STUDY PROTOCOL

PROTOCOL TITLE: PHYSICAL TELEREHABILITATION IN VETERANS WITH MULTIPLE SCLEROSIS

NCT02346734

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Study Settings. The two facilities that will recruit and follow patients for this study are the VAMC-Baltimore and the VAMC-Washington, DC. Both medical centers are located in Veteran Integrated Service Network (VISN) 5 and have major multidisciplinary MS Clinics. The clinics are staffed by neurologists, nurses, and a social worker all with expertise in MS. The majority of the MS clinic staff are funded through the MSCoE-East which also provides administrative support.

A National Veterans MS Surveillance Registry has been established by the MSCoE. This registry is based on VHA extant data from computerized databases. To assist with identifying valid cases of MS, the MSCoE-East developed a diagnostic algorithm.[2] This algorithm is based on the number of visits related to MS, service-connection for MS and use of MS-related medications. Overall sensitivity (0.93) and specificity (0.92) compared with chart adjudication of cases using the McDonald criteria, was high. As of 2010, this algorithm identified approximately 22,000 Veterans with MS that receive care within the VA healthcare system.

Using the validated MS cases from the algorithm noted above, a survey was developed and sent to a random national sample in 2008. All females were surveyed along with a stratified random sample of males. Details of the clinical and demographic features of the VA MS population have recently been reported by the MSCoE-East staff.[10] The mean age was 55 years, 82% were white and 61% were married. MS was diagnosed at a mean age of 38 years and the MS subtype breakdown was: relapsing-remitting (49%), secondary progressive (33%), primary progressive (14%) and progressive-relapsing (4%). In terms of neurologic disability, 51% were ambulatory, 16% required a cane to walk, 9% required bilateral support for ambulation, 22% were confined to a wheelchair and 2% were bedridden.

Subject Recruitment and Data Collection Procedures

The Study Sample. Eligible subjects will satisfy the following criteria: (1) age: 18-65, (2) confirmed diagnosis of MS based on McDonald criteria, (3) functional disability defined by the EDSS in the range of 2 to 6.5; (4) willingness and ability to use MS HAT platform with individual modifications based on preferred user interface. Subjects will be excluded from the study if they have (1) other musculoskeletal diagnoses, unstable cardiovascular, respiratory, metabolic or other conditions that would interfere with this study, (2) one or more exacerbations in the preceding 3 months, (3) received a course of steroid (IV or oral) within 60 days of screening; (4) significant cognitive impairment: Mini-Mental State Exam (MMSE) < 23. The patients will be also required to have a working telephone line in their home or a cell phone. Level of computer experience will not be a criterion for patient enrollment.

Subject Recruitment. During the project months 7-24, 138 subjects will enter the study. Participants will be randomly assigned to home telerehabilitation group or control group. In addition, at the beginning of the study (Months 2-3) 4 focus groups will be conducted in Veterans with MS with 8-10 subjects in each focus group. The subjects will be recruited via advertisements in local bulletin boards, university press and online announcements. The MSCoE disease registry will be used for patient enrollment.[2, 10]

Data Collection. The data collection schedule is given in **Table 8** for study outcomes. Each enrolled patient will be in the study for 6 months. For patients using an assistive device at the start of the trial, we will mandate they use the same device throughout the trial during each assessment point. The primary study points will include baseline (T1), 3-month (T2) and 6-month (T3) evaluations. Evaluation at each study point will consist of a complete functional status evaluation performed by the *blinded assessment team* in the outpatient clinic at the VAMC- Washington, DC or Baltimore VAMC.

Randomization plan. Following screening and consent for randomization, participants will be randomized to the MS HAT intervention or control. The study coordinator and co-PIs will confirm that all screening activities have occurred, that the participant meets eligibility criteria, and that all required baseline data have been collected. Individuals lacking proper documentation of eligibility or key data collection items will not be randomized. Randomization will be stratified by EDSS

(ranges 2.0-3.5 and 4.0-6.5) and we plan to use permuted block randomization within each EDSS stratum to allocate about half of the patients within each EDSS stratum into HAT group, and the rest into the usual care group. Permuted block randomization promotes periodic balance in the sense that sequential patients are distributed equally between groups. This is important for our study because our study enrolls patients sequentially, such that there may be systematic differences between patients entering at different times during the study. Randomized blocks of sizes 2 and 4 in random order will be used to create the randomization sequence for each stratum. The random sequence and allocation envelopes will be created and kept private by the data analyst; the study coordinator will then ascertain and communicate study group assignment to participants as described in the Section 4.5.4. Due to the nature of the intervention, both participants, the clinical management team, study coordinator and research assistants and technical staff will be aware of the patient assignments. However, the blinded assessment team will be unaware of study assignments throughout the study. Until the trial end, investigators, staff and participants will be masked to outcome data, with the exception of trial statistician, study coordinator, data analyst, and the Data Safety Monitoring Board.

Table 8. Data Collection Schedule

Outcome Test	**Baseline***	**3 months***	**6 months***
Demographics and disease history[1]	X		
EDSS[1]	X	X	X
MS Functional Composite (MSFC) [1]: Timed 25-foot walk (T25-FW) 9-hole peg test (9HPT) Paced Auditory Serial Addition Test	X	X	X
Modified Fatigue Impact Scale (MFIS) [1]	X	X	X
MS Impact Scale (MSIS-29) [1]	X	X	X
MS Self-Efficacy[1]	X	X	X
Symptom Checklist SCL-90[1]	X	X	X
Berg Balance Scale[2]	X	X	X
MS Walking Scale (MSWS-12) [2]	X	X	X
Modified Ashworth Scale[2]	X	X	X
MS QOL-54[1]	X	X	X
MOS Patient Adherence Measure[1]	X	X	X
Exercise Adherence (self-reported diary)	Monthly		
Client Satisfaction Questionnaire[2]	X	X	X
Patient-provider communication (IPC) [1]	X	X	X
Depressive symptoms (CES-D) [1]	X	X	X
Social Support and Networks[1]	X	X	X
Attitudinal Survey[2]			X

[1]Tests performed by the blinded nurse practitioner; [2]Tests performed by blinded Physical Therapist;
*All tests performed by the blinded assessment team (PT & NP pair)