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Adherence to physiotherapy-guided web-based exercise for persons living with moderate-to-severe multiple sclerosis: a randomized-controlled pilot study

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Practice Points:

- People with moderate-to-severe multiple sclerosis safely participated in physiotherapist prescribed home exercise over six months.
- A customized web-based platform was modified to include exercise options for users with advanced multiple sclerosis (giraffehealth.com).
- Wheelchair users in the web-based exercise group of this pilot study demonstrated the highest rates of exercise adherence.

Background: Options to support adherence with physical activity in moderate-to-severe MS are needed. The primary aim was to evaluate adherence to a web-based, individualized exercise program in moderate-to-severe MS. Secondary aims were to explore changes in MSIS-29, HADS, grip strength, T25FWT, and TUG.

Methods: Inclusion criteria were diagnosis of MS, internet access, residing within 300km of Saskatoon, and exercising less than twice weekly. Participants were randomized (2:1) to a physiotherapist-guided web-based home exercise program or physiotherapist-prescribed written home exercise program. The primary outcome was adherence (number of exercise sessions over 26 weeks). Secondary outcomes were described in terms of means and effect sizes.

Results: There were 48 participants: mean age 54.3y (SD 11.9), disease duration 19.5y (SD 11.0) and mean Patient-Determined Disease Steps 4.4 (SD 1.6). There was no significant difference in adherence between groups: web group (mean 38.9, SD 28.1); comparator group (mean 34.6, SD 40.8; U=198.5, p=.208, Hedges' g 0.13). Nearly 50% of participants (23/48) exercised ≥ twice per week for at least 13 of the 26 weeks. Adherence was highest in the web-based subgroup of wheelchair users. Medium effect sizes were found for HADS - anxiety subscale and in ambulatory participants for TUG. There were no adverse events.

Conclusions: There was no difference in exercise adherence between the web-based and active comparator groups. There was no worsening on secondary outcomes or adverse events, supporting the safety of web-based physiotherapy. More research is needed to determine if wheelchair users might be most likely to benefit from web-based physiotherapy.

53 Keywords: multiple sclerosis, exercise, adherence, physiotherapy, telerehabilitation

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Introduction:

Despite the benefits of physical activity, adherence with regular physical activity when living with multiple sclerosis (MS) can be challenging.[1-3] Physical activity programs must be flexible and evolve as MS symptoms and impairments change over time. Participation in physical activity may be enhanced through the provision of personalized programming with on-going monitoring and professional support.[4,5]

Physical activity specifically in people with more advanced disability is associated with improvements in cardiorespiratory and muscular fitness and quality of life over the short term.[6] Structured exercise involving strength training and/or aerobic exercise at least twice a week appears to be tolerated and safe in people with more advanced disability.[6] In advanced MS, supported programs with specialized equipment (i.e., bodyweight-supported treadmill walking, cycle ergometry, rowing or aquacise) are commonly reported. Access to professional support and specialized equipment for exercise is a challenge especially in areas with a high MS prevalence, yet low population density, as is the case in Saskatchewan, Canada.[7]

A key question remains concerning how best to support persons with MS in participating and adhering to their exercise programs. Various web-based approaches have been proposed to meet this challenge. A recent systematic review of web-based physical activity interventions concluded that web-based approaches increased physical activity levels among people with mild-to-moderate MS who were ambulatory.[8] The web-based interventions were largely of shorter duration

(i.e., <3 months) and included wait-list comparison groups.[8] More research is needed to determine if web-based approaches are also appropriate for increasing adherence to physical activity through structured exercise programs for people with more moderate-to-severe MS.

The primary objective of this Saskatchewan-based study was to improve physical activity adherence in moderate-to-severe MS through a personalized, physiotherapist-prescribed web-based exercise program over six months compared to a usual care exercise group. Secondary objectives of this pilot study were to explore changes in patient-reported symptoms according to the Multiple Sclerosis Impact Scale 29 (MSIS-29) and the Hospital Anxiety and Depression Scale (HADS) and changes in physical function as measured by the dominant hand dynamic grip strength, the Timed 25-Foot Walk Test (T25FWT), and the Timed Up and Go (TUG) test.

