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# Telerehabilitation for Lee Silverman Voice Treatment (Tele-LSVT)-Loud on voice intensity and voice use in daily living in people with multiple sclerosis: A protocol for a feasibility and pilot randomized controlled study

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## Abstract

**Objective:** Alterations in voice intensity and quality may constitute a social life limitation in people with multiple sclerosis (MS), but only 2% of cases receive speech therapy. Especially the Lee Silverman Voice Treatment (LSVT)-Loud is a highly effective intensive method for voice intensity, requiring subjects' repeated attendance at the clinic. Telerehabilitation may represent a feasible solution to bypass potential barriers related to speech therapy attendance, scaling up the beneficial effects of the treatment to a broader population. The proposed protocol aims to test the feasibility and the pilot efficacy of the LSVT-Loud delivered in telerehabilitation (Tele-LSVT-Loud), compared to the same treatment delivered in the clinic (LSVT-Loud).

**Methods:** A single-blinded, parallel, two-arm, pilot randomized (1:1 ratio) controlled trial will be performed involving 20 people with MS. Patients will be allocated to 4 weeks of Tele-LSVT-Loud by accessing a telerehabilitation platform at home or LSVT-Loud conventionally delivered in the clinic. Feasibility and pilot effectiveness will be evaluated three times: before (T0), after the treatment (T1), and 3-month follow-up (T2). Feasibility measures will include adherence, adverse events, user experience, motivation, engagement, and acceptability. Vocal intensity during a 1-minute monologue will be the primary outcome measure. Secondary outcome measures will be the vocal quality during a 1-minute monologue, sustained /a/ voice intensity, quality and stability, voice use in daily life, voice subjective perception in daily life, and quality of life.

**Results:** Expected results will be (1) high feasibility of Tele-LSVT-Loud and (2) a non-inferiority effect of Tele-LSVT-Loud compared with face-to-face treatment delivery on voice intensity and quality outcomes.

**Conclusions:** Tele-LSVT-Loud may be a feasible intervention for MS alteration in voice intensity and quality with a non-inferior effect compared to LSVT-Loud.

## Keywords

Telerehabilitation, speech therapy, multiple sclerosis, voice intensity, hypophonia, digital health

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## Background

Multiple sclerosis (MS) is currently one of the most common causes of chronic neurological disability in adults,<sup>1,2</sup> including speech, vocal, and communication disturbances in at least 62% of cases.<sup>3</sup> Among vocal disorders, reduced voice intensity or hypophonia<sup>4,5</sup> is predominant and highly impacts participation in social life.<sup>6,7</sup> MS people may experience difficulties in everyday conversations, such as when communication occurs in noisy, crowded environments, large groups of people, or on the phone. Though hypophonia significantly affects the social life of MS people, only 2% of MS hypophonic patients receive today specific treatment,<sup>8</sup> and studies investigating the effects of speech treatment in this clinical population are still sparse.<sup>8–11</sup> The paucity of evidence on interventions to improve voice quality in people with MS calls for the validation of effective dedicated methods for this population.



The LSVT-Loud is a well-documented, effective speech treatment for hypophonia.<sup>12,13</sup> The LSVT-Loud program adheres to key principles of motor learning and neural plasticity that are common mechanisms governing relearning in neurological conditions. For this reason, this method, first conceived to treat Parkinson's disease,<sup>12,13</sup> seems to be effective also in many other neurological conditions, such as cerebral palsy,<sup>14</sup> stroke and traumatic brain injury,<sup>15</sup> progressive supranuclear palsy,<sup>16</sup> and MS.<sup>17,18</sup> The recent works of Baldanzi et al.<sup>18</sup> and Crispiatico et al.<sup>19,20</sup> support the positive effects of the LSVT-Loud method in increasing voice intensity in MS. The effects of LSVT-Loud in MS may be related to the significant repetitions and task complexity increment over time, able to promote deconditioning and learned non-use. Deconditioning is, in fact, a substantial feature in the treatment of MS, where disability often leads to inactivity resulting in muscles' disuse. This inactivity often prevents people with MS from efficiently using their residual capacities.<sup>17</sup> Moreover, the role of high specificity and intensity of the LSVT-Loud on outcomes has been supported by Crispiatico et al.<sup>20</sup> Despite clear evidence that suggest the effectiveness of the LSVT-Loud method in increasing voice intensity in MS, several factors may prevent its agile use. First, the LSVT-Loud intensity requires patients' repeated attendance at a healthcare facility, which is, however, hindered by accessibility constraints related to distance barriers and/or neuromotor disability, such as balance impairment, postural instability, fatigue, and weakness. Moreover, people with MS are often still active workers, hardly including intensive interventions in their everyday routine. Also, repeated attendance at the clinic usually involves caregivers' availability when patients are not autonomous, with consequent time burden perception.

