



Original Research

# Perspectives From Persons With Multiple Sclerosis for a Comprehensive Real-World Change Therapy for Mobility



Victor W. Mark, MD <sup>a,b,c</sup>, Ritalinda D'Andrea Lee, PhD <sup>d</sup>,  
Edward Taub, PhD <sup>c</sup>, Gitendra Uswatte, PhD <sup>c,e</sup>

<sup>a</sup> Department of Physical Medicine and Rehabilitation, University of Alabama at Birmingham, Birmingham, Alabama, United States

<sup>b</sup> Department of Neurology, University of Alabama at Birmingham, Birmingham, Alabama, United States

<sup>c</sup> Department of Psychology, University of Alabama at Birmingham, Birmingham, Alabama, United States

<sup>d</sup> Claris Advocates, Georgetown, Texas, United States

<sup>e</sup> Department of Physical Therapy, University of Alabama at Birmingham, Birmingham, Alabama, United States

## KEYWORDS

Activities of daily living;  
Gait;  
Multiple sclerosis;  
Physical therapy modalities;  
Rehabilitation

**Abstract Objective:** To assess the personal perspectives of persons with multiple sclerosis (MS) on the acceptability of a novel physical therapy program that is designed to transfer gains from the clinic to their real-world lower extremity (LE) use, termed LE constraint-induced therapy (CIT). The program includes several behavior change techniques (prescribed home exercises, daily structured therapist interviews and problem solving for LE activities, keeping an activity diary) and a concentrated physical treatment schedule.

**Design:** Anonymous internet survey.

**Setting:** Participants accessed the survey from computers in the community.

**Participants:** Five hundred adults (N=500) were recruited from an MS support organization's registry for having indicated from mild to total limb spasticity because they were anticipated to have markedly impaired LE use in the community.

**Interventions:** Not applicable.

**Main Outcome Measures:** Participants were offered the options on a nonnumerical Likert scale of "Very likely," "Likely," "Neutral," "Unlikely," or "Very unlikely" to indicate their personal acceptability for each of 5 different key treatment procedures after these were explained. Totals for each option within each key procedure were analyzed for their acceptability.

**List of abbreviations:** BCT, behavior change technique; CIT, constraint-induced therapy; LE, lower extremity; MS, multiple sclerosis; NARCOMS, North American Committee of Multiple Sclerosis.

Supported by the North American Research Committee of Multiple Sclerosis.

Disclosures: none

Cite this article as: Arch Rehabil Res Clin Transl. 2022;4:100166

<https://doi.org/10.1016/j.arrct.2021.100166>

2590-1095/© 2021 The Authors. Published by Elsevier Inc. on behalf of American Congress of Rehabilitation Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Results:** Of the 281 persons who responded, 90% expressed interest in participating in LE CIT. A large majority of persons who completed the survey selected either “Very likely” or “Likely” for each key procedure (median=88%, range=65%-90%,  $P<.01$ ). This indicated strong acceptance for the procedures of LE CIT. In addition, more respondents who already had had previous physical therapy accepted LE CIT than did respondents who had not had physical therapy ( $P<.01$ ).

**Conclusions:** The results suggest there is strong acceptance of CIT for mobility with preliminary evidence of benefiting community LE use for persons with MS. The results support further clinical trials of LE CIT for persons with MS.

© 2021 The Authors. Published by Elsevier Inc. on behalf of American Congress of Rehabilitation Medicine. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

This study aims to understand whether mobility-disabled persons with multiple sclerosis (MS) would accept a novel, comprehensive form of physical training to improve spontaneous lower extremity (LE) use when given as a concentrated treatment schedule that includes a prescribed set of behavior change techniques (BCTs). The intervention was designed to transfer gains from supervised LE physical training in the clinic to unsupervised spontaneous LE use in the community.

From the perspectives of persons with MS, degraded mobility is one of the most devastating effects of the disease.<sup>1,2</sup> Managing impaired mobility is critical because their level of physical activity is generally lower than that of the general population.<sup>3</sup> Physical inactivity in turn is generally linked to diverse comorbid illnesses and increased health care costs.<sup>4,5</sup> These findings warrant attention because the worldwide prevalence of MS has been rising for the past several decades for unclear reasons.<sup>6</sup> Because there is as yet no generally accepted standard of evidence-based physical rehabilitation for MS, it is urgent to identify and test promising forms of rehabilitation that can improve mobility in the community for appreciably long periods for persons with MS.

