Promoting resilience after stroke in the survivor/caregiver dyad (ReStoreD): Pilot testing a couples-based intervention

Protocol Summary

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Sponsor:	NIH NATIONAL INST CHILD HLTH & HUMAN DEV
Principal Investigator:	Alexandra Terrill
Internal Staff and Sub-Investigators:	Cynthia Berg Meghan Berry Elizabeth Cardell Jackie Einerson Rebecca Hahnlein Kaitlin Huntington Kaitlyn Krogen Justin MacKenzie Jennifer Majersik RaeLynn Perez Lorie Richards Allison Ritchie Rachel Swan Eliza Young
External Sub-Investigators:	

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Background and Introduction

Almost 800,000 US residents experience a stroke each year (2), with a larger proportion surviving(3); thus, more stroke survivors are affected by the chronic sequelae of stroke. **Mood alteration, particularly in the form of depressive symptoms or apathy, occurs in over a third of all stroke survivors** (4) and is associated with increased disability and mortality, decreased participation, and poorer quality of life (5-7).

The majority of stroke survivors (80%) return to the community and rely on the support of an informal caregiver such as a spouse or partner (8). Unfortunately, spousal caregivers are often unprepared for the challenges of caring for a person with impairments, which can include changes in mood, mobility, behavior, speech, and cognition, leading to increased spousal burden and an altered relationship. These stroke outcomes often lead to depression for the person with stroke and the caregiver. **Stroke family caregivers are at significant risk of depression** (up to 50%(9)), which is associated with negative outcomes, including interference with rehabilitation and increased likelihood of re-hospitalization of stroke survivors (10), and social isolation and health declines for the caregivers (11). Importantly, research suggests that depressive symptoms in either member of the survivor-caregiver dyad (couple) increases depressive symptoms in the other (12).

Many significant psychosocial changes for stroke survivors and their partners may not occur until at least 6-12 months post-stroke when the couple is attempting to re-integrate into "normal" life. For example, there may be significant role changes (e.g., new caregiver role) and role losses or reversals (e.g., primary provider is no longer able to work). This can be a source of stress for both partners in the relationship. McKevitt et al. (2011) (13) found that nearly half (42%) of respondents with a partner at the time of stroke reported a negative change in the relationship. Social support and relationship harmony also deteriorate significantly from 1-3 years post-stroke while depressive symptoms increase (14). Couples with increased negativity in their relationships have worse psychological outcomes, including depression (15). A recent systematic review examining perceived changes in social support after stroke observed significant strain within the family unit after stroke and that this was associated with depression and severity of disability (16).

A new model is needed for stroke survivors and partner caregivers that focuses on the remaining relationship strengths in order to foster resilience in the couple. Despite the high prevalence and significant consequences of post-stroke depression, diagnosis and treatment of depressive symptoms in stroke survivors and caregivers are often inadequate. Support for efficacy of existing psychotherapeutic interventions for post-stroke depressive symptoms, such as cognitive-behavioral therapy, is mixed (17). Positive psychology interventions (PPIs) may be particularly useful as they aim to increase well-being by promoting positive emotions, thoughts and behaviors. Based on the broaden-and-build theory (18), PPI-induced positive emotions can broaden thought-action repertoires, which, in turn, create behavioral flexibility that over time builds personal resources such as resilience, social closeness, and even physical health (19). Research suggests that post-stroke positive emotionality is associated with improved function and social participation (20, 21). PPIs could be an effective treatment for stroke survivor *and* caregiver depressive symptoms.

Because of the reciprocal psychosocial effects of stroke (22), recent trends in the stroke

survivor/caregiver literature have espoused the **benefits of using a dyadic approach** (1, 23), with a recent review of caregiver and dyad interventions (1) supporting dyadic intervention use for targeting stroke survivor outcomes such as mood (depression and anxiety), social function, physical function and health-related quality of life (Class IIa; Level of Evidence A). Yet, dyadic interventions are scarce, rarely involving more than information and education (23-25). Interventions that include skill-building (e.g. problem solving, stress management, and goal setting) are recommended over those consisting of psychoeducation or support only. PPIs include these skill building components; for example, strategies to focus on the positive, deep breathing techniques for mindfully savoring a moment, and learning how to work toward a goal. However, findings for dyadic interventions are less clear for the caregiver's well-being (1). This is likely because existing dyadic interventions are focused on stroke survivor needs (1). **Our PPI is designed to respond to both caregiver and survivor needs** by having them complete PPI activities individually and together as a couple.

