



## Neuro rehabilitation effectiveness based on virtual reality and tele rehabilitation in people with multiple sclerosis in Argentina: Reavitelem study

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### ABSTRACT

Virtual Reality (VR) has emerged as a new treatment approach in neurorehabilitation (NR). REAVITELEM Study is a specific NR intervention program based on VR at center (VRC) and tele-rehabilitation (TR) in Argentina.

**Methods** First national multicenter study with a 12-week program intervention of VRC and TR. Participants were assessed at baseline, at 6th and 12th week. Phase I: recruitment and gather of 5 NR Centers from Argentina by the coordinator center (INEBA) to unify evaluation and intervention criteria. Phase II, all centers completed VRC and TR programs. Intervention was 30-minute session, twice a week for 12 weeks. Outcome measures: Expanded Disability Status Scale (EDSS), Fist and Key Pinch Dynamometry, Beck Depression Inventory-Fast Screen, Fatigue Severity Scale, Functional Independence Measure (FIM), International Questionnaire investigating Quality of life in MS (MusiQol) and a Visual Analogue Scale (VAS) of satisfaction after treatment.

**Results** A total of 54 PWMS (23 males) were recruited for VRC. Afterwards, 14 completed TR. The mean age for VRC was 44.72 (SD ± 13.74) and 41.71 (SD ± 10.5) for TR. The median EDSS was 4, 75 for VRC. At VRC, 42 have RRMS, 8 have SPMS and 4 PPMS. At TR, 13 have RRMS and 1 have SPMS. The VAS reported an excellent level of satisfaction after treatment with an average of 9, 02 (SD±1.35) in VRC and 9.42 (SD±0.66) in TR. There were significant differences for MusiQol, which improved from baseline to the post-intervention assessment at VRC ( $p < 0.001$ ) and at TR ( $p = 0.004$ ) as well as FIM post-intervention assessment at VRC ( $p = 0.02$ ) and TR ( $p = 0.04$ ).

**Conclusion** this study suggest that the NR treatment based on VR in MS in Argentina, is an additional effective tool, which favors improvements in the level of functioning in activities of daily living, quality of life, mood, and satisfaction with the treatment.

### 1. Introduction

Multiple sclerosis (MS) is a chronic degenerative disease that affects mostly young adults between 18 and 40 years of age and is the first cause of physical disability of non-traumatic origin in several countries (Reich et al., 2018; Comi et al., 2017). MS is characterized histo-pathologically by the presence of inflammatory plaques associated with the presence of

axonal damage (Reich et al., 2018; Trapp et al., 1998). In MS, axonal degeneration is thought to be one of the causal factors of the disability's irreversible progression seen in affected patients (Sormani et al., 2017; Moccia et al., 2017; Kappos et al., 2016).

Once the diagnosis is made, an early and individualized specific treatment for MS (based on the severity of the disease) could avoid radiological and physical disability in the medium/long-term.

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Currently, there is significant evidence supporting the importance of early treatment in MS to avoid disease progression and disability outcomes (Comi et al., 2017; Cristiano et al., 2020). Consequently, an individualized approach for targeting a treatment in a single patient has enabled neurologists to provide more effective and safer drug prescriptions for patients with MS (Comi et al., 2017; Giovannoni et al., 2015; Iacobaeus et al., 2020). Patients with negative prognostic factors and active disease from onset (at least two relapses in the previous year or a relapse with incomplete recovery associated with new and enhancing lesions at MRI) should start a more effective treatment as first choice (Comi et al., 2017; Soelberg Sorensen et al., 2019; Wattjes et al., 2021), while patients with a better prognosis would follow the strategy of lower-risk DMTs and receive intensified treatment only if the disease is not controlled (Comi et al., 2017; Soelberg Sorensen et al., 2019; Wattjes et al., 2021). Nevertheless, as the disease may still progress, neurorehabilitation is indicated to improve outcomes (Dombrov, 2011; Amatya et al., 2019; Amatya et al., 2015; Beer et al., 2012; Khan et al., 2008).

