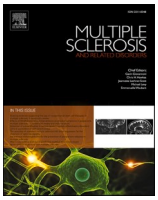
Multiple Sclerosis and Related Disorders 85 (2024) 105529

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



Under & Over: A randomised controlled study to develop an upper limb rehabilitation tool for people with Multiple Sclerosis

Alison Thomson [a,*], Andrea Stennett [a], Canan Metin [a], Jonathan Bestwick [a], Gavin Giovannoni [b], Ruth Dobson [a]

[a] Wolfson Institute of Population Health, Queen Mary University of London, London, UK
[b] Blizard Institute, Queen Mary University of London, London, UK

ARTICLE INFO

Keywords:
Multiple sclerosis
Upper limb
Rehabilitation

ABSTRACT

Background: Impairment of upper limb function is common in Multiple Sclerosis (MS). Rehabilitation remains a key strategy to manage symptoms and improve quality of life. The Under & Over study assessed the effectiveness of a rehabilitation programme in people with advanced MS.
Objective: To determine if repeated use of Under & Over can improve upper limb function for people with MS.
Methods: One hundred and six ($N = 106$) people with MS participated in this 3-month study. The primary outcome measure was the cardboard 9-hole peg test (c9HPT), with secondary outcomes including the EuroQol-5Dimensions, 5-Level Questionnaire (EQ5D-5 L) questionnaire. There were three arms**:** Arm 1a, the 'Daily Group', engaged with the Under & Over tool daily for 30 min. Arm 1b, the 'Free Use Group', used the same tool without time constraints, with the added feature of a community sharing platform. Arm 2, the 'Delayed Start Group', initially completed the c9HPT for three months before switching to the 'Free Use' programme.
Results: 43/106 (41 %) of those randomised completed the primary end point. No significant difference between c9HPT at baseline and 3 months was seen in Arm 1a or 1b. Participants in Arm 2 who had been completing the c9HPT 5 days a week for 3 months showed a training effect in the dominant hand (mean speed at baseline 0.0455 (s^{-1}), mean at 3 months 0.0341, difference 0.011; 95 % CI 0.0080 to 0.0148, $p < 0.001$). No significant difference was seen in c9HPT time following 3 months of active use of the Under & Over tool. The study faced significant limitations, notably in participant adherence, with fewer than half (43/106 (41 %)) completing the final assessment.
Conclusions: This study demonstrates how a small, engaged, and motivated group were able to complete a remote rehabilitation programme. Future remote intervention studies could benefit from incorporating adaptive engagement strategies, such as personalised reminders and participant-tailored activity adjustments, to enhance adherence and capture a broader spectrum of patient experiences.

1. Introduction

Impairment of upper limb function is a common clinical symptom for people living with Multiple Sclerosis (MS). Up to 75 % of people with MS have impairment of manual dexterity even in the early stages of disease (Bertoni et al., 2015), and as MS progresses, most people develop upper limb dysfunction in the form of tremor, loss of fine motor movement and weakness (Johansson et al., 2007). Loss of upper limb function has consequences for employability (Simmons et al., 2010), quality of life (Goverover et al., 2017), and performing activities of daily living such as eating, dressing and grooming (Yozbatıran et al., 2006). It can also have a devastating effect on creative and pleasurable activities such as painting, knitting, playing an instrument and handwriting. We have previously shown in an online survey that 314/360 (88 %) of people with MS attributed more importance to their upper limb function compared to lower limb function (Dubuisson et al., 2017a).

Despite this, walking ability dominates key areas of clinical practice and research, including in the evaluation of treatment efficacy. The most commonly used trial outcome measure and monitoring measure is the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983), which is heavily weighted on walking ability and can over or underestimate upper limb function (Ebers et al., 2008).

* Corresponding author at: Centre for Preventive Neurology, Wolfson Institute of Population Health, Queen Mary University of London, London, UK.
E-mail address: a.thomson@qmul.ac.uk (A. Thomson).

https://doi.org/10.1016/j.msard.2024.105529
Received 22 November 2023; Received in revised form 24 January 2024; Accepted 27 February 2024
Available online 1 March 2024

Rehabilitation remains a key strategy to manage symptoms and improve quality of life for people with MS (Khan et al., 2007). However, many rehabilitation interventions suffer from the same scotoma as DMT trials - the majority focus on walking ability and are trialled in people mildly or moderately affected by MS (Rietberg et al., 2005; Snook and Motl, 2009). Very few studies have focused on rehabilitation in people with advanced MS and there is a dearth of evidence focussing on upper limb rehabilitation (Lamers et al., 2016). Current rehabilitation tools and activities focus on measures of body functions and structures looking at the capacity to assess the maximal ability to execute a task or an action (e.g. the 9HPT is gold standard objective measure for manual dexterity (Fischer et al., 1999)) or an activity performance measure measuring the person's habitual performance of tasks in their normal environment (the ABILHAND (Penta et al., 2001). There are a range of upper limb rehabilitation tools in use, but few have been used in MS research and we are aware of only one developed specifically for people with MS (Lamers et al., 2016). For example the ABILHAND was originally developed for rheumatoid arthritis with subsequent versions developed for people with stroke (Penta et al., 1998). Although these have been validated for use with people with MS (Barrett et al., 2013) their transference from one condition to another poses problems in that the activities that are included lack relevance to the activities specific to living with MS. They also lack relevance to modern living. For example, they do not address challenges that may be commonly faced by people living with MS, such as self-catheterisation, and can further be influenced by mobility, again commonly affected in MS. Additionally, there is no mention of new technologies such as the use of touchscreen phones or tablets in the ABILHAND. In addition, of the rehabilitation studies that focus on the upper limb, only a few use bilateral tasks, yet the majority of activities completed in daily life require both upper limbs (Lamers et al., 2016). Therefore, an emphasis on the effectiveness of a bilateral upper limb rehabilitation programme is needed.

