Mass General Brigham

A Self-directed Positive Psychology Intervention for Individuals with Newly Diagnosed Multiple Sclerosis

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Institutional Review Board
Intervention/Interaction Detailed Protocol

Principal Investigator: Bonnie I. Glanz, PhD

Project Title: A Self-directed Positive Psychology Intervention for Individuals with Newly Diagnosed Multiple Sclerosis

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1. Background and Significance

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system that affects both physical and mental health. Mental health comorbidities including depression and anxiety are common [1-2] and health-related quality of life (HRQOL) is often reduced [3-4]. Several key elements of successful adaptation to MS have been identified including maintenance of emotional balance, preservation of healthy relationships, absence of psychological disorders, low levels of negative affect and high levels of positive affect [5].

Positive psychology (PP) uses systematic exercises such as writing a letter of gratitude or remembering a past success to increase the frequency and intensity of specific positive psychological constructs such as positive affect and optimism [6-7]. We have previously demonstrated the feasibility and acceptability of a five-week, at-home, trainer-guided PP intervention for individuals with MS [8]. The intervention was associated with significantly greater increases in positive affect, optimism, general health and resilience and decreases in anxiety in the intervention group compared to the controls. Despite the benefits of the trainer-guided PP trial, the program has several limitations. First, it requires funding for a dedicated study trainer limiting its scalability. Second, the improvements seen following the completion of the PP exercises may have been related to engagement with the study trainer and not the PP program itself. Third, the individuals who participated in the trial had a mean disease duration of more than 20 years and it is not clear if the observed findings apply across the disease course.

We would like to evaluate the feasibility, acceptability and efficacy of a self-guided version of the PP intervention in individuals with recently diagnosed with MS. An MS diagnosis creates a crisis for the individual and his/her family. Typical initial emotional responses include fear, denial, anger and resentment [9]. The introduction of techniques to increase positive emotional experiences early on in the disease course might promote successful adaptation to living with MS. If we are able to demonstrate the feasibility, acceptability and efficacy of a self-

directed PP program, it could be made available to all newly diagnosed patients seen at the Brigham Multiple Sclerosis Center.

2. Specific Aims and Objectives

Specific Aim 1: Evaluate the feasibility and acceptability of a five-week self-directed PP training intervention for newly diagnosed patients with MS. We will assess the feasibility of the intervention by calculating the proportion of subjects who complete four of the five weekly exercises. We will determine the acceptability of each exercise by having subjects rate the ease and utility of each exercise after it is completed.