This intervention is innovative in being **the first dyadic PPI aimed at couples coping with stroke to enhance mood and well-being.** Most traditional psychological approaches for stroke survivors focus on deficits and treatment of negative mood states, and have limited support for efficacy in treating post-stroke depressive symptoms (17). PPIs, in contrast, are based on enhancing psychological strengths and resources to increase well-being (26). Though not currently tested in stroke, PPIs have been effectively applied to various medical populations, including individuals with diabetes, spinal cord injury, or breast cancer (27-30), and have been shown to significantly increase well-being and decrease depressive symptoms (26, 31, 32) with long-lasting effects (28). PPIs carry little to no side effects, are less expensive and time consuming than psychotherapy, and involve minimal additional burden as they consist of brief, self-administered activities.

PPIs are typically targeted at the individual. However, due to the reciprocal nature of positive affect and positive close relationships (33), PPIs are ideally suited as a dyadic intervention. **In our innovative dyadic approach,** stroke survivors and caregivers complete PPIs each week on their own and together. Further, we are also examining **potential mechanisms of the dyadic PPI on couples' mood** trough interactions and shared emotional processes. Research on emotion co-regulation supports the notion that mood states among family members are correlated (34). By having participants complete PPI activities on their own we expect that individual positive emotion will increase. Through PPI activities completed together, couples will share in positive experiences, thereby increasing positive affectivity and strengthening social bonds. Together, this can foster a more positive environment over time, and effect a synergistic change in positive affect and well-being for the dyad. Couples with greater well-being may be better emotionally equipped to handle the stresses of stroke, potentially reducing depressive symptoms (10, 12). Although our intervention is developed for and will be tested in local, community-dwelling couples post-stroke, it is developed so that it is easy to administer using telehealth where the intervention could benefit those geographically or situationally isolated.

Preliminary Data

With internal funding (University of Utah's Consortium for Family and Health Research (C-FAHR)), we have collected preliminary feasibility data on the proposed dyadic PPI (IRB_00080565). We developed the positive psychology activities booklet to be used in our PPI

protocol and sent it to 5 clinical, stroke survivor and caregiver stakeholders for readability, acceptability and applicability. We modified materials based on their feedback.

To test PPI study design feasibility, we recruited participants via University-affiliated outpatient clinics; 5/8 respondent couples to 70 recruitment letters met eligibility criteria and enrolled. Four dyads (8 participants) were randomly assigned to PPI, 1 dyad to waitlist control. They completed assessments and were trained in the PPI activities in-person; they completed PPI activities at home. All PPI dyads completed the program, engaging in activities for at least 6 of 8 weeks. The control dyad withdrew due to caregiver health changes (80% retention). Seven out of 8 participants were at least "satisfied" with the intervention (*M*=3.5 out of 4), rated it at least "beneficial" (*M*=3.3), and found the activity booklet at least "helpful" (*M*=3.8). Questionnaire and interview data reflected participant satisfaction and benefit in mood, affect, dyadic coping, and quality of life. In post-intervention feedback, a participant (stroke survivor) noted: *"... it's hard to look at what's eating at you, and then to try to change that, because it's easier just to sit and do nothing than to show gratitude, to help people out, to savor things, to do all those things on that list. ... I was surprised that I'm very grateful to be alive... showing gratitude for others, for my wife, for my child, for my family, you can get stuck in this hole where everything is about you, and I was, am sick of that hole. So, doing the activities, it helped me tremendously."* These preliminary findings suggest strongly that the proposed PPI is feasible to implement with couples coping with stroke. Response rate, loss of enrollment due to eligibility, attrition, and participant feedback in this feasibility trial was used to inform the proposed larger pilot trial.

