Original Paper

# Upper Limb Impairment and the potential role of Virtual Reality in the Rehabilitation of the Upper Limb in Multiple Sclerosis: views of specialist clinicians and people with MS.

Amy Webster (MSc)a\*, Matthieu Poyade (PhD)b, Elaine Coulter (PhD)a, Lisa Forrest (MSc)a and Lorna Paul (PhD)a

a School of Health and Life Sciences, Glasgow Caledonian University, Glasgow, United Kingdom.

b School of Simulation and Visualisation, Glasgow School of Art, Glasgow, United Kingdom.

\*Corresponding Author: Amy Webster, School of Health and Life Sciences, Glasgow Caledonian University, Cowcaddens Road, Glasgow, G4 0BA. Email address: [Amy.Webster@gcu.ac.uk](mailto:Amy.Webster@gcu.ac.uk)

Word count: 7304

No. of tables: 3

No of figures: 2

No of Multimedia Appendices: 4

# Upper Limb Impairment and the potential role of Virtual Reality in the Rehabilitation of the Upper Limb in Multiple Sclerosis: views of specialist clinicians and people with MS.

## Abstract

**Background:** Finding enjoyable and effective long-term approaches to rehabilitation for improving upper limb (UL) function for people with multiple sclerosis (pwMS) is challenging. Using virtual reality (VR) could be a solution to this challenge however; there is a lack of reporting on pwMS’ and clinicians’ views on VR-based approaches and recommendations for games for rehabilitation.

**Objective:** To identify common UL problems and their related current therapeutic approaches in pwMS and 2) to explore the opinions of pwMS and specialist clinicians’ on VR and suggestions for development and design of VR games.

**Methods:** Separate focus groups were conducted with pwMS, recruited through the MS Society UK’s research network, and clinicians, recruited through the UK’s Therapists in MS network. Ten pwMS (two focus groups) and eight clinicians (five physiotherapists, two occupational therapists and one MS-nurse, two focus groups) were involved. Focus groups were recorded and transcriptions analyzed using theme-based content analysis (TBCA).

**Results:** People with MS commonly reported their UL problems interfered with activities of daily living (ADL) and resulted in the loss of meaningful hobbies such as writing. Many pwMS neglected UL exercise and found strategies for adapting to the UL impairments. Similarly, clinicians stated UL rehabilitation was neglected within their service and that it was challenging to find interesting treatment strategies. VR was suggested by both participant groups as a solution, being convenient for pwMS to access and could provide a more engaging and disguised approach to exercise. There were shared concerns with cybersickness and disengagement with using VR approaches. Both groups agreed games should be meaningful and adaptable for users, but suggested different VR activities, with clinicians suggesting games directly reflecting ADL and pwMS more abstract activity.

**Conclusions:** VR was well received by both pwMS and clinicians for UL rehabilitation. Recommendations are made for the development of VR rehabilitation games which are personalized and customizable for the varying ability of pwMS.

**Keywords:** virtual reality; multiple sclerosis; upper limb rehabilitation; co-production; activities of daily living; exercise games

## Introduction

Multiple sclerosis (MS) is an inflammatory demyelination disorder of the central nervous system that is estimated to affect 2.8 million people worldwide [1]. Over a third of people with MS (pwMS) have upper limb (UL) dysfunction, including weakness, tremor and spasms in one or both ULs [2]. This can result in difficulties with activities of daily living (ADL), negatively impacting quality of life and likelihood of remaining in employment [3, 4]. Problems specifically with dexterity are related to higher healthcare costs [5] and a higher association with depressive-like psychological measures compared to problems with lower limb function [6]. Rehabilitation and physical exercise improve motor function for pwMS [7, 8]. The evidence regarding UL rehabilitation is lacking in comparison to the lower limb, despite the high frequency of UL impairments and their impact on ADL [9]. In addition, there are particular challenges in finding effective yet motivating rehabilitation strategies in MS due to the long-term, progressive nature of the disease and diversity of symptoms [10].

Virtual reality (VR) is increasing in popularity in rehabilitation research and is proposed as a possible approach to encourage long term rehabilitation [11]. VR includes digital environments that often simulate real world experiences with reported benefits of high motivation and engagement, with real-time feedback [12]. VR has shown promising results within MS populations but this evidence is limited in comparison to stroke, especially regarding UL function [13]. Our systematic review, investigating the effect of VR in improving UL function in MS, found early, but limited, evidence suggesting VR has the potential to improve function in pwMS [14]. There was also a low number of drop outs in most studies within the review, supporting that VR could improve adherence compared to conventional rehabilitation, therefore VR could be useful in conditions like MS, where prolonged rehabilitation is required.

VR is often investigated alongside video games played within a VR setting, which can be commercially available or specifically tailored games designed with a target population in mind. Commercially available exercise games, targeted at a healthy population, can be unsuitable for disabled individuals, and lead to discouragement and anxiety [15]. It is beneficial to involve a sample of target users in the creation and development of effective VR based gamified approaches [16]. This process is known as co-production [17]. To date no studies have systematically co-produced VR games specifically for UL rehabilitation in pwMS.

Therefore, the aims of the current study were to determine the views of pwMS and specialist clinicians on UL (dys)function in MS, challenges faced by clinicians when delivering UL therapy, barriers and motivators for exercise in MS, opinions on VR and suggestions for development and design of VR games. These findings will guide the future development of VR applications and interventions for UL rehabilitation for pwMS.

## Methods

### Ethical Statement

Ethical approval for this study was given by the School of Health and Life Sciences Ethics Committee at Glasgow Caledonian University (ref: HLS/PSWAHS/20/002).

### Recruitment

The study aimed to recruit up to 12 pwMS and 12 specialist MS clinicians to take part in online focus groups. Sample size was determined in line with other similar studies’ design and general recommendations for qualitative analysis [18, 19]. To be included in the study pwMS were required to be aged 18 years or over, have a diagnosis of MS (self-reported) with self-reported UL impairment. Clinicians were required to have experience (any duration) in delivering MS rehabilitation within the NHS and/or third sector. In addition, all participants had to have access to, and ability to operate video conference software. There were no specified exclusion criteria. Participants with MS were identified through the MS Society UK’s research network who advertised the study to its members. Those who were interested in taking part contacted the research team directly, were emailed a participant information sheet and provided informed consent. In terms of recruitment of clinicians, the MS Trust Therapists in MS network advertised the study to its members. Interested clinicians contacted the research team, were emailed a participant information sheet and provided informed consent.

### Co-production Focus Groups

The focus groups for pwMS and clinicians were conducted separately with a maximum of five people per focus group. To comply with COVID regulations at the time, focus groups were held online using Zoom or MS Teams video conference software, this also provided an opportunity for recruitment of participants from across the UK and Ireland. The focus groups were conducted in a semi-structured style using a focus group schedule split broadly into three sections important for development of VR interventions for UL problems in MS: UL (dys)function and exercise/therapy; opinions on VR and suggestions for development and design of any developed VR games (Multimedia Appendix 1). In addition, clinicians were asked what information/feedback they would want from a patient’s VR therapy session. The questions included prompts which allowed more targeted responses from participants regarding their experiences and views [20]. Within the focus groups participants were shown three videos demonstrating different commercially available head mounted devices (HMDs) and hand tracking devices; 1) a non-immersive VR set up using a Leap Motion controller and computer monitor, which is a hand motion capture device that allows users to visualize their hand movements and interact with virtual environments; 2) immersive VR using the Oculus Rift HMD with a mounted Leap Motion device for hand tracking; 3) immersive VR utilizing the Oculus Quest, with in-built hand tracking (Figure 1; Multimedia Appendix 2). Videos were shown since participants were unable to try these devices, and to contextualize and demonstrate these different VR and motion capture devices, in terms of users interacting with environments, hand movements possible, and previous games developed from prior research. After watching the videos, participants were encouraged to share their initial thoughts on each of the technologies. The focus groups involving pwMS and clinicians lasted approximately 90 minutes 60 minutes respectively. The focus groups were facilitated by a female researcher (AW) who had been involved in recruitment of participants, and an additional senior, female researcher (LP) attended.

