An At-home Positive Psychology Intervention for Individuals with Multiple Sclerosis
A Phase 1 Randomized Controlled Trial

Melanie E. Freedman, BS; Brian C. Healy, PhD; Jeff C. Huffman, MD; Tanuja Chitnis, MD; Howard L. Weiner, MD; Bonnie I. Glanz, PhD

Background: Positive psychology (PP) uses targeted activities to increase the frequency and intensity of positive feelings and may improve overall well-being in medically ill populations. In this phase 1 randomized controlled trial, we examined the feasibility, acceptability, and potential impact of a 5-week, telephone-delivered PP intervention for individuals with multiple sclerosis (MS).

Methods: Participants were randomized 1:1 to a 5-week at-home PP intervention or a waitlist control condition. Participants engaged in weekly telephone calls with a study trainer and completed one PP exercise, such as recalling a past success, each week. Feasibility was determined by the number of sessions completed, and acceptability was assessed by weekly postexercise participant ratings of ease and utility. Efficacy was explored by examining between-group differences in changes from baseline on psychological variables, health-related quality of life, and self-reported functional activities at 5 and 10 weeks.

Results: Of 30 patients enrolled in the study, 28 (93%) completed all exercises. Ease scores ranged from 7.7 to 8.7 of 10 and utility scores ranged from 8.2 to 8.7 of 10. The PP intervention was associated with significantly greater increases (P < .05) in positive affect, optimism, state and trait anxiety, general health, and resilience in the intervention group versus the control group. Approximately half of the PP participants maintained at least 50% of the improvement at 10 weeks.

Conclusions: This 5-week, telephone-based PP intervention was feasible and acceptable to individuals with MS. Larger randomized controlled trials are warranted to further investigate the utility of this intervention to improve well-being and other health outcomes in MS. Int J MS Care. 2021;23:128-134.

Multiple sclerosis (MS) is a chronic autoimmune disease of the central nervous system that affects physical and mental health. Mental health comorbidities, including depression and anxiety, are common, and health-related quality of life (HRQOL) is often reduced. Several key elements of successful adjustment to MS and other chronic diseases have been identified, including maintenance of emotional balance, preservation of healthy relationships, absence of psychological disorders, low levels of negative
Positive psychology (PP) interventions use 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. Although most PP studies have been performed with healthy individuals or those with depression, preliminary studies of PP interventions for medically ill populations have shown improvements in psychological well-being. A recent 12-week study of a telephone-based PP intervention for patients with acute coronary syndrome (ACS) showed improvements in positive affect 12 and 24 weeks after the intervention. These improvements were associated with large effect size changes in depression and anxiety in the intervention group compared with the control condition.

There are very few PP studies in individuals with MS. In a single pilot randomized controlled trial using PP to promote resilience, 31 individuals with MS were randomized to receive the Everyday Matters intervention developed by the National Multiple Sclerosis Society or to a waitlist control group. The 6-week intervention was delivered via group teleconference and was supplemented with readings, videos, and online participation. There were significant group effects for resilience and satisfaction with roles, as well as trends for group effects in positive affect and well-being and depressive symptoms. Our research group previously performed a single-arm pilot study to assess the feasibility and acceptability of a 5-week in-person group PP intervention for individuals with MS. The utility of the group PP intervention to increase positive psychological constructs and HRQOL was also examined. At enrollment, participants were given a study participant manual that included an introduction and separate chapters for each week’s PP exercise. Participants attended one group meeting per week led by the study trainer to discuss the completed exercise and be introduced to the next exercise. All the participants completed the 5-week PP intervention. Participants demonstrated decreased depression and fatigue after 5 weeks of PP training compared with baseline. Despite considerable interest among individuals who were approached about participating in the group PP study, there was a high decline-to-participate rate. The most commonly cited barrier to study participation was the inability of individuals to commit to weekly in-person study visits.