For the past 40 years, physical training research for MS has focused on lessening bodily impairment.<sup>7</sup> Training regimens were directed to increase limb power, walking speed and endurance, and general physical fitness.<sup>8,9</sup> Accordingly, the most common forms of physical training in MS clinics are aerobic exercise, progressive resistance training, stretching, balance training, and respiratory training.<sup>10</sup> Outcome measures have primarily assessed maximal motor capacity within controlled laboratory environments (eg, timed 25-foot walking test, timed Up and Go, knee extension power). More than 200 clinical trials of physical training for MS to date have followed this course.<sup>11</sup> However, despite the substantial number of physical training trials for MS completed over the past decade, chronic physical inactivity of persons with MS has not budged.<sup>12-14</sup> Although degraded mobility is a primary concern for persons with MS, such trials have only rarely assessed mobility in the community, thus leaving uncertain how such interventions may be related to the personal perspectives of persons with MS.

In contrast, in recent years a small but growing number of therapies have aimed to change habitual self-care behaviors. Their research programs have been developing and testing therapies that used BCTs, which ideally target behaviors that are personally relevant in the community, using replicable techniques that include validated outcome

measures<sup>15</sup> and prescribed unsupervised practice in the real world.<sup>16</sup> Common techniques include behavioral contracting, goal setting, feedback, self-monitoring, motivational counseling, and problem-solving discussions with the treatment personnel.<sup>17-19</sup> In the view of MS stakeholders, incorporating personal perspectives in the content of a physical therapy and focusing attention on actual real-world behavior are essential to prolong posttreatment behavioral changes.<sup>20</sup>

Outpatient therapies that used BCTs to improve physical activity for MS have typically been scheduled for 12 weeks or more and seldom included supervised physical training.<sup>21</sup> However, although these trials were usually immediately successful, the gains were generally not retained more than 3 months.<sup>22</sup> An exception was a concentrated form of supervised physical therapy that applies BCTs and immerses participants in systematically prescribed, unsupervised activities outside of the laboratory or clinic. LE constraint-induced therapy (CIT) combines supervised massed, task-oriented physical LE practice for 3.5 h/d for consecutive weekdays for 3 consecutive weeks with BCTs. The techniques include behavioral contracting, goal setting, feedback, prescribed unsupervised home practice of activities, self-monitoring (including daily activity diary keeping and reporting on compliance with homework task assignments), daily administration of a structured interview, motivational counseling, and regular problem-solving discussions with the therapist.<sup>23</sup> In a case series of persons with chronic mobility disability from progressive MS (N=4),<sup>24</sup> the participants significantly gained on the Lower Extremity Motor Activity Log,<sup>25</sup> a validated patient-reported outcome of LE use in the community, with a very large treatment effect size ( $d'$ )=3.3. Moreover, there was no decrement at 1-year follow-up, and 2 participants maintained their gains out to 4-year follow-up. This case series suggests that LE CIT is safe and can produce improved spontaneous LE use in the community on a persistent basis.

Because most therapies that have applied BCTs for MS are given for several weeks with sessions spaced a day to a week apart, consistent with conventional outpatient physical therapy schedules,<sup>26</sup> we wished to understand whether mobility-impaired persons with MS would accept LE CIT, which is given daily, 3.5 h/d, 5 consecutive weekdays each week, for 3 consecutive weeks (52.5 hours of treatment). On the one hand, the relatively short schedule that marks LE CIT could mitigate the risk of attrition during treatment.<sup>27</sup> On the other hand, the concentrated and comprehensive treatment might be difficult for some persons with MS to

accommodate. Despite the concentrated treatment schedule and multiple components included in LE CIT, we hypothesize that a majority of persons with impaired mobility from MS would accept LE CIT. The results of this study of stakeholders' perspectives could help to indicate whether future, more expanded clinical trials of LE CIT for MS could be recommended.