Methods:

This single-blinded pilot study invited people with MS with moderate-to-severe disability. We advertised for the study at the Saskatchewan MS Clinic and through the MS Society of Canada. Inclusion criteria were: clinically-definite MS; moderate-to-severe disability (Patient-Determined Disease Steps (PDDS) score of 2-7),[9,10] and ability to access the internet from current living environment. Consent was obtained to access the medical records from the treating neurologist to confirm MS diagnosis for participants not recruited through the MS clinic. Exclusion criteria were: current participation in exercise twice a week or more; residence greater than

300 kilometers from Saskatoon, Saskatchewan, Canada, or severe cognitive impairment. Participants needed to demonstrate an ability to provide informed consent according to the clinical judgement of the research physiotherapists. No formal cognitive assessment tool was utilized to determine eligibility. The 300 kilometers maximum distance, if not able to travel to Saskatoon for assessment visits, was chosen to allow the physiotherapists time to complete a home-visit assessment in one day. No monetary incentives were awarded for participating in or completing the study.

Participants were randomly assigned in a 2:1 ratio to either a web-based exercise group (intervention) or usual care exercise group (active comparator). We chose to allocate more participants to the intervention group since this approach can be advantageous in early trials exploring the feasibility or safety of an intervention.[11] This study was the first study we are aware of which explored including wheelchair users in a web-based exercise intervention. Randomization was stratified according to self-reported method of usual community mobility: those reporting not using wheeled mobility, and those using wheeled mobility the majority of the time. Randomized lists were created before the first participant's first visit using an online service (www.random.org). Data collection occurred from March 2017 to October 2018. This study was approved by the University of Saskatchewan Biomedical Research Ethics Board and registered on ClinicalTrials.gov (NCT03039400).

Interventions

At the baseline in-person visit, physiotherapists created and prescribed exercise programs. Physiotherapists discussed maintaining function as part of the goal setting process (i.e., exercises for trunk control in sitting, upper-limb function for self-care and lower-limb function for transfers). Programs were individualized in terms of exercises, level of difficulty, and number of sets and repetitions. A minimum of twice per week exercise sessions for six months was prescribed for all participants (2x 26 weeks = 52 exercise diary entries). Physiotherapists informed their participants to expect one follow-up phone call from the physiotherapist at the end of the first week. The purpose of the follow-up phone call was to ensure that participants could access their exercise programs and that they had no questions or concerns about their program.

Nine physiotherapists were trained on the study protocol; seven provided exercise prescription and blinded assessments, and two provided only blinded assessments. Training of physiotherapists on the study protocol occurred in small groups or individual sessions all led by a physiotherapist researcher (SJD). All physiotherapists providing exercise prescription for the study had expertise in neurorehabilitation and a minimum of 5 years' experience working with people living with MS.

Intervention arm. Those in the web-based group had their exercise program set up at the baseline in-person visit on webbasedphysio.com (now www.giraffehealth.com). The website contains exercises (videos, text and audio description), which are individually prescribed by a physiotherapist at an initial

assessment.[12,13] The physiotherapist is able to review the electronic exercise diaries and remotely alter the exercises in response to comments from participants. The inventory of exercises and the educational materials were previously developed with input from people living with MS in the UK with mild to moderate disability.[13] For this pilot study, a half-day focus group was held with two patient advisors with advanced disability secondary to MS, a physiatrist (KK) and four experienced physiotherapists, including the orginator of webbasedphysio (LP). The purpose of the focus group was to create additional inventory of exercises for the web-based platform acceptable to people with more advanced disability. Additions included seated versions of existing exercises and novel exercises that focused on core and upper-extremity strength. Participants in the web-based intervention arm were informed that every two weeks for the 6-month intervention period, the treating physiotherapist would review their online exercise diary and remotely alter their exercise program as appropriate by changing exercises, level of difficulty, and/or number of repetitions. Participants were also invited to contact their physiotherapist for a change in their program as needed. Online exercise diaries (web group) were collected on an ongoing basis.

Comparator arm. Those in the usual care exercise group were given a written, home-based exercise program consistent with the most common method for exercise prescription practice for outpatient physiotherapy services at our site. Participants were asked to keep an exercise diary, in paper format, and mail it to the study coordinator at study midpoint (3 month) and endpoint (6 month). For this group,

physiotherapists did not review the exercise diaries. Participants were advised that they could email their physiotherapist to request a change in their program as needed.

Demographic information including sex, age, PDDS,[9,10] disease duration, typical community ambulation status (walk vs. wheel), and residence location were collected. PDDS is a self-assessment measure of disability status, primarily oriented to walking. For example, category 2 (moderate disability) notes no limitations in walking but acknowledges significant problems that limit activities in other ways. For category 7 (wheelchair/scooter), a wheelchair is the main form of mobility and walking is limited to less than 25 feet.

