

Delivering the Lee Silverman voice treatment-loud method in-site versus telerehabilitation in people with multiple sclerosis: Feasibility evidence of a non-inferiority pilot randomized

Original

Delivering the Lee Silverman voice treatment-loud method in-site versus telerehabilitation in people with multiple sclerosis: Feasibility evidence of a non-inferiority pilot randomized controlled trial / Vitali, C., Fusari, G., Cacciatore, D.M., Smecca, G., Baldanzi, C., Carullo, A., Rovaris, M., Cattaneo, D., Baglio, F., Isernia, S.. - In: DIGITAL HEALTH. - ISSN 2055-2076. - ELETTRONICO. - 11:(2025), pp. 1-13. [10.1177/20552076251326222]

Availability:

This version is available at: 11583/3008487 since: 2026-03-10T09:01:19Z

Publisher:

SAGE

Published

DOI:10.1177/20552076251326222

Terms of use:

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

Publisher copyright

(Article begins on next page)

Delivering the Lee Silverman voice treatment-loud method in-site versus telerehabilitation in people with multiple sclerosis: Feasibility evidence of a non-inferiority pilot randomized controlled trial

DIGITAL HEALTH
Volume 11: 1–13
© The Author(s) 2025
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/20552076251326222
journals.sagepub.com/home/dhj



Chiara Vitali^{1,*}, Giulia Fusari^{1,3,*}, Diego Michael Cacciatore¹, Giulia Smecca¹,
Cinzia Baldanzi¹, Alessio Carullo², Marco Rovaris¹, Davide Cattaneo^{1,3},
Francesca Baglio¹ and Sara Isernia¹ 

Abstract

Objective: Telerehabilitation may overcome accessibility barriers related to the Lee Silverman Voice Treatment (LSVT)-Loud for dysphonia rehabilitation in multiple sclerosis (MS). The present study provides the feasibility evidence on patient-relevant structural and procedure effects of a pilot randomized controlled trial comparing LSVT-Loud telerehabilitation (Tele-LSVT-Loud) versus standard delivery.

Methods: Twenty-one people with MS (six males) with dysphonia were 1:1 randomly allocated to 4 weeks of LSVT-Loud in-site or Tele-LSVT-Loud at home accessing a telemedicine platform. The feasibility of Tele-LSVT-Loud compared to LSVT-Loud was evaluated considering adherence rate, safety (adverse events), technology interaction (User Experience Questionnaire), intrinsic motivation to the treatment (Intrinsic Motivation Inventory), and perceived rehabilitation experience (individual qualitative interviews) during and after the intervention program.

Results: Thirty-one percent of eligible subjects were unavailable to follow in-site treatment. Drops-outs were higher in the LSVT-Loud than Tele-LSVT-Loud group (4 versus 1). Also, the adherence rate of synchronous sessions was 68.75% in the LSVT-Loud compared to 87.5% in the Tele-LSVT-Loud group, related to greater difficulty in integrating the treatment into a daily routine, as mentioned in the qualitative interview. No relevant adverse events were observed in both groups. The user experience with technology in the Tele-LSVT-Loud group was positive. The interviews revealed a positive therapeutic alliance, regardless of the delivery path. Interestingly, only people in the Tele-LSVT-Loud group judged equivalent the therapist-user relationship in in-site and telerehabilitation settings.

Conclusions: Telerehabilitation promotes the feasibility of LSVT-Loud. The modality of delivery is a relevant factor in determining eligibility and adherence to a voice rehabilitation program in MS.

Keywords

Telerehabilitation, multiple sclerosis, voice, feasibility, digital health, speech therapy

Submission date: 14 November 2024; Acceptance date: 18 February 2025

¹IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy

²Department of Electronics and Telecommunications, Politecnico of Turin, Turin, Italy

³Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

*The first two authors equally contributed to the work.

Corresponding author:

Sara Isernia, IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy.

Email: sisernia@dongnocchi.it



Background

Tele-speech therapy has been recently suggested as a safe and efficient alternative to in-person rehabilitation for voice disorders,¹ with the potential to lessen extra costs, distance-, time-consuming issues, and caregiver burden, often hindering rehabilitation accessibility. However, tele-rehabilitation for voice disorders is still poorly adopted, and skepticism remains among people experiencing voice disorders and caregivers about the capacity of telepractice to equally surrogate in-person sessions.²

Multiple Sclerosis (MS) is one of the most common central nervous system neuroinflammatory diseases accumulating physical disability in young adult age,³ and potentially impacts speech and voice,^{4,5} consequently provoking dysarthria (motor speech changes) and dysphonia (voice changes) conditions.⁶ In particular, dysarthria is identified as the most prevalent expressive communication deficit in MS, with an estimated prevalence of around 45%,⁷ potentially affecting all speech subsystems including respiration, phonation, resonance, articulation, and prosody, along with impairments in receptive and expressive language.⁸ The primary dysarthric characteristics in MS include slowed speech, increased frequency and duration of pauses (often with inappropriate onset), impaired loudness control, mono-pitch, imprecise articulation of consonants, asthenic or strained voice quality, and reduced respiratory capacity. Even mild dysarthria is highly common in MS and can significantly affect the individual's quality of life, underscoring the importance of early detection and management. When considering dysphonia, speech-language pathologists perceptually rated people with MS as vocally impaired in 45% to 91% of the cases.⁷ Voice impairment in people with MS is perceptually characterized by pitch instability, asthenia, hoarseness, and breathy voice. Glottal inefficiency, reduced loudness control, and vocal instability (both short-term and tremor-like) are key features, with studies highlighting glottal inefficiency as a determinant factor in voice deterioration. Phonatory asthenia and strain, as well as impaired pitch and loudness control, affect about 30% of cases. Moreover, the acoustic analysis showed increased jitter (frequency perturbation) and shimmer (amplitude perturbation), indicating short-term instability in pitch and loudness.⁹ Long-term tremor-like instability has proven to be a strong predictor for distinguishing people with MS from healthy individuals, though findings on fundamental frequency remain inconsistent across studies.¹⁰

Few studies on specific treatments for speech and voice disorders in people with MS have been documented. Among these, expiratory muscle strength training,¹¹ which improved respiratory strength without significant changes in voice production or quality of life, and the work by Crispiatico et al.¹² on the use of Lee Silverman Voice Treatment (LSVT)-Loud have been reported.

The LSVT-Loud is a standardized speech rehabilitation method^{13,14} based on motor learning and neural plasticity

principles to enhance voice intensity and quality. The works of Sapir et al., Baldanzi et al., and Crispiatico et al.^{12,15–17} demonstrated the effect of LSVT-Loud treatment on dysphonia in MS. Although the impact of this method on MS voice impairment, some barriers hamper its accessibility, for which telerehabilitation may be a solution. LSVT-Loud especially requires intensive continuous adherence and attendance in the clinic: people receiving the treatment have to participate in four sessions per week with the therapists for a total of four weeks and they have to complete autonomous practice seven days a week for the period of the intervention. This commitment often hardly fits with the work demands of people of adult age, or with people with reduced motor autonomy, often requiring the assistance of a caregiver. Importantly, in some cases, voice disorders in MS may occur in advanced phases of the disease, when the physical disability level is impactful. In this context, the possibility of accessing the treatment at a distance in a telerehabilitation setting may scale up the target of patients who can be candidates for voice rehabilitation.