Exercise training can improve functional activities and decrease the rate and extent of disability in MS (Casuso-Holgado et al., 2018; Khalil et al., 2018; Khan et al., 2009). However, lack of access to neurorehabilitation, especially if one lives in a remote area where there are fewer options or where there are healthcare/medical facilities but no MS experts, may render it difficult to engage in traditional healthcare facility training programs (Kalron et al., 2020).

Telerehabilitation could facilitate rehabilitation in MS by providing service delivery in the natural environment, that is, in patient homes (Amatya et al., 2015; Kalron et al., 2020; Bendixen et al., 2009; Brennan et al., 2009; Chumbler et al., 2012; Constantinescu et al., 2010; Hailey et al., 2011). However, success depends on many factors, most of which are compounded in developing countries (Bendixen et al., 2009; Brennan et al., 2009; Chumbler et al., 2012; Constantinescu et al., 2010; Hailey et al., 2011). This strategy has been on the rise in recent years, especially during the pandemic period, with the development of new technologies that included videoconferencing, remote monitoring of signs and activity (e.g., via electronic monitors), and distribution of specialized and individualized information via electronic mechanisms (e.g., email or Internet posting of newsletters or videos) (Kalron et al., 2020; Bendixen et al., 2009; Brennan et al., 2009; Chumbler et al., 2012; Constantinescu et al., 2010; Hailey et al., 2011). Telerehabilitation has proven to be beneficial for MS by increasing physical activities (i.e., daily walking), decreasing fatigue, and improving cognitive function, mobility, balance, participation, and quality of life (Amatya et al., 2019; Amatya et al., 2015; Kalron et al., 2020). However, scarce data has been evaluated in affected patients in our region.

Virtual rehabilitation (VR) is a component of telerehabilitation (Casuso-Holgado et al., 2018; Massetti et al., 2016). VR and interactive games enable high-intensity, task-oriented multisensory feedback training and can enhance motor learning and training by combining motor and cognitive demands in an attractive and interactive way, motivating participants to deal with the game's demands and not just the movements (Casuso-Holgado et al., 2018; Massetti et al., 2016; Maggio et al., 2019). Trials investigating the benefits of VR in MS have demonstrated a wide range of promising results (Casuso-Holgado et al., 2018), not only in functional aspects of the disease but also in pain and emotions of affected patients (Massetti et al., 2016; Shaw et al., 2021). Despite existing information in MS, there are currently no studies in Latin America concerning telerehabilitation and VR in the disease.

We developed the following study to assess a standardized and specific neurorehabilitation intervention program based on VR and TR effectiveness, its functional impact on activity limitations, and the quality of life in MS patients in Argentina.

## 2. Methods

### 2.1. Centers included and study design

This was a prospective cohort multicenter study that collected patient-level data in Argentina.

The study was conducted between January 2018 and October 2019. Participant centers included five (5) centers in five (5) cities of different regions of Argentina.

A specific case report form was designed, and neurologists from different neurological centers transferred the data from their medical records. Centers were selected based on their experience in managing neurorehabilitation MS patients as well as for acting as referral centers for clinical practice and academic research in Argentina.

Patients received VR intervention at study centers for 12 weeks. A selected group of patients then continued with the intervention for 12 weeks via in-home telerehabilitation. The design of the intervention is presented in Fig. 1.

Ethical approval and written or verbal informed consent was obtained at each participating center as per local institutional regulations.

### 2.2. Patient selection

Patients were eligible for inclusion if they had a diagnosis of clinically definite MS (Thompson et al., 2018; Polman et al., 2011), were at least 18 years old at diagnosis, had an Expanded Disability Status Scale (EDSS) score of < 7 at study inclusion, and had no history of relapse activity (defined as the appearance of a new neurological symptom lasting more than 24 h, in the absence of clinical intercurrent, followed by a period of clinical stability or improvement of at least 30 days) or corticosteroids during the last 60 days of study inclusion.

Patients were excluded if they presented cognitive impairment, significant fatigue (fatigue impact scale >4) and/or psychiatric comorbidity (depression and anxiety) at study entry. Patients with other neurological illnesses or musculoskeletal disorders other than MS; with cardiovascular, respiratory, or metabolic illness or other conditions which may interfere with the study; those suffering a relapse or hospitalization in the last 3 months prior to commencement of the assessment protocol or during the process of the therapeutic intervention; or the presence of visual disorders not corrected by optical devices were also excluded.