The #ThinkHand campaign raised awareness and initiated discussions amongst people with MS, clinicians, charities, pharmaceutical companies and regulators to realise the importance and work towards generating evidence to improve treatment aimed at preserving upper limb function for people with advanced MS. Meaningful patient involvement enabled a complete understanding of the detrimental impact that loss of hand and arm function plays in a person's life, and the specific upper limb challenges faced by people with advanced MS. One outcome of this campaign was a design-led exploration of alternative ways to measure, record and account for people's experiences of change in hand and arm function in everyday life (Thomson, 2019). The Under & Over tool, used in this study is one of these designs.

The Under & Over study was designed to assess the effectiveness of a rehabilitation programme aimed at improving upper limb function in people with advanced MS. By using a design-led rehabilitation tool in a remote study setting, the real-life effectiveness of the programme can be better understood. The utilisation of a remote study setting was strategically chosen to accommodate the specific needs of individuals with advanced MS, who often encounter substantial mobility limitations (Kalb et al., 2020). By leveraging the capabilities of digital platforms, the study was designed to be accessible to participants regardless of their location, thus enabling a more diverse and expansive cohort. This approach aligns with the evolving landscape of clinical research, where the emphasis on patient-centred methodologies is paramount (Engle et al., 2021). A remote setting also ensures that the intervention can be seamlessly integrated into the daily lives of participants, fostering an environment that accurately reflects the practical application of the rehabilitation tool.

2. Methods

2.1. Study design and patients

The primary aim of this study was to develop and evaluate an engaging everyday activity to improve upper limb function in people with MS. Objectives were to determine if repeated use of Under & Over can improve upper limb function for people with MS compared to participants on the waiting-list and to explore different engagement strategies involving a digital community of people with MS. In order to be eligible for inclusion, potential participants needed to be aged $\geq$18 years old (there was no upper age limit) with a diagnosis of MS for >6 months; have an EDSS score of $\geq$6 measured using the WebEDSS; be able to understand and communicate in English; have access to a computer; and able to give online informed consent. Participants who did not meet the inclusion criteria or are unable to use their hands due to pain or any other factor that impedes their ability to engage with the study interventions were excluded from participation. Potential participants completed an online questionnaire and gave informed consent. This information was screened by the research team prior to enrolment on the study platform and posting of the study pack.

The study was administered entirely remotely through a dedicated study website (www.underandover.study), which was used for recruitment, baseline, outcome measurement and to host the rehabilitation programme. Recruitment involved a series of targeted strategies, including advertising via MS charities (MS Society and The MS Trust), the MS Research Blog, twitter account, and direct contact to eligible MS patients who had provided consent to be contacted about research. Study recruitment took place over a 3-month period (January – April 2021).

2.2. Sample size calculation, randomisation and blinding

A priori power calculations indicated that 120 participants were required, based on an estimated initial baseline speed (expressed as the proportion of the c9HPT task achieved in one second; the reciprocal of time taken to complete the task) of 0.0305. Using the assumption that a study close mean speed would be 0.0299 per second in the wait list arm and 0.0359 per second in the rehab group (equating to times of 32.8 (baseline), 33.4 (wait list) and 27.9 (intervention) seconds respectively) with a standard deviation of 0.01 in each group, power calculations were based on 80 % power to achieve a statistical significance level of 0.05.

Participants were randomised by the researcher in a 2:1 allocation ratio to either the immediate rehabilitation group or the wait list group. The allocation sequence was concealed and sequentially organised. The immediate rehabilitation group was subdivided into Daily and Free Use subgroups. Due to the nature of the study, participants and researchers were not blinded to group allocation. However, the study statistician was blinded to group allocation during the data analysis phase.

2.3. The under & over tool

The Under & Over tool consisted of a 40×40 cm plastic board with 9 holes in a grid pattern, two shoelaces and a series of patterns to complete (Fig. 1). The aim of the activity was to thread the shoelaces through the holes to create a pattern while exercising hand and arm movement and control. A digital booklet provided a series of patterns to enhance engagement with the rehabilitation activity.

2.4. Study procedures

Study procedures are summarised in Fig. 2. Instructions for each study Arm were as follows:

Arm 1a- Daily Group: Participants were asked to complete the Under & Over tool for up to 30 min per day, 5 days per week for 3 months. They were instructed to complete patterns in a specific order.
Arm 1b - Free Use Group: Participants were asked to complete the Under & Over tool for an unspecified time, 5 days per week for 3 months. They were given free choice about the pattern they wished

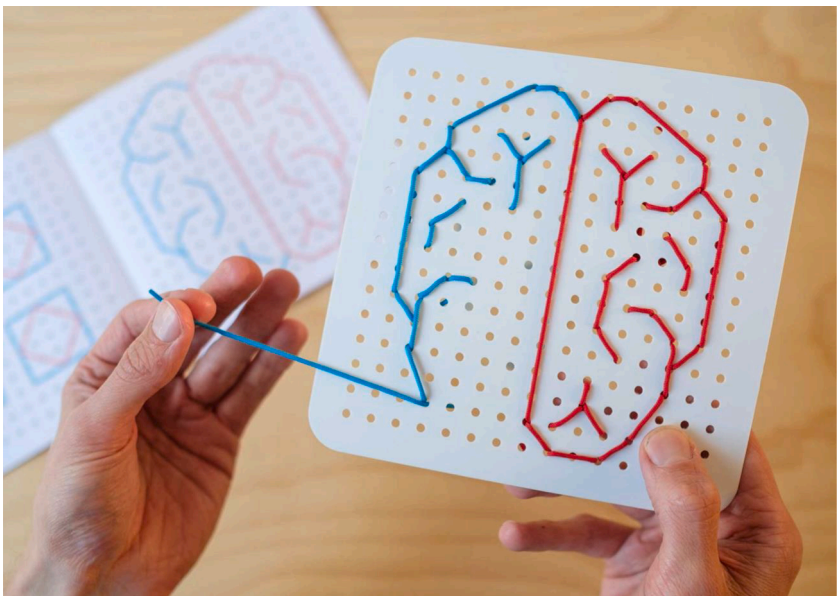


Fig. 1. The Under & Over tool.