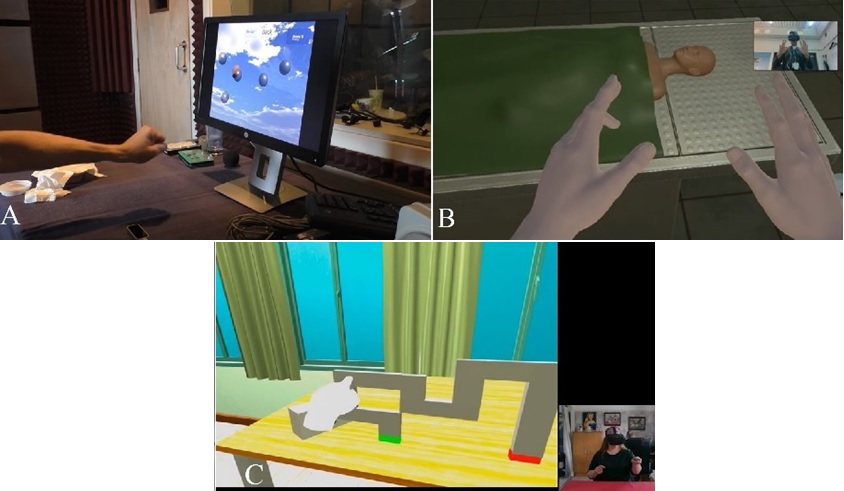


Figure 1: Stills from videos shared with participants during focus groups, demonstrating different VR technology. A) Video 1 showing Leap Motion only [21]; B) Video 2 showing Leap Motion and Oculus Rift; and C) Video 3 showing Oculus Quest [22].

### Data Analysis

All focus groups were audio recorded and transcribed verbatim. Qualitative analysis of the data was performed based on Theme-Based Content Analysis (TBCA) as described by Neale and Nichols [23]. This qualitative method groups responses into content related themes to enable researchers to view the user preferences easier and has been used to influence the development, or evaluation, of a VR environment [23-25]. TBCA is a flexible qualitative data analysis method which involves five key steps 1) data collection; 2) data collation; 3) raw theme definition and classification; 4) higher order theme selection; and 5) presentation of classification matrix [23]. Due to the large number of higher order themes, we added an additional step by grouping the higher order themes into main themes. The raw themes were assigned independently by two researchers in the pwMS (AW & LF) and clinicians (AW & LP) transcripts. After agreement on the raw themes, the responses were then independently grouped by two researchers (AW & LP) into higher order themes. Any discrepancies in assigning themes were resolved through consultation with a third reviewer if necessary. Once the higher order themes were determined, main themes, were determined by two researchers (AW & LP). The main themes with their associated raw and higher order themes are presented in tables. The raw and higher order themes were quantified manually within the matrix based on the number of responses to display popularity or consensus [23] and example quotes for each for each higher order theme were included. Focus groups of pwMS and clinicians were analyzed separately and then the findings compared to allow between the two groups.

## Results

### Participant Demographics

Ten pwMS were recruited to the study and took part in one of two focus groups; each of which had five participants. The majority of participants with MS were female (7 female; 3 male), mean age of 56.4 (± 16.5) years with a mean time since diagnosis of 14.4 (± 12.3) years. Participants had varying MS types (Table 1).

Table 1: Demographic details for people with MS

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Participant ID** | **Age (years)** | **Sex** | **MS Type** | **Time since diagnosis (years)** |
| P1 | 60 | F | SPMS | 30 |
| P2 | 38 | F | RRMS | 4 |
| P3 | 68 | M | SPMS | 35 |
| P4 | 58 | F | SPMS | 1 |
| P5 | 42 | F | SPMS | 11 |
| P6 | 28 | F | RRMS | 3 |
| P7 | 56 | F | PPMS | 5 |
| P8 | 70 | M | PPMS | 16 |
| P9 | 60 | M | SPMS | 12 |
| P10 | 84 | F | SPMS | 27 |
| Mean ± SD | 56.4 ± 16.5 |  | | 14.4 ± 12.3 |

Abbreviations: F (female); M (male); PPMS (primary progressive MS); RRMS (relapse and remitting MS); SD (standard deviation); SPMS (secondary progressive MS).

Eight clinicians were recruited (five physiotherapists, two occupational therapists and one MS specialist nurse), six participants worked in the National Health Service and two in other settings. There were two focus groups for clinicians with four participants in each. All clinicians were female, mean age of 46.2 (± 9.6) years and the mean length of experience was 17.9 (±10. 2) years.

### People with MS - Theme Based Content Analysis (TBCA)

Following TBCA of the focus groups of pwMS, 20 higher order themes were determined based on the grouping of the assigned raw themes. These 20 higher order themes were grouped into four main themes: 1) Impact of MS on the Upper Limb; 2) Exercising with MS; 3) People with MS’ Views on Virtual Reality; and 4) Recommendations for Development and User Requirements (Table 2). A full version of this table, including more example quotes from participants, is available as Multimedia Appendix 3.

Table 2: Main, Higher Order and Raw Themes from TBCA People with MS Focus Groups

|  |  |  |
| --- | --- | --- |
| **Main Theme** | **Higher Order Themes (No. of Responses)** | **Raw Themes (No. of Responses)** |
| Impact of MS on the Upper Limb | Interference with Functional Activities (35) | Dressing (8); Eating (6); Dropping Items (5); Writing (5); Grooming (3); Dependence on Others for ADLs (3); Carrying Items (3); Travelling (2) |
| Symptoms and Signs that Impact Activities (25) | Fatigue (10); Numbness (6); Sensory Overload (4); Weakness (3); Tremors (2); Proprioception (2); Coordination (1) |
| Strategies People with MS Adopt to Assist with Activities of Daily Living (24) | Strategies for Functional Activities (8); Adapting (7); Making Difference (5); Technology Assistance (2); Mobility-assistance Equipment (2) |
| Struggle with Loss of Meaningful Activities and Skills (14) | Loss of Skills (6); Impact of Losing Ability to Write (4); Keeping Meaningful Activities (4) |
| Upper Limb Actions People with MS Find Difficult (13) | Dexterity (6); Range of Motion (4); Grip (3) |
| Sharing and Sympathy (13) | Sharing Strategies (4); Sharing Advice on Exercise (4); Taking Advice (3); Sympathising (2) |
| Difficulty with Progression and Unpredictable nature of MS (10) | Variation in MS (6); Unpredictable (2);  Progression (2) |
|  |  |  |
| Exercising with MS | Views and Attitudes on Exercise (49) | Maintenance (10); Negative Perceptions of exercise (8); Keeping muscle strength (8); Determined to Exercise (7); Benefits of Exercise (6); Multitask Approach (4); Legs Focus (3); In control (3) |
| Previous Experience of Upper Limb Rehabilitation/ Exercise (40) | Outcomes from UL Exercise/Rehab (12); Neglecting UL Exercise or Rehabilitation (10); UL Equipment (6); UL Physiotherapy (4); Driven for UL exercise (3); UL Exercise Resources (3); Adherence (2) |
| Barriers to Exercise (28) | Personal Barriers (8); Environmental Barriers (8); COVID Barriers (7); Verbal Disengagement (5) |
| Facilitators to Exercise (28) | Verbal Encouragement (10); Health Care Professionals (8); MS Centre (4); Gym Facilitators (3); Pushing self for Results (3) |
| Adverse Effects of Exercise (11) | Induce Symptoms (4); Tiring (3); Recovery time after exercise (2); Affecting Socializing (1); Overdoing Exercise (1) |
| Approaches to Exercise used by People with MS (26) | Routine (7); Exercise Bikes (6); Exercise Aims (5); Low Impact/Stretching Exercise (4); Physiotherapy Approaches (4) |
| Views on Group versus Individual Exercise (26) | Competition in Exercise (10); Motivation of group exercise (5); Downsides of group Exercise (5); Importance of socializing in Exercise (2); Camaraderie (2); Enjoyment (1); Interest in Group Exercise (1) |
|  |  |  |
| People with MS’ Views on VR | Positive Views on VR (55) | Home Use (9); Outcome Benefits (6); Personal Opinions on VR (5); Fun (5); Adaptable (5); Positives of Technology (5); Wireless Convenience (5); Accessibility Convenience (4); Incentives (3); Meaningful (3); Online Socializing (2); Immersion (1) |
| Negative Views on VR (40) | Cybersickness (17); HMD Discomfort (6); Technology Discomfort (5); HMD Dislike (3); Disengagement (3); Accessibility Concerns (3); Unsuitability (3) |
| Views on Trying or Participating in VR Rehabilitation (25) | Openness to VR (12); Challenging (4); Safety Considerations (3); Need Results (2); Technology Considerations (2); Unsuitable for them (2) |
|  |  |  |
| People with MS’ Recommendations for Development and User Requirements | Considerations for Development of VR Games (84) | Mindful of Target Audience (9); Tracking Progress (8); Discouragement of Feedback (8); Knowing UL Outcomes (7); End Result (6); Score Targets (6);  Challenging Self (6); Competition in Games (5); Education (5);  Time Feedback (4); Supervision (4) Community Involvement (3); Multipurpose (3); Continuous development (3); Be Fun (3); Hardware (2); Learning Patterns Concern (2) |
| Suggestions for VR Activities (36) | Suggested UL Actions (9); Game Ideas (7); Real Life vs. Abstract Tasks (4); Haptic Activities (4); Strength in Games (4); Writing and Drawing (3); Demonstrated Games (3); Additional Objectives (2); Atmosphere (1) |
| Importance of Choice (23) | Offer Different Movements (8); Having Variety of Games (6); Personal preferences (6); Variety of Different Levels (3) |