Given the potential impact of PP interventions on psychological well-being, and the need to assess remotely delivered PP interventions, we conducted a phase 1 randomized controlled trial of a 5-week, at-home, telephone-delivered PP intervention for individuals with MS. The primary aim was to assess the feasibility and acceptability of this approach. We also explored the impact of PP training on positive affect, a target of PP interventions that is sensitive to change and has been linked to better health outcomes in a variety of chronic diseases (including asthma and diabetes), other psychological variables, HRQOL, and self-reported functional activities. Finally, we determined whether changes observed after PP training were maintained at 10 weeks.

Methods
Participants
Participants were recruited from the Comprehensive Longitudinal Investigation of Multiple Sclerosis at Brigham and Women’s Hospital, Partners MS Center (CLIMB). CLIMB is an ongoing, prospective observational cohort study that began enrolling participants in 2000. Inclusion criteria include 18 years of age or older and a diagnosis of MS or clinically isolated syndrome according to the revised McDonald criteria. To date, more than 2500 participants have been enrolled. All patients seen at Partners MS Center who were enrolled in CLIMB were eligible to participate. Study flyers were given to treating neurologists to be distributed to eligible patients at the time of their routine visits to the MS center. Patients were not approached if they were currently participating in other research studies apart from CLIMB or were eligible to participate in other research studies at the same visit. Study flyers were also posted at the MS center. Interested individuals met with a member of the study staff to learn about the study in more detail. Study recruitment began March 12, 2018, and ended January 17, 2019. This study was approved by the Partners Human Research Committee at Brigham and Women’s Hospital, and all the participants provided written informed consent.

Procedures
All the participants completed a patient-reported outcome (PRO) battery in REDCap, a secure web application for building and managing online surveys. Using a computerized random number generator, participants were randomized to the intervention group or to a waitlist control group (Figure S1, published in the online version of this article at ijmsc.org). At the beginning of the intervention phase (phase 1: weeks 1–5), participants in the intervention group were given a PP intervention manual and asked to complete 5 weeks of PP exercises, one exercise per week. At the completion of each exercise, participants rated the ease and utility of the exercise. The waitlist control group had no study activities during

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the first 5 weeks after enrollment. At the completion of the intervention phase, all the participants were e-mailed a link to complete the PRO battery in REDCap. At the beginning of the extension phase (phase 2: weeks 6-10), participants in the control group received their study participant manual in the mail. They completed the PP intervention as described previously. The intervention group did not complete any study activities during the extension phase. At the completion of the extension phase, all the participants were e-mailed a link to complete the PRO battery.

Study Intervention

The PP intervention consisted of 5 weeks of PP training using the exercises detailed in Table 1. These exercises have all been described by Huffman et al.31 and are well-accepted and easy for participants to complete. The study trainer (M.E.F.) was a baccalaureate-level research assistant with experience completing telephone and in-person study assessments with medically ill patients for numerous studies, including two PP intervention trials. She worked under the supervision of a psychiatrist (J.C.H.) and received training using a standard trainer manual that included optional scripts to describe PP and the weekly exercises as well as suggestions to help facilitate brainstorming. Finally, she received didactic teaching from MS experts on the basics of MS care and shadowed in the MS clinic to better understand the experiences of patients with MS. During the study, physician study staff members were available by telephone or pager to intervene, if needed, due to participant discomfort or to answer specific questions about the study.

Before beginning the intervention, the study trainer spoke with each participant to introduce PP as an approach that focuses on improving positive emotions through the practice of simple exercises that are designed to make people feel more hopeful, grateful, and happy. During the weekly calls, the study trainer introduced the exercise and helped brainstorm ways to complete it. The calls were also used to review completed exercises and their effects on well-being. The study trainer discussed with participants how individuals can translate the skills learned from completing exercises into skills that can be used in everyday life. During the final call, the study trainer identified the two to three skills that resonated most with participants and discussed how to implement them going forward.