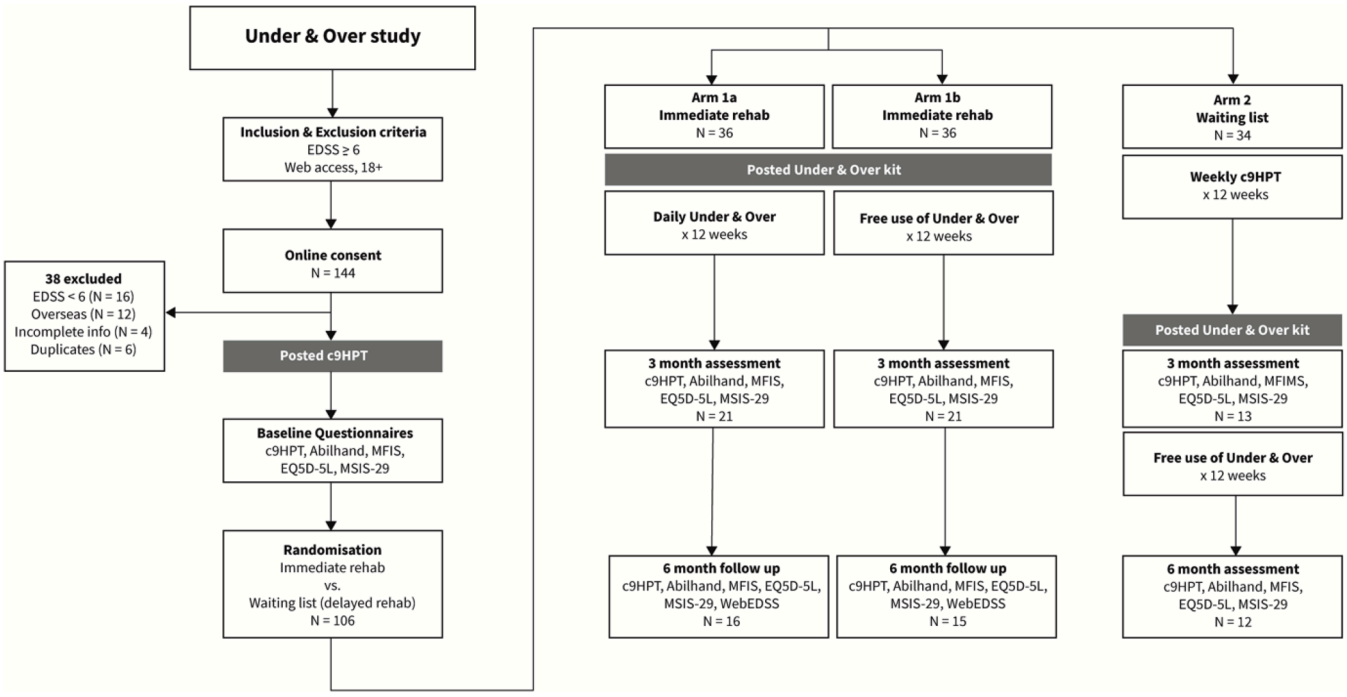


Fig. 2. Study procedures and flow of participants through study. c9HPT = cardboard 9 Hole Peg Test, MSIS-29 = Multiple Sclerosis Impact Scale, MFIS = Modified Fatigue Impact Scale, ABILHAND = Manual Ability Measure, EQ5D-5 L = EuroQol 5-Dimension, 5-Level Questionnaire.

to complete, and were given the option to create their own patterns. These participants had access to a community sharing section of the study website where they could upload photographs of their patterns and view other participants' patterns over the 3-month period.

Arm 2 - Delayed Start Group (wait list arm): For the first three months of the study, participants were asked to complete the c9HPT 5 days a week. After three months, they followed the same instructions as Arm 1b.

Participants were asked to complete a daily questionnaire on the study platform to record their activity that day. Questions asked include, the time taken to complete the activity, which pattern was attempted, proportion of the pattern completed and a free text box for further comments. A questionnaire was circulated to all participants at the end of the study to gather feedback on their experience overall.

2.5. Outcome measures

Outcome measurements were collected at baseline, 12 weeks and 24 weeks (see Fig. 2). The primary outcome measure was the "Cardboard 9-hole peg test" (c9HPT). We have previously demonstrated validity of the cardboard version of the 9-hole peg test in people with MS (Dubuisson et al., 2017b); with the added value that it can be posted to participants homes and removes the need for in person visits. It is a quantitative