#### Impact of MS on the upper limb

The most common higher order theme was ‘Interference with Functional Activities’ with 35 responses (Table 2). Participants reported a wide range of activities they found difficult due to their MS, the most frequent being ADLs including personal care, eating and carrying heavy items. ‘Symptoms and Signs that Impact Activities’ had the second highest number of responses (N = 25) where participants particularly noted the impact of fatigue on activity (N = 10), however sensory problems such as numbness and pins and needles were also highlighted. Other MS symptoms impacting UL function were e.g. weakness, tremors, co-ordination problems. In ‘Strategies People with MS Adopt to Assist with ADL’ (N = 24), as a result of losing function, participants discussed the use of assistive equipment e.g. button fasteners and specialized cups and voice control. Other strategies were using their less affected hand or pacing to manage fatigue. The remaining four higher order themes had fewer responses. In brief, dexterity, range of joint movement and grip were the main ‘Upper Limb Actions People with MS Find Difficult’ (N = 13). These were often compounded by the unpredictability and progressive nature of MS (‘Difficulty with Progression and Unpredictable nature of MS’; N = 10). Participants reported the emotional impact of losing the ability to carry out personal and meaningful activities specifically as a consequence of loss of UL function (‘Struggle with Loss of Meaningful Activities and Skills’ N = 14). With one participant stating:

“I used to be a writer and it was very, very hard because I couldn’t write anymore… I was really motivated [to relearn writing], felt really cut off from the world” (P8, age 70 male with PPMS)

The final higher order theme was ‘Sharing and Sympathy’ (N = 13 responses), where participants empathized and shared experiences and suggestions of assistive equipment.

#### Exercising with MS

Most responses under this main theme related to ‘Views and Attitudes on Exercise’ (N = 49) (Table 2). Participants were motivated to exercise with a “use it or lose it” attitude and a desire to, if not improve then at least maintain, their function and prevent further deterioration. Participants also described negative perceptions of exercise such as finding it “very boring” and guilt from not participating in exercise. In ‘Previous Experience with Upper Limb Rehabilitation/Exercise’ (N = 40), many participants discussed not undertaking any UL exercise or rehabilitation, currently or previously. Many UL programs previously undertaken by some aimed to build strength, reduce pain and improve hand function; with variable outcomes. There were similar numbers of responses in terms of ‘Barriers to Exercise’ (N = 28) and ‘Facilitators to Exercise’ (N = 28). Personal barriers to exercise included co-morbidities, MS symptoms (fatigue, pain bladder and bowel), difficulty using exercise equipment and expense. COVID had negatively impacted on the participants’ exercise due to services closing down. Environmental barriers to exercise included lack of local facilities and not having space to exercise at home. Verbal encouragement was described as both a barrier (could be off putting) and a facilitator (motivating) to exercise. Other facilitators were seeing improvements, feeling motivated, and the attitudes of healthcare professionals, personal trainers and carers. Conversely healthcare professionals with lack of experience in MS lead to adverse effects for pwMS, such as feeling exhausted (‘Adverse Effects of Exercise’ N = 11). Participants undertook many different forms of exercise (‘Approaches to Exercise used by People with MS’ N = 26) including exercise bikes, Pilates and yoga, dog walking and gym exercises. There were varying ‘Views on Group versus Individual Exercise’ (N = 26). Some found competition within a group to be motivating while others did not, with one participant suggesting social support and camaraderie was more important than competition:

“I’m not too fussed about being in competition with others, but if it was a more social thing that would maybe encourage me to perhaps join in a group that’s doing something together” (P4, age 58 female with SPMS)

Negative aspects of group exercise included the fear of letting others down.

#### Views on Virtual Reality

The initial reaction to VR was positive (‘Positive Views on VR’ N = 55) (Table 2). Participants stated it looked fun or enjoyable with the potential to improve or maintain muscle strength, dexterity, and spatial awareness, especially with repeating the actions and concurrently perhaps learning a new skill (e.g. piano playing):

“I think [VR’s] still very good because… it’s… maintaining those motor skills that is so easily slip away when you’re not using them” (P9, age 60 male with SPMS)

There were positive comments in relation to the convenience and accessibility of VR facilitating exercise at home at a time to suit, eliminating travel to physiotherapy and gyms. Participants highlighted that the wireless HMD was more convenient being portable and not needing a computer. The advantage of linking up with others online was raised. However, ‘Negative Views on Virtual Reality’ (N = 40) related to concerns regarding cybersickness, linked to dizziness and balance problems:

“With MS a lot of people suffer from nausea or motion sickness. That can be a concern for the headsets” (P6, age 28 female with RRMS)

Other negative responses related to the HMD; discomfort regarding weight, usability concerns, wearing with glasses and being disconnected from the real world. A few participants raised that interest in VR may reduce over time. Participants were also concerned about fatigue and the usefulness of VR for UL sensory dysfunction. The majority of participants were open to trying VR (‘Views on Trying or Participating in VR Rehabilitation’) but would like to understand the benefits, long term outcomes and any safety issues.