### 2.3. Intervention

Previous to patient inclusion, all treating centers were trained in how to implement the VR for MS patients. Once inclusion was completed, institutional VR was delivered to affected patients by VirtualRehab®, a bespoke neurorehabilitation application that has been commercially available for many years (O'Neil et al., 2018). The software requires a personal computer and a supported optical tracking device, including Kinect v2 (Microsoft Corporation, Redmond, WA), Orbbec Astra (Orbbec, China), and Intel D435 (Intel, Santa Clara, CA) for gross motor activities or the LEAP motion (Leap Motion Inc, San Francisco, CA) for fine motor activities (O'Neil et al., 2018). The system uses a standard display monitor and PC hardware. Training content consists of sixteen different "exergames" for gross motor task-oriented exercise and seven games for fine motor therapy. Each "exergame" featured customizable intensity and target placement to increase relevance and participation for different patient-specific impairment profiles. VirtualRehab® securely archives patient data on a cloud server or in local storage, allowing clinicians to review and augment therapy programs remotely if required, and supports the application of the system in telerehabilitation settings (O'Neil et al., 2018). Institutional VR was applied for "body" as well as for "hands." Each patient was assessed by the Principal Investigator (PI) of each center at study entry. All included patients made the same frequency of sessions (two sessions per week for 12 weeks) and

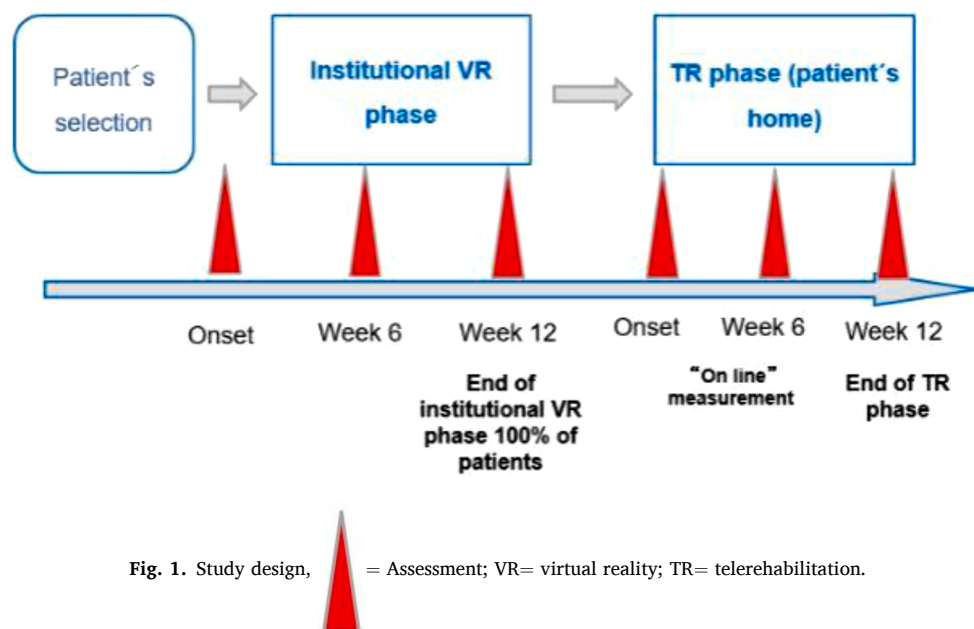


Fig. 1. Study design, = Assessment; VR= virtual reality; TR= telerehabilitation.

every session last 30 min. Re-evaluation of objectives for every patient was done during the continuous evaluation of every patient. Telerehabilitation was implemented in the same manner, with the exception that VR was applied for “body” and only for patients who had the technical requirements in their homes for installing the system. Therefore, not all patients included in the institutional VR group were followed during the 12 weeks of telerehabilitation.

#### 2.4. Variables collected

All variables were collected from patient medical records and transferred into a specifically designed digital database.

Patients' selection and clinical variables collected was done by treating neurologist. All other assessments were performed by occupational therapists and/or physical therapists trained in the use of the measures (each therapist always performed the same measures with all patients in all evaluation periods) and blinded to the intervention received by the subjects. The following outcome measures were used in both groups at the beginning of the intervention, at the end, and in a follow-up period.