In response to these barriers, recent digital rehabilitation solutions may be adopted. Especially telerehabilitation, namely, technology-enabled rehabilitation care service

delivered out of the clinic and allowing monitoring at distance,<sup>21,22</sup> constitutes an alternative to the conventional face-to-face delivery. Telerehabilitation may allow bypassing typical barriers obstructing treatment attendance,<sup>21,23</sup> such as accessibility issues, health services overburden, and costs. In fact, healthcare platforms and mobile devices offer migration of care from the clinic to the patient's home,<sup>24</sup> integrating rehabilitation into the person's daily routine and social life and promoting healthcare self-management.<sup>25</sup> Telerehabilitation strategies are in line with multifaceted approaches to the modern management of patients,<sup>26</sup> empowering subjects to take control of their medical needs while enabling personalized care, choice, and personal control. Especially, by including the rehabilitation program in daily routine, the patient has an active role, empowered and engaged in their own care management, with consequences also on perceived care outcomes.<sup>27</sup> A large number of trials support the feasibility of telerehabilitation approaches in MS and compare their effectiveness with standard rehabilitation practice,<sup>21,28–30</sup> also showing an enhancement of perceived participation in social activities after treatment attendance.<sup>24</sup> In the context of speech therapy, pioneer digital computerized interventions were proposed, especially for the language domain in aphasia post-stroke conditions.<sup>31</sup> Also, speech therapy telerehabilitation delivery gained attention,<sup>32</sup> with latest contributions supporting its viability to treat language disturbances at distance<sup>33</sup> and showing a good attitude of speech therapists toward the adoption of this new delivery path.<sup>34,35</sup> However, evidence supporting telerehabilitation for the treatment of voice intensity and quality in neurological conditions are still scarce, even if its utility in the clinical setting is acknowledged. In fact, the voice treatment guidelines mentioned telerehabilitation as a valid solution during the pandemic emergency period.<sup>36</sup> The paucity of evidence of voice telerehabilitation includes the work of Dias et al.,<sup>37</sup> which tested the efficacy of the LSVT-Loud method delivered by telerehabilitation in Parkinson's disease, reporting non-inferiority effects compared to conventional delivery paths. Recently, Crispiatico et al.<sup>19</sup> showed that LSVT-Loud could be a valid treatment to increase voice intensity in MS, but no evidence is available on the efficacy of voice treatment delivered by telerehabilitation. Given the beneficial effects of LSVT-Loud treatment in telerehabilitation in other neural conditions often suffering from hypophonia or reduced voice intensity,<sup>12,14–16</sup> it is plausible to assume that LSVT-Loud delivered to people with MS by telerehabilitation is a feasible solution with a non-inferior effect compared to LSVT-Loud delivered in the clinic.

The proposed trial aims to test the feasibility of the LSVT-Loud program delivered by telerehabilitation (Tele-LSVT-Loud) in people with MS and to pilot explore its efficacy compared to the same treatment conventionally delivered in the clinic (LSVT-Loud).