In the present randomized controlled trial, we tested the feasibility of patient-relevant structural and procedure effects of the LSVT-Loud treatment delivered in telerehabilitation (Tele-LSVT-Loud) compared to the in-person conventional modality (LSVT-Loud) in a group of people with MS in need of vocal intervention.¹⁸

This study reports the evidence on the feasibility of the Tele-LSVT-Loud, by exploring indicators of patient-relevant structural and procedure effects, such as recruitment practicability, adherence, safety, and acceptability with both quantitative and qualitative approaches (mixed methods).

Method

The present study reports the feasibility results of the “*Telerehabilitation for Lee Silverman Voice Treatment (Tele-LSVT)-Loud on voice intensity and voice use in daily living in people with multiple sclerosis*” project trial.

The protocol of the study is detailed in Vitali et al.¹⁸ and registered as a clinical trial on clinicaltrials.gov (identifier NCT05930379). The study has been approved by the Don Gnocchi Ethics Committee (protocol number 03_29/03/2023) and conducted and reported in accordance with the CONSORT guidelines (the CONSORT checklist is reported in Supplemental materials).

Trial design and setting

This is a single-blind (assessors), randomized (1:1), parallel two-arm, controlled trial conducted at the IRCCS Don Carlo Gnocchi Foundation ONLUS of Milan (Italy).

Participants were recruited from the clinic's Multiple Sclerosis Rehabilitation Center by the clinicians, enrolled in the study, and randomly allocated to the experimental or control (active comparator) arms (1:1 ratio). The two conditions, experimental and control, consisted of 4 weeks of speech therapy for voice intensity based on the LSVT-Loud method.¹⁴ In the experimental condition, the therapy was administered in telerehabilitation (Tele-LSVT-Loud), while in the control condition, it was delivered in-site as the conventional modality (LSVT-Loud). Feasibility was assessed during and after the treatment period (for details, see reference¹⁸).

Study population

Participants were considered eligible to take part in the research and enrolled in the study by neurologists and/or physiatrists whether they fulfilled the following criteria: (1) age >18 years; (2) MS diagnosis based on criteria of McDonald,¹⁹ (3) mild-to-severe voice symptoms reported (as confirmed by two speech therapists), (4) preserved cognitive functions (Mini-Mental State Examination score >24 points), (5) possibility to use 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, (7) expressing agreement to participate in the study by signing the informed consent form, (8) absence of dysphonia related to other diseases than MS, (9) absence of comorbidity such as other neurological conditions different from MS, (10) absence of history of laryngeal cancer, radiotherapy, head-neck trauma or intubation, (11) absence of visual/hearing disability, (12) absence of major psychiatric comorbidities, (13) do not have attended LSVT-Loud speech therapy in the last 6 months.

Sample size has been a priori estimated using G*Power software (3.1 version) (see Vitali et al.¹⁸ for details).

Randomization

A computer-based 1:1 randomization ratio was performed by a researcher not involved in the assessment. The randomization was set within two strata based on the baseline vocal intensity level measured with the 1-min monologue test with an in-air microphone located 30 cm from the mouth (SPL < 60 dB; SPL ≥ 60 dB). Only assessors and researchers performing statistical analysis, but not speech therapists conducting the rehabilitation sessions and participants were blind to the allocation. Rehabilitators assigned participants to interventions.

Trial interventions

In both arms, the LSVT-Loud method¹⁴ was delivered by a speech therapist (LSVT-Loud licensed) with the same frequency, intensity, and time, as follows:

frequency: 1 synchronous session 4 times/week for 4 weeks + autonomous practice 7 times/week for 4 weeks.

intensity: the session was customized according to the patient's functional abilities to ensure the progression of difficulty in rehabilitation session.

time: the synchronous sessions last about 60 min, while the autonomous practice lasts about 5–10 min in addition to the synchronous session (4 times a week) or 30 min (3 times a week).

The two conditions, Tele-LSVT-Loud and LSVT-Loud, differed for the type of synchronous intervention which was delivered in telerehabilitation at home versus the conventional face-to-face delivery in the clinic, respectively. The Tele-LSVT-Loud synchronous sessions were delivered by accessing a digital platform (Maia Platform, <https://abmedica.it/prodotti-ab-medica/maia>), clicking on a link sent by mail allowing starting the videoconference with the therapist.

Further details about trial intervention are published elsewhere.¹⁸

Measures

The baseline measures were evaluated by an assessor blind to the group allocation in an individual session at T0. Feasibility measures were assessed during and after the treatment (T1).

Baseline measures

Clinical profile: MS form, disease duration, pharmacological treatment, and Expanded Disability Status Scale (EDSS²⁰) score were collected by consulting the medical record.

Global cognitive level: the Montreal Cognitive Assessment scale²¹ was administered to evaluate cognitive function, obtaining a total score ranging from 0 to 30, with a higher score indicating a greater cognitive level.

Fatigue: the Modified Fatigue Impact Scale²² was self-administered to assess the perceived fatigue. The higher total score (range 0–84) refers to a greater effect of fatigue on everyday activities. A score of 38 is reported as the cutoff above which subjects are considered fatigued.

Technological expertise: an *ad-hoc* questionnaire²³ on technological expertise was self-administered, allowing evaluating the familiarities with technology (total range score 1–5, the greater score the higher familiarity) and the perceived skill in technology use (total range score 1–5, the greater score the higher skill).

Voice intensity: 1-min monologue was recorded by an in-air microphone. The dB SPL (mean and standard deviation) was extracted to assess the average voice intensity.

Voice impairment impact: the Voice Handicap Index (VHI²⁴) was used to assess the perceived impact of voice disorder on quality of life. The greater the score indicates

a higher disability (score range 0–120), and a cutoff of 12 can be considered to rate the disability related to a voice disorder.

Quality of life: the World Health Organization Disability Assessment Schedule 2.0 (WHODAS²⁵) was self-administered to evaluate the impact of health issues on the functioning domain. A total score ranging from 0 to 144 was interpreted in terms of a greater score as a higher disability.

Feasibility measures

Adherence: the session attendance was registered by the therapist for the synchronous rehabilitation activity, while the completed autonomous practice was reported by the participants in a structured diary, in which they also indicated eventual reasons for non-attendance (see Supplemental material for details). Moreover, adherence issues were addressed during the weekly interview with the psychologist (see below). An attendance rate was computed by summing the number of attended sessions, dividing the sum by the total number of the program sessions, and multiplying by 100 (range 0–100, with 100 referring to the higher adherence rate).

Adverse events: participants were invited to report eventual adverse events occurring during and after the treatment in the structured diary. Also, adverse events were investigated weekly during the interview (see below).

Telerehabilitation platform user experience: the User Experience Questionnaire (UEQ²⁶) was administered after the treatment period, and 6 scores were obtained related to different user experience domains: attractiveness, perspicuity, efficiency, dependability, stimulation, novelty. Standardized scores for each domain were computed according to Schrepp et al.²⁶ indications: the range of the scale is between –3 (horribly bad) and +3 (extremely good). A score of +1.5 is interpreted as a good experience with technology.

