum Reade, Revalidatie Friesland, Revant, Rijnlands Revalidatiecentrum, RMC Groot Klimmendaal, Scheper Ziekenhuis, Sint Maartenskliniek, Sophia Revalidatie, Tolbrug Revalidatie, ViaReva, and Stichting Onbeperkt Sportief.

Financial Disclosures: The authors declare no conflicts of interest.

Funding/Support: None.

References

1. Merkelbach S, Schulz H, Kölmel HW, et al. Fatigue, sleepiness, and physical activity in patients with multiple sclerosis. J Neurol. 2011;1:74-79.

2. Brañas P, Jordan R, Fry-Smith A, Burls A, Hyde C. Treatments for fatigue in multiple sclerosis: a rapid and systematic review. Health Technol Assess. 2000;4:1-61.

3. World Health Organization. Global recommendations on physical activity for health, 2010. Accessed February 9, 2015.

http://whqlibdoc.who.int/publications/2010/9789241599979_eng.pdf

4. Amato MP, Ponziani G, Rossi F, Liedl CL, Stefanile C, Rossi L. Quality of life in multiple sclerosis: the impact of depression, fatigue, and disability. Mult Scler. 2001;7:340-344.

5. Motl RW, Snook EM, McAuley E, Scott JA, Douglass ML. Correlates of physical activity among individuals with multiple sclerosis. Ann Behav Med. 2006;32:154-161.

6. Sutherland G, Andersen MB. Exercise and multiple sclerosis: physiological, psychological, and quality of life issues. J Sports Med Phys Fitness. 2001;41:421-432.
7. Antcliff D, Campbell M, Woby S, Keeley P. Assessing the psychometric properties of an activity pacing questionnaire for chronic pain and fatigue. *Phys Ther.* 2015;95:1274-1286.

8. Birkholtz M, Aylwin L, Harman RM. Activity pacing in chronic pain management: one aim, but which method? part one: introduction and literature review. *Br J Occup Ther.* 2004;67:447-452.

9. Chalder T, Goldsmith KA, White PD, Sharpe M, Pickles AR. Rehabilitative therapies for chronic fatigue syndrome: a secondary mediation analysis of the PACE trial. *Lancet Psychiatry.* 2015;2:141-152.

10. Murphy SL, Kratz AL. Activity pacing in daily life: a within day analysis. *Pain.* 2014;155:2630-2637.

11. Nielson WR, Jensen MP. Relationship between changes in coping and treatment outcome in patients with fibromyalgia syndrome. *Pain.* 2004;109:233-241.

12. Abonie US, Sandercock GR, Heesterbeek M, Hettinga FJ. Effects of activity pacing in patients with chronic conditions associated with fatigue complaints: a meta-analysis. *Disabil Rehabil.* 2018;42:613-622.

13. Karsdorp P, Vlaeyen JWS. Active avoidance but not activity pacing is associated with disability in fibromyalgia. *Pain.* 2009;147:29-35.

14. Nijs J, Paul L, Wallman K. Chronic fatigue syndrome: an approach combining self-management with graded exercise to avoid exacerbations. *J Rehab Med.* 2008;40:241-247.

15. Abonie US, Edwards AM, Hettinga FJ. Optimising activity pacing to promote a physically active lifestyle in medical settings: a narrative review informed by clinical and sports pacing research. *J Sports Sci.* 2020;38:590-596.
16. Abonie US, Hoekstra F, Seves LB, van der Woude LHV, Dekker R, Hettinga FJ. Associations between activity pacing, fatigue and physical activity in adults with multiple sclerosis: a cross sectional pilot study. *J Funct Morphol Kinesiol.* 2020;5:1-10.

17. Seves BL, Hoekstra F, Schoenmakers JWA, et al. Test-retest reliability and concurrent validity of the Adapted Short QUestionnaire to ASsess Health-enhancing physical activity (Adapted-SQUASH) in adults with disabilities [published online ahead of print December 9, 2020]. *J Sports Sci.* doi:10.1080/02640414.2020.1850983

18. Krupp LB, LaRocca NG, Muir-Nash J, Steinberg AD. The Fatigue Severity Scale: application to patients with multiple sclerosis and systemic lupus erythematosus. *Arch Neurol.* 1989;46:1121-1123.

19. Selim AJ, Rogers W, Fleishman JA, et al. Updated US population standard for the Veterans RAND 12-item Health Survey (VR-12). *Qual Life Res.* 2009;18:43-52.