**Table 1.** SPIRIT diagram for the schedule of enrollment and interventions in a parallel arm study design.

Period				
Timepoint		Baseline	Post-allocation	
		T0	T1	T2
<b>Enrollment</b>				
	Eligibility screen	X		
	Informed consent	X		
	Recruitment	X		
	Allocation	X		
<b>Interventions</b>				
	Tele-LSVT-Loud			
	LSVT-Loud			
<b>Assessments</b>				
	<i>Demographic characteristics</i> Age Education Sex	X		
	<i>Clinical characteristics</i> EDSS Disease onset Disease duration Pharmacological treatment MS form	X		
	<i>Global cognitive level</i> MONTreal Cognitive Assessment	X		
	<i>Fatigue</i> Modified Fatigue Impact Scale	X		
	<i>Technological expertise</i> Ad hoc questionnaire	X		
	<i>Voice intensity and quality</i> 1-minute monologue voice intensity and quality Sustained /a/ voice intensity quality and stability Daily life voice intensity and quality (Vocal Holter)	X	X	X
	<i>Quality of life</i> Voice Handicap Index World Health Organization Disability Assessment Schedule 2.0	X	X	X

(continued)

Table 1. Continued.

Period	Timepoint		
	Baseline T0	Post-allocation T1 T2	
Technology experience User Experience Questionnaire Intrinsic Motivation Inventory		X	
Feasibility Adherence Ad hoc individual interview		X	
Safety Adverse events		X	

T0 = baseline (pre-intervention phase); T1 = post-treatment assessment; T2 = follow-up assessment (3 months after treatment). EDSS = Expanded Disability Status Scale; MS = multiple sclerosis.

## Materials and methods

The protocol of the study has been designed and reported in line with the “Standard Protocol Items: Recommendations for Interventional Trials” (SPIRIT) guidelines (Table 1, Figure 1). The study will be conducted according to the Declaration of Helsinki, the principles of Good Clinical Practice, and in accordance with local legislation in participating countries.

### Trial design and setting

The study design consists of a single-blinded, randomized, parallel, two-treatment arm controlled clinical trial. Participants will be recruited from the MS Rehabilitation Unit of the IRCCS Don Carlo Gnocchi Foundation ONLUS of Milan (Italy).

After enrollment in the study and baseline evaluation, MS patients will be 1:1 randomly allocated to the experimental or control condition. The experimental group will follow 4 weeks of LSVT-Loud delivered in telerehabilitation (Tele-LSVT-Loud), while the control group will be administered the same treatment in the clinic (conventional modality; LSVT-Loud). Feasibility and pilot effectiveness will be evaluated during and after treatment administration. Outcome measures will be assessed at baseline (T0), after treatment (T1), and follow-up (3 months after T1). Figure 1 reports the trial work plan.

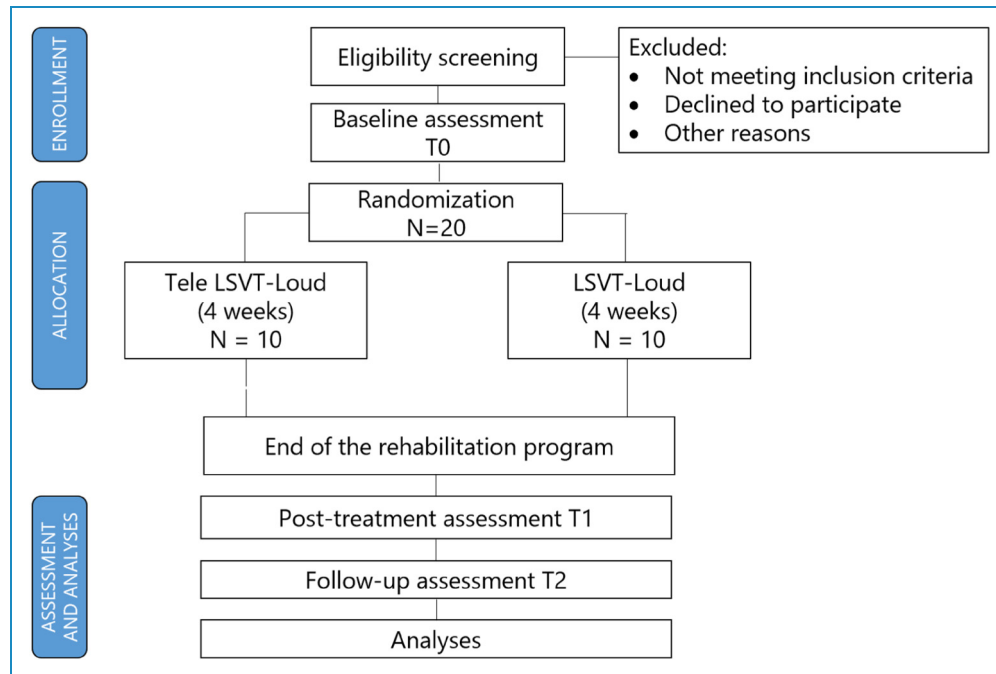
### Sample size

An a priori sample size calculation was performed using the G\*Power software (3.1 version) on the primary outcome measure. A sample size of 20 subjects (10 subjects per condition) was adequate to detect a statistical power (1-β) =