#### 2.5. Variables collected were

- Demographic: age at study entry, gender, place of residence and years of education.
- Clinical variables: date of disease onset, MS phenotype, current treatment for MS and Expanded Disability Status Scale (EDSS) (Kurtzke, 1975; Reich et al., 2018)
- Fatigue: the instrument used to evaluate fatigue was the Fatigue Severity Scale (Krupp et al., 1989), one of the most commonly used scales for the assessment of fatigue in MS attributed to a multifactorial origin. It consists of nine items that are assessed by the patient with a score between 0 and 7. The cut-off point of this scale is arbitrary, with a score of 5 used by most authors as the reference value to distinguish the presence or absence of the symptom. The result is interpreted as a percentage measure.
- Motor deficit: the instrument used was the Fugl-Meyer Assessment of Motor Recovery (Fugl-Meyer et al., 1975). The scale is an instrument-specific, performance-based impairment index. It is designed to assess motor functioning, balance, sensation, and joint functioning in patients with motor deficit.

- Health-related quality of life: this was assessed using MusiQoL (Fernandez et al., 2011), a specific instrument designed to assess quality of life in MS.
- Depression: measured by Beck depression inventory II (Benedict et al., 2003).
- Hand grasps: measured by Fist and Key Pinch Dynamometry (Kellor et al., 1971).
- NHPT (Nine Hole Peg Test) (Oxford Grice et al., 2003).
- Functional Independence: the instrument to assess this outcome was the Functional Independence Measure (FIM) (Dickson and Kohler, 1995). FIM is an instrument that was developed as a measure of disability for a variety of populations and is not specific to any diagnosis.
- Daily activities: the instrument used was the Lawton and Brody Instrumental Activities of Daily Living (IADL) Scale (Lawton and Brody, 1969). The scale is used to assess independent living skills of an individual and measures functional ability as well as declines and improvements over time.
- Visual Analogue Scale (Aitken, 1969): measurement of feelings (satisfaction with VR and TR) was done using visual analogue scales. It was done at the end of the institutional VR phase in patients that continues TR at the beginning and at the end.

#### 2.6. Statistical analysis

As previously mentioned, two study periods were designed: the institutional period, where VR was provided in MS patients at study centers during the first 12 weeks, and then the telerehabilitation period during the following 12 weeks (Fig. 1).

Patients were measured at study entry at week six and week twelve of VR and at baseline week 6 and 12 in telerehabilitation. Descriptive values were presented, and later a comparative analysis was performed between pre and post paired test between groups. Each patient was his own control. The statistical analysis was performed using the SPSS statistical software system (SPSS Inc., Chicago, IL; version 22.0). The Shapiro-Wilk test was used to screen all data for normality of distribution. The Friedman test was also used, which is a non-parametric test for repeated measurements in related samples. A Bonferroni correction was performed to adjust for multiple testing. With 3 comparisons, a p value < 0.05 was considered statistically significant. In the event that there were significant differences, the Wilcoxon test was performed, which

allows two related samples to be compared. Additionally, the Mann-Whitney test for non-related samples was used to compare variables, and significant values were considered as  $p < 0.05$ .

### 3. Results

A total of fifty-four patients were included during the first stage of the study. These were patients that received the intervention at an institutional setting. Most of patients were RRMS patients (42), mean age 44.7 years, who received DMT to control the disease. The remainder of the baseline characteristics at study entry are displayed in Table 1.

Institutional VR was implemented during the following 12 weeks for fifty-four patients. An improvement in functional aspects of upper limb dexterity was observed (Nine-hole Peg Test, right and left) as well as for hand grasps after the 12 weeks of intervention (Table 2). Also, a significant difference in depression index, daily activity scales (L&B scale), FIM and quality of life was observed between pre and post intervention ( $p$  0.023, 0.039, 0.01, and  $<0.001$ , respectively, Table 2); however, no differences were observed in fatigue ( $p = 0.23$ ). No safety issues were detected and no drop out during the study period was observed.