Outcomes

The primary outcome of exercise adherence was calculated as number of exercise sessions over the study period of 26 weeks. All participants were asked to keep an exercise diary, detailing their participation in their prescribed exercise sessions. If participants met the recommended participation adherence of exercise sessions twice per week, they would have participated in at least 52 exercise sessions over the study period.

Secondary outcomes included the MSIS29, the HADS, dynamic grip strength and fatigability, the T25FWT, the TUG test, and a falls history. The MSIS29 is a multiple sclerosis-specific symptom measure which inquires about symptom impact on day-to-day life in the past two weeks.[14] The HADS is a brief measure containing

fourteen questions.[15] It is designed to detect the presence and severity of anxiety and depression and has been validated in a MS population. Dynamic grip strength and fatigability were measured for the dominant hand using a portable hand dynamometer. Participants performed fifteen maximum voluntary contractions in a row. Hand-grip fatigability was calculated as a percentage decrease from the maximum voluntary contraction in the first three squeezes to the maximum voluntary contraction in the last three squeezes.[16] The T25FWT and TUG tests are validated measures for the assessment of mobility in MS and were utilized with ambulatory participants.[17,18] Assessments were completed at the baseline appointment prior to the physiotherapist learning of the participant's random assignment. Study exit (6-month) assessments were completed by a physiotherapist blinded to the participant's group assignment. Blinded physiotherapists also collected fall history in the previous three months by participant self-report at baseline and study exit.

Analyses

For the primary outcome, adherence was described using means (standard deviations) and the distributions between groups were compared at six months using the Mann-Whitney *U* test. Hedges' *g* was calculated for effect size. Hedges' *g* is a member of the Cohen's *d* family of effect sizes and is interpreted in a similar manner – as a proportion of the pooled standard deviation. Cohen proposed conventions for interpreting these effect sizes as small (d=0.2), medium (d=0.5), or large (d=0.8).[19] Adherence was carried out on an intention-to-treat basis. We chose

to replace all missing values for exercise adherence with zero as this approach is the most conservative approach, making the assumption for the worst possible adherence outcome – i.e., no exercise done. In order to explore the differences in adherence between those who were community walkers and those who were community wheelchair users, means (SD) were calculated.

For exploration of the secondary outcomes, means (SD) were described at baseline and six months. Effect sizes for paired data (Cohen's $d_z = t/\sqrt{n}$) were calculated for within-group changes in secondary outcomes for the web group, comparator group, and total study sample. Analysis of secondary outcomes was carried out only on available data. For returned patient-reported questionnaires, missing items were replaced with the participant's scale mean.

Results:

Forty-eight people participated in the study: 32 in the web group and 16 in the comparator group. Demographics are summarized in Table 1. Nine participants withdrew from the study prior to the midpoint: six (19%) from the web group and three (19%) from the comparator group (see Consort diagram, Figure 1). Reasons for withdrawal were hospitalization unrelated to the study protocol (n=1), personal reasons related to relocation or family stressors (n=3), and no reason provided (n=5). No adverse events were reported related to the study protocol. Twenty-one of 48 participants (44%) reported no falls in the three months prior to baseline; 13/48 (27%) reported one fall; 8/48 (17%) reported two falls; and 6/48 (13%) reported three or more. In the three months prior to study exit, 20/36 (56%)

reported no falls, 8/36 (22%) reported one fall, 2/36 (6%) reported two falls and 6/36 (17%) reported three or more falls (12 were missing falls data at study end).

[Table 1 about here]

[Figure 1 (CONSORT diagram) about here]

Mean number of exercise sessions for the web group was 38.9 (*SD*=28.1) and 34.6 (*SD*=40.8) for the comparator group. The difference between group distributions for primary adherence outcome was not statistically significant (*U*=198.5; *p*=.208). Hedges' *g* was 0.13. Percentages of participants completing at least two exercise sessions in each week of the study are displayed in Figure 2. Considering the entire sample, almost 50% of participants (23/48) exercised two or more times per week for at least half of the 26-week study period.

Of the 32 diaries to be returned from the 16 participants in the comparator group originally enrolled, only 16 diaries were returned. This resulted in a disproportionate volume of missing data being replaced with zeroes in the comparator group for the adherence analyses.

[Figure 2 about here]

Exploratory analyses: The highest group mean of exercise sessions was seen in community wheelchair users in the web-based exercise group (mean=51.6, SD=28.9; Table 2).