20. Arends S, Hofman M, Kamsma YP, et al. Daily physical activity in ankylosing spondylitis: validity and reliability of the IPAQ and SQUASH and the relation with clinical assessments. *Arthritis Res Ther.* 2013;15:R99.

21. Wagenmakers R, van den Akker-Scheek I, Groothoff JW, et al. Reliability and validity of the Short Questionnaire to Assess Health-Enhancing Physical Activity (SQUASH) in patients after total hip arthroplasty. *BMC Musculoskelet Disord.* 2008;9:141.

22. Hays RD. *RAND 36 Health Status Inventory.* Harcourt Brace & Company; 1998.

23. Ware JE Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care.* 1996;34:220-233.
24. Whitehead L. The measurement of fatigue in chronic illness: a systematic review of unidimensional and multidimensional fatigue measures. *J Pain Symptom Manage.* 2009;37:107-128.

25. Smedal T, Beiske AG, Glad SB, et al. Fatigue in multiple sclerosis: associations with health-related quality of life and physical performance. *Eur J Neurol.* 2011;18:114-120.

26. *SPSS Statistics for Windows.* Version 24.0. IBM Corp; 2016.

27. Charlton C, Rasbash J, Browne WJ, Healy M, Cameron B. *MLwiN.* Version 3.00. University of Bristol, Centre for Multilevel Modelling; 2017.

28. Murphy SL, Kratz AL, Williams DA, Geisser ME. The association between symptoms, pain coping strategies, and physical activity among people with symptomatic knee and hip osteoarthritis. *Front Psychol.* 2012;3:326.

29. Enoka RM, Duchateau J. Translating fatigue to human performance. *Med Sci Sports Exerc.* 2016;48:2228-2238.

30. Heine M, van den Akker LE, Blikman L, et al. Real-time assessment of fatigue in patients with multiple sclerosis: how does it relate to commonly used self-report fatigue questionnaires? *Arch Phys Med Rehabil.* 2016;97:1887-1894.

31. Janardhan V, Bakshi R. Quality of life in patients with multiple sclerosis: the impact of fatigue and depression. *J Neurol Sci.* 2002;205:51-58.

32. Abonie US, Hettinga FJ. Effect of a tailored activity pacing intervention on fatigue and physical activity behaviours in adults with multiple sclerosis. *Int J Environ Res Public Health.* 2020;18:17.
Table 1. Descriptive statistics of the 68 study participants

| Variable                  | Value       |
|---------------------------|-------------|
| Age, y                    | 45.2 ± 10.9 |
| Body mass index<sup>a</sup> | 26.8 ± 6.3  |
| Male sex                  | 22 (32.4)   |

Note: Values are given as mean ± SD or number (percentage).

<sup>a</sup>Calculated as weight in kilograms divided by height in meters squared.
This in-press manuscript has been peer reviewed and accepted for publication by the International Journal of MS Care and appears here in nearly final form. It has been edited and received author approval. Essential corrections may still be made later in the proof stage, before publication in a print issue. Once published in an issue, the paper will be removed from the Online First section and appear in that issue's table of contents. Meanwhile, the manuscript is citable using the DOI, which appears on the first page.

Table 2. Outcome measures 14, 33, and 52 weeks after rehabilitation

| Variable                        | 14 weeks          | 33 weeks          | 52 weeks          |
|---------------------------------|-------------------|-------------------|-------------------|
|                                 | Mean ± SD         | Missing, No.      | Mean ± SD         | Missing, No.      | Mean ± SD         | Missing, No.      |
| Physical activity, min/wk       | 1990.32 ± 1395.06 | 25                | 2029.47 ± 1311.07 | 27                | 1650.53 ± 702.6   | 40                |
| Health-related quality of life  | 36.00 ± 8.61      | 30                | 37.31 ± 8.30      | 40                | 38.47 ± 7.29      | 46                |
| Fatigue                         | 5.22 ± 0.96       | 29                | 5.09 ± 1.21       | 37                | 5.09 ± 0.96       | 44                |
| Engagement in activity pacing   | 3.86 ± 0.64       | 29                | 3.82 ± 0.64       | 38                | 3.84 ± 0.59       | 45                |
| Perceived risk of overactivity  | 3.63 ± 0.80       | 29                | 3.56 ± 0.74       | 38                | 3.42 ± 0.88       | 45                |
Table S1. Multilevel modeling analysis of activity pacing association with physical activity while controlling for demographics, fatigue and perceived risk of overactivity from 14 weeks to 52 weeks postrehabilitation