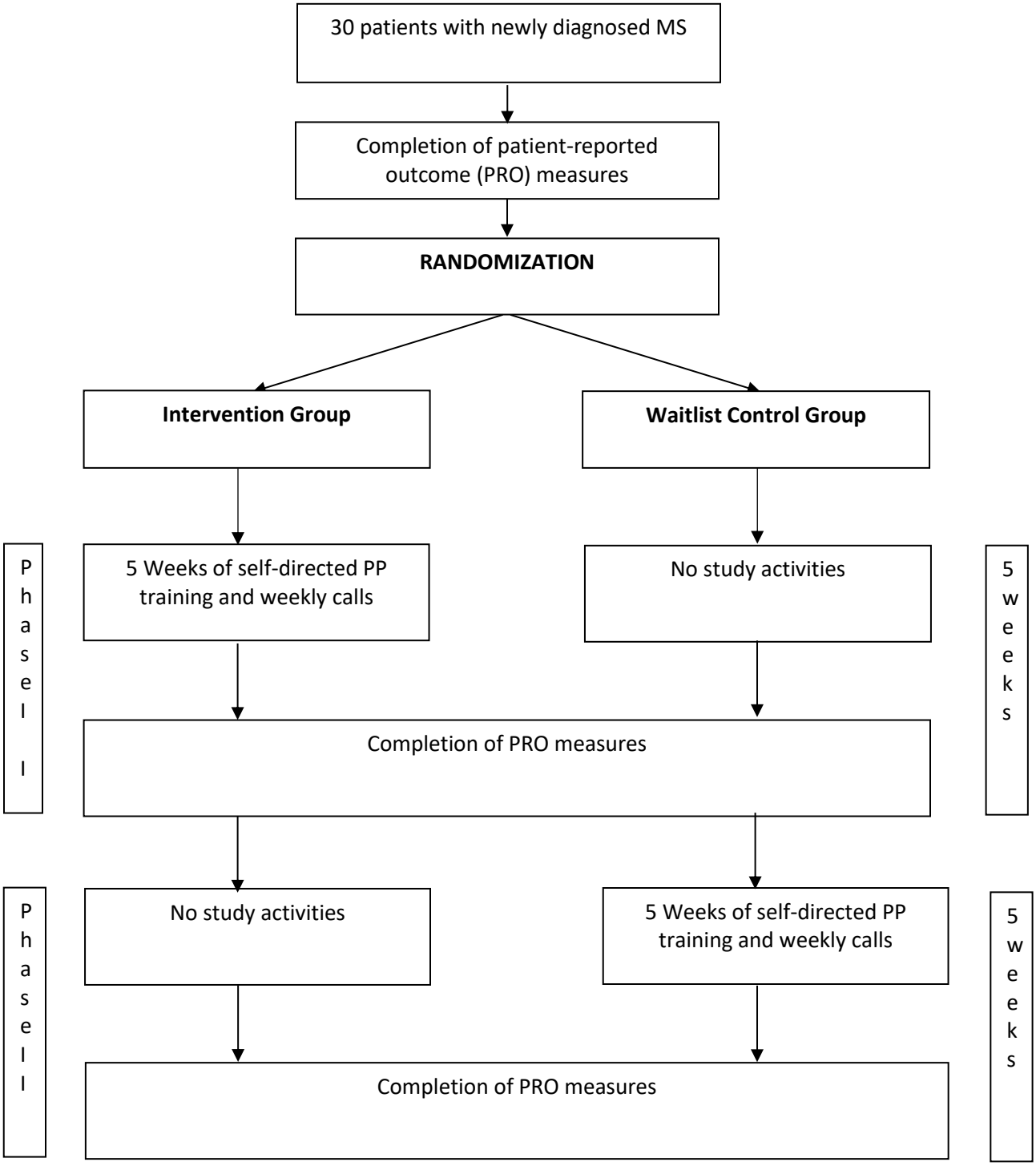
Specific Aim 2: Examine the efficacy of PP training to improve positive affect, emotional function and HRQOL. We will compare positive affect in subjects in the intervention and control group at the completion of the intervention phase. We will also assess between-group differences in depression, anxiety, fatigue, resilience and HRQOL following the intervention phase.

Specific Aim 3: Determine if improvements in positive affect, emotional function and HRQOL following PP training are maintained. For subjects in the intervention group who demonstrate a benefit from PP intervention, we will determine if that benefit is maintained by comparing positive affect, depression, anxiety, fatigue, resilience and HRQOL at the completion of the intervention and extension phases.

3. General Description of Study Design

This is a phase I randomized controlled trial (RCT) to examine the feasibility, acceptability and efficacy of a self-directed PP training intervention to increase positive affect in newly diagnosed patients with MS. The RCT will include a five-week intervention phase and a five-week extension phase.

Schema:


30 patients with newly diagnosed MS
Completion of patient-reported outcome (PRO) measures
RANDOMIZATION
Intervention Group
Waitlist Control Group
Phase I
5 Weeks of self-directed PP training and weekly calls
No study activities
5 weeks
Completion of PRO measures
Phase II
No study activities
5 Weeks of self-directed PP training and weekly calls
5 weeks
Completion of PRO measures

4. Subject Selection

Thirty subjects with newly diagnosed MS will be enrolled at the Brigham MS Center.

Inclusion criteria:

1. Diagnosis of MS according to the McDonald 2017 diagnostic criteria with onset of symptoms within the last 2 years
2. Age 18-65
3. Ability to speak, read and write in English

Exclusion criteria:

1. Moderate or marked cognitive abnormalities identified by the treating neurologist during routine clinical visits to the Brigham MS Center that would preclude meaningful participation in the PP exercises.

All newly diagnosed MS patients seen at the Brigham MS Center will be eligible to participate. Patients will be approached by their physicians at the time of their routine clinical visits to the center. Interested individuals will meet with a member of the research staff to learn about the study in more detail. Flyers will also be posted at the Brigham MS Center.