Outcome Measures

The primary outcome measures were the feasibility and acceptability of the intervention. To assess feasibility, we calculated the proportion of participants who reported having completed at least four of the five exercises before their weekly conversations with the study trainer. In addition, we examined exercise-specific ratings of ease and utility to measure the acceptability of each exercise. Ease and utility were measured using Likert scales scored from 0 to 10, one for ease of completion (0 = very difficult; 10 = very easy) and one for overall utility (0 = not helpful; 10 = very helpful). Ease and utility scores were recorded by participants at the completion of each PP exercise.

At enrollment, 5 weeks, and 10 weeks, participants completed a battery of PRO measures in REDCap. The PRO battery included the following: the Positive and Negative Affect Schedule (PANAS),22 the Life Orientation Test–Revised,32 the Center for Epidemiologic Studies Depression Scale (CES-D),24 the State-Trait Anxiety Inventory,25 the Medical Outcomes Study 36-item Short Form Health Survey (SF-36),26 the Work Productivity and Activity Impairment Questionnaire,27 the Brief Resilience Scale,28 and the Perceived Stress Scale.29 The key psychological construct was the positive affect scale of the PANAS due to the previously demonstrated effects of PP on positive affect.30 The PANAS is a well-validated measure of positive affect that has been shown to be responsive to change.14

Statistical Analysis

The sample size of 30 total participants for this trial was chosen to ensure that we could estimate the proportion who would complete the intervention with precision of approximately ±0.05. With a sample size of 15 per group, we had 80% power to detect a difference between groups of 0.74 times the SD at the two-sided 0.05 level using the analysis of covariance (ANCOVA) model assuming a within-subject correlation of 0.7 (Stata routine: sampsi). The proportion of participants who completed the intervention and the associated 95% CI were used to estimate feasibility. The mean ease and utility scores and 95% CIs were used to estimate acceptability.

### Table 1. Description of positive psychology exercises

| Week | Exercise                        | Description |
|------|---------------------------------|-------------|
| 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. |
Secondary outcomes included the PRO measures listed previously. We estimated the differences between groups on PRO measures using the ANCOVA model. In the ANCOVA model, the postintervention scores were compared between groups controlling for baseline scores. To confirm the results, including participants with missing data, we also estimated the difference using a common baseline model with a random intercept, and the results were similar (data not shown). We estimated the within-person change using all available participants by comparing the scores immediately before the intervention with postintervention measurement in participants from both groups (intervention and waitlist control) using a longitudinal model with a random intercept. Finally, we assessed whether at least 50% of the change from baseline to the 5-week time point on each of the outcome measures was maintained at the 10-week time point for participants in the intervention group.

Results
Thirty patients were enrolled in the study. Eighty percent of participants in the intervention group were female compared with 73% in the waitlist control group. The mean ± SD age of participants in the intervention group was 54.5 ± 7.2 years and in the waitlist control group was 54.2 ± 4.7 years (mean difference = 0.3 [95% CI, −4.2 to 4.8] years, \( P = .89 \)). Both groups had a mean disease duration of slightly more than 21 years (mean difference = −0.2 [95% CI, −7.3 to 7.0] years, \( P = .96 \)). The mean ± SD Expanded Disability Status Scale score in the intervention group was 3.0 ± 2.3 compared with 3.2 ± 2.3 in the waitlist control group (mean difference = −0.2 [95% CI, −1.9 to 1.5], \( P = .78 \)). Baseline PRO scores for both groups are presented in Table S1. At baseline there were no significant differences between groups on any of the PRO measures. One participant in the intervention group and one in the waitlist control group withdrew or were withdrawn from the study before beginning the intervention: one did not have time to participate and the other did not return telephone calls to schedule the first at-home training session. The remaining participants completed all five study exercises and follow-up assessments. The estimated feasibility of the intervention was 93% (95% CI, 78% to 99%). The estimated average ease and utility scores of each exercise are presented in Table 2. The exercises received generally high scores for each measure, with remembering past successes, enjoyable and meaningful activities, and gratitude for positive events receiving the highest scores.