#### Recommendations for Development and User Requirements

With regards ‘Considerations for Development of VR games’ (N = 84), a variety of UL movements was desirable with clarity in terms of the aim and outcome in relation to the UL being important (Table 2). Competition within the VR games; interacting with others or challenging themselves were frequently discussed as being motivating. Tracking improvements during VR gameplay was vital to some participants, including monitoring improvements in score, exercise time (rather than countdown which could be stressful), progressive challenges. The games should offer the ability to challenge users, with one participant saying:

“That challenge to try and be better the next time, whereas if you’ve got no idea… you’ve got nothing to fight against or to work against” (P10, age 84 female with SPMS)

Conversely other participants emphasized the potential demotivating effect of feedback given the progressive nature of MS, by warning score feedback should not be “disheartening”, therefore should optional to the user. There was a strong feeling that the VR games should be “fun” with abstract gameplay potentially being more fun. Participants felt demonstrations and supervision to assess progress were important. They also stated the VR games had to account for the differences in ability of pwMS and that older people may need more basic VR games. The idea of the VR games having an educational outcome or learning a new skill was suggested to help with engagement. Participants suggested reaching, punching and other aerobic activities could be incorporated (‘Suggestions for VR Activities’ (N = 36)). Having haptic approaches was frequently proposed with gripping, squishing games such as kneading bread. Participants proposed activity with a cognitive element such as a puzzle or maze, and whole limb movements such as Whack-a-mole or writing/drawing. Participants liked the VR piano which had been demonstrated. There was a variety of opinions in terms of abstract or real-life activity with most preferring abstract games but some ADL type activity also suggested. ‘Importance of Choice’ (N = 23) related to having variety in games, UL movements and levels of difficulty with abstract games or real-life gamified tasks, with one participant declaring:

“I’d like to make sure I’m not doing a whole lot of exercises that are all doing the same things… Got to be mixing them up: one for coordination, one for dexterity” (P1, age 60 female with SPMS)

### Clinicians Theme Based Content Analysis (TBCA)

From the clinician focus groups there were 15 higher order themes grouped into four main themes: 1) Current Methods and Challenges for Delivering Upper Limb Rehabilitation; 2) Clinicians’ Views on Virtual Reality; 3) Recommendations for Development and User Requirements; and 4) Implementation of Virtual Reality into Practice (Table 3). A full version of this table, including more example quotes from participants, is available as Multimedia Appendix 4.

Table 3: Main, Higher Order and Raw Themes from TBCA Clinician Focus Groups

|  |  |  |
| --- | --- | --- |
| **Main Themes** | **Higher Order Themes (No. of Responses)** | **Raw Themes (No. of Responses)** |
| Current Methods and Challenges for Delivering Upper Limb Rehabilitation | Challenges Clinicians Face when Delivering Exercise for People with MS (52) | MS-specific challenges (13); Patient Adherence (11); Service Challenges (9); UL related challenges (7); Patient Differences (6); Challenges with current methods of delivery (4); COVID impacts (2) |
| Recommended Upper limb Exercises for People with MS (29) | Actions (10); Systematic Approach (7); Functional Tasks (6); Strength and range of movement (5); Relapse care (1) |
| Experience with Long Term, Progressive Condition (24) | Deterioration (11); Acceptance in Patients (8); Difficulty with Patient Improvements (5) |
| Factors Clinicians Consider when Prescribing Exercise for the Upper Limb (22) | Meaningful and Patient Focused (9); Patient Assessments (6); Symptoms (4); Repetition (3) |
| Current Methods of Upper Limb Exercise Delivery for People with MS (15) | Technological Approaches (4); Programmes (4); Accessible Equipment (3); Clinician Routines (2); Patient Lead (2) |
| Socializing in Exercise (14) | Social motivation (6); Support (5); Recommending social exercise (3) |
|  | | |
| Clinicians’ Views on Virtual Reality | Positive Views on VR (50) | Solutions to current challenges (10); Personal Opinions on VR (7); Facilitating movements/tasks (6); VR-specific qualities (6); Meaningful (5); Engagement (5); Visualisation (4); Novel (3); Cognitive appeal (2); Adaptability (2) |
| Negative Views on VR (38) | Disengagement (10); Cybersickness and safety (8); HMD discomfort (7); Accessibility concerns (5); Feedback concerns (5); Validity concerns (3) |
| Questioning Benefits and the Unknowns of VR (14) | Questioning Purpose of VR (4); Questioning Benefits of VR (4); Neural Mechanisms (3); Research (2); Different VR systems (1) |
|  | | |
| Clinicians’ Recommendations for Development and User Requirements | Considerations for Developing VR Games for People with MS (41) | Communication between clinician and patient (12); Purposeful (7); Social components (5); Selecting tasks (4); Slower tasks (3); Competition (3); Feedback for clinician (3); Positive Feedback (2); End point (2) |
| Suggestions for VR Activities (18) | ADL Activities (6); Hobbies (6); Objectives (6) |
| Importance of Choice (15) | Preferences (6); Having Variety (5); Set Up (4) |
|  | | |
| Implementation of VR into Practice | Suggestions for Incorporation of VR into Practice (18) | Home use (7); VR in Clinics (7); Long term treatment (4); |
| Challenges with Implementation of VR into Practice (24) | Funding (7); Demanding on Services (6); Availability of Equipment (5); Risk (3); Adjustment (2); Uncertainty of Practice (2) |
| Finding the Target Audience for VR (8) | Who would use VR (3); Niche Group (3); Age (2) |

#### Current Methods and Challenges for Delivering Upper Limb Rehabilitation

‘Recommended UL Exercises for People with MS’ (N = 29) included strength training and active movements related to functional activity such as hand to mouth movements (Table 3). Treatment for the UL often involved equipment such as Therabands and Theraputty but also technology such as the Gloreha robotic system and functional electrical stimulators with different models of care for UL exercises described as part of community-based classes, within third sector organizations and online programs (‘Current Methods of UL Exercise Delivery for People with MS’ (N = 15)). Within ‘Factors Clinicians Consider when Prescribing Exercise for the UL’ (N = 22) most responses were regarding meaningful, goal focused exercises. Clinicians also considered the patient’s symptoms e.g. spasticity, pain, and the ability of patients. The importance of repetition of movement was reinforced. Most responses were in relation to ‘Challenges Clinicians Face when Delivering Exercise for People with MS’ (N = 52). Clinicians expressed that UL-focused exercise was neglected compared to the lower limb and the challenge of making UL exercise interesting:

“A bit more difficult for upper limb things… it’s much easier to maybe… go for a walk with somebody or you know, or cycle or whatever. Upper limb is maybe a wee bit more difficult” (C6, PT)

Clinicians also mentioned the use of Theraputty described as “juvenile” and lists of exercises “boring”.

Service related challenges included limited time and capacity to see patients and large geographical areas to cover. Other challenges were keeping patients engaged long term with exercise, especially at home, and finding an activity that would be attractive to patients. Under ‘Experience with Long Term, Progressive Condition’ (N = 24) clinicians raised being realistic about improvements with a progressive condition whilst also keeping patients motivated, minimizing deterioration or maintenance, rather than improving.

“Trying to motivate people with progressive MS, you’re trying to get them to continue to maintain where they are rather than improve” (C5, OT)

Clinicians expressed the positive benefits of ‘Socializing in Exercise’ (N = 14) for support and motivation.

#### Clinicians’ Opinions on Virtual Reality

Clinicians were very positive about VR (N = 50) describing it as being interactive, fun, meaningful and a novel potential approach to rehabilitation which could help engagement (Table 3). They were positive about the escapism aspect and the potential to improve mental health:

“What appeals about VR stuff is that it is focused and takes you into a different place… You’re doing tai chi on a beautiful, Japanese garden rather than actually in your grumpy living room… I think even that in terms of the escapism aspect, maybe from a mental wellbeing” (C1, PT)

Clinicians liked the visual feedback to help with e.g. co-ordination, but which could also reinforce movements and introduce a cognitive component. Clinicians commented that VR provided the opportunity to undertake activities not possible within the clinic and to exercise without the activity seeming like exercise. The majority of the ‘Negative Views of VR’ (N = 38) were regarding patient safety using VR headsets; cybersickness, including dizziness and disorientation, specifically in patients with vestibular issues. Other general concerns with HMDs were usability with glasses, the weight of the HMD and feeling claustrophobic. Clinicians suggested that VR activities should not be too simplistic to avoid patronizing patients and at an appropriate skill level. The longevity of engagement of patients after the initial novelty was questioned. Clinicians also questioned the use of VR for activities that can be done in the real world and similarly how VR activities might translate to real function. The importance of feedback on the quality of movement as well as the quantity was highlighted. Finally, accessibility and digital poverty were also raised. The final higher order theme was ‘Questioning Benefits and the Unknowns of VR’ (N = 14) where some clinicians felt there was insufficient evidence on the purpose and benefits of VR and its effect on neural mechanisms.