5. Subject Enrollment

Individuals with MS will be given a copy of the consent document to review. They will have the opportunity to discuss the study with their physician as well as other members of the research study staff prior to giving consent. Individuals may choose to enroll at the time of their clinical visit, or they may enroll at a later date. Consent will be obtained by study investigators or research coordinators listed on the protocol.

6. STUDY PROCEDURES

Enrollment Visit (60 minutes)
Subjects will be enrolled at the Brigham MS Center at the Brigham and Women's Hospital. At enrollment, subjects will be consented and assigned a study subject ID. Subjects will complete a battery of PRO measures in REDCap, a secure web application for building and managing online surveys. The PRO measures include:

1. Positive and Negative Affect Scale (PANAS) [11] is comprised of two 10-item mood scales, one measuring positive affect and the other negative affect.

2. Life Orientation Test-Revised (LOT-R) [12] is a 6-item measure of optimism and pessimism and the most widely used measure of optimism.

3. NeuroQoL [13] is a set of self-report measures developed through a collaborative, multisite NINDS-sponsored research initiative to construct psychometrically-sound and clinically-relevant HRQOL tools for individuals with neurological conditions such as stroke, MS and Parkinson's disease. It covers 12 domains including Ability to Participate in Social Roles and Activities, Anxiety, Cognitive Function, Depression, Emotional and Behavioral Dyscontrol, Fatigue, Lower Extremity Function, Positive Affect and Well-Being, Satisfaction with Social Roles and Activities, Sleep, Stigma and Upper Extremity Function.

4. Brief Resilience Scale (BRS) [14] is a 6-item scale that measures the ability to bounce back or recover from stress.

After enrollment, a computerized random number generator will be used to randomize subjects to the intervention or control group.

Intervention Phase (5 weeks)
In the intervention phase (Phase I: Weeks 1-5), subjects randomized to the intervention group will be given the study participant manual and asked to set up a time for weekly phone calls with the study coordinator. They will complete five weeks of PP exercises, one exercise per week. They will be asked to rate their mood prior to and after completing each exercise. They will also be asked to rate the ease and utility of each exercise. The weekly calls with the study coordinator will be used to document and discuss the ease and utility scores recorded by subjects at the completion of the weekly exercise. The control group will have no study activities during the intervention phase and will be considered a wait-list control. At the completion of the intervention phase, all subjects will be emailed a link to complete PRO measures in REDCap.

Extension Phase (5 weeks)
In the extension phase (Phase II: Weeks 6-10), subjects in the control group will receive their study participant manual in the mail. They will be contacted by the study coordinator to set up weekly phone calls. They will complete the PP intervention as described above. The intervention group will complete no study activities in the extension phase. At the completion of the extension phase, all subjects will be emailed a link to complete PRO measures.

Intervention: The PP intervention consists of five weeks of self-directed PP training using the following exercises:

1. Gratitude for positive events: Recall three positive events that occurred in the past week and write about the events and how the events made you feel.

2. Personal strengths: Complete a brief survey of personal strengths and select a strength such as perseverance or humility and use it deliberately in the next 24 hours. Write about how you used the strength and how you felt while using it.

3. Gratitude letter: Recall another individual's kind act that resulted in joy, relief, serenity or other positive feelings. Write a letter to the person describing feelings of gratitude associated with this event.

4. Enjoyable and meaningful activities: Intentionally complete three acts in a single day – a pleasurable act done alone, a pleasurable act done with others and a meaningful or important act.

5. Remembering past successes: Focus on a time when you experienced success and write about the event and the positive feelings and thoughts you had during the event

These exercises have all been described by Huffman et al. [10, 15]. Exercises may require anywhere from 15 minutes to several hours to complete.

7. Risks and Discomforts

There are no major risks associated with participating in the study. Subjects may experience discomfort writing about emotional aspects of their lives. If they do experience discomfort, they may choose not to complete the weekly PP assignments. If they feel their participation is becoming too burdensome or is exacerbating ongoing symptoms, they have the option to decline further participation and withdraw from the study. They may also be referred to a mental health provider at the Brigham MS Center.

8. Benefits

This is a pilot study designed to determine the feasibility, acceptability and efficacy of a self-directed PP training program for individuals with newly diagnosed MS. If the results suggest that self-directed PP training is feasible, acceptable and effective, it may be offered as a no cost, innovative tool for increasing positive affect, decreasing depression and anxiety and improving HRQOL in patients with newly diagnosed MS.