Intrinsic motivation for the treatment: the Enjoyment subscale of the Intrinsic Motivation Inventory (IMI²⁷) was administered to explore the motivation of the participants toward the treatment program at T1. The higher score (range 1–7) was interpreted as a greater intrinsic motivation.

Perceived treatment experience (engagement, acceptability, and feasibility): an individual semi-structured interview was weekly performed by a psychologist at the end of each week of rehabilitation program (4 interview sessions in total) to explore treatment experience during the rehabilitation period. The interview track was implemented, tested, and refined during round table meetings by telerehabilitation experts (see Supplemental materials for details). The following themes (coding units) were explored: adherence issues, adverse events, motivational drivers, expectations about treatment, the impact of the treatment on daily routine, perceived fatigue, technology accessibility, and relationship with the therapist. The individual interviews were recorded and verbatim transcribed.

Statistical analysis

The statistical analysis was performed using the R software (version 4.3.3. retrieved from: <https://www.r-project.org/>). Variables' distributions were checked using quantile-quantile and histogram plots and means, medians, frequencies, interquartile ranges, and standard deviations were reported as descriptive statistics as appropriate. Unpaired *t*-test (*t*) or Mann-Whitney (*U*) were run to test group differences.

A content qualitative analysis was also performed on interview transcripts by three researchers (psychologists, two women and one man) using QDA Miner Lite (version 2.0.8. retrieved from: <https://provalisresearch.com/products/qualitative-data-analysis-software/>). Also, the final interpretation of qualitative data included two expert speech therapists. The analysis followed different steps: (1) segmentation of text based on coding units defined during the implementation of the interview (see “Measures” section): in this phase, the three researchers first worked independently in double-blind modality, then agreement was checked and disagreements were collegially discussed and solved, (2) for each coding unit, categories were collegially proposed and discussed, (3) significant themes and relevant meanings for the study aims were highlighted and discussed in round tables including both psychologists and speech therapists.

Missing data related to the drops from the treatment at the beginning of the program and consequently affected measures assessing the rehabilitation experience (weekly interviews and questionnaires on motivation and technology experience). Descriptive and qualitative analyses of these measures were performed only on participants who did not drop out of the treatment.

Results

The trial enrollment started in June 2023, and the last follow-up occurred in August 2024.

Eligibility

Figure 1 depicts the CONSORT diagram of the trial.

Among 70 people with MS with rehabilitation needs, 90% ($n = 63$) were eligible for the research, fulfilling inclusion criteria. Among these, only 33% ($n = 21$) were available to be recruited (see Figure 1). In fact, the remaining 67% ($n = 42$) were not recruited due to their unavailability to follow the in-site treatment (31%, $n = 13$) or the impossibility of participating in an intensive rehabilitation program, net of the delivery modality (69%, $n = 29$). In detail, among the 13 people unavailable to follow the in-site treatment, 62% reported transportation barriers, 7% had family issues, and 31% did not further justify the unavailability reasons. Finally, among the 29 people

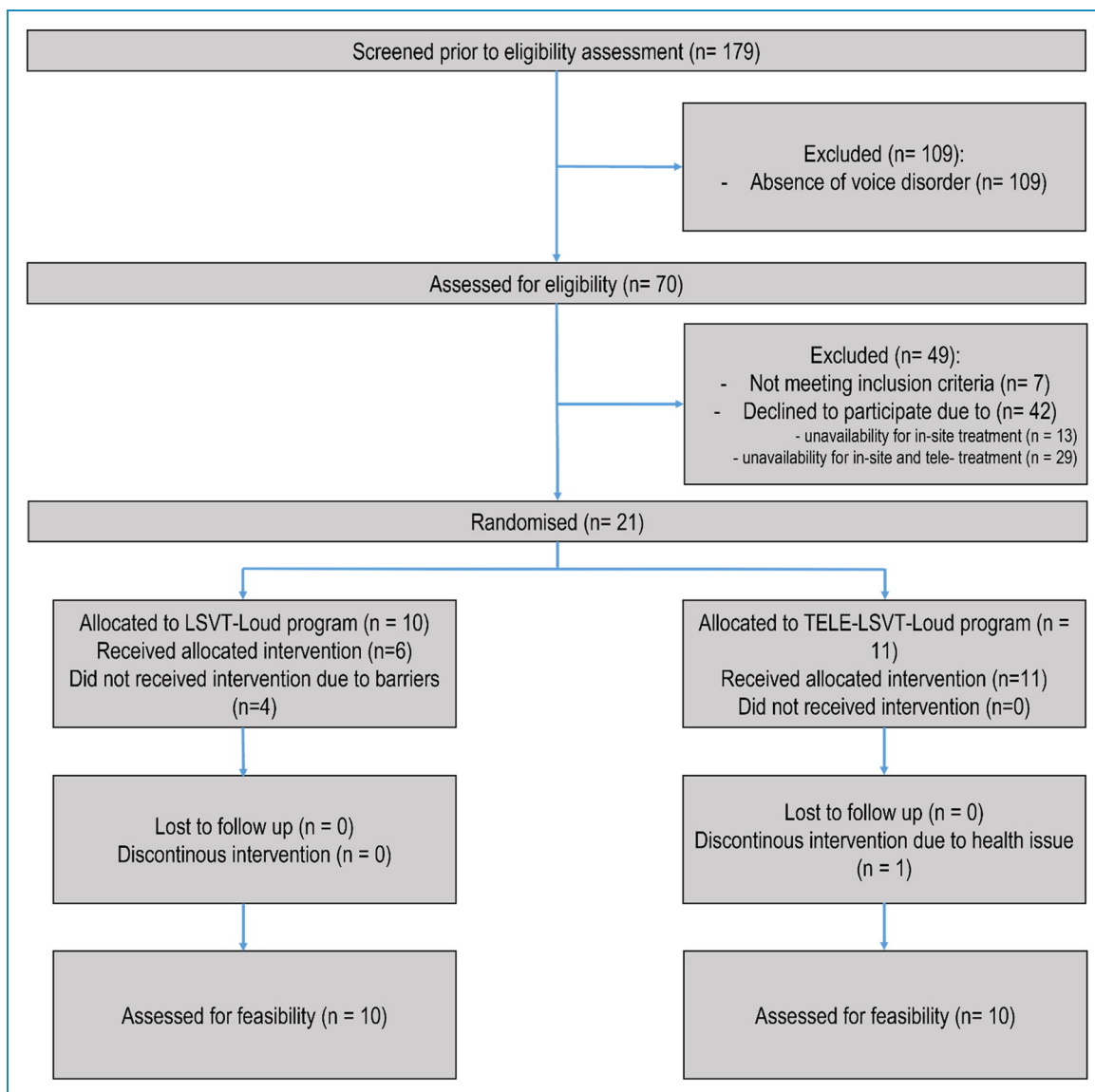


Figure 1. CONSORT diagram of the study.

reporting impossibility to participate net of the delivery modality, 17% reported limited autonomy issues, 59% health conditions worsening, and 24% unwillingness to participate. The unwillingness to participate was mainly due to two factors: some patients reported that they did not have the time to devote to the treatment, mainly due to work commitments; others did not consider the speech problem relevant enough to devote the effort required.