0.80 and standardized effect size (f) = 0.30, with a statistical threshold of  $\alpha < 0.05$  to test the Tele-LSVT-Loud non-inferiority effect compared to the LSVT-Loud program, using a repeated measure ANOVA model (two levels between factors, condition; three-levels within factor, time; time × condition interaction).

### Study population, recruitment, and randomization

According to the sample size calculation (see the paragraph above), 20 patients with MS will be recruited according to the inclusion criteria (see the paragraph below). Participants will be contacted by their referring neurologist whether they fulfill the inclusion criteria for enrollment in the study (see “Inclusion and exclusion criteria”). In addition, the research study open enrollment will be disseminated within the IRCCS Don Gnocchi Foundation by means of flyers. When potential participants express their intention to take part in the study, the study protocol will be clearly explained to them. They will be informed that their participation would be subjected to the presence of some inclusion and exclusion criteria (see “Inclusion and exclusion criteria”) and that they will not be able to choose which arm of the study they will be assigned to. Therefore, they must be available for both face-to-face treatment and telerehabilitation (see below). After enrollment in the study, participants will be randomly allocated to the experimental or control condition using a web-based allocation concealment and a computer-based algorithm by an independent researcher. The randomization will be computed with a 1:1 ratio and will be stratified based on the baseline vocal intensity level (two blocks: block 1, SPL < 60 dB; block 2, SPL ≥ 60 dB, as measured with in-air microphone at a distance of 30 cm, during a



**Figure 1.** The trial work plan.

1-minute monologue; see “Acoustical measures”). Both speech–language therapists and participants will not be blind to the allocation. Instead, the assessors will be blinded to the patients’ arm allocation. Also, the researcher performing statistical analysis will be masked for the group allocation.

### Inclusion and exclusion criteria

The inclusion criteria will be (1) age > 18; (2) diagnosis of MS based on McDonald’ criteria<sup>38,39</sup>; (3) exhibit mild-to-severe voice symptoms (as confirmed by two speech–language therapists); (4) Mini-Mental State Examination > 24<sup>40</sup>; (5) availability of a personal computer and internet connection at home; (6) stable pharmacological treatment with dopamine agonists and/or steroids in the last 3–6 months, if any; and (7) agreement to participate in the study with the signature of the informed consent form.

The exclusion criteria will be (1) the presence of dysphonia related to other diseases; (2) the presence of comorbidity such as other neurological conditions different from MS; (3) a history of laryngeal cancer, radiotherapy, or head–neck trauma or intubation; (4) the presence of visual/hearing problems; (5) presence of major psychiatric comorbidities; and (6) participation in voice rehabilitation sessions with conventional treatment or LSVT-Loud in the last 6 months.

### Trial interventions

Participants will be randomly allocated to two treatment conditions: Tele-LSVT-Loud (experimental condition) and LSVT-Loud (active comparator).

The LSVT-Loud method will be delivered by an expert LSVT-Loud speech therapist (LSVT-Loud certified) and will be adopted in both conditions with the same rehabilitation frequency (F), intensity (I), and time (T)<sup>41</sup>:

F: Synchronous LSVT-Loud sessions will be held 4 times a week for 4 weeks + LSVT-Loud autonomous practice 7 times a week for 4 weeks;

I: Sessions will be personalized and customized according to the patient’s functional abilities to ensure the progression of difficulty in rehabilitation sessions;

T: Each synchronous session will last about 60 minutes, each autonomous practice will last about 5–10 minutes in addition to the synchronous session (4 times a week) or 30 minutes (3 times a week).