After the 12 weeks of institutional VR phase, telerehabilitation was implemented during the following 12 weeks in fourteen patients in which technical and logistic aspects were allowed. In that group, a sustained improvement in functional aspects of upper limb dexterity was observed (Nine-hole Peg Test, right and left) as well as in hand grasps after the 12 weeks of intervention (Table 3). Also, a significant difference in depression index, FIM, and quality of life was observed between

**Table 1**  
Baseline characteristics of included patients in VR and TR periods.

	VR Institutional	Tele Rehabilitation
<b>N</b>	<b>54</b>	<b>14</b>
<b>Mean age, years (range)</b>	44.7 (18–77)	41.7 (25–58)
<b>Female/male</b>	31 – 23	6 – 8
	57.4% / 42.6%	42.9% / 57.1%
<b>MS phenotype</b>		
PPMS	4	1
SPMS	8	0
RRMS	42	13
<b>Scholarship</b>		
0–7 years	3	3
7 - 12 years	20	4
> 12 years	31	7
<b>Laboral status</b>		
Full time job	18	7
Part time job	9	1
License*	4	0
Retired	5	1
Retired due to disability	10	3
Unemployed	8	2
<b>DMT</b>		
Yes/no	42 – 12	10 – 4
<b>EDSS (Median, Min, Max)</b>	4.0 (1–7)	
<b>BDI-II (Mean: Phase onset – Phase end)</b>	3.3 – 3.47	4.6 – 3.5
<b>FIM (Mean: Phase onset – Phase end)</b>	111.69 – 113.66	112–112.57
<b>FIS (Mean: Phase onset – Phase end)</b>	3.31 – 3.46	3.29 – 3.18
<b>MusiQoL (Mean: Phase onset – Phase end)</b>	70.65 – 77.36	68.15 – 74.26
<b>VaS (Mean VR phase end, TR phase onset-end)</b>	8.9	9.02 – 9.43

VR= virtual reality; TR= telerehabilitation; MS= multiple sclerosis; PPMS= primary progressive multiple sclerosis; SPMS= secondary progressive multiple sclerosis; RRMS= relapsing remitting multiple sclerosis; DMT= disease modifying treatment; EDSS= expanded disability status scale; BDI= Beck depression index; FIM= functional independence measure; FIS= fatigue impact scale; VaS= Visual Analogue Scale; MusiQoL= Multiple sclerosis quality of life; \* License= the patient is employed but circumstantially does not go to work due to a medical authorization (for example, carrying out a neurorehabilitation program).

**Table 2**  
Functional measurements during week 0 and 12 in institutional VR program ( $n = 54$ ).

	Baseline (mean)	Week 12 (mean)	P value (week 0–12)
<b>EDSS</b>	4	4	1
<b>Nine-hole Peg Test right</b>	27.3	23.99	0.04
<b>Nine-hole Peg Test left</b>	31.4	26.9	0.003
<b>DIN right</b>	31.4	34	0.5
<b>DIN left</b>	27.3	30.4	0.037
<b>DIN grip right</b>	9.3	8.3	0.6
<b>DIN grip left</b>	16	16.7	0.8
<b>DGI</b>	3.6	2.8	0.06
<b>BDI-II</b>	3.3	3.47	0.023
<b>FIS</b>	3.31	3.46	0.23
<b>Fugl-Meyer</b>	62.6	63.3	0.3
<b>FIM</b>	111.69	113.66	0.01
<b>Lawton &amp; Brody</b>	6.2	6.5	0.039
<b>MusiQoL</b>	70.65	77.36	$<0.001$
<b>Vas</b>	N /A	8.9	N /A

VR= virtual reality; TR= telerehabilitation; MS= multiple sclerosis; PPMS= primary progressive multiple sclerosis; SPMS= secondary progressive multiple sclerosis; RRMS= relapsing remitting multiple sclerosis; DMT= disease modifying treatment; EDSS= expanded disability status scale; BDI= Beck depression index; FIM= functional independence measure; FIS= fatigue impact scale, VaS= Visual Analogue Scale; MusiQoL= Multiple sclerosis quality of life; N/A Not applicable.