measure of arm and hand function and is widely used in people with MS both in clinical and research settings. Quality of life was assessed using the EuroQol-5 Dimension (EQ-5D-5 L) (EuroQol Group, 1990). It is a validated (Fogarty et al., 2013) self-reported questionnaire consisting of two components: The EQ-5D descriptive component and the EQ visual analogue scale (EQ VAS). The Multiple Sclerosis Impact Scale (MSIS-29) is a measure of the impact of MS on daily life activities (Hobart, 2001). It consists of 20 items associated with a physical scale and 9 items with a psychological scale. All items have 5 response options: 1 "not at all" to 5 "extremely". The MSIS-29 is valid and reliable in people with MS (Riazi et al., 2002). The Modified Fatigue Impact Scale (MFIS), a valid and reliable measure in people with MS (Amtmann et al., 2012; Learmonth et al., 2013) was used to measure fatigue. Participants rated the impact of fatigue over the past 4 weeks on a 21-item scale. The items were grouped in terms of physical, cognitive, and psychosocial function. The scale ranges from 0 to 84 where a higher score indicates greater impact of fatigue on daily activities. The ABILHAND questionnaire, a valid outcome measure used in people with MS (Barrett et al., 2013), was used to assess the perceived ease or difficult that participants experience when performing bilateral upper limb tasks. Participants rated 23 bilateral tasks using a 3-point ordinal scale (ease, difficult, impossible). Data on sociodemographic profile, MS specific information were collected at baseline only.

2.6. Patient involvement

The study was designed based on an active and longstanding patient and public involvement (PPI) programme. Following INVOLVE principles (INVOLVE, 2015), patients were involved in the development of the study protocol, reviewing participant information, study design and testing of the online study platform. There was a specific remote patient testing group all with an EDSS of ≥6 to ensure the platform and the patterns were appropriate for a range of upper limb abilities.

2.7. Ethical approval

Yorkshire & The Humber-Leeds West Research Ethics Committee reviewed and approved the study (Reference 20/YH/0259).

2.8. Data analysis

The c9HPT, the primary outcome measure was used to determine whether the Under and Over tool improved upper limb function in people with MS. The outcome of two successful trials for each hand (dominant and non-dominant) were used as outlined in the MS Functional Composite Manual (Fischer et al., 1999). A 20 % increase in score between the assessment time points (baseline, 3 months and 6 months) was considered clinically significant.

Baseline demographics (e.g. Age, Gender, Ethnicity), MS characteristics (e.g. EDSS, Type of MS), self-reported questionnaires (e.g. MSIS-29, MFIS, ABILHAND and EQ-5D-5 L), relapse, adverse events and adherence information were analysed using descriptive statistics. Comparisons between groups were analysed using mann-Whitney *U* tests. Quantitative analysis was performed using Stata software version 17 (StatCorp, College Station, Texas).

Qualitative analysis was performed using LancsBox for macOS software (v6.0.0, LancsBox Software, Lancaster University corpus toolbox) on participant open text daily and weekly responses. Keyword analysis was used to identify significant key words or phrases within large quantities of text.

3. Results

3.1. Participants

One hundred and twelve ($N = 112$) people with MS consented to take part in the study. 6 did not meet the inclusion criteria or were duplicates, and 106 people were randomised. There were no significant differences between groups (Table 1). The majority of participants had progressive MS, and most reported significant upper limb impairment (average ABILHAND score 25) and high levels of fatigue (MFIS mean scores of 50.1, 52.3 and 50.7).

3.2. Dropout rate and missing data

The primary end point (c9HPT) was completed by 43/106 (41 %) of those randomised – 16/36 in Arm 1a, 15/37 in Arm 1b and 12/33 in Arm 2 (Table 2). The majority of people did not state any reason for not completing the study; where these were given, key reasons include ill health (e.g. fatigue, tiredness) or bereavement as a result of the COVID-19 pandemic.

3.3. Changes in scores

No significant difference between c9HPT at baseline and 3 months was seen in Arm 1a or 1b (Fig. 3). Participants in Arm 2 who had been completing the c9HPT 5 days a week for 3 months showed a training effect in the dominant hand (mean speed at baseline 0.0455, mean at 3 months 0.0341, difference 0.011; 95 % CI 0.0080 to 0.0148, $p < 0.001$) (Fig. 3). No significant difference was seen in c9HPT time following 3 months of active use of the Under & Over tool (Table 2). This lack of effect persisted in a multivariable model controlling for age, gender and EDSS. Post-hoc comparisons were performed between and within groups at 3 and 6 months and found no statistically significant p-values (data not shown).

At 6 months, fatigue (as measured by MFIS) was lower across all the groups with a change score of 4 (Arms 1a and 1b) and 6 points (Arm 2). At 6 months participants in Arm 1a scored on average 10 points lower

Table 1
Baseline demographics and MS characteristics of study participants.

	Mean scores (SD)		
	Arm 1a	Arm 1b	Arm 2
No. of patients	36	36	34
Age (years; mean [SD])	54.2 (9.7) (*n* = 32)	52.3 (9.6) (*n* = 27)	55.6 (8.1) (*n* = 24)
Gender	27F / 8 M/ 1 Other	28F / 8M	23F / 11 M
Type of MS			
Relapsing MS	8	10	6
Secondary Progressive MS	17	13	17
Primary Progressive MS	8	6	6
Not specified	3	7	5
EDSS	Median 6.5	Median 6.5	Median 6.5
Most recent relapse			
None for at least a year	11	12	16
In the past three to six months	8	5	3
Unknown/not specified	17	19	15
Ethnicity			
White (British, Irish, other)	32	28	28
Black or Black British - Caribbean	0	0	1
Asian or Asian British - Indian	1	1	0
Unknown/not specified	3	7	5
Cohabitation			
Spouse/partner	25	21	17
Living alone/Other	5	7	9
Unknown/not specified	4	8	8
Current employment:			
In paid employment	7	4	8
Retired	12	8	6
Unable to work	11	12	7
Unemployed and looking for work	1	1	0
At home and not looking for work (e.g. housewife/husband)	1	1	3
Other/missing Data	4	10	10
No. of hours worked	7 (13)	8 (13.7)	13 (15.9)

Table 2
Cardboard 9HPT scores at baseline, 3 months and 6 months. Time shown as inverse of the time in seconds (s^{-1} = 1/seconds).