“I think it’s important to think about how is [VR] different to just doing [activities] in real life as well… What can you augment in your rehab through this virtual reality that you can’t just do in real life anyway?” (C7, PT)

#### Recommendations for Development and User Requirements

Under ‘Considerations for Developing VR Games for People with MS’ (N = 41) clinicians discussed the importance of the VR games having purposeful activity, translation of tasks into real life and having an endpoint (Table 3). The games should consider movements of individual joints of the UL with extension movements at the wrist and fingers being important as where pwMS lose the most function. Games should incorporate strength, co-ordination, proprioception and range of motion exercise as well as exercises for the core. Feedback was important, with clinicians able to monitor the program. Clinicians were not interested in scores for the games but wished feedback on the quality of the movements and patient engagement. Clinicians stated that undertaking VR activities with others or in group settings with elements of competition was desirable. Clinicians gave ‘Suggestions for VR activities’ (N = 18), including ADL activities such as putting on makeup, writing or chopping vegetables, and hobbies such as pottery, sewing or piano playing. Clinicians raised the ‘Importance of Choice’ (N = 15), in the VR set up, choice of games and choice within games e.g. levels of difficulty, to appeal to as many people as possible:

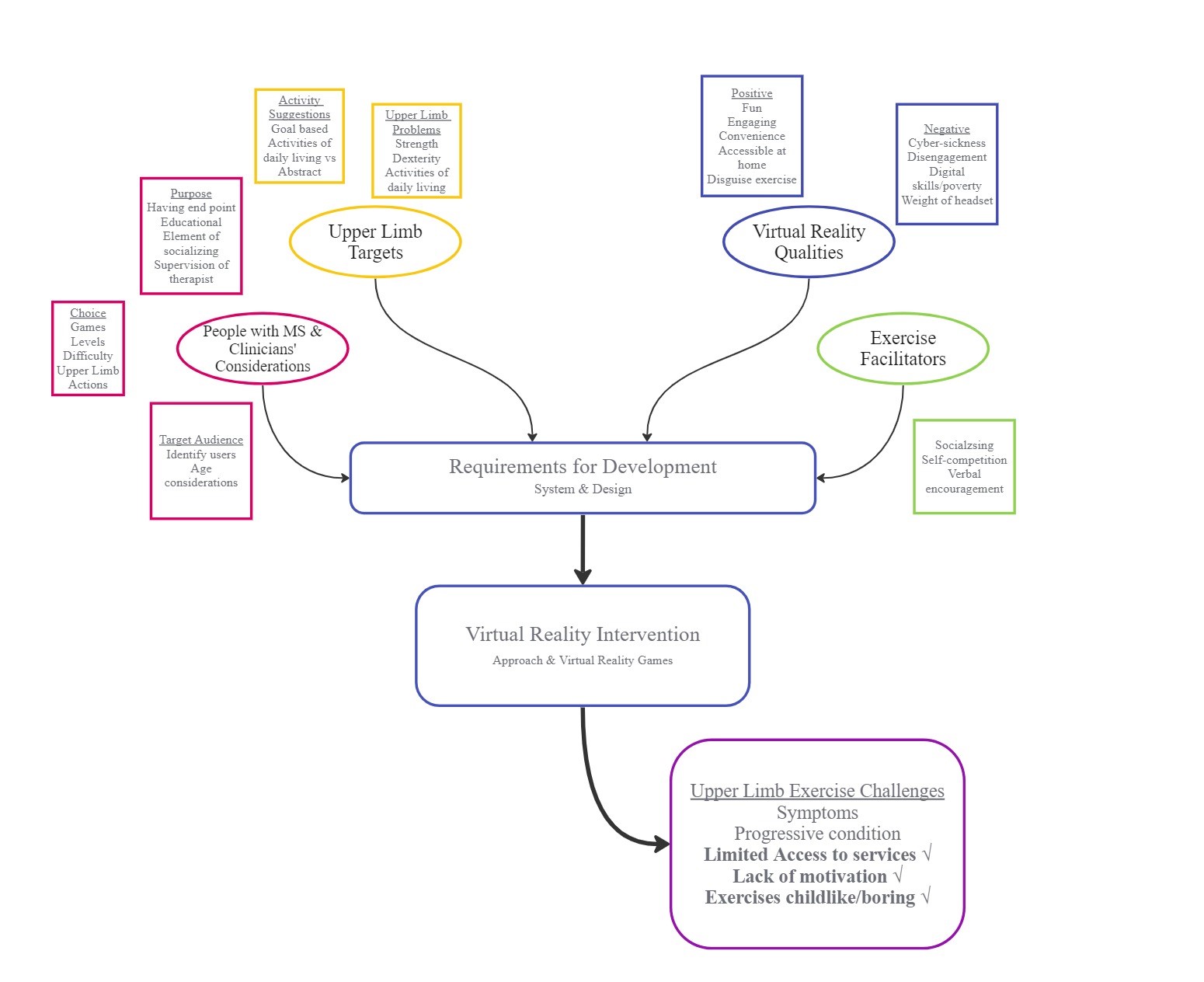
“I think, it is about having a variety of things that push as many buttons with patients that you can manage and cover as many options as you can” (C2, PT)

#### Implementation of Virtual Reality into Practice

Under ‘Suggestions for Incorporation of VR into Practice’ (N = 18) clinicians felt long term, regular use of VR was needed for positive outcomes (Table 3). Home use was felt to encourage frequent use with clinicians monitoring progress remotely, thus saving in person contact time. There were a number of ‘Challenges with Implementation of VR into Practice’ (N = 24) with cost and funding (service and individual) being the most commonly reported which included potential increased demand on services.

“I know if I brought it to my bosses they would want a breakdown of cost of monthly rate, how are we going to utilise it, how often are we going to utilise it. What figures could we get from this particular item and what outcomes could we achieve” (C4, MS Specialist Nurse)

Equipment related challenges were ownership, availability, supply of equipment and infection control. A full risk assessment would be required before implementation and guidance needed on intervention duration and frequency. Clinicians discussed for whom VR would be appropriate for, in terms of age or other factors and identified this as an area for future research (‘Finding the Target Audience for VR’ (N = 8)).

Figure 2: Flow diagram of the results from TBCA of people with multiple sclerosis and clinicians’ co-production focus groups and how this will guide the requirements for developing virtual reality based games/interventions, which will aim to tackle certain achievable upper limb exercise challenges within MS.

## Discussion

### Principle Findings

This study aimed to explore the views of pwMS and clinicians on UL impairment associated with MS and the potential role of VR as a rehabilitation approach to address this impairment. The discussion will focus on the combined findings from the two groups of participants; pwMS and clinicians (Figure 2). This figure is a visual representation of the principle findings, based on the higher number of responses assigned, which should inform the development of VR application and interventions aiming to improve UL function for pwMS, and how VR could tackle challenges of existing UL exercise raised by clinicians and pwMS in this study. The findings agree with previous studies, that pwMS commonly have UL impairments which impact on function, including problems with dexterity and ADLs, which leads to loss of meaningful activities [26-28]. Despite UL difficulties, UL exercise was neglected due to e.g. MS symptoms such as fatigue, lack of motivation and dislike of exercise and the challenges for clinicians of time constraints and finding appropriate therapies that were not childlike or boring. Lack of focus on UL rehabilitation has been reported previously in MS [9] and in other long term neurological conditions such as stroke [29]. The progressive and unpredictable nature of MS was raised by both groups and consequently clinicians raised the importance of setting realistic expectations with therapy; sometimes focusing on maintenance of function sometimes rather than improvement.

Both groups (pwMS and clinicians) were optimistic about the use of VR and believed VR could be a solution to their exercise challenges. Positive comments including avoiding travelling, being accessible, and being engaging or fun addressed the identified barriers for UL rehabilitation. This concurs with previous VR studies [30, 31] and specifically in UL rehabilitation in MS, with a recent home based, feasibility study using the Oculus Quest 2 VR headset in which participants described VR as fun, interesting and innovative [32]. Participants in the study by Kamm et al [32] suggested adding difficulty levels and scoring to their exercises, competitive elements previously described to be motivating by pwMS using non-immersive exercise games delivered through the Nintendo Wii [33]. In the present study both groups were especially positive regarding the immersive approach of the Oculus Quest. Participants thought the escapism properties and visualization of movements could potentially ‘disguise exercise’ which may occur with the ‘fun’ element of VR reducing the perception of exertion during exercise [34], therefore encouraging more UL therapy.