## Methods

This study was supported by the North American Research Committee on Multiple Sclerosis (NARCOMS). This organization maintains a registry of approximately 38,000 individuals who have self-reported MS and agreed to participate in surveys. At present PubMed lists 103 such survey studies since 2004. The institutional review board of the investigators' university approved this study.

NARCOMS facilitated this survey for the present study by randomly selecting 500 individuals who (1) were living in the United States, (2) reported a spasticity score from 2-5 (2="mild," prompting modest changes of activities; 5="total," indicating daily interference with many self-care activities),<sup>28</sup> and (3) were not participating in other NARCOMS studies. Although the participants who were readily available for this survey had reported specifically their level of spasticity rather than impaired mobility, it was anticipated that mild-severe spasticity would be associated with ambulatory difficulty, as was found in a prior NARCOMS survey.<sup>29</sup>

A cover letter was emailed to the 500 individuals, which indicated that LE CIT had preliminarily improved community walking in MS and asked recipients for their opinions concerning participating in a possible clinical trial for this treatment. Survey responses were collected anonymously with *survey.monkey*, which assured the recipients that the results would not be used to enroll them as potential participants.

The internet survey was designed to require no more than 5 minutes. One of the authors (R.D.L.) herself has MS, is impaired in mobility, and participated in designing the survey. Recipients were first asked to indicate whether they ever had physical therapy for MS. The next question asked whether the recipient would be interested in participating in a physical therapy that has research evidence suggesting it could improve walking if it were made available at no cost. Recipients who responded "no" were asked not to continue the survey.

The next question addressed procedures of LE CIT. For brevity, we selected 5 key procedures. Each was to be answered from a Likert scale without associated numerical point values with one of the following options concerning how likely the participant would undergo the specific procedure: "Very likely," "Likely," "Neutral," "Unlikely," or "Very unlikely." The selections of either "Very likely" or "Likely" will be considered together to indicate acceptance of each procedure. The key procedures were (1) "Going to the physical therapy site 5 days a week for 3.5 hours each weekday for 3 weeks," (2) "Doing specific activities with the legs outside the treatment setting that are assigned for each day of the 3-week therapy period," (3) "Being interviewed by your therapist each day of the 3-week therapy period about how well you are using your legs," (4) "Having a 30-minute problem-solving discussion with your therapist on each day of

treatment to solve any difficulties with your leg use," and (5) "Keeping an activity diary during your 3-week participation in the program."

The survey's final questions requested the participant's year of birth, year of MS diagnosis, the subtype of MS as understood by the participant, and the participant's sex.

## Data analysis

Chi-square goodness-of-fit tests were used to evaluate whether participants expressed a preference for taking part in a study of LE CIT and would be likely to carry out the 5 key procedures. In formal terms, the chi-square tests evaluated whether the observed distribution of responses to a particular question were significantly different from a perfectly random distribution, that is, an equal number of participants endorsing each degree of preference. A Bonferroni correction was applied to these statistical tests, that is,  $\alpha$  was set to 0.01, because responses regarding how likely participants were to carry out the key procedures were likely to be correlated. Fisher exact tests were used to evaluate whether how likely participants were to carry out the 5 key procedures depended on experience with physical therapy;  $\alpha$  was set to 0.01. Test statistic and *df* values are not reported for the Fisher exact test because their calculation is unnecessary for this test. Fisher exact tests are used instead of chi-square tests of independence because the expected value of some of the cells in the contingency analysis tables was <5.<sup>30</sup> Statistical Analysis Software<sup>a</sup> was used to conduct these tests. Other aspects of the data were characterized using descriptive statistics. This study was approved by our university's institutional review board.

## Results

A total of 281 persons responded to the survey, that is, 56% of the 500 who were contacted to participate. The majority (77%) of the responders indicated that they had physical therapy for their MS. In response to the query whether they would consider a course of physical therapy with research evidence to benefit walking if it were offered at no cost, the interest was strong ( $\chi^2 [1, n=281]=177, P<.05$ ). Ninety percent endorsed participation in such a treatment. The remainder did not, either because they did not need such treatment ( $n=15$ ) or were not interested ( $n=14$ ).