**Table 3**  
Functional measurements during week 0 and 12 in telerehabilitation program ( $n = 14$ ).

	Baseline (mean)	Week 12 (mean)	P value (week 0–12)
<b>EDSS</b>	4	4	1
<b>Nine-Hole Peg Test right</b>	27.3	26.7	0.8
<b>Nine-hole Peg Test left</b>	31.4	25	0.05
<b>DIN right</b>	30.4	37.8	0.06
<b>DIN left</b>	30.9	31.3	0.8
<b>DIN grip right</b>	9.5	10.1	0.07
<b>DIN grip left</b>	8.9	9.2	0.7
<b>DGI</b>	13.7	13.8	0.9
<b>BDI-II</b>	4.6	3.5	0.03
<b>FIS</b>	3.29	3.8	0.70
<b>Fugl-Meyer</b>	62	62	1
<b>FIM</b>	112	112.57	0.3
<b>Lawton &amp; Brody</b>	6.3	6.7	0.33
<b>MusiQoL</b>	68.15	74.26	$<0.001$
<b>VaS</b>	9.02	9.43	$<0.001$

VR= virtual reality; TR= telerehabilitation; MS= multiple sclerosis; PPMS= primary progressive multiple sclerosis; SPMS= secondary progressive multiple sclerosis; RRMS= relapsing remitting multiple sclerosis; DMT= disease modifying treatment; EDSS= expanded disability status scale; BDI= Beck depression index; FIM= functional independence measure; FIS= fatigue impact scale, VaS= Visual Analogue Scale; MusiQoL= Multiple sclerosis quality of life.

pre and post intervention ( $p$  0.03, 0.0 and  $<0.001$ , respectively, Table 3). However, no differences were observed in fatigue ( $p = 0.23$ ).

A total of 14 patients completed the entire protocol of institutional VR and then TR. In those patients, when we analyzed FIM and MusiQoL we observed sustained improvement in both scales during both time periods (Figs. 2 and 3).

### 4. Discussion

This is the first multicenter study to evaluate the effectiveness of VR applied at institutions and then in a TR setting in MS patients in Argentina. Patients improved motor and functional aspects during the

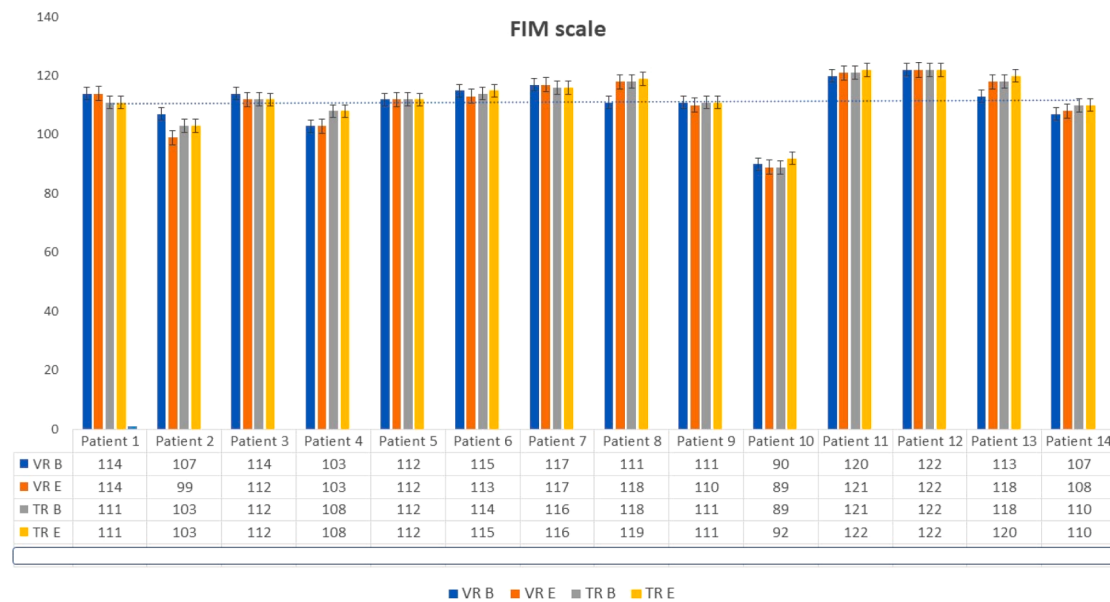


Fig. 2. FIM scale in patients that completed institutional VR and TR program, FIM= functional independence measure, VR= virtual reality; TR= telerehabilitation, VRB= virtual rehabilitation baseline; VRE= virtual rehabilitation end; TR= telerehabilitation baseline; TRE= telerehabilitation end.