Negative views about VR were also expressed, mainly the potential for cybersickness. Cybersickness is thought to be caused by conflict of stimuli, leading to nausea, disorientation and pain in the eyes and head [35]. Woman are more susceptible to cybersickness [36], which is relevant in MS with a higher number of females affected. Although cybersickness with VR has been reported previously in pwMS [37], there are development strategies for reducing cybersickness such as designing VR activity with less overall movement within the virtual environment. Cybersickness is however thought to reduce over time with exposure to VR [38]. There were unnecessary concerns raised for those wearing glasses as the HMD can accommodate glasses, but there were valid concerns about the weight of the HMD for some users. Disengagement was another concern both groups expressed, with limited data on long-term adherence to VR in MS rehabilitation. Exercise is a behavioral intervention and long-term adherence to exercise can be supported by evidence based behavior change techniques (BCTs) [39]. These BCTs, such as goal setting, rewards and feedback (see below), can be incorporated into VR games/activity to support longer term engagement in UL exercise. While VR can be more engaging than other methods of exercise [40] frequent performance, feedback on progress and adjusting levels of difficulty can maximize VR engagement for those with long-term neurological conditions [41]. Finally, clinicians had specific concerns regarding digital poverty, the technical ability of the pwMS and insufficient technical services to support VR.

Considerations for VR game development align with user-centred design principles for VR in motor rehabilitation in stroke, such as being fun, tracking progress, having an element of competition, challenging oneself and providing feedback [42], and are not specific to any clinical population. Participants raised that VR development should be mindful of the different end users (pwMS) who may differ in ability and preferences. Clinicians suggested VR would appeal to younger individuals with MS, whereas pwMS felt older pwMS might need more basic gameplay. While there is some but limited evidence for lower usability scores for older VR users compared to younger users, there can be higher user enjoyment [43], and there is moderate evidence for good usability of VR in older populations [44], therefore this concern may be overly cautious. Consideration of the end user links to the importance of choice when designing VR interventions, with a variety of games to appeal to as many as possible. Participants felt the games should include different movements, levels of immersion, level of difficulty or feedback on performance (discussed below). Accommodating individual preferences is a key element for the design of VR games for rehabilitation, as it increases user engagement [45]. However, our previous systematic review found that a choice of games was rarely included in VR interventions in MS [14].

There were differing views in terms of the type of feedback people wished from VR. Some pwMS wanted to track scores and visualize results, which is supported by reward theories for users during both entertainment and serious games [46]. Conversely, concerns were raised about feedback potentially being discouraging or demotivating especially given the variable nature of MS. As an example, countdown timers provide slight pressure to motivate players to increase engagement [47] however pwMS in the present study felt they could be stressful. Feedback on the duration of exercise completed was appealing to pwMS, as reported previously [19]. As well as the quantity of VR exercise clinicians also wished feedback on the quality of movement when performing the games. Rehabilitation often involves highly repetitive movements to stimulate neuroplasticity however stroke-specialist therapists have also previously reported concerns that quality of movement in UL VR rehabilitation maybe sacrificed for a good gaming outcome [18] although this has not been explored in pwMS. Both groups were interested in the reported outcomes of using VR approaches which, if positive, would increase engagement.

Clinicians and pwMS felt VR activity had to be related to the patient’s personalized and meaningful goals, which is known to increase motivation in physiotherapy settings [48], however is often neglected in VR regimes [14]. Goals need to be adjusted over time in a progressive condition such as MS and to avoid disengagement as raised earlier. Participants with MS frequently stated that their goals related to improvement but also maintenance of ability and the prevention of further deterioration. In terms of suggestions for VR activities, the groups differed with clinicians suggesting ADL or hobby simulations and pwMS being more ambivalent, stressing activity to be fun with variety of real life and abstract VR games. Previous studies of VR have often involved ADL activities such as cooking or other kitchen activity [49, 50]. Although VR can provide a safe environment to practice ADL for people with mobility issues [51] pwMS in the current study were less interested in ADL, especially kitchen simulations. Both groups suggested an ‘end result’ such as creating a drawing, or learning a new skill would be positive and facilitate a feeling of accomplishment. There were also suggestions from the pwMS to incorporate haptic activities such as grabbing, gripping. However, the user is not able to receive tactile feedback when interacting with a virtual environment and handheld controllers may need to considered for some VR activities [52]. Another solution could be to incorporate pseudo haptics, the use of different stimuli, such as visual or auditory stimuli, to mimic a variety of haptic properties in a virtual environment [53]. This is an emerging field that could be explored in VR for pwMS. Likewise, since many of the participants suggested finger-related exercises, it is important that VR systems utilize good hand-tracking motion capture devices to allow visualization of the movement of fingers and wrists within a VR setting.

Many pwMS were supportive of VR for home use, as being more convenient and accessible. However, there was recognition that users needed demonstration of the technology and a level of clinician supervision. Assessing quality of movements and monitoring of patient progress are reported challenges for VR home use [54]. A recent small study found VR to be feasible for home based UL rehabilitation in pwMS, after three supervised sessions [32] but larger studies of home based VR for UL rehabilitation are required. There was agreement in both groups that an element of social interaction could be considered within development of the VR games. Generally there is lack of evidence on the effect of socialization within UL therapy but it may improve adherence and motivation [55] and better outcomes [56]. Specifically in relation to VR there is some evidence that social aspects increase motivation through competition [57], but participants in our study were more interested in self-competition rather than competing against others. This is similar to a study of a walking app for MS, where users were less interested in sharing their goals or achievements with others [58].

### Strengths and Limitations

Recruiting participants through online sources may result in a biased sample, as those comfortable with technology and access to online services are more likely to take part. Being online allowed the involvement of pwMS with varying abilities and clinicians who worked in the NHS and the third sector across the UK. However, the online nature meant it was not possible for participants to physically test the VR equipment and explore their reactions. While it can also be challenging to engage all participants in online focus groups, this was resolved by asking questions using participants’ names or by getting participants to use the raise hand function within the video conference software and encourage discussion between participants.

Regarding the TBCA methodology, which groups responses into themes to quantify them, but does not allow consideration of the interaction between participants. Participants had a number of specific questions, such as long-term outcomes of using immersive VR, the optimal target users for VR (level of disability) and the extent of translation of VR activity into ‘real life’ function. However, there is currently a lack literature to provide responses to these questions, which highlights areas for future research.

### Conclusions

This is the first study exploring the views of pwMS and clinicians in terms of VR for UL rehabilitation for pwMS and has highlighted the current challenges in UL rehabilitation even though UL impairment is common and impacts meaningful activity. Overall, pwMS often found dexterity-related activities difficult which impacted multiple ADLs and challenges faced in therapy related to motivation, lack of resources and difficulty finding interesting UL exercises. There was positive support for VR for UL exercise. Overall, to improve engagement and satisfaction for the user this study suggests any VR games developed for pwMS 1) be fun and engaging, 2) have clear aims related to the individual user’s goals, 3) offer personalization such as a variety of games (abstract and ADL based), different movements, levels of difficulty and methods of feedback, 4) monitor quality as well as quantity of movement during game play, 5) incorporate design features to reduce the potential for cybersickness, 6) consider if the games can incorporate education or skill development, 7) incorporate aspects of social interaction, 8) consider including haptic properties. The findings support the need for the creation of bespoke serious games rather than using commercially available exercise games, which can discourage users with motor dysfunction [15, 59]. Overall future development of VR games for UL rehabilitation should focus on a personalized and customizable approach to encourage long term engagement of users to improve meaningful outcomes for pwMS.