Participants

In total, 21 subjects were 1:1 randomized in Tele-LSVT-Loud and LSVT-Loud group. Table 1 reports baseline characteristics of the two groups, which were matched. Both groups showed an equally good level of familiarity and perceived competence toward technological devices.

Adherence

The Tele-LSVT-Loud group reported a high adherence to the synchronous rehabilitation sessions (median = 87.50%, 95% CI = 63.46–100.00) but a low adherence to the autonomous practice (median = 57.14%, 95% CI = 32.11–76.98). In contrast, the LSVT-Loud group showed a low adherence rate both to synchronous (median = 68.75%, 95% CI = 21.22–86.38) and autonomous practice (median = 5.36%, 95% CI = 0.52–58.77).

In more detail, 72.72% of Tele-LSVT-Loud participants attended more than 80.00% of the synchronous sessions, versus 50% of people in the LSVT-Loud group. Concerning the autonomous practice, in both groups, only 3 participants attended the rehabilitation with an adherence equal to or higher than 80.00%. Moreover, in both groups, 1

Table 1. Baseline characteristics of the Tele-LSVT-Loud and LSVT-Loud group.

	Tele-LSVT-Loud	LSVT-Loud	comparison test (<i>p</i>)
<i>N</i>	11	10	
Sex (M:F)	3:8	3:7	0.890
Age (mean, 95% CI)	55.09 (48.18–62.00)	54.00 (47.26–60.74)	0.803
Education (median, 95% CI)	13.00 (11.64–15.63)	12.50 (10.09–15.71)	0.515
Technology familiarity (mean, 95% CI)	3.64 (3.04–4.23)	3.60 (3.10–4.10)	0.918
Technology competence (mean, 95% CI)	3.07 (2.48–3.66)	3.16 (2.83–3.49)	0.783
EDSS (median, 95% CI)	6.50 (4.98–7.48)	6.50 (4.88,7.41)	0.803
MS form (RR:SP:PP)	7:2:2	6:2:2	0.985
Disease duration (y, mean, 95% CI)	23.70 (17.74–29.71)	22.30 (13.04–31.56)	0.770
MS pharmacological treatment (%)	100.00	80.00	0.128
Immunomodulatory/immunosuppressive (%)	63.00	50.00	0.558
glatiramer acetate	18.18	10.00	
teriflunomide	18.18	0.00	
ozanimod	9.09	0.00	
ocrelizumab	0.00	10.00	
ofatumumab	9.09	0.00	
interferon beta	9.09	10.00	
fingolimod	0.00	20.00	
Symptomatic drug (%)	36.37	30.00	0.763
Previous rehabilitation experience (%)	100	100	1.000
Previous speech therapy experience (%)	45.50	70.00	0.256
Previous telerehabilitation experience (%)	27.30	10.00	0.314
MoCA (mean, 95% CI)	24.55 (21.36–27.73)	23.10 (20.43–25.76)	0.450
MFIS (mean, 95% CI)	38.30 (27.12–50.14)	43.50 (28.27–58.72)	0.596
dB SPL 1-min monologue (mean, 95% CI)	71.40 (69.20–73.60)	71.30 (69.50–73.00)	0.904
VHI (mean, 95% CI)	33.91 (21.96–45.85)	50.20 (33.36–67.04)	0.088
WHODAS (mean, 95% CI)	43.33 (31.72–54.94)	43.05 (28.78–57.31)	0.972

95%CI: 95% confidence interval; EDSS: Expanded Disability Status Scale; MS: multiple sclerosis; RR: relapsing remitting; SP: secondary progressive; PP: primary progressive; y: years; MoCA: Montreal Cognitive Assessment Scale; MFIS: the Modified Fatigue Impact Scale; dB SPL: decibel sound pressure level; VHI: Voice Handicap Index; WHODAS: World Health Organization Disability Assessment Schedule.

subject withdrew from the treatment program after attending the first 2 sessions. Finally, in the LSVT-Loud group only, 3 participants withdrew from the study during the first session of the treatment due to costs related to transport and time barriers.

Non-attendance issues

The statements collected during the interviews were categorized into the following motive types for session non-attendance: health issues, overlapping commitments, unexpected events, unwillingness, and technical issues.

Interestingly, the two groups reported a different trend of motive types: in Tele-LSVT-Loud and LSVT-Loud group overlapping commitments were mentioned in 26% versus 56% of cases; health issues were highlighted for 38% versus 16% of non-attended sessions; unexpected events were reported for 8% versus 28% times, respectively. Also, the unwillingness was mentioned only in the Tele-LSVT-Loud group by one participant who referred to the unattended autonomous activity. Finally, technical issues were reported in 12% of cases in the Tele-LSVT-Loud group.

Analyzing similarities and differences between statements within each motive type, the specific unexpected events were different in the two groups. Especially, while

the Tele-LSVT-Loud group mainly mentioned family emergencies, the LSVT-Loud group most reported unexpected events due to barriers, such as climate and transport issues (see Table 2).

Factors potentially influencing adherence

Fatigue. Based on MFIS score measured at baseline, 52.4% (11/21) of participants were categorized as “fatigued” (score ≥ 38), 5 in Tele-LSVT-Loud and 6 in LSVT-Loud group, equally distributed in the two groups. By investigating the perceived fatigue during the treatment period through the interview, no significant difference emerged between the two groups. Interestingly, participants who showed an adherence $< 80\%$ in both groups reported no or low perceived fatigue. Instead, participants with high adherence were those who reported fatigue during the 4 weeks of treatment (all participants scoring above 38 points on MFIS).

Integration in daily life. During the interviews, 50% of participants who attended the LSVT-Loud program on-site mentioned difficulties in keeping time dedicated to the rehabilitation versus only 10% of the Tele-LSVT-Loud group. In detail, the time of the session plus the one to reach the clinic clashed with the daily duties’ organization

Table 2. Motives of non-attendance in the Tele-LSVT-Loud and LSVT-Loud participants.

Non-attendance motive	Sessions' type		Tele-LSVT-Loud	LSVT-Loud
	S	A	% Example	% Example
	health issues	X	X	38 «I had a migraine attack» «I had a severe cold»
overlapping commitments	X	X	26 «I had a doctor's visit» «I got overwhelmed with duties»	56 «I'm often busy, after the session with the therapist the swimming pool...» «I had the renewal patent issue...»
unexpected events	X	X	9 «I needed to walk my brother to the hospital» «I had a family emergency»	28 «It was raining, and I couldn't come to the hospital with the motorized wheelchair. If only there was an underground tunnel...» «There was the strike of the public transport! » «The elevator of the metro was broken! » «I had a personal issue»
unwillingness		X	15 «I had no excuse»	0 -
technical issues	X		12 «I had a new PC, I can't set the audio» «connection problems»	0 -

A: autonomous practice; S: synchronous sessions. % is computed on the total number of motives reported in the interviews.