[Table 2 about here]

Results for secondary outcomes are displayed in Table 3. The means at study exit were not lower than at baseline with moderate effect sizes seen for improvement in both groups for the HADS – anxiety subscale (dz=0.58) and among ambulatory participants for the TUG (dz=0.61). Medium effect sizes were also found for the MSIS-29 in the web-based group (dz=0.65).

[Table 3 about here]

Discussion:

There was no difference in the primary outcome of adherence between the web-based and active comparator groups. Similar to other web-based exercise studies, there were no adverse events related to participating in the exercise intervention. This pilot study invited only people who reported exercising less than twice a week to participate. During the study, nearly 50% of participants (23/48) exercised two or more times per week for at least half of the 26 week study period. There was a wide range of variability in participation in the exercise sessions, with some people reporting more than twice-weekly sessions. In the web-based group on any given week 28% to 69% of the participants exercised at least twice per week. In comparison, in the active comparator group adherence ranged between 25% and 50%. Lowest rates of adherence were observed towards the end of the study for both groups. This participation rate in twice-weekly exercise is comparable to the six-month, multi-centre trial (n=90) with webbasedphysio, except the previously reported multi-centre trial included only ambulatory people.[12]

Comparing our adherence results with other web-based exercise research in multiple sclerosis is challenging, since methods for defining and measuring adherence are not consistent in the literature.[20] Studies reporting internet-delivered physical activity interventions for people with MS commonly describe physical activity levels measured by self-report questionnaire or describe objective activity levels with accelerometer data.[21-24] A focus on activity levels may be appropriate for people with mild-to-moderate MS. For people with more advanced disability and in the absence of clear exercise guidelines for those with more advanced MS, it would seem appropriate to first consider participation adherence (i.e., is the person safely participating in regular exercise?).

Participation adherence data are also important from a service provider perspective,[20] especially for those with restricted access to services who may have more advanced disability or who reside in more rural settings. In the present study, half of the participants had their primary place of residence outside of larger city centres and nearly one third were community wheelchair users. In order to better understand participation and access to structured exercise in MS as a means of physical activity, describing the place of residence of people with MS and the severity of their MS may be relevant.

We employed stratified randomization according to ambulatory status based on the belief that wheelchair users may experience lower exercise adherence. The data suggest this was not the case; overall, wheelchair users reported higher adherence rates and wheelchair users in the web-based group had the highest mean adherence rate. These data were unexpected given that prior research supports

decreased participation in exercise and physical activity with advancing disability.[25] These exploratory results are limited by small group; however, the results provide preliminary support that the web-based platform was helpful to some wheelchair users for overcoming exercise barriers. Further research with this platform or similar platforms in wheelchair users is needed.

In the exploratory analysis of the secondary outcomes, for all the secondary outcomes, the means did not worsen in the web-based group between baseline and six months. This is encouraging given the progressive nature of MS, the longer duration of this exercise trial and the inclusion of people with more advanced disability. However our selection of physical function outcomes were limited in this study. Strength asymmetry may not consistently have a dominant-non-dominant pattern and functional tasks rely on other factors besides grip strength.[16] It would have been prudent to include other functional tasks as outcome measures. The exercise prescription process in this study was individualized with the goal of prioritizing function. As such, core, upper-limb strength and sit-stand transfers were targeted, which may be important for the maintenance of longer-term independence.[26] The goal-setting process of linking specific exercises with longer-term goals and priorities of people with more advanced MS was facilitated by physiotherapists with experience in MS. This process for goal setting could influence study results. For example, a functional goal to maintain sit to stand transfers in order to stay living at home alone with MS as long as possible might encourage longer term adherence with a sit stand exercise prescription.

Limitations of this pilot study included incomplete data ascertainment due to dropouts, missing diaries from the active comparator group and challenges scheduling the blinded final assessments. We also did not collect baseline data pertaining to possible important predictors of exercise behavior in order to better characterize our study sample. The dropout rate in this study was 20%, similar to other physical activity studies involving people with progressive MS with higher levels of disability.[22] Reasons for dropping out of our study were reassuringly not related to the intervention; yet reasons for dropping out were not disclosed for five of the participants. Sixteen of the 32 comparator-group diaries were not returned and six participants in the active comparator group submitted no exercise diaries at all. All missing data were replaced with zeros in the intention-to-treat analysis with a disproportionate amount of missing data in the comparator group. We can therefore be confident that the sensitivity to detect between-group differences in adherence was not reduced by the handling of missing data. Exercise adherence is under-reported in this study since all missing data are unlikely to equate with zero exercise. Despite this, exercise adherence in this study in both groups still increased compared to that reported by participants at their screening baseline. We did not collect pre-randomization exercise baseline behavior through diaries or other data potentially predictive of future exercise behaviour (i.e., cognitive function, MS course, attributions and self-efficacy for exercise[27] and, caregiver support[28]). Larger scale, powered studies are required to improve our understanding of the potential benefits of web-based exercise interventions and the predictors for adherence with web-based platforms is warranted.