### Acknowledgements

The authors wish to give thanks to all the participants who took part in this study, as well as the MS Society, UK for the funding this study (Grant no: 115).

### Authors Contributions

AW, MP, EC and LP designed and conceptualized this study. AW, LF and LP performed the analysis. AW and LP wrote and prepared the manuscript, with support from MP, EC and LF.

### Conflict of Interest

The authors report no conflicts of interest.

### Abbreviations

ADL: Activities of daily living

HMD: Head mounted device

MS: Multiple sclerosis

OT: Occupational therapist

PPMS: Primary progressive multiple sclerosis

PT: Physiotherapist

PwMS: Person/people with multiple sclerosis

RRMS: Relapse and remitting multiple sclerosis

SPMS: Secondary progressive multiple sclerosis

TBCA: Theme based content analysis

UL: Upper limb

VR: Virtual reality

## References

1. Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the atlas of MS. Mult Scler. 2020;26(14):1816-21. doi: 10.1177/1352458520970841
2. Marrie RA, Cutter GR, Tyry T, et al. Upper limb impairment is associated with use of assistive devices and unemployment in multiple sclerosis. Mult Scler Relat Disord. 2017;13:87-92. doi: 10.1016/j.msard.2017.02.013.
3. Simmons RD, Tribe KL, McDonald EA. Living with multiple sclerosis: Longitudinal changes in employment and the importance of symptom management. J Neurol. 2010;257(6):926-36. doi: 10.1007/s00415-009-5441-7.
4. Goverover Y, Genova H, Deluca J, et al. Impact of Multiple Sclerosis on Daily Life In: Chiaravalloti, N., Goverover, Y. (eds) Changes in the Brain. New York: Springer; 2017 p. 145-65. doi: 10.1007/978-0-387-98188-8\_7
5. Koch MW, Murray TJ, Fisk J, et al. Hand dexterity and direct disease related cost in multiple sclerosis. J Neurol Sci. 2014;341(1-2):51-4. doi: 10.1016/j.jns.2014.03.047.
6. Alonso RN, Eizaguirre MB, Cohen L, et al. Upper limb dexterity in patients with multiple Sclerosis: An important and underrated morbidity. Int J MS Care. 2021;23(2):79-84. doi: 10.7224/1537-2073.2019-083.
7. Dalgas U, Ingemann-Hansen T, Stenager E. Physical exercise and MS recommendations. Int Ms J. 2009;16(1):5-11.
8. Etoom M, Khraiwesh Y, Lena F, et al. Effectiveness of physiotherapy interventions on spasticity in people with multiple sclerosis: A systematic review and meta-analysis. Am J Phys Med Rehabil. 2018;97(11):793-807. doi: 10.1097/PHM.0000000000000970.
9. Lamers I, Maris A, Severijns D, et al. Upper limb rehabilitation in people with multiple sclerosis: A systematic review. Neurorehabil Neural Repair. 2016;30(8):773-93. doi: 10.1177/1545968315624785.
10. Burks JS, Bigley GK, Hill HH. Rehabilitation challenges in multiple sclerosis. Ann Indian Acad Neurol. 2009;12(4):296. doi: 10.4103/0972-2327.58273
11. Howard MC. A meta-analysis and systematic literature review of virtual reality rehabilitation programs. Comput Hum Behav. 2017;70:317-27. doi: 10.1016/j.chb.2017.01.013
12. Porras DC, Siemonsma P, Inzelberg R, et al. Advantages of virtual reality in the rehabilitation of balance and gait: Systematic review. Neurology. 2018;90(22):1017-25. doi: 10.1212/WNL.0000000000005603.
13. Maggio MG, Russo M, Cuzzola MF, et al. Virtual reality in multiple sclerosis rehabilitation: A review on cognitive and motor outcomes. J Clin Neurosci. 2019;65:106-11. doi: 10.1016/j.jocn.2019.03.017.
14. Webster A, Poyade M, Rooney S, et al. Upper limb rehabilitation interventions using virtual reality for people with multiple sclerosis: A systematic review. Mult Scler Relat Disord. 2021;47:102610. doi: 10.1016/j.msard.2020.102610.
15. Plow M, Finlayson M. A qualitative study exploring the usability of nintendo wii fit among persons with multiple sclerosis. Occup Ther Int. 2014;21(1):21-32. doi: 10.1002/oti.1345.
16. Kristensson P, Matthing J, Johansson N. Key strategies for the successful involvement of customers in the co‐creation of new technology‐based services. Int J Serv Ind Manag. 2008;19(4):474-91 doi: 10.1108/09564230810891914.
17. Windasari NA, Visita L. User engagement mechanisms of online co-design service: Does user innovativeness matter? Asian Acad Manag J. 2019;24(1). doi: 10.21315/aamj2019.24.1.3.
18. Schmid L, Glässel A, Schuster-Amft C. Therapists’ perspective on virtual reality training in patients after stroke: A qualitative study reporting focus group results from three hospitals. Stroke Res Treat. 2016;2016:6210508. doi: 10.1155/2016/6210508.
19. Vasileiou, K., Barnett, J., Thorpe, S. et al. Characterising and justifying sample size sufficiency in interview-based studies: systematic analysis of qualitative health research over a 15-year period. BMC medical research methodology. 2018:18:1-18 doi: 10.1186/s12874-018-0594-7.
20. Jiménez TR, Orozco M. Prompts, not questions: Four techniques for crafting better interview protocols. Qual Sociol. 2021;44(13):507-28. doi: 10.1007/s11133-021-09483-2.
21. Webster A, Poyade M, Rea P, et al. The co-design of hand rehabilitation exercises for multiple sclerosis using hand tracking system. In: Rea, P. (eds) Adv Exp Med Biol. Switzerland (AG), Springer, Cham; 2019;1120:83-96. doi: 10.1007/978-3-030-06070-1\_7
22. Hollywood R, Poyade M, Paul L, et al. Proof of concept for the use of immersive virtual reality in upper limb rehabilitation of multiple sclerosis patients. In: Rea, P. (eds) Adv Exp Med Biol. Switzerland (AG), Springer, Cham; 2022;1356:73-93. doi: 10.1007/978-3-030-87779-8\_4.
23. Neale H, Nichols S. Theme-based content analysis: A flexible method for virtual environment evaluation. Int J Hum Comput Stud. 2001;55(2):167-89. doi: 10.1006/ijhc.2001.0475.
24. Junus IS, Santoso HB, Isal RYK, et al. Usability evaluation of the student centered e-learning environment. Int Rev Res in Open and Distributed Learning. 2015;16(4):62-82. doi: 10.19173/irrodl.v16i4.2175.
25. Latham B, Poyade M, Finlay C, et al. New tools in education: Development and learning effectiveness of a computer application for use in a university biology curriculum. In: Rea, P. (eds) Adv Exp Med Biol. Switzerland (AG), Springer, Cham; 2019:29-46. doi: 10.1007/978-3-030-14227-8\_3.
26. Bertoni R, Lamers I, Chen CC, et al. Unilateral and bilateral upper limb dysfunction at body functions, activity and participation levels in people with multiple sclerosis. Mult Scler. 2015;21(12):1566-74. doi: 10.1177/1352458514567553.
27. Cattaneo D, Lamers I, Bertoni R, et al. Participation restriction in people with multiple sclerosis: Prevalence and correlations with cognitive, walking, balance, and upper limb impairments. Arch Phys Med Rehabil. 2017;98(7):1308-15. doi: 10.1016/j.apmr.2017.02.015.
28. Newsome SD, von Geldern G, Shou H, et al. Longitudinal assessment of hand function in individuals with multiple sclerosis. Mult Scler Relat Disord. 2019;32:107-13. doi: 10.1016/j.msard.2019.04.035.
29. Meadmore KL, Hallewell E, Freeman C, et al. Factors affecting rehabilitation and use of upper limb after stroke: Views from healthcare professionals and stroke survivors. Top Stroke Rehabil. 2019;26(2):94-100. doi: 10.1080/10749357.2018.1544845.