“three hours pass for treatment and round-trip ... this is the time I remove from my daily routine”). In general, participants mentioned that the intensity of the treatment was a critical feature making it difficult to continue attending the program beyond a short period (1 month) (“I lack time to do things, but it is for one month, ok...”). Nevertheless, these issues did not lead people to drop out of the program. Interestingly, 2 participants in the Tele-LSVT-Loud group reported being worried about disturbing their neighbor during the speech therapy sessions (synchronous sessions and autonomous practice) in telerehabilitation.

Motivation. The two groups showed comparable high intrinsic motivation to the rehabilitation program (IMI-E score scale) (Tele-LSVT-Loud median = 5.57, 95% CI = 4.87–6.25; LSVT-Loud median = 6.14, 95% CI = 5.62–6.42). Six motivational levers prompting session attendance emerged by the qualitative interview, which were not related to the modality of the treatment delivery: (1) *the treatment efficacy on voice* (88% cases): hoping and perceiving a voice improvement which consisted in an increased voice aspects (tone, strength, and control) or in daily living social communication, or a higher autonomy in daily living (especially in cases in which voice commands are crucial to interact in the environment); (2) *social relationships with clinicians* (37% cases): grateful feelings toward people caring for them; (3) *contributing to science* (31% cases): pride feelings to be part of a research project, to have a role in something important for themselves, but even more, for posterity who will access rehabilitation in the future; (4) *trust in staff experience* (12% cases): a sense to be “in good hands”; (5) *space of my own* (19%): taking the treatment program as a dedicated moment for themselves, to cultivate having a space

exclusively for them; (6) *a way to spend time* (6%): taking the project opportunity to pass the time.

Adverse events

In both groups (Tele-LSVT-Loud and LSVT-Loud), no relevant adverse events were observed. Subjects reported only mild and transient events (Grade 1, see Table 3). These events were categorized into: (1) voice/throat-related symptoms (e.g. discomfort in the throat, vocal cords discomfort, hoarseness, voice fatigue, lowered voice); (2) non-voice/throat-related symptoms (e.g. headache, fatigue, muscle tension, feeling of dizziness). They were mainly reported during the first out of four weeks of treatment for both groups and occurred equally during or after treatment.

In the Tele-LSVT-Loud group, mild and transient events were reported in 12% of total sessions attended by the participants, while in the LSVT-Loud group they occurred in the 6% of total sessions attended (Table 3).

Only participants in the Tele-LSVT-Loud group reported non-voice/throat-related symptoms, in the first week and during treatment session.

User experience with technological system

Tele-LSVT-Loud participants expressed a positive evaluation of their experience with the technological system in each UEQ domains: mean attractiveness = 2.33 (95% CI = 1.79–2.87); mean perspicuity = 2.43 (95% CI = 1.90–2.96); mean efficiency = 1.75 (95% CI = 1.28–2.22); mean dependability = 1.52 (95% CI = 1.03–2.01); mean stimulation = 2.09 (95% CI = 1.51–2.67); mean novelty = 2.11 (95% CI = 1.50–2.73).

Table 3. Adverse events in the Tele-LSVT-Loud and LSVT-Loud groups.

	Tele-LSVT-Loud	LSVT-Loud
Common terminology criteria for adverse events	AE/total attended sessions in the group	AE/total attended sessions in the group
Grade 5 <i>Death related to AE</i>	0.00	0.00
Grade 4 <i>Life-threatening consequences; urgent intervention indicated</i>	0.00	0.00
Grade 3 <i>Severe or medically significant but not immediately life-threatening; hospitalization; disabling; limiting self-care ADL</i>	0.00	0.00
Grade 2 <i>Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL</i>	0.00	0.00
Grade 1 <i>Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated</i>	0.12	0.06

AE: adverse events. % is computed on the total number of AE reported in the interviews and the diaries.

In the individual interviews, all subjects in the Tele-LSVT-Loud group reported a good experience in the interaction with the telerehabilitation system. In only 2 cases (20%), the subjects reported a low perceived self-efficacy in the use and handling of technological devices at the beginning of the program. These subjects reported negative feelings about the devices' use, especially anxiety. However, these subjects mentioned an increment in self-efficacy during the last weeks of treatment (beginning of the treatment: "I can use nothing of these things anymore"; end of the treatment: "I thought different afterwards"). Three subjects (30%) advised about technical issues mostly related to their low expertise in the use of technology. Among these, two subjects improved their technological ability during the sessions' treatment, while a participant continued to experience difficulties in handling the PC without the assistance of a caregiver. Regarding the need for assistance, only this latter participant referred to the necessity of caregiver support to manage the technological systems during the session. Notably, when the participants were asked to compare the telerehabilitation experience with the conventional face-to-face delivery, all Tele-LSVT-Loud participants reported telerehabilitation as more comfortable than face-to-face modality for different reasons: increased perceived easiness in accessing the sessions (100%), better management of daily commitment (60%), less burden on the caregiver (30%), saving time in reaching the clinic (20%), less stress and fatigue (10%). In sum, 90% of Tele-LSVT-Loud participants declared that telerehabilitation is preferable to the conventional modality, while the only subject with the opposite position changed opinion after the second week of the treatment.

Relationship with therapist

In the interview, the actual relationship with the therapist was investigated. Also, the beliefs about the difference

Table 4. Beliefs of Tele-LSVT-Loud participants toward the relationship with the therapist in the in-site program versus the beliefs of the LSVT-Loud participants toward the relationship with the therapist in telerehabilitation at the fourth week of treatment.

Relationship with therapist	Tele-LSVT-Loud	LSVT-Loud
No difference between delivery paths	80%	16.66%
Face-to-face delivery increased patient-therapist relationship	10%	83.34%
Telerehabilitation delivery increased patient-therapist relationship	10%	0%

between the "face-to-face" and "at-distance" relationship with the clinicians were explored both from the point of view of people in the Tele-LSVT-Loud and LSVT-Loud groups. All subjects reported a positive relationship with the therapist. In the Tele-LSVT-Loud group, eight individuals (80%) reported that the relationship with the therapist would have been the same whether they attended in-clinic sessions, with two of them changing their position after the first week of the program from "the relation would have been stronger in the in-site treatment" into "there would be no difference". Also, one subject (10%) judged that the telerehabilitation delivery increased the patient-therapist relationship by making the treatment less hospitalized ("When I go to the rehabilitation session in the clinic, I'm there as a patient. Now I make the therapist enter my home... and these things go beyond the clinical session. It gives you something more... I'm not going to do a visit!"). In this group, only one subject (10%) said the patient-therapist relationship would have been better in the in-site treatment (see Table 4).

In the LSVT-Loud group, only 16% of participants believed that the relationship with the therapist would be the same in telerehabilitation and in-site treatment. Sixty-six percent of the group reported that face-to-face delivery increased patient-therapist relationships. Finally, one of the participants reported that the relationship would have been equal in the two conditions only whether the first sessions had been delivered face-to-face and then the treatment continued in telerehabilitation (see Table 4).

Discussion

In the present work, we presented the feasibility evidence on patient-relevant structural and procedure effects of an RCT on the LSVT-Loud program delivered in telerehabilitation to people with MS, adopting a mixed-method approach.