Cardboard 9 Hole Peg Test scores	N	Mean	SD
Arm 1a - Dominant hand			
Baseline	31	0.031	0.014
3 months	21	0.036	0.015
6 months	16	0.033	0.014
Arm 1a - Non-dominant hand			
Baseline	31	0.028	0.012
3 months	21	0.029	0.012
6 months	16	0.032	0.017
Arm 1b - Dominant hand			
Baseline	29	0.033	0.012
3 months	18	0.032	0.012
6 months	15	0.033	0.014
Arm 1b - Non-dominant hand			
Baseline	28	0.029	0.011
3 months	17	0.029	0.014
6 months	15	0.077	0.183
Arm 2 - Dominant hand			
Baseline	26	0.037	0.013
3 months	13	0.046	0.017
6 months	12	0.040	0.016
Arm 2 - Non-dominant hand			
Baseline	27	0.032	0.010
3 months	13	0.042	0.016
6 months	12	0.035	0.016

than baseline on the physical subscale of the MSIS-29 (see Table 3).

3.4. Study adherence

Adherence data indicated that in general people fell into two groups: (1) well engaged and completing the tool 5 days per week, (2) poorly engaged and completing the tool 0 days per week. The group not completing the tool on any days increased throughout the study period, reflecting the increasing lack of engagement by participants in Arms 1a and 1b, however participants in Arm 2 who started completing the tool 5 days a week continued to do so throughout the study period. 40 participants responded to the end of study questionnaire. 89 % had a positive experience of participating in the study and 61 % managed to stay motivated. 7 % felt face to face would have been preferable.

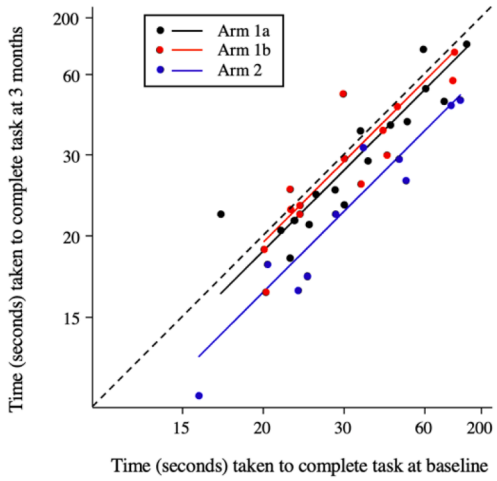
3.5. Qualitative analysis

Participants who completed the study for a majority of 5 days a week used words such as 'enjoy', 'fun', and 'great' in their daily and weekly feedback to describe completing the patterns, suggesting their overall experience was positive. Participants also reported feeling positive when seeing progress in completing the patterns using key words such as 'improve' and 'better'. Participants who completed the study for 0 days a week, reported key words such as 'tired' and 'fatigue'. Difficulty levels of the rehabilitation tool may have played a role in participants non-completion rates, for example the commonly occurring key words relating to this are 'difficult', 'struggl*', 'challeng*', 'hard', 'demanding', 'complicate*' and 'strain'.

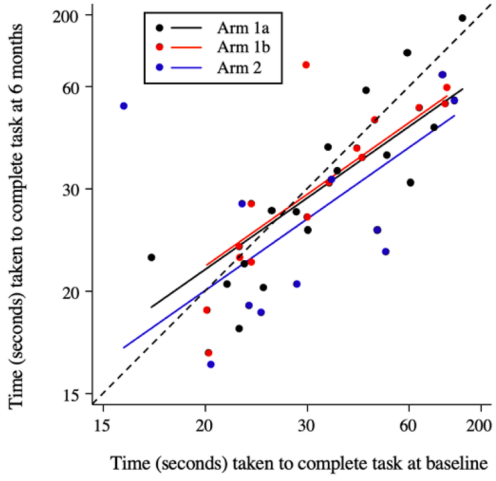
Participants from both adherence groups reported multitasking while completing the Under & Over activity with activities such as "watching TV" and "having a phone call". The poor adherence group reported the word "distrat*" while the group with good adherence reported the words 'podcast' and 'music' when describing other activities. Further open text analysis showed that individual participants reported experiencing improvements in their overall dexterity, hand coordination, sensitivity, handwriting and ability to knit.

3.6. Engagement

7 videos were available on the study website and platform, including information on the study process (recruitment, baseline and randomisation information), Q&A's with the study team, talks by clinical experts and technology support. The videos were viewed 2366 times. Participants who were following Arms 1b and 2 had the option to create their own patterns and upload these to the study platform for other participants to view. 41 new patterns were created and uploaded. There were 71 discussions between study participants on the study platform and 47 of these discussions received replies from other study participants.



Arm 1b v Arm 1a p = 0.396
Arm 2 v Arm 1a p < 0.001
Arm 2 v Arm 1b p < 0.001



Arm 1b v Arm 1a p = 0.870
Arm 2 v Arm 1a p = 0.415
Arm 2 v Arm 1b p = 0.342

Fig. 3 a. (left): Time taken for 9-hole peg test at 3 months versus baseline according to group (Arm 1a = black, Arm 1b = red, Arm 2 = blue). Points to the right of the line of identity (dashed) show an improvement at 3 months. b (right): Time taken for 9-hole peg test at 6 months versus baseline according to group (Arm 1a = black, Arm 1b = red, Arm 2 = blue). Improvement is not sustained at 6 months.