Table 3 displays the between-group comparisons of change from baseline on all PROs at 5 weeks. A statistically significant difference between the groups was observed for the key psychological construct, positive affect (estimated group difference = 7.4 [95% CI, 3.2 to 11.6]). There were also significant differences between the intervention and waitlist control groups on measures of optimism, anxiety, the general health subscale of the SF-36, and resilience. The within-subject change on each of the outcome measures is provided in Table S2. The measures that showed a significant treatment effect also showed a significant change with time when both groups of participants—those in the intervention group who completed the intervention during phase 1 (weeks 1-5) and those in the waitlist control group who completed the intervention during phase 2 (weeks 6-10)—were combined. Results of several other measures, including the CES-D and the SF-36 role physical, vitality, and mental health subscales, also showed a significant change with time across all participants.

Finally, we assessed whether the improvements on PROs were maintained for the additional 5 weeks of follow-up in the intervention group (Table S3). In general, the observed improvements were maintained for approximately 50% of participants.

Discussion
This study found that a 5-week, telephone-delivered PP intervention was feasible and well-accepted by individuals with MS. Ninety-three percent of participants who enrolled in the study completed the PP intervention. In addition, participants provided mean scores on ratings of ease and utility that ranged between 7.7 and 8.7 of 10, suggesting that a remotely delivered PP intervention is a good option for individuals with MS. Our research group previously reported the results of a pilot study of a group PP intervention for individuals with MS. Compared with the group PP trial, we found that the at-home, remotely delivered PP intervention study was much easier to enroll. In addition, all the participants in the group PP trial were female. The willingness of males to participate in the at-home PP study suggests that there is an interest among men to explore PP, but
Table 3. Estimation of treatment effect during first study period

| Outcome                      | Change, mean ± SD | Estimated difference (95% CI) | P value |
|------------------------------|-------------------|-------------------------------|---------|
| PANAS positive affect        | 4.9 ± 4.5; n = 12 | −3.2 ± 5.8; n = 13            | 7.4 (3.2 to 11.6) | .001* |
| PANAS negative affect        | −2.6 ± 9.4; n = 13| −0.3 ± 4.5; n = 11            | −0.7 (−6.6 to 5.1) | .799 |
| LOT-R                        | 2.1 ± 3.4; n = 14 | −1.3 ± 2.5; n = 14            | 3.3 (0.8 to 5.8)  | .011* |
| CES-D                        | −2.1 ± 2.9; n = 14| 0 ± 5.7; n = 12               | −1.9 (−5.0 to 1.2) | .225 |
| STAI state anxiety           | −3.2 ± 6.1; n = 14| 3.4 ± 8.1; n = 14             | −6.0 (−11.5 to −0.5) | .034* |
| STAI trait anxiety           | −3.3 ± 4.9; n = 14| 2.7 ± 6.9; n = 14             | −5.7 (−10.4 to −1.0) | .012* |
| SF-36                        |                   |                               |         |
| Physical functioning         | −1 ± 3.3; n = 11  | 0.3 ± 3.2; n = 13             | −1.7 (−4.5 to 1.0) | .210 |
| Role physical                | 4.2 ± 6.3; n = 14 | 1.1 ± 9; n = 13               | 4.1 (−1.9 to 10.1)  | .175 |
| Bodily pain                  | 0.1 ± 8.3; n = 14 | −0.2 ± 7.5; n = 14            | 1.1 (−5.1 to 7.4)  | .708 |
| General health               | 1.1 ± 4; n = 14   | −2.9 ± 3.9; n = 14            | 4.0 (0.9 to 7.1)  | .013* |
| Vitality                     | 1.4 ± 4.2; n = 14 | 0.3 ± 7.7; n = 14             | 1.6 (−3.4 to 6.7)  | .519 |
| Social functioning           | 3 ± 6.7; n = 13   | 2.4 ± 9.2; n = 14             | 1.2 (−4.8 to 7.1)  | .687 |
| Role emotional               | −3.6 ± 9.4; n = 14| −4.3 ± 12.3; n = 14           | 0.1 (−8.2 to 8.5)  | .976 |
| Mental health                | 2.9 ± 4.6; n = 14 | −0.8 ± 6.6; n = 14            | 3.6 (−0.9 to 8.1)  | .109 |
| Physical composite score     | 0.9 ± 4.2; n = 11 | 0.3 ± 5.4; n = 13             | 0.7 (−3.7 to 5.0)  | .755 |
| Mental composite score       | 0.5 ± 6; n = 11   | −1.4 ± 6.3; n = 13            | 2.2 (−3.1 to 7.5)  | .403 |
| WPAI                         |                   |                               |         |
| Work time missed             | −1 ± 4.9; n = 9   | −1.9 ± 10.8; n = 6            | 1.3 (−7.9 to 10.5) | .765 |
| Work impairment              | 1.2 ± 24.7; n = 8 | 3.3 ± 10.3; n = 6             | −0.9 (−24.1 to 22.3) | .934 |
| Overall work impairment      | 0.1 ± 22.1; n = 9 | 0.5 ± 15.6; n = 6             | 1.0 (−22.4 to 24.3) | .930 |
| Activity impairment          | 0 ± 26.9; n = 14  | 5 ± 23.5; n = 14              | −6.6 (−25.5 to 12.3) | .480 |
| BRS                          | 0.1 ± 0.4; n = 13 | −0.3 ± 0.5; n = 14            | 0.4 (0.0 to 0.7)  | .033* |
| PSS                          | −0.4 ± 2.8; n = 14| −1.1 ± 2.7; n = 14            | 0.5 (−1.7 to 2.6)  | .657 |