Of the 252 who endorsed the treatment, a small number ( $n=11$ ) did not complete the survey. Those who both endorsed participation in LE CIT and completed the survey, heretofore referred to as survey completers ( $n=241$ , or 48% of the total), were primarily women (73%) and had a mean age of  $58\pm 8.6$  years (range, 31-79 years). Survey completers reported that they had either relapsing-remitting MS (52%), secondary-progressive MS (38%), primary-progressive MS (10%), or did not select a specific condition (8%). The mean chronicity of MS disease was  $19.0\pm 9.4$  years.

Table 1 summarizes the distribution of the acceptability of the 5 key procedures of LE CIT that were presented. As shown by table 1, the majority of the survey completers selected either "Very likely" or "Likely" options for each of the 5 key procedures, thus indicating of their strong

**Table 1** Distribution of degrees of acceptance by survey completers (n=241 for all procedures) for undergoing 5 key procedures of LE CIT

Response	Schedule Daily PT for 3 wk		Home Exercises		Daily Interview Real-World Leg Use		Problem-Solving Discussion		Activity Diary	
	n	%	n	%	n	%	n	%	n	%
Very likely	102	41.6	146	59.8	154	63.4	143	59.1	142	58.5
Likely	58	23.7	74	30.3	62	25.5	59	24.4	77	31.7
Subtotal	160	65.3	220	90.1	216	88.9	202	83.5	219	90.2
Neutral	27	11.0	16	6.6	18	7.4	27	11.2	19	7.8
Unlikely	34	13.9	5	2.0	5	2.1	10	4.1	2	0.8
Very unlikely	24	9.8	3	1.2	4	1.6	3	1.2	3	1.2
Subtotal	85	34.7	24	9.8	27	11.1	40	16.5	24	9.8
Total completers	245		244		243		242		243	

NOTE. "Subtotal" rows sum the participants for each key procedure who on upper row selected either "Very likely" or "Likely," thus indicating totals who accepted each procedure, and on lower row, participants who did not accept each procedure. Abbreviation: PT, physical therapy.

**Table 2** Percentage of participants indicating whether they would be likely to participate in an LE CIT trial by PT history

Participate in LE CIT Trial	Have had PT		Not Have Had PT	
	n	%	n	%
Yes	202	93.5	49	76.6
Not needed	8	3.7	7	10.9
Not interested	6	2.8	8	12.5
Total respondents	216		64	

Abbreviation: PT, physical therapy.

acceptance of the procedures of LE CIT. The Schedule procedure, indicating treatment for 5 d/wk, 3.5 h/d, for 3 weeks, had the least of "Very likely" and "Likely" responses, but nonetheless this procedure was accepted by 65% of the respondents.

The other 4 key procedures were more strongly accepted by the survey completers, ranging from 82%-90% acceptance. The median acceptance (ie, proportion of respondents who selected either "Very likely" or "Likely") across the 5 procedures was 88%. For all 5 procedures, the distribution of responses was significantly different from a uniform distribution, that is, one that reflected no preference ( $\chi^2 [4, n \geq 242] > 86, P < .01$ ).

There was a marked difference in the distribution of those expressing interest in participating in an LE CIT research trial in relation to whether the respondents already had physical therapy ( $P < .01, n = 280$ ). As shown by [table 2](#), respondents who already had physical therapy strongly endorsed participating in the projected research study, while those who had not had physical therapy indicated less interest in undergoing the projected research, although most of the latter group also expressed interest in such participation.

The distribution of the responses regarding acceptance of the individual key procedures also changed markedly when considering whether completers had already undergone physical therapy ([table 3](#)). Regarding the Schedule, the proportion of completers who responded with either "Very likely" or "Likely" was 72% among those with physical therapy experience, while it was 45% among those without physical therapy experience ( $P < .01$ ). For 2 of the other procedures, the effect of history of physical therapy on the acceptance rate was significant ( $P < .01$ ); 92% of participants who had physical therapy accepted undergoing daily interviews compared with those without physical therapy (80%); 87% of participants who had physical therapy vs 71% without physical therapy endorsed problem-solving discussions. For the other 2 procedures, there was a trend of effect of physical therapy experience on acceptance rates: home exercises (93% of those with physical therapy vs 82% of those without physical therapy,  $P = .03$ ) and maintaining an activity diary (93% of those with physical therapy vs 80% of those without physical therapy,  $P = .01$ ).