Table 3
Patient Reported Outcome Measures at baseline, 3 and 6 month follow up. The number taking part in each assessment at each time point is given in brackets. MSIS-29 = Multiple Sclerosis Impact Scale, MFIS = Modified Fatigue Impact Scale, ABILHAND = Manual Ability Measure, EQ5D-5 *L* = EuroQol 5-Dimension, 5-Level Questionnaire. * **Absolute difference between Arm 1a and 2 at 3 months −17.49 (95 %CI −31.57 to −3.4); $p = 0.016$.**

	Arm 1a	Arm 1b	Arm 2
MSIS-29			
Physical (mean; SD [n])			
Baseline	60.3; 18.7	62.8; 23.2	65.8; 17.1 (25)
3 months	(29)	(28)	66.3; 19.2 (14)
6 months	55.3; 21.2	64.5; 23.9	60.2; 25.9 (11)
	(19)	(17)	
	50.1; 17.8	64.7; 24.0	
	(16)	(13)	
Psychosocial (mean; SD			
[n])	36.0; 21.2	41.8; 24.2	44.3; 23.1 (25)
Baseline	(29)	(28)	43.7; 21.4 (14)
3 months	36.5; 21.5	42.6; 30.6	41.4; 28.0 (11)
6 months	(19)	(17)	
	31.1; 14.1	42.1; 31.5	
	(16)	(13)	
MFIS (total score)			
MFIS (Mean; SD [n])			
Baseline	50.1; 11.0	52.3; 15.8	50.7; 9.8 (26)
3 months	(30)	(29)	50.8; 11.3 (15)
6 months	47.4; 14.0	52.3; 18.7	44.4; 16.3 (12)
	(19)	(17)	
	45.5; 6.9 (13)	47.9; 19.0	
		(14)	
ABILHAND			
Score (mean; SD [n])			
Baseline	25.3; 10.2	24.9; 9.8 (28)	25.6; 10.1 (27)
3 months	(32)	23.8; 10.1	24.0; 9.5 (14)
6 months	25.2; 10.7	(17)	25.1; 10 (12)
	(22)	27.2; 11.2	
	25.6; 10.3	(12)	
	(17)		
EQ5D-5 L (VAS)			
Score (mean; SD [n])			
Baseline	56.8; 19.5	55.0; 21.4	54.4; 16.8 (27)
3 months	(29)	(25)	44.8; 21.2 (13)
6 months	61.5; 17.9	51.7; 26.6	*
	(15)	(17)	46.3; 25.1 (12)
	57.9; 23.5	52.4; 22.5	
	(17)	(12)	

3.7. Adverse events

19 participants experienced at least one adverse event (AE), with 23 AEs in total (see supplementary data). No serious adverse events were reported.

4. Discussion

This study is the first fully remote study examining the effect of a targeted upper limb rehabilitation tool. Whilst we were unable to demonstrate an effect of the Under & Over tool on upper limb function, the meaningful improvement in both fatigue as measured by MFIS across all groups (Rooney et al., 2019) and on the physical subscale of the MSIS-29 (Costelloe et al., 2007; Phillips et al., 2014) for those in the Daily Under & Over group (Arm 1a) indicates some responsiveness to the intervention or due to participation in the study.

The study population were older adults with advanced MS. Although the outcome measures were not able to capture statistical change in this population following the intervention, participants expressed subjective improvements in their feedback, demonstrating the challenge of selecting appropriate outcome measures in this group. This study also highlights the importance of utilising patient reported outcomes to gain added insights about efficacy of interventions.

It is important to note that the 9HPT is intended to be administered by healthcare professionals as an outcome measure, used at specific time intervals within clinical practice and research. It is not intended to be used remotely (independent of healthcare professionals) and repeatedly by the same person with the aim of getting better, or faster at completing the activity. However, this study has shown how repeated use of outcome measures can result in statistically significant change even when used remotely. Future studies could include a preliminary practice phase to mitigate the learning effect on tests like the 9HPT and consider using complementary measures less prone to practice-related improvements. Extended follow-up durations could also help distinguish between short-term learning gains and sustained functional benefits.

There are important limitations to this study. Study adherence was relatively poor, with <50 % completing the final assessments. This is an issue in many rehabilitation studies, especially those designed to be remote, and affects the ability to obtain statistical significance (Argent et al., 2018). Nonetheless, this study was conducted during the COVID-19 pandemic, and this could have also had an impact on adherence. Interpretation of the findings must be approached with consideration of this constraint. Future research should focus on increasing and sustaining participant numbers and improving adherence strategies to robustly assess the efficacy of interventions.

It is interesting to note that in the presence of free choice there was a greater risk of lower adherence to the rehabilitation programme. This suggests some people prefer a structured programme of activities to follow with limited options for customisation, or change. Remote studies require high levels of motivation from the participant and support from the research team to stay engaged and complete the rehabilitation programme, and understanding how best to deliver this remains an important area of research.

4.1. Recommendations for remote rehabilitation studies

Delivering research studies fully remotely can improve inclusivity by reducing burden and cost of travel, and allowing disabled participants to take part within the comfort of their home. Our findings align with the current research integrating digital technologies in neurorehabilitation, reinforcing its potential to improve motor and cognitive functions in MS patients (Manuli et al., 2020; Maggio et al., 2023). The enhanced upper limb functionality observed with remote rehabilitation tools underscores the promising application of digital technologies in managing MS, despite the challenges in remote study adherence and participant engagement. However, remote studies are not without challenges, including limited interactions which can affect study adherence and reporting of adverse events, restrictions of validated digital outcome measures and the potential for digital exclusion.

Incorporating more reminders or contact with participants to try to increase adherence needs to be balanced with the need to respect participant choice to drop out for any reason, as some people reported feeling guilty for withdrawing. It remains beneficial to emphasise to study participants that sharing reasons for withdrawal is important, as it can improve the design of future studies. In our study, assessing qualitative data from those with poor compliance sheds light on possible reasons for dropout – in this case tiredness and fatigue predominate, both of which are major symptoms in MS. It is likely that a lack of a noticeable positive impact of the intervention in these participants also contributed to their reasons for not completing the assessments.