The first evidence of feasibility regards the practicability of the recruitment in the trial. The enrollment period was longer than expected, given the large number of eligible people who were not available for recruitment. In fact, over half of the eligible people needing voice rehabilitation expressed their inability to participate. Some of them stated that participation in the in-site treatment would have entailed a disproportionate effort (about 30%), while the rest mentioned their impossibility to participate in the treatment, regardless of the delivery modality for their health conditions. In the former case, people could not benefit from a voice rehabilitation program due to distance, cost, and time barriers related to intensive in-site treatment, which inevitably hampered their access to the treatment. This evidence hints at two relevant considerations: first, the scarce practicability of recruitment in a short time reflects the impracticability of the in-site LSVT-Loud

program for most people with MS needing voice rehabilitation, often with a long disease history and a high level of disability, and, second, the need of the telerehabilitation modality is central to guarantee the access to care to all people with voice disorders who experience barriers.

The barriers heavily impacted the adherence of people who followed the LSVT-Loud method in the clinic. We observed a noticeably lower attendance at the in-site than the telerehabilitation program, which became apparent as an adherence minor of 68% in the in-clinic versus 87% of sessions of the at-home participants for the synchronous sessions, as expected.^{18,28–30} A similar result was previously found by Covert et al.³¹ who observed a higher adherence in telerehabilitation participants than ones in in-site. Even when people had access to the treatment, the delivery modality influenced their chances to profit from the optimal dose of the rehabilitation, with plausible impacts of underdosing on efficacy.^{32,33} Interestingly, when we qualitatively investigated reasons for discontinued attendance during the program, we found that people in the LSVT-Loud group were prone to miss sessions due to unexpected events for which adhering to the treatment session would have undermined the daily routine management. On the other hand, unexpected events rarely were reasons to miss the sessions for people in telerehabilitation. The flexibility of telerehabilitation modality compared to the in-site delivery has been previously highlighted in studies exploring enablers and barriers of telehealth for MS.^{34,35} In fact, people with MS acknowledge telerehabilitation has the potential to lessen travel time, enhance scheduling flexibility, and reduce the caregiver burden. Moreover, another proof of the higher feasibility of Tele-LSVT-Loud than LSVT-Loud was that 40% of people in the in-site treatment abandoned the program during the first week. In detail, they referred to having taken part in the study hoping to be allocated to the telerehabilitation program and having difficulties following the in-site treatment. Finally, an interesting aspect to be reported concerns the autonomous practice, which was mainly related to the least adherence in both groups (only 3 subjects completed 80% of sessions in each group). This evidence suggests the need to introduce strategies to increase the patient's engagement during the autonomous practice to support adherence.^{36,37}

When qualitatively exploring potential factors that explain the lower adherence and attendance rate to the in-site than telerehabilitation treatment, we found a huge role of the treatment integration in the daily routine. In detail, people attending telerehabilitation were prone to perceive high compatibility of the treatment modality with their daily routine, differently than participants who followed the intervention in the clinic, which inevitably demand an additional effort in terms of time and reorganization of duties, family, and work activities. Our findings trace a previous contribution that sought to identify acceptability issues related to telerehabilitation experience in

people with neurological disorders.³⁸ Especially users highlighted the convenience of in-home rehabilitation, allowing minimized traveling time to reach the clinic and access care and freeing caregivers to the duty to accompany their loved ones to the hospital.

Two factors expected to play a role on people' adherence, motivation and fatigue, provided unforeseen evidence. We did not find a meaningfully higher motivation in the telerehabilitation group than in the in-site group. All people attending the program reported a substantial intrinsic motivation to follow the intervention. The reasons would be related to motivational drivers common to the two groups concealing relevant rehabilitation and affiliation needs such as treatment efficacy, social relationships, and contributing to science, as collected in the qualitative interviews. As previously suggested,³⁸ these motivational levers contribute to lessening the perceived effort for engaging in the program. Also, the levers reported matched with another qualitative study investigating people with MS perspective on online rehabilitation,³⁹ reporting the fulfillment of a need to exercise and the desire to advance the MS research as the main motivations driving the intervention attendance. Nevertheless, even if we did not find differences in motivation levels and motivational drivers between people in in-site and telerehabilitation treatment, the drop-out of 40% of the in-site participants inevitably prevented us from investigating the level of intrinsic motivation in this sub-group.

Concerning fatigue, the one-week interviews revealed that less than half of the participants reported treatment-related fatigue by the end of the fourth week. Some participants experienced physical fatigue only during the early phase of rehabilitation, likely due to the process of learning and adapting to the program. This observation aligns with previous research demonstrating the positive effects of rehabilitation, including intensive programs, on reducing perceived fatigue in people with MS.^{40,41} However, several participants reported fluctuating or increasing cognitive and psychosocial fatigue over the course of the treatment, primarily due to the challenge of integrating intensive rehabilitation into their daily schedules. In conclusion, fatigue in MS does not appear to be a barrier to sustaining participation in intensive rehabilitation programs. However, clinicians should be mindful of the potential contribution of travel-related fatigue and the cognitive demands of managing clinic visits, which may exacerbate overall fatigue perceptions in people with MS. These factors should be considered when determining the mode of treatment delivery. In this context, telerehabilitation may offer a viable solution by minimizing travel-related fatigue, providing greater flexibility, and reducing caregiver burden.

The analysis of adverse events showed that, as expected,¹⁸ LSVT-Loud treatment was safe regardless of the mode of delivery. In fact, no major and permanent

adverse events ever occurred, consistent with a recent study by Sackley and colleagues,⁴² which found only minimal and transient problems (e.g. vocal strain) at an acceptable rate compared to the level of benefit provided by the treatment. In our study, the highest number of reports occurred in the Tele-LSVT-Loud group. Notably, non-voice/speech-related symptoms occurred only in the Tele-LSVT-Loud group, including symptoms related to respiratory management and muscle tension, probably because these are more difficult to monitor remotely. In fact, in traditional face-to-face therapy, therapists can provide immediate manual adjustments and hands-on guidance to assist with breath control and muscle relaxation, potentially reducing the occurrence of such symptoms. In contrast, telerehabilitation relies heavily on verbal instructions and patient self-monitoring, which may pose challenges for certain aspects of therapy, such as respiratory or muscle tension management. Despite the irrelevance of this symptomatology, we believe it is essential to inform clinicians delivering Tele-LSVT-Loud about the potential need for enhanced feedback and monitoring during online sessions. Speech therapists should ensure that patients are provided with clear, detailed instructions on breath control and muscle relaxation exercises and should proactively monitor for signs of strain or tension during teletherapy sessions to minimize the occurrence of such issues.

From the technological experience point of view, participants reported an intermediate familiarity and perceived competence toward technology. As expected,¹⁸ people in telerehabilitation globally expressed a positive opinion on the easiness of use, learning, effort level, perceived novelty, and motivation in using the Tele-LSVT-Loud system. Importantly, the few cases that referred to difficulties in the interaction with the system due to their unfamiliarity with technology at the beginning of the intervention changed their mind after the first period of the program. This evidence supports the viability of the online delivery of the LSVT-Loud program, both to people familiar and unfamiliar with technological systems. In this regard, previous works highlighted the critical role of usability in increasing the satisfaction of MS people following telerehabilitation interventions.⁴³ In the present trial, the only participant who reported a negative experience with using technology during the program was a person dependent on the caregiver in handling the systems to access the session due to a high level of disability (EDSS = 8.5), especially restricted upper limb mobility. As reported by the technology acceptance model,⁴⁴ the perceived ease of use gravely impacts on the behavioral intention of utilizing a system, and the ease of use is in turn influenced by the level of disability in neurological disorders.⁴⁵ In light of increasing access to telerehabilitation for people with a high disability level, the use of smarter or *ad-hoc* devices, such as smartphones instead of computers, could permit people with motor impairment to undergo treatment with more autonomy.