## Discussion

A significant majority of the participants in our study who completed the survey accepted all of the 5 key procedures

**Table 3** Percentage of survey completers likely or very likely to undergo key LE CIT procedures by PT history

Procedure	Have had PT		Not have had PT	
	n	%	n	%
Schedule	138	71.5	22	44.9
Home exercises	180	93.3	40	81.6
Daily interviews	177	91.7	39	79.6
Problem solving	167	86.5	35	71.4
Activity diary	180	93.3	39	79.6
Total completers	193		49	

Abbreviation: PT, physical therapy.

of LE CIT that were presented. The positive pilot findings of LE CIT<sup>24</sup> coupled with the findings of the present study support expanded clinical trials of LE CIT for persons with MS.

Most of the participants in our study had undergone physical therapy, yet 90% of the respondents expressed interest in participating in physical rehabilitation research. This high level of interest may reflect a perception among survey respondents either that their physical therapy had not been adequate to improve their mobility or that the novelty of LE CIT may persuade respondents to undergo this comprehensive program. In a prior survey of NARCOMS registrants on their perspective of their spasticity treatment, which included physical therapy, a considerable majority viewed the treatments as inadequate.<sup>29</sup> Because the great majority of physical rehabilitation trials have not reported sustained improved LE use in the community, which is highly important from the perspective of persons with MS, further research is needed to evaluate the efficacy of behavior-based methods of physical training over the long-term.

LE CIT differs considerably from other forms of physical rehabilitation, both in its content and schedule. The general CIT program, whether for the upper extremities or the LEs, does not simply involve intensive practice with the more impaired limb(s). Instead, it combines supervised massed practice with other techniques derived from evidence-based behavioral science,<sup>31</sup> which focus on improving LE use in everyday situations outside the treatment setting.

LE CIT is generally provided daily, several hours each weekday, over 3 consecutive weeks. In our studies of LE CIT, the real-world gains do not maximize until the third week of treatment, which supports the length of the course. The treatment is administered over consecutive weeks, rather than in a more distributed schedule, to mitigate the possibility of an attenuated outcome resulting from participant attrition (eg, because of interruption and rescheduling treatment because of illness or therapist vacation or changes in availability of transportation).<sup>27</sup> Fatigue ratings at the end of the 3 weeks of treatment either did not change or declined in our case series of LE CIT, compared with the pretreatment levels.<sup>24</sup> This suggests that the treatment generally does not aggravate fatigue, which is consistent with other forms of physical training for MS.<sup>32</sup>

This concentrated treatment schedule was less endorsed by the responders than for the other key practice points that were evaluated, although a significant majority of survey completers nonetheless accepted the schedule as was described. The concentrated dose of LE CIT may be difficult

for some persons with MS, particularly if they are employed or reside far from the treating facility. At present it is undetermined whether changing the schedule of LE CIT for MS may affect the results, although our research with upper extremity CIT after stroke (unpublished results) or MS<sup>33</sup> suggests that a more distributed schedule of treatment does not diminish outcome.

### Study limitations

Participants were selected primarily because they had complained of LE spasticity rather than limited mobility per se. However, as noted, the majority of participants who have LE spasticity also have impaired mobility.<sup>29</sup> Therefore this sample may be considered representative in general of persons with MS who have impaired mobility.

This internet survey was designed such that it did not inquire the demographic characteristics of individuals who declined to participate, to minimize their time investment. As a result, this study is unable to describe the demographic characteristics of those individuals who declined to complete the survey, and thus we cannot determine whether demographic variables may have affected their interest to undergo the survey.