In detail, each synchronous session of the LSVT-Loud method consists of “daily tasks,” which are always the same, and “hierarchical exercises.” The daily tasks consist of 30 minutes of activities: (a) maximum duration sustained vowels, (b) maximum frequency range, and (c) repetition of 10 functional phrases, while the hierarchical exercises consist of 30 minutes of reading and conversation exercises that progress in difficulty by increasing the duration and complexity of the tasks.

Speech–language therapists train the subjects to perform the exercises autonomously. Each autonomous session of the LSVT-Loud method consists of 10-minute exercises in addition to the synchronous session four times a week

and 15-minute exercises twice a day the remaining 3 days of the week.

A detailed description of the intervention has been published.<sup>13</sup>

The two treatment conditions will differentiate only for the type (T) of synchronous intervention. Especially, in the Tele-LSVT-Loud intervention, speech therapy sessions will be delivered by telerehabilitation, while in the LSVT-Loud condition, the intervention will be conventionally delivered *face to face* in the clinic. In detail, in the Tele-LSVT-Loud group, the synchronous sessions will be administered through a digital telerehabilitation platform (Maia Platform, <https://abmedica.it/prodotti-ab-medica/maia>). The speech–language therapist and patient will have access to the platform with their credentials. From the therapist’s side, the telerehabilitation platform portal will allow the planning of synchronous rehabilitation sessions during the intervention period. Once the therapist plans a rehabilitation session through the portal, the patient will receive a link to connect to the synchronous session by mail 48 hours before starting the session. The patient will participate in the synchronous session using the personal PC at home by clicking the link received by mail and accessing a telepresence system (videoconference system).

## Measures

An evaluation battery will be administered to participants at the baseline (T0), after the treatment (T1), and at the 3-month follow-up (T2) (see Table 1), including both output measures to test the feasibility of the Tele-LSVT-Loud intervention and outcome measures to pilot test its efficacy compared to the conventional LSVT-Loud.

**Feasibility measures.** **Adherence to the treatment** will be registered by the therapist for the synchronous sessions (in telepresence or in the clinic). Moreover, the participants will fill a structured diary in which they report their attendance at the autonomous practice. Also, they will note their perceived experience related to the treatment adherence and eventual reasons for not participating in some sessions. Attendance to at least 80% of the session will be considered a high level of adherence.

**Adverse events** will be investigated during the rehabilitation period. Patients will be invited to list adverse events occurring during the therapy and outside of the sessions in the structured diary. Moreover, a weekly semi-structured interview by a psychologist will be aimed at exploring possible safety issues experienced during the rehabilitation attendance (e.g. excessive vocal fatigue or breathlessness).

**Telerehabilitation platform user experience** will be assessed by the User Experience Questionnaire (UEQ)<sup>42</sup> at T1. The UEQ is a 26-item scale (semantic differential scale: each item consists of two opposite adjectives, e.g.

boring vs. exciting) that allows calculating six different domains: (1) attractiveness (overall impression of the system), (2) perspicuity (easily to learn how to use the system), (3) efficiency (user’s effort to solve tasks), (4) dependability (feeling of control of the interaction with the system), (5) stimulation (motivation to use the system), and (6) novelty (innovation and creation of the system). The mean of the item score of each domain will be standardized based on a data benchmark.<sup>42</sup>

**Intrinsic motivation for the treatment** will be measured by the Intrinsic Motivation Inventory – Interest/Enjoyment subscale (IMI-IE<sup>43</sup>) after treatment. IMI-IE consisted of a pool of seven items 7-point Likert scale<sup>44</sup> ranging from (1) “Absolutely Not” to (7) “Absolutely Yes.” A total score (average of the item scores) will be considered, and a higher score will be considered as a greater motivation level.

**Perceived treatment engagement, acceptability, and feasibility** will be investigated by performing individual *ad hoc* interviews during and after the rehabilitation protocol period. In detail, the individual *ad hoc* interviews will be weekly administered to each patient at the end of each week of treatment (four individual interviews for each patient). The track of the individual interview will be implemented during round table meetings of telerehabilitation experts, which will be involved in the track testing and refinement. The interviews will be recorded, and then the registration will be verbatim transcribed.

## Effectiveness measures

**Acoustical measures.** All the acoustical measures were collected following published recommendations, and<sup>14,45,46</sup> mouth-to-microphone distance is kept at 30 cm in a quiet room.