Finally, the last issue we explored was the relationship with the therapist in the two delivery paths. In general, all the participants built a good relationship with the therapist, both face-to-face and at a distance. Importantly, we also sought to extrapolate stereotypes on the therapeutic alliance in telerehabilitation from the point of view of people who experienced only face-to-face modality: in detail, participants in in-site treatment were prompted to imagine how would have been the therapeutic alliance whether intervention would have been delivered at a distance. Instead, people who followed telerehabilitation were asked to report their judgment on the relationship built and whether it would have been constructed in a face-to-face modality. To this concern, the position of the two groups was completely different. People who did not follow telerehabilitation stretched to shift toward face-to-face superiority in guaranteeing a deeper relationship with the therapist. On the contrary, people who experienced telerehabilitation judged no difference between the relationship built in telerehabilitation and the one that would have been built if the treatment had been delivered in the clinic. More substantially, people in telerehabilitation who started the program stating that they would have preferred a face-to-face modality to have a stronger relationship with therapists changed their position after the initial week of the program. This finding suggests that people who approach online therapies for the first time can present a distorted view of the treatment due to an engrained stereotype leading to think that (synchronous) telerehabilitation leads to a more detached relationship with the therapist than the standard in-site intervention. Clinicians may be aware of this evidence when they start a telerehabilitation program with a patient and adopt adequate strategies to face eventual reluctance in undertaking the intervention at a distance or alliance ruptures, with potential impacts on treatment effects.⁴⁶ The subjective perception of the therapeutic alliance in tele-speech therapy has been investigated by Freckmann et al.,⁴⁷ suggesting that rehabilitation at a distance does not provide a negative influence on therapist–client rapport. Moreover, a systematic review of videoconferencing interventions for long-term conditions supports the feasibility of this delivery modality, assuring a good level of therapeutic alliance.⁴⁸

This work is not free from limitations. First, the sample size of people who fully adhered to the intervention is small, and, given the longer-than-expected recruitment period, we could not prolong the enrolment phase to include additional subjects in the research. This issue may have undermined the power of the study. In retrospect, some standardized measures, such as the motivation and fatigue scales, should have been administered twice instead of once before/after the treatment, allowing us to capture the perceived experience trend with a quantitative approach. Similarly, we qualitatively investigated the beliefs about the relationship with the therapists in

telerehabilitation only after the first week of treatment, and this timing may have introduced a bias and did not allow us to evaluate the stereotypes on tele-speech therapy. Future research should overcome these limits. Another final consideration is the area of enrolment, a metropolitan city, which is not representative of some needs in rural conditions, which may encounter internet connections issues.

Conclusion

In conclusion, the modality of treatment delivery (in-site versus telerehabilitation) is a relevant factor in determining eligibility for an intensive voice rehabilitation program in people with MS. Telerehabilitation promotes higher adherence than conventional in-site modality and is a safe and feasible way to deliver the intervention for people experiencing accessibility barriers and a high level of disability.

Acknowledgements: The authors thank all the participants in the present research and Silvia Di Benedetto for the support in the recruitment of participants. GF thanks 40th cycle of the PhD program in Translational Medicine for its valuable support.

Author's note: Giulia Fusari, Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy.

Contributorship: CV, DC, FB, and SI made a substantial contribution to the concept or design of the work. CV, DC, GF, and SI developed the design and methodology. CV, DMC, GF, and GS performed the investigation. DMC, GS, and SI performed the formal analysis. CV, GF, and SI wrote the manuscript. All authors reviewed and commented on the drafts. All authors read and approved the final manuscript.

Declaration of conflicting interests: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval: The study was approved by the Ethics Committee of IRCCS Don Carlo Gnocchi Foundation and was registered as a clinical trial on clinicaltrials.gov (identifier: NCT05930379). Participants were fully informed of the aims and procedures of the project. A reporting procedure ensured that any serious adverse events were reported to the Chief Investigator. Informed written consent was obtained from all participants before the study initiation.

Funding: The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the FISM – Fondazione Italiana Sclerosi Multipla – cod. 2022/PR-Single/016 and by the Italian Ministry of Health (Ricerca Corrente program 2025–2027).

Guarantor: SI.

ORCID iD: Sara Isernia  <https://orcid.org/0000-0002-0849-3984>

Supplemental material: Supplemental material for this article is available online.

References

1. Farmani E, Fekar Gharamaleki F and Nazari MA. Challenges and opportunities of tele-speech therapy: before and during the COVID-19 pandemic. *J Public Health Res* 2024; 13: 22799036231222115.
2. Lam JHY, Lee SMK and Tong X. Parents' and Students' perceptions of telepractice services for speech-language therapy during the COVID-19 pandemic: survey study. *JMIR Pediatr Parent* 2021; 4: e25675.
3. Jakimovski D, Bittner S, Zivadinov R, et al. Multiple sclerosis. *Lancet* 2024; 403: 183–202.
4. Hartelius L and Svensson P. Speech and swallowing symptoms associated with Parkinson's disease and multiple sclerosis: a survey. *Folia Phoniatr Logop* 1994; 46: 9–17.
5. Feijó AV, Parente MA, Behlau M, et al. Acoustic analysis of voice in multiple sclerosis patients. *J Voice* 2004; 18: 341–347.
6. Dimitriou N, Bakirtzis C, Nteli E, et al. Adaptation and validation of the Greek version of the speech pathology-specific questionnaire for persons with multiple sclerosis (SMS). *Int J Speech Lang Pathol* 2024; 26: 59–67.
7. Noffs G, Perera T, Kolbe SC, et al. What speech can tell us: a systematic review of dysarthria characteristics in multiple sclerosis. *Autoimmun Rev* 2018; 17: 1202–1209.
8. Plotas P, Nanousi V, Kantanis A, et al. Speech deficits in multiple sclerosis: a narrative review of the existing literature. *Eur J Med Res* 2023; 28: 52.
9. Konstantopoulos K, Vikelis M, Seikel JA, et al. The existence of phonatory instability in multiple sclerosis: an acoustic and electroglottographic study. *Neurol Sci* 2010; 31: 259–268.
10. Hartelius L, Buder EH and Strand EA. Long-term phonatory instability in individuals with multiple sclerosis. *J Speech Lang Hear Res* 1997; 40: 1056–1072.
11. Chiara T, Martin D and Sapienza C. Expiratory muscle strength training: speech production outcomes in patients with multiple sclerosis. *Neurorehabil Neural Repair* 2007; 21: 239–249.
12. Crispiatico V, Baldanzi C, Napoletano A, et al. Effects of voice rehabilitation in people with MS: a double-blinded long-term randomized controlled trial. *Mult Scler* 2022; 28: 1081–1090.
13. Fox CM, Morrison CE, Ramig LO, et al. Current perspectives on the Lee Silverman Voice Treatment (LSVT) for individuals with idiopathic Parkinson disease. *Am J Speech Lang Pathol* 2002; 11: 111–123.
14. Ramig LO, Countryman S, O'Brien C, et al. Intensive speech treatment for patients with Parkinson's disease: short-and long-term comparison of two techniques. *Neurology* 1996; 47: 1496–1504.
15. Sapir S, PawJas A, Ramig L, et al. Effects of intensive phonatory-respiratory treatment (LSVT[®]) on voice in individuals with multiple sclerosis. *NCVS Status Progress Rep* 1999; 14: 141–147.
16. Baldanzi C, Crispiatico V, Foresti S, et al. Effects of intensive voice treatment (the lee silverman voice treatment [LSVT