The participants were asked to answer the survey questions supposing that treatment would be provided without charge as part of a study. The provision of treatment at no personal cost is standard for research clinical trials. It is possible that the acceptability of the treatment could have been different if participants were required to arrange payment for their treatments. The cost of CIT has been raised as a barrier to treatment<sup>34</sup> because it is labor intensive and many American insurance programs do not reimburse for it. Although the American health care system generally does not reimburse for treatment involving extensive therapist time and effort, such restrictions may not apply to other parts of the world. According to a recent survey, 25% of European MS rehabilitation clinics offer CIT.<sup>10</sup> Telemedicine adaptations of upper extremity CIT have preliminarily been successful, pointing to ways to control cost and improve access to treatment.<sup>35,36</sup> These advances may support later trials to adapt telemedicine methods for LE CIT.

### Conclusions

This survey found that persons with MS and moderate-severe spasticity would accept a comprehensive physical therapy that would combine intensive supervised physical training with several BCTs. It will be important to further develop physical therapy programs to improve mobility in the community for persons with MS, given the limited progress for improving mobility following the more widely practiced forms of bodily impairment training or forms of therapy that applied BCTs without supervised task-oriented training. The present study suggests that in a research setting, LE CIT would be strongly accepted by persons with MS.

### Supplier

- Statistical Analysis Software, SAS Institute, Gary, NC.

## Corresponding author

Victor W. Mark, MD, Department of Physical Medicine and Rehabilitation, University of Alabama at Birmingham, 1717 Sixth Ave South, SRC 190, Birmingham, AL, 35233. E-mail address: [vmark@uabmc.edu](mailto:vmark@uabmc.edu).

## Acknowledgment

We thank Tuula Tyry, PhD, Program Manager for NARCOMS, for facilitating accessing the participant registry for this survey.