The acoustical tasks will be recorded using a portable high-quality (24 bit/96 kHz) recorder with an integrated in-air microphone (Roland, R-05) and the device Vocal Holter (VH), which consists of a contact microphone placed in a collar worn around the neck and a device for data acquisition, processing, and storage that can be worn in a pocket during the day. The contact microphone measures the skin vibrations caused by the activity of the vocal cords. Besides the voice indicators, local temperature and relative humidity are also measured during monitoring. The sound pressure level (SPL, dB) values are obtained from both a calibrated in-air microphone and the contact microphone of the VH device, which is subjected to a personal calibration using an embedded microphone in air that is located at 22 cm from the mouth of the involved subject (length guaranteed by the removable telescopic antenna integrated into the device). The same in-air microphone was previously calibrated against a pressure calibrator, which provides an SPL level of 94 dB via a signal at a frequency of 1 kHz.

The following acoustic parameters will be obtained: sound pressure level (SPL) expressed in decibel (dB), fundamental frequency  $f_0$  expressed in Hertz (Hz), harmonic-to-noise ratio (HNR) (dB), cepstral peak prominence smoothed CPPS (dB), local shimmer (%), and local jitter (%). These outcomes are commonly used in studies of voice treatment with LSVT-Loud method.<sup>46–48</sup> It is worth noting that the collection of all these parameters for the evaluation of voice quality guarantees an adequate intra-subject reliability and a valid interpretation of results.<sup>49,50,51</sup>

The average vocal intensity of 1 minute of monologue (SPL, dB) will be recorded simultaneously through the air and contact microphones. This is an objective, acoustic measure with established reliability.<sup>46</sup> As this measure is the primary outcome, it will be collected at baseline, post-treatment, and follow-up. Participants will be requested to speak about simple and familiar topics at a comfortable frequency and intensity level. A specific task identical for each participant will be given: “Please speak for at least a minute, explaining ‘how to make coffee,’ ‘how you feel today,’ and ‘what is scheduled for the day.’” The PRAAT software (www.praat.org) will analyze the voice parameters recorded with the microphone in air, while the VH device extracts the acoustical parameters from the voice samples recorded via the contact microphone.

**Intensity of sustained vowel /a/ (SPL/a/, dB)** will be evaluated simultaneously through the in-air and contact microphones at baseline, post-treatment, and follow-up. All participants will be requested to sustain the vowel /a/ as long as possible at a comfortable frequency and intensity level. A specific task, identical for each participant, will be given: “Take a deep breath and say /a/ as long as you can.”<sup>14</sup> The mean intensity measured in decibels (SPL, dB) of three repetitions of the vowel /a/ will be considered. The PRAAT software (www.praat.org) will analyze the voice parameters recorded with the microphone in air. VH extracts the parameter from the voice samples recorded via the contact microphone. Sustained /a/ voice quality and stability will be measured by means of the parameters CPPS, HNR,  $f_0$ , local shimmer, and local jitter.

**The intensity of voice in daily life** will be measured (SPL, dB), and the voice quality will be assessed through the parameters CPPS, HNR, and  $f_0$ . Participants’ voices will be monitored for about 4 hours of consecutive speech by means of the VH device. To this aim, they were instructed to wear the VHM after the evaluation session before returning to their daily routine.

**Quality of life measures. The patient’s voice self-assessment and quantification of the impact of the voice disorder on their daily life** will be measured by the Voice Handicap Index (VHI<sup>52</sup>) at baseline, post-treatment, and follow-up. VHI is a standardized 30-item questionnaire, divided into three subscales covering functional, emotional, and physical aspects of voice disorders.