30. Dias P, Silva R, Amorim P, et al. Using virtual reality to increase motivation in poststroke rehabilitation. IEEE Comput Graphics Appl. 2019;39(1):64-70. doi: 10.1109/MCG.2018.2875630.
31. Pagliari C, Di Tella S, Jonsdottir J, et al. Effects of home-based virtual reality telerehabilitation system in people with multiple sclerosis: A randomized controlled trial. J Telemed Telecare. 2021:1357633X211054839. doi: 10.1177/1357633X211054839.
32. Kamm CP, Blättler R, Kueng R, et al. Feasibility and usability of a new home-based immersive virtual reality headset-based dexterity training in multiple sclerosis. Mult Scler Relat Disord. 2023:72:104525. doi: 10.1016/j.msard.2023.104525.
33. Forsberg A, Nilsagård Y, Boström K. Perceptions of using videogames in rehabilitation: A dual perspective of people with multiple sclerosis and physiotherapists. Disabil Rehabil. 2015;37(4):338-44. doi: 10.3109/09638288.2014.918196
34. Palacios-Cena D, Ortiz-Gutierrez RM, Buesa-Estellez A, et al. Multiple sclerosis patients' experiences in relation to the impact of the kinect virtual home-exercise programme: A qualitative study. Eur J Phys Rehabil Med. 2016;52(3):347-55.
35. LaViola Jr JJ. A discussion of cybersickness in virtual environments. ACM Sigchi Bulletin. 2000;32(1):47-56. doi: 10.1145/333329.333344.
36. Stanney K, Fidopiastis C, Foster L. Virtual reality is sexist: But it does not have to be. Front Robot AI. 2020;7:4. doi: 10.3389/frobt.2020.00004.
37. Kalron A, Frid L, Fonkatz I, et al. The design, development, and testing of a virtual reality device for upper limb training in people with multiple sclerosis: Single-center feasibility study. JMIR Serious Games. 2022;10(3):e36288. doi: 10.2196/36288.
38. Kemeny A, Chardonnet J, Colombet F. Getting rid of cybersickness. irtual Reality, Augmented Reality, and Simulators. Switzerland (AG), Springer, Clam 2020. doi: 10.1007/978-3-030-59342-1.
39. Michie S, Van Stralen MM, West R. The behaviour change wheel: A new method for characterising and designing behaviour change interventions. Implement Sci. 2011;6(1):1-12. doi: 10.1186/1748-5908-6-42.
40. Mouatt B, Smith AE, Mellow ML, et al. The use of virtual reality to influence motivation, affect, enjoyment, and engagement during exercise: A scoping review. Front Virtual Real. 2020;1:564664. doi: 10.3389/frvir.2020.564664.
41. Zimmerli L, Jacky M, Lünenburger L, et al. Increasing patient engagement during virtual reality-based motor rehabilitation. Arch Phys Med Rehabil. 2013;94(9):1737-46. doi: 10.1016/j.apmr.2013.01.029.
42. Charles D, Holmes D, Charles T, et al. Virtual reality design for stroke rehabilitation. In: Rea, P. (eds) Adv Exp Med Biol. Switzerland (AG), Springer, Cham; 2020;1235:53-87. doi: 10.1007/978-3-030-37639-0\_4.
43. Lorenz M, Brade J, Klimant P, et al. Age and gender effects on presence, user experience and usability in virtual environments–first insights. PloS One. 2023;18(3):e0283565. doi: 10.1371/journal.pone.0283565.
44. Tuena C, Pedroli E, Trimarchi PD, et al. Usability issues of clinical and research applications of virtual reality in older people: A systematic review. Front HumNeurosci. 2020;14:93. doi: 10.3389/fnhum.2020.00093
45. Lohse K, Shirzad N, Verster A, et al. Video games and rehabilitation: Using design principles to enhance engagement in physical therapy. J Neurol Phys Ther. 2013;37(4):166-75. doi: 10.1097/NPT.0000000000000017.
46. Richter G, Raban DR, Rafaeli S. Studying gamification: the effect of rewards and incentives on motivation. In: Reiners, T, Wood, L (eds) Gamification in Education and Business. Springer, Cham; 2015:21-46. doi: 10.1007/978-3-319-10208-5\_2.
47. Yildirim IG. Time pressure as video game design element and basic need satisfaction. Proceedings of the 2016 CHI Conference Extended Abstracts on Human Factors in Computing Systems; 2016 May 7-12; San Jose (CA, USA). p. 2005-11. doi: 10.1145/2851581.2892298.
48. Dekker J, de Groot V, Ter Steeg AM, et al. Setting meaningful goals in rehabilitation: Rationale and practical tool. Clin Rehabil. 2020;34(1):3-12. doi: 10.1177/0269215519876299.
49. Høeg ER, Becermen B, Bruun-Pedersen JR, et al. Co-creating virtual reality applications for motor rehabilitation with physiotherapists In: Brooks A, Brooks, EI (eds) Interactivity, Game Creation, Design, Learning, and Innovation. 8th EAI International Conference, ArtsIT 2019, and 4th EAI International Conference, DLI 2019, Aalborg, Denmark, November 6–8, 2019. Springer; 2020. p. 379-89. doi: 10.1007/978-3-030-53294-9\_26.
50. Pau M, Cocco E, Arippa F, et al. An immersive virtual kitchen training system for people with multiple sclerosis: A development and validation study. J Clin Med. 2023;12(9):3222. doi: 10.3390/jcm12093222.
51. Lee JH, Ku J, Cho W, et al. A virtual reality system for the assessment and rehabilitation of the activities of daily living. Cyberpsychol Behav. 2003;6(4):383-8. doi: 10.1089/109493103322278763.
52. Knierim P, Kosch T, Schwind V, et al. Tactile drones-providing immersive tactile feedback in virtual reality through quadcopters. Proceedings of the 2017 CHI Conference Extended Abstracts on Human Factors in Computing Systems; 2017 May 6-11, Denver (CO, USA). p. 433-6. doi: 10.1145/3027063.3050426.
53. Collins K, Kapralos B. Pseudo-haptics: Leveraging cross-modal perception in virtual environments. Senses Soc. 2019;14(3):313-29. doi: 10.1080/17458927.2019.1619318.
54. Threapleton K, Drummond A, Standen P. Virtual rehabilitation: What are the practical barriers for home-based research? Digit Health. 2016;2:2055207616641302. doi: 10.1177/2055207616641302.
55. Clarke R, Coote S. Perceptions of participants in a group, community, exercise programme for people with multiple sclerosis. Rehabilitation Res Prac. 2015;2015:123494. doi: 10.1155/2015/123494.
56. Arntzen EC, Straume BK, Odeh F, et al. Group-based individualized comprehensive core stability intervention improves balance in persons with multiple sclerosis: A randomized controlled trial. Phys Ther. 2019;99(8):1027-38. doi: 10.1093/ptj/pzz017.
57. Anderson-Hanley C, Snyder AL, Nimon JP, et al. Social facilitation in virtual reality-enhanced exercise: Competitiveness moderates exercise effort of older adults. Clinical Interv Aging. 2011:275-80. doi: 10.2147/CIA.S25337.
58. Geurts E, Van Geel F, Feys P, et al. WalkWithMe: personalized goal setting and coaching for walking in people with multiple sclerosis. Proceedings of the 27th ACM Conference on User Modeling, Adaptation and Personalization; 2019 June 9-12 Larnaca, Cyprus. p. 51-60. doi: 10.1145/3320435.3320459.
59. Cuesta-Gomez A, Sanchez-Herrera-Baeza P, Ona-Simbana ED, Martinez-Medina A, Ortiz-Comino C, Balaguer-Bernaldo-de-Quiros C, Jardon-Huete A, Cano-de-la-Cuerda R. Effects of virtual reality associated with serious games for upper limb rehabilitation inpatients with multiple sclerosis: Randomized controlled trial. J Neuroeng Rehabil. 2020:13;17(1):90. doi: 10.1186/s12984-020-00718-x.