Abbreviations: BRS, Brief Resilience Scale; CES-D, Center for Epidemiologic Studies Depression Scale; LOT-R, Life Orientation Test–Revised; PANAS, Positive and Negative Affect Schedule; PP, positive psychology; PSS, Perceived Stress Scale; SF-36, 36-item Short Form Health Survey; STAI, State-Trait Anxiety Inventory; WPAI, Work Productivity and Activity Impairment Questionnaire.

*Statistically significant.

perhaps not in a group setting. This may reflect a lack of time to make weekly visits to the MS center or a lack of comfort sharing experiences with a group. It is possible that remotely delivering the intervention better addresses the needs of male patients. Finally, we found that participants who enrolled in the at-home PP trial had higher average disability scores than participants who enrolled in the group PP trial. It is likely that at-home interventions are more accessible to individuals with increased MS-related disability. Taken together, these findings suggest that the delivery of psychosocial interventions that can be accessed remotely may be of increasing interest to individuals with MS.

We observed a significant increase in positive affect, the key psychological construct, in individuals who completed the PP intervention in phase 1 compared with waitlist controls. We also observed improvements in optimism, anxiety, general health, and resilience after PP training. Positive affect has previously been identified as an important element in the successful adjustment to chronic disease. Positive affect has also been linked to superior health outcomes, including lower mortality rates in the general population and reduced morbidity in individuals with chronic diseases, including asthma and diabetes. When we examined the within-subject change across all study participants after the intervention, we found positive effects on the following outcome measures: positive affect, optimism, depression, anxiety, role physical, general health, vitality, mental health, and resilience. These findings demonstrate that a PP intervention that distinctly focuses on an individual’s strengths is a potentially novel way to improve mental health and function in individuals with MS. In addition, the ease of delivery of the intervention and the ease of completion of the PP exercises make it a scalable intervention.