Participants have to rate each statement using a 5-point scale scored from 0 (never) to 4 (always); the maximum score is 120 (worst score). The score of 12 at the VHI test should be considered as a threshold for rating the handicap caused by voice disorders. The VHI has been demonstrated to be an effective tool to evaluate self-perception of voice quality in people with MS, which correlates with the Grade Roughness Breathiness Asthenia Strain scale score.<sup>4</sup>

**The perceived quality of life** will be measured by the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0<sup>53</sup>) at baseline, post-treatment, and follow-up. WHODAS 2.0 covers six domains of functioning including cognition, mobility, self-care, getting along, life activities, and participation. Scores assigned to each item are on a 5-point scale ranging from (0) “none” to (4) “extreme” with higher scores indicating a higher disability. The 36-item version will be administered, and both summary scores (score range 0–144 with higher numbers indicating higher disability) and domain-specific scores for the six different functioning domains (especially in cognition, life activities, and participation domain will be considered; score range 0–24 for each domain with higher numbers indicating higher disability). The WHODAS 2.0 has been reported as a valid measure to assess and monitor disability impact on quality of life in people with MS.<sup>54</sup>

#### Other measures

–The clinical profiles of patients routinely reported in their medical records will be collected at baseline. In details, MS form, disease duration, pharmacological treatment, and Expanded Disability Status Scale score<sup>55</sup> will be considered.

–The global cognitive level will be investigated at baseline by the Montreal Cognitive Assessment scale.<sup>56</sup> The scale evaluates attention, executive functions, memory, language, visuospatial abilities, abstraction, calculation, and orientation abilities, providing a total score ranging from 0 to 30 (a higher score indicates a greater global cognitive level).

–The perceived level of fatigue will be measured at baseline by the Modified Fatigue Impact Scale,<sup>57</sup> a self-report 21-item 5-point Likert scale.<sup>44</sup> The questionnaire evaluates the perceived fatigue in terms of physical, cognitive, and psychosocial function. Total score ranges from 0 to 84, with a higher score indicating a greater effect of fatigue on daily life activities.

–The technological expertise will be evaluated at baseline to take account of participants’ different levels of competence at baseline, which may influence their attitude in using telerehabilitation systems. This variable would allow to test whether a high proficiency in technology use is required to access LSVT-Loud treatment via telerehabilitation. Moreover, it would enable investigating whether participants’ technology expertise impacts their perceived usability toward telerehabilitation system. Technology familiarity and expertise will be explored by a 12-item

*ad hoc* questionnaire exploring the frequency of use and the perceived competence in the use of technological devices and systems, such as PC, tablets, internet, smartphones, social networks, videogames, and apps). For each technology, subjects will be invited to rate their level of familiarity and skills in the use on a 5-point Likert scale.<sup>44</sup> Two separate total scores will be obtained for the frequency of use and the perceived competence in the use by averaging the item scores (score range 1–5. A higher score indicates greater familiarity and perceived competence).

### Data collection

The anamnestic and clinical profile, global cognitive level, perceived fatigue, and technological expertise will be evaluated at T0. The feasibility measures will be collected during and after treatment (T1). In detail, during the treatment period, adherence and adverse events will be investigated by the therapist and reported in the patient diary. Also, weekly individual *ad hoc* interviews will be performed to evaluate safety issues, motivational drivers, previous and actual expectations, accessibility issues, therapist–patient interaction, and perceived effects of the treatment on quality of life. At T1, the user experience and intrinsic motivation related to the treatment will be assessed. The effectiveness measures (primary and secondary) will be collected at T0, T1, and T2.

### Statistical analysis

Statistical analysis will be performed on quantitative data using IBM SPSS Statistics (version 28) and jamovi software (version 2.3) (<https://www.jamovi.org>).

Descriptive statistics (frequencies, medians, means, interquartile ranges, standard deviations) will be run both for baseline, feasibility, and efficacy measures. Correlations between feasibility and clinical baseline measures will be tested. Unpaired comparisons will be performed to test group differences (Tele-LSVT-Loud vs. LSVT-Loud) in feasibility measures at T1. According to the CONSORT guidelines, changes in primary and secondary outcome measures will be tested. Eventual missing data will be handled by adopting an intention-to-treat approach. A  $2 \times 3$  repeated measures ANOVA model will be adopted to test the interaction between condition (two levels between factor: Tele-LSVT-Loud vs. LSVT-Loud) and time (three levels within factor: T0, T1, T2). Visual inspection of residual plots will be performed to assess deviations from homoscedasticity or normality or presence of influential point. Post hoc analysis will also be run to observe pairwise comparisons adjusting for multiple comparisons. A significant statistical threshold of  $\alpha < 0.05$  will be considered.