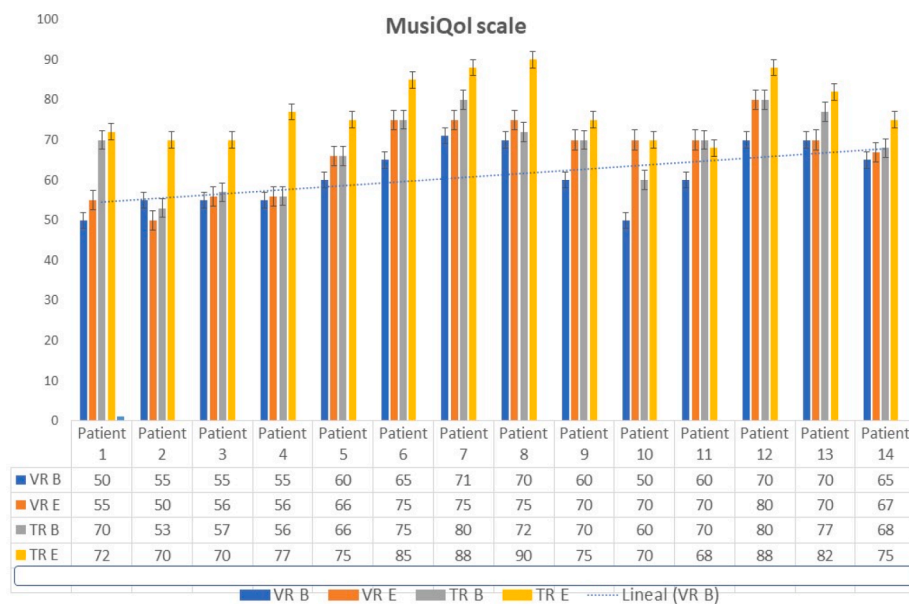


Fig. 3. MusiQoL scale in patients that completed institutional VR and TR program, MusiQoL= Multiple sclerosis quality of life, VR= virtual reality; TR= telerehabilitation, VRB= virtual rehabilitation baseline; VRE= virtual rehabilitation end; TR= telerehabilitation baseline; TRE= telerehabilitation end.

12 weeks applied, as well as other aspects such as a decrease in depression and an improvement in daily activity scales and quality of life. During the TR, the improvement was maintained throughout the period that the intervention was provided (12 weeks). It is important to highlight that a significant increase was observed in FIM in the VR ( $p = 0.01$ ) and TR phases ( $p = 0.02$ ), with FIM being an important measurement of the effectiveness of the intervention applied during both phases. As previously mentioned, FIM is not only a measurement of motor functions but also of functional independence as well (Dickson and Kohler, 1995). It is important to highlight in our study the high adherence to institutional VR during the first phase in all included patients, as well as in the 14 patients that were included during the TR phase, and the increased satisfaction with the intervention, as demonstrated with the VaS in VR and TR (Tables 2 and 3).

This study included two sequential and complementary stages: In the

initial one, the patients carried out a specific virtual reality (VR) program at the specialized neurorehabilitation center and under the supervision of a professional.

In the second stage the patients performed at their homes (outside the neurorehabilitation center), using a telerehabilitation (TR) program with remote professional supervision. Both phases are part of the same study whose objective was to evaluate the persistence of the results achieved during the first stage, even at the patient's home (TR phase).