This study did not focus on improving specific health behaviors or treatment adherence. Previous research, however, has suggested that increases in positive affect may affect these outcomes. Peterson et al randomized patients after percutaneous coronary intervention to the patient education control group or the positive affect/
self-affirmation intervention group. Participants in both groups received educational workbooks, a pedometer, and a behavioral contract for a physical activity goal. Participants in the positive affect/self-affirmation intervention group also received a positive affect workbook chapter, bimonthly inductions of positive affect by telephone, and small mailed gifts. Participants were followed up for 12 months. Significantly more participants in the intervention group than in the control group achieved an increase of 336 kcal/wk or more at 12 months (54.9% vs 37.4%). In a study that examined the usefulness of a combined PP and motivational interviewing intervention after an ACS, patients with ACS were randomized to a 12-week, telephone-delivered PP–motivational interviewing intervention or an attention-matched, motivational interviewing–based health education control condition. Participants who underwent PP–motivational interviewing completed 9 to 15 more minutes of moderate-to-vigorous physical activity per day and took 1600 to 1800 more steps per day (as measured by an accelerometer) than control participants. Future studies of PP interventions in MS should incorporate health behaviors as additional outcome measures. Two outcomes that might be considered are exercise and treatment adherence. The benefits of exercise, including improvements in muscle strength, flexibility, and fatigue, have been well-described in MS, and regular exercise is commonly recommended. Even with the introduction of oral medications, treatment adherence remains a problem in MS. Increasing adherence is likely to have a positive effect on patient outcomes and may also lower the cost of MS care. This may be a promising next step for future PP studies in MS.

When we examined whether improvements seen in participants in the intervention group were maintained 5 weeks postintervention, we found that the benefits were maintained in approximately 50% of participants, suggesting that additional work or booster sessions may be required to maintain the benefits of PP training. The use of booster or continuation sessions has previously been addressed in the PP literature. In a study aimed at identifying the optimal components of an 8-week PP-based intervention for patients with ACS, researchers found that continuing the intervention beyond the 8 weeks via booster sessions was associated with greater physical activity, but this finding did not reach statistical significance. The booster sessions took place 2, 4, and 6 weeks after completion of the program and focused on the ongoing use of PP skills in daily life. Given that the intervention studied in MS was a 5-week rather than an 8-week program, it is possible that the booster sessions would play a more important role in maintaining the effects of the PP training. Future work should focus on optimization of the PP program for individuals with MS. The chronic nature of the disease suggests that skills that can be developed and maintained throughout the course of the disease are needed.

The present study has several limitations. First, this phase 1 randomized controlled trial had a small sample size and a large number of outcome measures, which may have limited our ability to see statistically significant changes in HRQOL and other psychological outcomes. Second, it is possible that engagement with the study trainer, and not the PP program, explains the findings. Third, this study was subject to self-selection bias, which may limit the external validity of the findings. Participant characteristics, including income and disability level, as well as physician characteristics, such as support or attitude toward psychosocial interventions, have all been shown to influence participation in psychosocial trials. Fourth, this intervention required a significant amount of time on the part of the study trainer and funding for the trainer’s time. Future work might explore the feasibility and acceptability of an at-home, self-guided PP program that would not require a dedicated study trainer. If successful, this self-guided intervention could be made available to a much larger number of individuals with MS.

In conclusion, the results of this study support the feasibility, acceptability, and potential efficacy of a 5-week, telephone-delivered PP intervention to improve well-being in individuals with MS. The shift from in-person to at-home PP training improved the accessibility of the program, making it possible to provide the intervention to a much larger and more diverse group of individuals. Similarly, the booster sessions were well-received, with approximately 50% of participants maintaining the benefits of PP training 5 weeks after the intervention.

**PRACTICE POINTS**

- Psychosocial interventions aimed at increasing positive emotional experiences may help lessen the psychological impact of living with MS.
- We examined the feasibility, acceptability, and potential impact of a 5-week, at-home positive psychology intervention for individuals with MS.
- The intervention was feasible and acceptable and associated with increases in positive affect, optimism, state and trait anxiety, general health, and resilience.

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of participants, including males, working individuals, and those with disabling disease. Larger trials are warranted to further investigate the utility of PP training to improve psychological well-being and to examine its effect on a wide range of health outcomes in MS.

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