To test the non-inferiority effect of Tele-LSVT-Loud with respect to LSVT-Loud, the lower limit of the confidence interval (CI) of acoustic measures will be assessed.

According to the extension of the CONSORT 2010 Statement,<sup>58</sup> the non-inferiority effect will be demonstrated if the lower bound of the two-sided  $(1-2\alpha) \cdot 100\%$  CI for the treatment effect (change after treatment) will be below the margin (greater than  $-0.5$ ), with a significant level  $\alpha < 0.05$ .

Whether clinically relevant results will be observed on the effectiveness of Tele-LSVT-Loud protocol, data will be useful to compute the sample size required to get a precise estimate of treatment effects in subsequent larger Phase III randomized control trials.

### Discussion

Though voice and speech impairments are widely present in people with MS, only 2% of patients receive specific targeted therapy.<sup>8</sup> The LSVT-Loud is a highly specific and intensive intervention that has been demonstrated to be effective in increasing the voice intensity and quality in people with MS.<sup>18–20</sup> Although the intensity of the treatment (dose) contributes to the intervention effectiveness, it also may lead patients to experience accessibility barriers, with consequent difficulties in adhering to and completing the treatment.

To overcome the challenges associated with conducting *face-to-face* intensive treatment, it has been proposed to deliver LSVT-Loud by telerehabilitation. The present proposed protocol investigates the feasibility and pilot efficacy of the LSVT-Loud delivered by telerehabilitation compared to the conventional delivery modality (*face to face* in the clinic).

As the first result, the high feasibility of Tele-LSVT-Loud will be verified. Based on previous studies investigating the feasibility of telerehabilitation protocols for MS<sup>21,24,30</sup>, a higher compliance and acceptability of Tele-LSVT-Loud compared to the standard LSVT-Loud intervention are expected. Especially the telerehabilitation delivery modality may be able to break down distance barriers and travel time dedicated to reaching the clinic to participate in the sessions. Additional potential barriers related to telerehabilitation can be the technological proficiency of the users and the usability of the system. However, recent data showed that the usability and acceptability of the telerehabilitation systems were high in subjects with chronic diseases despite the medium–low level of the technological proficiency of the patients.<sup>23</sup> This study's findings link patients' usability experience to their behavioral intention to use the system, primarily due to their perceived utility for their own health condition, in agreement with validated technology acceptance models.<sup>59</sup>

It is also expected to observe minimal adverse events during the Tele-LSVT-Loud, according to previous trials testing the safety-related issues of telerehabilitation protocols.<sup>23,60</sup> Also, moving the setting of the rehabilitation from the clinic to the home has been reported to enhance the patient's engagement in the treatment and his/her

activation in healthcare plan self-management.<sup>61</sup> This may assure to observe a high intrinsic motivation in the treatment of subjects attending Tele-LSVT-Loud. Eventually, the low complexity of the patient's side platform portal and the synchronous communication of the telerehabilitation sessions lead us to posit a good user experience in the interaction with the technology. Moreover, we will test whether clinical characteristics influence feasibility perception of the intervention (e.g. a higher disability may affect the perceived usability of the system).

Concerning the pilot effectiveness, previous contributions reporting the non-inferiority effect of Tele-LSVT-Loud in Parkinson's disease<sup>37</sup> may support our hypothesis to find similar results also in the MS population. Vocal intensity disturbances usually affect people with a medium-to-long disease duration and a moderate-to-high disease history. We expect to include in the study people with approximately 5–8 EDSS score. The maintenance of the same dose of the treatment both in Tele-LSVT-Loud and LSVT-Loud, in terms of frequency, intensity, and time, leads to assume the same beneficial effects of the LSVT-Loud method in the two conditions. Given the reduced sample size of the trial, these results will be used to compute the sample size for future randomized controlled trials. In these future studies, the impact of the clinical characteristics on the outcomes will also be investigated.

Our pilot results will pave the way for a telerehabilitation approach for voice treatment in people with MS. Specifically, it will provide evidence of the feasibility of a well-known method, the LSVT-Loud, for improving voice intensity and quality delivered by a telerehabilitation approach. The study findings may support the adoption of telemedicine digital tools to overcome accessibility constraints related to intensive and high-dose speech therapies for MS.

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