A recent systematic review of 9 randomized controlled trials summarized the effects of interventions with VR in people with MS, compared to conventional intervention or no intervention, with special attention in the following outcomes: functional mobility, fatigue, quality of life, and balance (Nascimento et al., 2021). Of the 9 included studies, four in the intervention group used games from Nintendo Wii® and five used games from Microsoft Kinect®, all non-specific platforms for

rehabilitation (Nascimento et al., 2021). In relation to the comparison group, there were variations between the articles, as some studies used control groups with no exercises, and others used conventional exercises or a combination of them (Nascimento et al., 2021). In terms of functional mobility, despite studies reporting improvements in groups that underwent intervention (VR or other), no significant differences between groups were observed (Nascimento et al., 2021). The same pattern of results was found in the following measurement MSWS-12, 6MWT or 10MWT (Nascimento et al., 2021). Regarding fatigue and quality of life, there was a greater improvement in the RV group compared to the traditional exercise group (Nascimento et al., 2021). Quality of life was evaluated in three of the 9 studies and showed a better improvement on VR when compared with no intervention (Nascimento et al., 2021). Regarding balance, the Berg Balance Scale (BBS) was the most used scale to evaluate this outcome. In 5 studies the VR groups showed an improvement in balance when compared with no intervention. When results of balance were pooled in a meta-analysis against the traditional exercise group, there was a significant favorable effect for the VR groups (fixed effect; MD = 3.84; 95% CI: (2.54 to 5.14); I<sup>2</sup> = 4%; *p* = 0.35). In conclusion, this systematic review of 9 control trials showed that VR is as equally effective as conventional intervention in improving functional mobility in MS but, regarding quality of life, fatigue, and balance, it promotes an improvement equal to or greater than the conventional exercises (Nascimento et al., 2021). However, these observations should be interpreted with caution due to the methodological differences and dosimetry of trainings between the included studies and, also, due to the methodological quality of some of the included studies (Nascimento et al., 2021). It is important to mention that no intervention was done via telerehabilitation (Nascimento et al., 2021). Currently, there is one clinical trial that is recruiting patients to evaluate the effect of a telerehabilitation virtual reality intervention on functional upper limb activities in people with MS (the TEAMS pilot randomized controlled trial) (Kalron et al., 2020). In that study, twenty-four MS patients will be recruited at two MS centers (in Italy and Israel). Participants will complete a total of three assessments focusing on upper limb functions. Both groups will receive 16 training sessions focusing on functional upper limb activities. The home-based telerehabilitation VR intervention will comprise a custom-made software program running on a private computer or laptop and MS patients will perform several activities of daily living (ADL) functions associated with self-care, dressing, and meal preparation (Kalron et al., 2020).

Our study has many limitations that should be mentioned: first, the small number of centers included second, the short follow up times of included patients; and third, the low number of patients included during the telerehabilitation process. This latter limitation was caused by two factors: the availability of an internet connection to be able to continue the telerehabilitation in patient homes; and the lack of hardware to implement VR in their homes. A recent report performed in Argentina showed that despite an increase in the coverage and penetration of the Internet in Argentina over the past two years due to the pandemic, only 45% of the country had Internet coverage, most of which was centralized in large cities (batimes). This generated a significant limitation at the moment of implementation of the study since many patients did not have internet coverage to continue with VR during the telerehabilitation process. Another difficulty was the absence of laptops or desktops to install VR software in personal computers. As the software is not compatible with smartphones, only patients with available hardware were able to continue with the telerehabilitation process.

Despite that many methodological aspects are related to these issues (before and after analysis), it is important to highlight the limitations. In a real-world setting, Internet connections and the availability of hardware that allows the installment of the VR software could limit the use of this intervention, especially in clinical practice.

The extended use of these new technological tools in Neuro-rehabilitation encounters economic barriers specially in low-income countries. It is essential to obtain, as in any rehabilitation strategies,

an adequate balance between the availability of high-quality resources and the access for all users who request it. The potential utility of these rehabilitation techniques is to reach people who live far from specialized centers and optimize the care of patients with MS by using this rehabilitation approach with the use of low-cost, low-tech devices (smartphones and other portable devices) that are widely distributed, especially in low-income countries.

In conclusion, we observed an improvement in many functional aspects that affect the implementation of institutional VR and the tele-rehabilitation phase in MS patients in Argentina. However, its implementation still needs to be optimized to improve its use in clinical practice.

## 5. Funding

The study was carried out with an unrestricted grant for research from Novartis Argentina. The funder of the study had no role in the study design, data collection, data analysis, data interpretation, nor in the writing of the report. The corresponding author had full access to all data in the study and holds final responsibility for the decision to submit for publication.

## Author declaration

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us. We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property

## Declaration of Competing Interest

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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