## References

- LaRocca NG. Impact of walking impairment in multiple sclerosis: perspectives of patients and care partners. *Patient* 2011;4:189-201.
- van Asch P. Impact of mobility impairment in multiple sclerosis 2—patients' perspectives. *Eur Neurol Rev* 2011;6:115-20.
- Sasaki JE, Motl RW, Cutter G, Marrie RA, Tyry T, Salter A. Factors associated with excessive sitting time in multiple sclerosis. *Mult Scler Relat Disord* 2018;21:71-7.
- Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. *Lancet* 2012;380:219-29.
- Ding D, Lawson KD, Kolbe-Alexander TL, et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. *Lancet* 2016;388:1311-24.
- Rotstein DL, Chen H, Wilton AS, et al. Temporal trends in multiple sclerosis prevalence and incidence in a large population. *Neurology* 2018;90:e1435-41.
- Mark VW. Retention of physical gains in the community following physical training for multiple sclerosis: a systematic review and implications. *Semin Neurol* 2021;41:177-88.
- Latimer-Cheung AE, Pilutti LA, Hicks AL, et al. Effects of exercise training on fitness, mobility, fatigue, and health-related quality of life among adults with multiple sclerosis: a systematic review to inform guideline development. *Arch Phys Med Rehabil* 2013;94:1800-28.
- Sá MJ. Exercise therapy and multiple sclerosis: a systematic review. *J Neurol* 2014;261:1651-61.
- Martinková P, Freeman J, Drabinová A, et al. Physiotherapeutic interventions in multiple sclerosis across Europe: regions and other factors that matter. *Mult Scler Relat Disord* 2018;22:59-67.
- Dalgas U, Hvid LG, Kwakkel G, et al. Moving exercise research in multiple sclerosis forward (the MoXFo initiative): developing consensus statements for research. *Mult Scler J* 2020;26:1303-8.
- Casey B, Coote S, Byrne M. Activity matters: a web-based resource to enable people with multiple sclerosis to become more active. *Transl Behav Med* 2019;9:120-8.
- Aminian S, Motl RW, Rowley J, Manns PJ. Management of multiple sclerosis symptoms through reductions in sedentary behaviour: protocol for a feasibility study. *BMJ Open* 2019;9:e026622.
- Kinnett-Hopkins D, Adamson B, Rougeau K, Motl RW. People with MS are less physically active than healthy controls but as active as those with other chronic diseases: an updated meta-analysis. *Mult Scler Relat Disord* 2017;13:38-43.
- Abraham C, Wood CE, Johnston M, et al. Reliability of identification of behavior change techniques in intervention descriptions. *Ann Behav Med* 2015;49:885-900.
- Plow M, Finlayson M. Beyond supervised therapy: promoting behavioral changes in people with MS. *Mult Scler J* 2019;25:1379-86.
- Conn VS, Hafdahl AR, Brown SA, Brown LM. Meta-analysis of patient education interventions to increase physical activity among chronically ill adults. *Pat Educ Couns* 2008;70:157-72.
- Heath GW, Parra DC, Sarmiento OL, et al. Evidence-based intervention in physical activity: lessons from around the world. *Lancet* 2012;380:272-81.
- Michie S, Richardson M, Johnston M, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. *Ann Behav Med* 2013;46:81-95.
- Heesen C, Bruce J, Feys P, et al. Adherence in multiple sclerosis (ADAMS): classification, relevance, and research needs. A meeting report. *Mult Scler J* 2014;20:1795-8.
- Sangelaji B, Smith CM, Paul L, Sampath KK, Treharne GJ, Hale LA. The effectiveness of behaviour change interventions to increase physical activity participation in people with multiple sclerosis: a systematic review and meta-analysis. *Clin Rehabil* 2016;30:559-76.
- Coulter EH, Bond S, Dalgas U, Paul L. The effectiveness of interventions targeting physical activity and/or sedentary behaviour in people with multiple sclerosis: a systematic review. *Disabil Rehabil* 2020;42:594-612.
- Taub E, Uswatte G, Mark VW, et al. Method for enhancing real-world use of a more affected arm in chronic stroke: transfer package of constraint-induced movement therapy. *Stroke* 2013;44:1383-8.
- Mark VW, Taub E, Uswatte G, et al. Constraint-induced movement therapy for the lower extremities in multiple sclerosis: case series with 4-year follow-up. *Arch Phys Med Rehabil* 2013;94:753-60.
- Dos Anjos S, Mark VW, Rodriguez CM, Morris DM, Uswatte G, Taub E. Reliability and validity of the Lower-Extremity Motor Activity Log (LE-MAL) for measuring real-world leg-use in adults with multiple sclerosis. *Arch Phys Med Rehabil* 2021;102:626-32.
- Kalron A, Feys P, Dalgas U, et al. Searching for the "active ingredients" in physical rehabilitation programs across Europe, necessary to improve mobility in people with multiple sclerosis: a multicenter study. *Neurorehabil Neural Repair* 2019;33:260-70.
- Lai B, Kim Y, Wilroy J, Bickel CS, Rimmer JH, Motl RW. Sustainability of exercise intervention outcomes among people with disabilities: a secondary review. *Disabil Rehabil* 2019;41:1584-95.
- Rizzo MA, Hadjimichael OC, Preiningerova J, Vollmer TL. Prevalence and treatment of spasticity reported by multiple sclerosis patients. *Mult Scler* 2004;10:589-95.
- Bethoux F, Marrie RA. A cross-sectional study of the impact of spasticity on daily activities in multiple sclerosis. *Patient* 2016;9:537-46.
- Siegel S. Nonparametric statistics for the behavioral sciences. New York: McGraw-Hill Book Company Inc; 1956.
- Taub E, Uswatte G, Elbert T. New treatments in neurorehabilitation founded on basic research. *Nat Rev Neurosci* 2002;3:228-36.
- Pilutti LA, Greenlee TA, Motl RW, Nickrent MS, Petruzzello SJ. Effects of exercise training on fatigue in multiple sclerosis: a meta-analysis. *Psychosom Med* 2013;75:575-80.

33. Mark V, Taub E, Bashir K, et al. Constraint-induced movement therapy can improve hemiparetic progressive multiple sclerosis. Preliminary findings. *Mult Scler* 2008;14:992-4.
34. Viana R, Teasell R. Barriers to the implementation of constraint-induced movement therapy into practice. *Top Stroke Rehabil* 2012;19:104-14.
35. Lum PS, Uswatte G, Taub E, Hardin P, Mark VW. A tele-rehabilitation approach to delivery of constraint-induced movement therapy. *J Rehabil Res Dev* 2006;43:391-400.
36. Borstad AL, Crawfis R, Phillips K, et al. In-home delivery of constraint-induced movement therapy via virtual gaming. *J Patient Cent Res Rev* 2018;5:6-17.