9. Statistical Analysis

To assess the feasibility of the intervention (Specific Aim 1), our goal is to demonstrate that the proportion who will complete four out of five exercises is greater than 0.5. Given our sample size of 30 subjects, we will have 80% power to detect a difference if the true proportion of subjects who will complete four out of five exercises is 0.75 using a one sample binomial test of proportions (Stata routine: *power oneproportion*). For the comparison of the treatment groups in terms of PRO measures (Specific Aim 2), the intervention effect will be estimated using analysis of covariance (ANCOVA) model. In the ANCOVA model, the post-intervention scores

will be compared between the groups controlling for baseline scores. All outcome measures (PANAS, LOT-R, NeuroQoL and BRS) will be compared using the same model. To assess whether benefits of the PP intervention are maintained at 10 weeks (Specific Aim 3), we will first calculate the change from baseline to week 5 for each of the outcome measures. For the subjects who experience a benefit of the intervention, we will then assess if at least 50% of the benefit was maintained at the 10-week time point. The proportion of subjects who maintained the benefit will be reported.

10. Monitoring and Quality Assurance

Bonnie Glanz, the PI, will be responsible for assuring the validity and integrity of the data collected, and adherence to the IRB-approved protocol. The study team will meet weekly to review subject recruitment, subject satisfaction and study progress. Adverse events associated with the study will be reported to the PI within 24 hours of knowledge of the event. The PI will report adverse events or other unanticipated problems to PHRC as described in the PHRC policy on Adverse Event Reporting and Unanticipated Problems Involving Risks to Subjects or Others.

11. Privacy and Confidentiality

- ☒ Study procedures will be conducted in a private setting
- ☒ Only data and/or specimens necessary for the conduct of the study will be collected
- ☒ Data collected (paper and/or electronic) will be maintained in a secure location with appropriate protections such as password protection, encryption, physical security measures (locked files/areas)
- ☐ Specimens collected will be maintained in a secure location with appropriate protections (e.g. locked storage spaces, laboratory areas)
- ☒ Data and specimens will only be shared with individuals who are members of the IRB-approved research team or approved for sharing as described in this IRB protocol
- ☒ Data and/or specimens requiring transportation from one location or electronic space to another will be transported only in a secure manner (e.g. encrypted files, password protection, using chain-of-custody procedures, etc.)
- ☒ All electronic communication with participants will comply with Mass General Brigham secure communication policies
- ☒ Identifiers will be coded or removed as soon as feasible and access to files linking identifiers with coded data or specimens will be limited to the minimal necessary members of the research team required to conduct the research
- ☒ All staff are trained on and will follow the Mass General Brigham policies and procedures for maintaining appropriate confidentiality of research data and specimens
- ☒ The PI will ensure that all staff implement and follow any Research Information Service Office (RISO) requirements for this research
- ☐ Additional privacy and/or confidentiality protections

12. References

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APPENDIX A

Data Monitoring Committee / Data and Safety Monitoring Board Appendix

- *To be completed for studies monitored by Data Monitoring Committee (DMC) or Data and Safety Monitoring Board (DSMB) if a full DMC/DSMB charter is not available at the time of initial IRB review.*
- *DMC/DSMB Charter and/or Roster can be submitted to the IRB later via Amendment, though these are not required.*

A Data Monitoring Committee (DMC) or Data and Safety Monitoring Board (DSMB) will be convened for safety monitoring of this research study. The following characteristics describe the DMC/DSMB convened for this study (Check all that apply):

☐ The DMC/DSMB is independent from the study team and study sponsor.

☐ A process has been implemented to ensure absence of conflicts of interest by DMC/DSMB members.

☐ The DMC/DSMB has the authority to intervene on study progress in the event of safety concerns, e.g., to suspend or terminate a study if new safety concerns have been identified or need to be investigated.

☐ Describe number and types of (i.e., qualifications of) members:
Click or tap here to enter text.

☐ Describe planned frequency of meetings:
Click or tap here to enter text.

☐ DMC/DSMB reports with no findings (i.e., "continue without modifications") will be submitted to the IRB at the time of Continuing Review.

☐ DMC/DSMB reports with findings/modifications required will be submitted promptly (within 5 business days/7 calendar days of becoming aware) to the IRB as an Other Event.