This study was also subject to the limitations related to design and measurement in most exercise adherence studies. A limitation of the randomized design is that randomization removes choice from participants regarding how they would like their exercise adherence supported. Some participants, randomized to the active comparator in this study, expressed disappointment and this perhaps contributed to the high number of non-returned exercise diaries in the active comparator group. Future research aimed to increase exercise adherence might consider more pragmatic study designs, such as those which permit patient choice in selecting from a range of interventions that appeal most to the participant.

Diarizing was utilized as a measurement tool for adherence. However, diarizing is also a form of self-monitoring which may promote exercise beyond what is current usual practice and knowing that monitoring is occurring may change behavior.[29] While we aimed to minimize the monitoring in the comparator group to emulate usual care and facilitate physiotherapist support and monitoring in the web-based group, this approach resulted in different diarizing methods for each group. The web-based group exercise was diarized only through the web-based online platform allowing real-time monitoring by the physiotherapists. The comparator group were only asked to submit paper diaries at study midpoint (3 months) and endpoint (6 months). Unfortunately a significant limitation of this study was missing diaries in the comparator group. One advantage of the online web-based diary format is that participants did not need to return diaries since exercise adherence could be reviewed remotely through the web-based program. Participants in both groups were still required to diarize their exercise. Challenges

with diarizing as a means of measuring adherence may have impacted exercise adherence outcomes.

There are also limitations with having a usual care comparator group. While it is relevant to include usual care or active care comparison groups since any new interventions addressing physical activity participation should aim to achieve at least the same rates of participation as usual care with additional benefits (i.e., lower costs, improved accessibility at the population level). In reality, usual care is currently not standardized for access to support for physical activity. Some individuals in the comparator group may have received more support for physical activity than their usual care for physical activity.

There are other limitations and challenges with web-based physiotherapist-prescribed exercise that we experienced in the conduct of this study. There were limitations in the accessibility of the internet for some and the challenge of changing established models of care. There was a continued desire for face-to-face contact between participants and prescribing therapists. Qualitative inquiry into web-based programs to date is limited and a more comprehensive understanding of the challenges warrant further study.[8] There may be opportunities to improve adherence with web-based exercise platforms with augmented patient-provider interactions and coaching[2] and through social media supports.[30]

In moderate-to-severe MS personalised home-based exercise programs of six months duration were well tolerated without evidence of systematic decline in patient-reported outcomes or measured function. A web-based approach is one method that provides a safe way to facilitate participation in physical activity. Web-

based approaches provide a widely-accessible means of delivering personalized and professionally-guided support for some individuals with multiple sclerosis. Further research is needed to determine which individuals may be most likely to benefit from this approach.

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Competing Interests:

Sarah Donkers, Darren Nickel, Shyane Wiegers, and Katherine Knox have no disclosures related to this research. Lorna Paul is co-inventor of the web-based physiotherapy platform and now a director of the social enterprise Giraffe Healthcare. However she was not involved with any data collection or analysis.

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Figure Legends:

Figure 1. CONSORT diagram

Figure 2. Percentage of participants exercising at least twice per week

Table 1. Demographics at baseline			
	Web group (n=32)	**Comparator group (n=16)**	**Total (N=48)**
Females n (%)	20 (63%)	11 (69%)	31 (65%)
Mean age years	54.6y (SD=11.9)	53.8y (SD=12.2)	54.3y (SD=11.9)
Mean PDDS	4.2 (SD=1.6)	4.8 (SD=1.7)	4.4 (SD=1.6)
Mean disease duration from onset	20.0y (SD=11.3)	18.4y (SD=10.7)	19.5y (SD=11.0)
Community wheelchair users n (%)	9 (28%)	5 (31%)	14 (29%)
Residence n (%)			
City	18 (56%)	6 (38%)	24 (50%)
Small city	7 (22%)	2 (13%)	9 (19%)
Town	4 (13%)	6 (38%)	10 (21%)
Rural	3 (9%)	2 (13%)	5 (10%)