This study also contributes further understandings about the utilisation of rehabilitation tools outside the clinical environment. The impact of external factors whilst completing the tool was notable. Distraction led to lower study engagement, demonstrating the importance of providing advice about surroundings when carrying out study interventions.

5. Conclusion

This study demonstrates how a small, engaged and motivated group

were able to complete a remote rehabilitation programme. This study also highlights that repeated use of the c9HPT can result in statistically significant improvements in performance. Although this is not how the tool is intended to be used in clinical practice, it blurs the boundaries between what can be considered an outcome measure, and what is a rehabilitation tool. We demonstrate the importance of providing multiple ways to enable people to record their experiences to report change in their own words, enabling the measurement of impact not captured by standardised outcome measures. We demonstrate that it is feasible and acceptable to deliver a remote upper limb rehabilitation study to people with advanced MS, and that future studies need to be open to delivering interventions in a variety of ways to best meet the needs of people with MS.

Declaration of competing interest

The Author(s) declare(s) that there is no conflict of interest.

Acknowledgements

We would like to thank the members of the Barts MS Advisory Group for their input and feedback during the study development process. A further group of people with MS tested the Under & Over tool and gave valuable feedback on the design of the tool and remote aspects of the study - thank you all for your contributions.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The Under & Over study was supported by Roche. All authors vouch for data accuracy, reviewed all drafts, and approved the final manuscript.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2024.105529.

References

Amtmann, D., Bamer, A.M., Noonan, V., Lang, N., Kim, J., Cook, K.F., 2012. Comparison of the psychometric properties of two fatigue scales in multiple sclerosis. Rehabil. Psychol. 57, 159–166. https://doi.org/10.1037/a0027890.

Argent, R., Daly, A., Caulfield, B., 2018. Patient Involvement With Home-Based Exercise Programs: can Connected Health Interventions Influence Adherence? JMIR. MHealth UHealth 6. https://doi.org/10.2196/mhealth.8518 e47.

Barrett, L.E., Cano, S.J., Zajicek, J.P., Hobart, J.C., 2013. Can the ABILHAND handle manual ability in MS? Mult. Scler. 19, 806–815. https://doi.org/10.1177/1352458512462919.

Bertoni, R., Lamers, I., Chen, C.C., Feys, P., Cattaneo, D., 2015. Unilateral and bilateral upper limb dysfunction at body functions, activity and participation levels in people with multiple sclerosis. Mult. Scler. 21, 1566–1574. https://doi.org/10.1177/1352458514567553.

Costelloe, L., O'Rourke, K., Kearney, H., McGuigan, C., Gribbin, L., Duggan, M., Daly, L., Tubridy, N., Hutchinson, M., 2007. The patient knows best: significant change in the physical component of the Multiple Sclerosis Impact Scale (MSIS-29 physical). J. Neurol., Neurosurg. Psychiatry 78, 841–844. https://doi.org/10.1136/jnnp.2006.105759.

Dubuisson, N., Baker, D., Thomson, A., Marta, M., Gnanapavan, S., Turner, B., Giovannoni, G., Schmierer, K., 2017a. Disease modification in advanced MS: focus on upper limb function. Mult. Scler. 23, 1956–1957. https://doi.org/10.1177/1352458517717811.

Dubuisson, N., Bauer, A., Buckley, M., Gilbert, R., Paterson, A., Marta, M., Gnanapavan, S., Turner, B., Baker, D., Giovannoni, G., Schmierer, K., Thomson, A., 2017b. Validation of an environmentally-friendly and affordable cardboard 9-hole peg test. Mult. Scler. Relat. Disord. 17, 172–176. https://doi.org/10.1016/j.msard.2017.08.002.

Ebers, G.C., Heigenhauser, L., Daumer, M., Lederer, C., Noseworthy, J.H., 2008. Disability as an outcome in MS clinical trials. Neurology 71, 624–631. https://doi.org/10.1212/01.wnl.0000313034.46883.16.

Engle, R.L., Mohr, D.C., Holmes, S.K., Seibert, M.N., Afable, M., Leyson, J., Meterko, M., 2021. Evidence-based practice and patient-centered care: doing both well. Health Care Manage. Rev. 46, 174–184. https://doi.org/10.1097/HMR.0000000000000254.

EuroQol Group, 1990. EuroQol–a new facility for the measurement of health-related quality of life. Health Policy 16, 199–208. https://doi.org/10.1016/0168-8510(90)90421-9.

Fischer, J.S., Rudick, R.A., Cutter, G.R., Reingold, S.C., National MS Society Clinical Outcomes Assessment Task Force, 1999. The Multiple Sclerosis Functional Composite measure (MSFC): an integrated approach to MS clinical outcome assessment. Multiple Sclerosis 5, 244–250. https://doi.org/10.1177/135245859900500409.

Fogarty, E., Walsh, C., Adams, R., McGuigan, C., Barry, M., Tubridy, N., 2013. Relating health-related Quality of Life to disability progression in multiple sclerosis, using the 5-level EQ-5D. Mult. Scler. 19, 1190–1196. https://doi.org/10.1177/1352458512474860.

Goverover, Y., Genova, H.M., DeLuca, J., Chiaravalloti, N.D., 2017. Impact of Multiple Sclerosis on Daily Life. In: Chiaravalloti, N.D., Goverover, Y. (Eds.), Changes in the Brain. Springer, New York, New York, NY, pp. 145–165. https://doi.org/10.1007/978-0-387-98188-8_7.