- LOUD]) in subjects with multiple sclerosis: a pilot study. *J Voice* 2022; 36: 585.e581–585.e513.
17. Crispatico V, Baldanzi C, Bertuletti M, et al. Factors associated with treatment-related changes in voice volume in people with multiple sclerosis. *Int J MS Care* 2023; 25: 1–7.
 18. Vitali C, Fusari G, Baldanzi C, et al. 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. *Digit Health* 2023; 9: 20552076231218150.
 19. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol* 2018; 17: 162–173.
 20. Kurtzke JF. Rating neurologic impairment in multiple sclerosis: an expanded disability status scale (EDSS). *Neurology* 1983; 33: 1444–1452.
 21. Conti S, Bonazzi S, Laiacona M, et al. Montreal cognitive assessment (MoCA)-Italian version: regression based norms and equivalent scores. *Neurol Sci* 2015; 36: 209–214.
 22. Fisk JD, Ritvo PG, Ross L, et al. Measuring the functional impact of fatigue: initial validation of the fatigue impact scale. *Clin Infect Dis* 1994; 18: S79–S83.
 23. Rossetto F, Mestanza Mattos FG, Gervasoni E, et al. Efficacy of telerehabilitation with digital and robotic tools for the continuity of care of people with chronic neurological disorders: the TELENEURO@REHAB protocol for a randomized controlled trial. *Digit Health* 2024; 10: 20552076241228928.
 24. Jacobson BH, Johnson A, Grywalski C, et al. The voice handicap Index (VHI). Development and validation. *Am J Speech-Lang Pathol* 1997; 6: 66–70.
 25. Federici S, Bracalenti M, Meloni F, et al. World health organization disability assessment schedule 2.0: an international systematic review. *Disabil Rehabil* 2017; 39: 2347–2380.
 26. Schrepp M, Hinderks A and Thomaschewski J. Construction of a benchmark for the user experience questionnaire (UEQ). *Int J Interact Multim Artif Intell* 2017; 4: 40–44.
 27. McAuley E, Duncan T and Tammen VV. Psychometric properties of the intrinsic motivation inventory in a competitive sport setting: a confirmatory factor analysis. *Res Q Exerc Sport* 1989; 60: 48–58.
 28. Di Tella S, Pagliari C, Blasi V, et al. Integrated telerehabilitation approach in multiple sclerosis: a systematic review and meta-analysis. *J Telemed Telecare* 2020; 26: 385–399.
 29. 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* 2024; 30: 344–355.
 30. Isernia S, Pagliari C, Jonsdottir J, et al. Efficiency and patient-reported outcome measures from clinic to home: the human empowerment aging and disability program for digital-health rehabilitation. *Front Neurol* 2019; 10: 1206.
 31. Covert LT, Slevin JT and Hatterman J. The effect of telerehabilitation on missed appointment rates. *Int J Telerehabil* 2018; 10: 65–75.
 32. Roy N. Optimal dose-response relationships in voice therapy. *Int J Speech Lang Pathol* 2012; 14: 419–423.
 33. Baker E. Optimal intervention intensity. *Int J Speech Lang Pathol* 2012; 14: 401–409.
 34. Gopal A, Bonanno V, Block VJ, et al. Accessibility to telerehabilitation services for people with multiple sclerosis: analysis of barriers and limitations. *Int J MS Care* 2022; 24: 260–265.
 35. Landi D, Ponzano M, Nicoletti CG, et al. Patient’s point of view on the use of telemedicine in multiple sclerosis: a web-based survey. *Neurol Sci* 2022; 43: 1197–1205.
 36. Sardi L, Idri A and Fernández-Alemán JL. A systematic review of gamification in e-health. *J Biomed Inform* 2017; 71: 31–48.
 37. Brown M, O’Neill N, van Woerden H, et al. Gamification and adherence to web-based mental health interventions: a systematic review. *JMIR Ment Health* 2016; 3: 39.
 38. Chen Y, Zheng K, Dodakian L, et al. A qualitative study on user acceptance of a home-based stroke telerehabilitation system. *Top Stroke Rehabil* 2020; 27: 81–92.
 39. Knox KB, Nickel D, Donkers SJ, et al. Physiotherapist and participant perspectives from a randomized-controlled trial of physiotherapist-supported online vs. paper-based exercise programs for people with moderate to severe multiple sclerosis. *Disabil Rehabil* 2023; 45: 1147–1153.
 40. Hameau S, Bensmail D, Roche N, et al. Adaptations of fatigue and fatigability after a short intensive, combined rehabilitation program in patients with multiple sclerosis. *J Rehabil Med* 2018; 50: 59–66.
 41. Heine M, van de Port I, Rietberg MB, et al. Exercise therapy for fatigue in multiple sclerosis. *Cochrane Database Syst Rev* 2015; 2015: Cd009956.
 42. Sackley CM, Rick C, Brady MC, et al. Lee Silverman voice treatment versus NHS speech and language therapy versus control for dysarthria in people with Parkinson’s disease (PD COMM): pragmatic, UK based, multicentre, three arm, parallel group, unblinded, randomised controlled trial. *Br Med J* 2024; 386: e078341.
 43. Özden F, Özkeskin M, Ekici E, et al. Opinions, satisfaction and expectations of individuals with multiple sclerosis about telerehabilitation services. *Clin Neurol Neurosurg* 2024; 237: 108162.
 44. Brennan DM and Barker LM. Human factors in the development and implementation of telerehabilitation systems. *J Telemed Telecare* 2008; 14: 55–58.
 45. Rossetto F, Borgnis F, Isernia S, et al. System integrated digital empowering and teleRehabilitation to promote patient activation and well-being in chronic disabilities: a usability and acceptability study. *Front Public Health* 2023; 11: 1154481.
 46. Miciak M and Rossetini G. Looking at both sides of the coin: addressing rupture of the therapeutic relationship in musculoskeletal physical therapy/physiotherapy. *J Orthop Sports Phys Ther* 2022; 52: 500–504.
 47. Freckmann A, Hines M and Lincoln M. Clinicians’ perspectives of therapeutic alliance in face-to-face and telepractice speech-language pathology sessions. *Int J Speech Lang Pathol* 2017; 19: 287–296.
 48. Steel K, Cox D and Garry H. Therapeutic videoconferencing interventions for the treatment of long-term conditions. *J Telemed Telecare* 2011; 17: 109–117.