PDDS: Patient Determined Disease Steps

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Table 2. Mean number of exercise sessions for community walkers and community wheelchair users over 26 weeks.*			
	Web group	**Comparator group**	**Total**
Community walkers (Mean PDDS=3.75; SD=1.39; median=4)	34.0 (SD=26.8) n=23	34.0 (SD=45.3) n=11	34.0 (SD=33.2) n=34
Community wheelchair users (Mean PDDS=6.07; SD=0.73; median=6)	51.6 (SD=28.9) n=9	36.0 (SD=33.5) n=5	46.0 (SD=30.3) n=14
Total	38.9 (SD=28.1) n=32	34.6 (SD=40.8) n=16	

*target number of sessions/participant = 2xweek x 26 weeks= 52 sessions

PDDS - Patient-Determined Disease Steps

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Table 3. Secondary outcomes			
Outcome	**Web Group**	**Comparator Group**	**Total Sample**
MSIS29 physical scale	M_{base}=38.4 (SD=15.4) M_{exit}=36.2 (SD=18.9) d_z = 0.26 (n=25)	M_{base}=38.1 (SD=10.4) M_{exit}=35.1 (SD=14.8) d_z = 0.20 (n=11)	M_{base}=38.3 (SD=13.9) M_{exit}=35.8 (SD=17.5) d_z = 0.23 (n=36)
MSIS29 psychological scale	M_{base}=29.9 (SD=18.1) M_{exit}=25.3 (SD=18.9) d_z = 0.65* (n=25)	M_{base}=29.5 (SD=16.4) M_{exit}=26.8 (SD=18.9) d_z = 0.13 (n=11)	M_{base}=29.8 (SD=17.4) M_{exit}=25.8 (SD=18.6) d_z = 0.32 (n=36)
HADS anxiety scale	M_{base}=7.6 (SD=4.2) M_{exit}=6.2 (SD=4.3) d_z = 0.58* (n=25)	M_{base}=7.8 (SD=4.2) M_{exit}=6.4 (SD=4.4) d_z = 0.53* (n=11)	M_{base}=7.7 (SD=4.1) M_{exit}=6.3 (SD=4.3) d_z = 0.58* (n=36)
HADS depression scale	M_{base}=7.0 (SD=4.0) M_{exit}=6.2 (SD=3.9) d_z = 0.35 (n=25)	M_{base}=6.1 (SD=3.5) M_{exit}=5.6 (SD=3.6) d_z = 0.25 (n=11)	M_{base}=6.8 (SD=3.8) M_{exit}=6.0 (SD=3.8) d_z = 0.33 (n=36)
TUG	M_{base}=15.6s (SD=14.0) M_{exit}=13.1s (SD=10.5) d_z = 0.62* (n=18)	M_{base}=20.5s (SD=19.5) M_{exit}=17.6s (SD=14.5) d_z = 0.56* (n=8)	M_{base}=17.1s (SD=15.7) M_{exit}=14.5s (SD=11.8) d_z = 0.61* (n=26)
T25FW	M_{base}=9.0s (SD=6.1) M_{exit}=8.9s (SD=6.6) d_z = 0.04 (n=17)	M_{base}=20.3s (SD=30.9) M_{exit}=15.9s (SD=17.2) d_z = 0.29 (n=8)	M_{base}=12.6s (SD=18.2) M_{exit}=11.1s (SD=11.3) d_z = 0.17 (n=25)
Dominant-hand maximal voluntary contraction	M_{base}=27.2kg (SD=10.6) M_{exit}=29.3kg (SD=13.0) d_z = -0.29 (n=23)	M_{base}=29.8kg (SD=10.7) M_{exit}=29.1kg (SD=10.7) d_z = 0.12 (n=10)	M_{base}=28.0kg (SD=10.5) M_{exit}=29.2kg (SD=12.2) d_z = -0.18 (n=33)

Dominant-hand dynamic fatigue index	M_{base}=19.1% (SD=23.5) M_{exit}=7.5% (SD=10.8) d_z = 0.49 (n=23)	M_{base}=16.1% (SD=10.6) M_{exit}=11.6% (SD=21.7) d_z = 0.30 (n=10)	M_{base}=18.2% (SD=20.4) M_{exit}=8.7% (SD=14.7) d_z = 0.44 (n=33)

MSIS29= Multiple Sclerosis Impact Scale 29; HADS = Hospital Anxiety Depression Scale;

TUG= Timed Up and Go; T25FW= Timed 25 Foot Walk; * medium effect size

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