Hobart, J., 2001. The Multiple Sclerosis Impact Scale (MSIS-29): a new patient-based outcome measure. Brain 124, 962–973. https://doi.org/10.1093/brain/124.5.962.

INVOLVE, 2015. Public Involvement in research: Values and Principles Framework.

Johansson, S., Ytterberg, C., Claesson, I.M., Lindberg, J., Hillert, J., Andersson, M., Widén Holmqvist, L., von Koch, L., 2007. High concurrent presence of disability in multiple sclerosis: associations with perceived health. J. Neurol. 254, 767–773. https://doi.org/10.1007/s00415-006-0431-5.

Kalb, R., Brown, T.R., Coote, S., Costello, K., Dalgas, U., Garmon, E., Giesser, B., Halper, J., Karpatkin, H., Keller, J., Ng, A.V., Pilutti, L.A., Rohrig, A., Van Asch, P., Zackowski, K., Motl, R.W., 2020. Exercise and lifestyle physical activity recommendations for people with multiple sclerosis throughout the disease course. Mult. Scler. 26, 1459–1469. https://doi.org/10.1177/1352458520915629.

Khan, F., Turner-Stokes, L., Ng, L., Kilpatrick, T., Amatya, B., 2007. Multidisciplinary rehabilitation for adults with multiple sclerosis. Cochrane Database Syst. Rev. https://doi.org/10.1002/14651858.CD006036.pub2.

Kurtzke, J.F., 1983. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). Neurology. 33 https://doi.org/10.1212/WNL.33.11.1444.

Lamers, I., Maris, A., Severijns, D., Dielkens, W., Geurts, S., Van Wijmeersch, B., Feys, P., 2016. Upper Limb Rehabilitation in People With Multiple Sclerosis: a Systematic Review. Neurorehabil. Neural Repair. 30, 773–793. https://doi.org/10.1177/1545968315624785.

Learmonth, Y.C., Dlugonski, D., Pilutti, L.A., Sandroff, B.M., Klaren, R., Motl, R.W., 2013. Psychometric properties of the Fatigue Severity Scale and the Modified Fatigue Impact Scale. J. Neurol. Sci. 331, 102–107. https://doi.org/10.1016/j.jns.2013.05.023.

Maggio, M.G., Stagnitti, M.C., Rizzo, E., Andaloro, A., Manuli, A., Bruschetta, A., Naro, A., Calabrò, R.S., 2023. Limb apraxia in individuals with multiple sclerosis: Is there a role of semi-immersive virtual reality in treating the Cinderella of neuropsychology? Mult. Scler. Relat. Disord. 69, 104405. https://doi.org/10.1016/j.msard.2022.104405.

Manuli, A., Maggio, M.G., Tripoli, D., Gullì, M., Cannavò, A., La Rosa, G., Sciarrone, F., Avena, G., Calabrò, R.S., 2020. Patients' perspective and usability of innovation technology in a new rehabilitation pathway: an exploratory study in patients with multiple sclerosis. Mult. Scler. Relat. Disord. 44, 102312 https://doi.org/10.1016/j.msard.2020.102312.

Penta, M., Tesio, L., Arnould, C., Zancan, A., Thonnard, J.L., 2001. The ABILHAND questionnaire as a measure of manual ability in chronic stroke patients: rasch-based validation and relationship to upper limb impairment. Stroke 32 (7), 1627–1634. https://doi.org/10.1161/01.str.32.7.1627. PMID: 11441211.

Phillips, G.A., Wyrwich, K.W., Guo, S., Medori, R., Altincatal, A., Wagner, L., Elkins, J., 2014. Responder definition of the Multiple Sclerosis Impact Scale physical impact subscale for patients with physical worsening. Mult. Scler. 20, 1753–1760. https://doi.org/10.1177/1352458514530489.

Riazi, A., Hobart, J.C., Lamping, D.L., Fitzpatrick, R., Thompson, A.J., 2002. Multiple Sclerosis Impact Scale (MSIS-29): reliability and validity in hospital based samples. J. Neurol. Neurosurg. Psychiatry 73, 701–704. https://doi.org/10.1136/jnnp.73.6.701.

Rietberg, M.B., Brooks, D., Uitdehaag, B.M., Kwakkel, G., 2005. Exercise therapy for multiple sclerosis. Cochrane Database Syst. Rev. https://doi.org/10.1002/14651858.CD003980.pub2.

Rooney, S., McFadyen, D.A., Wood, D.L., Moffat, D.F., Paul, P.L., 2019. Minimally important difference of the fatigue severity scale and modified fatigue impact scale in people with multiple sclerosis. Mult. Scler. Relat. Disord. 35, 158–163. https://doi.org/10.1016/j.msard.2019.07.028.

Simmons, R.D., Tribe, K.L., McDonald, E.A., 2010. Living with multiple sclerosis: longitudinal changes in employment and the importance of symptom management. J. Neurol. 257, 926–936. https://doi.org/10.1007/s00415-009-5441-7.

Snook, E.M., Motl, R.W., 2009. Effect of exercise training on walking mobility in multiple sclerosis: a meta-analysis. Neurorehabil. Neural Repair. 23, 108–116. https://doi.org/10.1177/1545968308320641.

Thomson, A., 2019. Re-doing patient experience through design-led research. https://doi.org/10.25602/GOLD.00026288.

Yozbatıran, N., Baskurt, F., Baskurt, Z., Ozakbas, S., Idiman, E., 2006. Motor assessment of upper extremity function and its relation with fatigue, cognitive function and quality of life in multiple sclerosis patients. J. Neurol. Sci. 246, 117–122. https://doi.org/10.1016/j.jns.2006.02.018.