| Physical activity, minutes per week | Model 1     | Model 2     | Final model |
|-----------------------------------|-------------|-------------|-------------|
| **Fixed Factors**                 | P           | P           | P           |
| Constant                          | 0.01 (0.20) | 0.01 (0.21) | -0.10 (0.20) |
| **Variables**                     |             |             |             |
| Sex (female)                      | .933        | .938        | .576        |
| Age                               | .968        | .720        | .691        |
| Body mass index                   | .358        | .329        | .181        |
| Fatigue                           | .087        | .14 (0.24)  | .02 (0.25)  |
| Risk of overactivity              | .175        | .175        | .643        |
| Engagement in pacing              | .151        | .151        | .890        |
| Fatigue x risk of overactivity    |             |             |             |
| Fatigue x engagement in pacing    | .844        | .844        | .02 (0.09)  |
| **Random effects**                |             |             |             |
| Level 1 (within time points)      |             |             |             |
| Constant                          | 0.41 (0.07) | 0.41 (0.07) | 0.40 (0.06) |
| Level 2 (between individuals)     |             |             |             |
| Constant                          | 0.52 (0.13) | 0.55 (0.14) | 0.48 (0.12) |
| Δ Deviance                        | <.001       | 116.68      | 120.77      | 129.01      |
| Deviance empty model              | 470.54      | 470.54      | 470.54      |

\[ \beta = \text{Standardized regression coefficients from the complete regression model accounting for all variables.} \]

\[ \text{SE} = \text{Standard error} \]

Model 1 = age, sex and body mass as covariates, and fatigue as confounder

Model 2 = perceived risk of overactivity as confounder and engagement in pacing as independent variables

Model 3 = age, sex and body mass were covariates, fatigue and perceived risk of overactivity as confounders, engagement in pacing as independent variable, and the interaction terms of fatigue with engagement in pacing and perceived risk of overactivity

Note: Physical activity was the dependent variable.
Table S2. Multilevel modeling analysis of activity pacing association with health-related quality of life while controlling for demographics, fatigue and perceived risk of overactivity 14 weeks to 52 weeks postrehabilitation

| Health-Related Quality of Life | Model 1 | Model 2 | Final model |
|-------------------------------|---------|---------|-------------|
| **Fixed Factors**             |         |         |             |
| Constant                      | -0.21 (0.16) | -0.21 (0.19) | -0.27 (0.16) |
| **Variables**                 |         |         |             |
| Sex (female)                  | 0.27 (0.19) | 0.30 (0.23) | 0.35 (0.19) |
| Age                           | 0.22 (0.09) | 0.15 (0.11) | 0.27 (0.09) |
| Body mass index               | -0.25 (0.09) | -0.29 (0.11) | -0.32 (0.09) |
| Fatigue                       | -0.38 (0.08) | <.001    | -0.33 (0.08) |
| Risk of overactivity          | 0.728   | 0.03 (0.08) | 0.627 (0.04) |
| Engagement in pacing          | -0.23 (0.09) | <.001    | -0.15 (0.09) |
| Fatigue x risk of overactivity| .040    | -0.13 (0.06) |             |
| Fatigue x engagement in pacing| .974    | 0.00 (0.07) |             |
| **Random Effects**            |         |         |             |
| Level 1 (within time points)  |         |         |             |
| Constant                      | 0.38 (0.06) | 0.38 (0.05) | 0.36 (0.06) |
| Level 2 (between individuals) |         |         |             |
| Constant                      | 0.26 (0.08) | 0.46 (0.12) | 0.25 (0.08) |
| △ Deviance                    | <.001   | 58.30   | <.001      |
| Deviance empty model          | 378.83  | 470.54  | 470.54     |

β = Standardized regression coefficients
SE = Standard error

Model 1 = age, sex and body mass as covariates, and fatigue as confounder
Model 2 = perceived risk of overactivity as confounder and engagement in pacing as independent variables
Model 3 = age, sex and body mass were covariates, fatigue and perceived risk of overactivity as confounders, engagement in pacing as independent variable, and the interaction terms of fatigue with engagement in pacing and perceived risk of overactivity

Note: Health-related quality of life was the dependent variable.