Purpose and Objectives

We have developed a dyadic (couples-based) positive psychology intervention (PPI) protocol to simultaneously target stroke survivors (≥6months since stroke) and their partner caregiver. Preliminary data from a small sample suggest that the PPI protocol is feasible in this population (IRB_00080565). We will now test this intervention and explore potential pathways for its efficacy of through the following aims:

> **Aim 1.** To determine preliminary efficacy of the PPI in 24 couples with depressive symptoms in a randomized waitlist control pilot trial on mood and well-being. *H1a: The PPI will improve well-being and mood as assessed by established outcome measures in survivors and caregivers from pre- to post-intervention. H1b: Improvements in well-being and mood will be greater in the PPI vs. control group.*
>
> **Aim 2.** To determine if the PPI improves quality of interactions in couples during stressful discussion and collaborative problem-solving tasks. *H2: The PPI will enhance the emotional tone of the couple's interactions from pre- to post-intervention as measured by observational interaction coding.*
>
> **Exploratory Aim 3.** To determine whether increases in mood in one partner leads to improvement in mood in the other partner over time as assessed by weekly self-report. *H3: Increases in mood in one partner will be positively associated with increase mood in*

the other partner and vice-versa; i.e. be synergistic across couples.

Study Population

Age of Participants: 18+, no upper limit

Sample Size:
At Utah: 70
All Centers:

Inclusion Criteria:
Inclusion criteria are:

1) Couples consisting of one partner who had an ischemic or hemorrhagic stroke ≥ 6 months ago and a cohabiting partner (living together ≥ 1 year) who self-identifies as the caregiver and is willing to enroll in the study.

2) Either one or both partner(s) report depressive symptoms as assessed by the PROMIS-Depression measure (no formal diagnosis is required).

3) Both partners must be community-dwelling adults age 18 years and older.

4) Both partners must be able to understand printed English instructions

Exclusion Criteria:
Exclusion criteria are:

1) Either partner does not consent to participate.

2) The caregiving partner has had a stroke or other major neurological condition.

3) Either partner is unable to understand printed English instructions.

4) Either partner has significant cognitive impairment (as assessed by the Telephone Interview for Cognitive Status, TICS).

Note: As this is a pilot study, we are restricting participation to only those who are able to understand printed English instructions and have mild/no cognitive impairment. We anticipate expanding inclusion criteria for future trials.

Design

Survey/Questionnaire Research

Prospective Clinical Research
Randomized
Phase I Clinical Trial
Other

Randomized wait-list controlled pilot trial of a behavioral intervention

Study Procedures

Recruitment/Participant Identification Process:

Based on preliminary feasibility data (see Preliminary Studies), we are estimating 80% retention but will conservatively plan for only 70%. To ensure a total of 24 dyads (12 PPI, 12 control) for pilot data analysis, we plan to enroll 35 couples.

Participants will be recruited through University-affiliated clinics, stroke- and caregiver-related support groups, research participant databases, and the University of Utah's Clinical Trials webpage. We have established relationships with these clinics to assist with recruitment, including the Outpatient Rehabilitation Psychology Clinic, Neurology Stroke Clinic, Rehabilitation and Wellness Clinic, and Stroke Rehabilitation Clinic. Research assistants (RAs) will recruit in clinics. We will also provide study information to staff and health care providers along with recruitment letters to hand out to interested potential participants (referral).

We will also distribute study flyers to local support groups (e.g. aphasia, stroke survivor, caregiver support groups). Finally, we will also send recruitment letters to people listed in research participant databases. Recruitment materials will state that they can contact us for more information about study participation. Responding to the letter/flyer is not consent to participate, just for information. Interested people will be pre-screened on the phone for minimum inclusion criteria (couple with one partner having had stroke 6 or more months ago, both are willing to participate, one or both partners are reporting some depressive symptoms).

Informed Consent:

Description of location(s) where consent will be obtained:

Consent will be obtained during participants' first in-person visit prior to completing baseline survey material in the Occupational Therapy Life Skills Clinic.

Description of the consent process(es), including the timing of consent:

Once participants have been screened on the phone or at the clinic, they will receive a copy of the informed consent for their review. Consent will be obtained at the beginning of their first in-person visit prior to completing baseline survey material. The investigator or research assistant will review the informed consent document with the participant. Participants will have an opportunity to review materials on their own and ask questions prior to consenting to participate (or opt out of participating). Both members of participant couples will sign a single consent document.

Procedures:

Potential participants will be screened verbally over the phone (if responding to recruitment letter or flyer or referral from clinic) or in person (if seen at clinic). If screened in person, this will be done in a clinic room where privacy and confidentiality can be maintained. Potential participants will be asked about time since stroke, whether they are experiencing mood changes or have difficulty enjoying things they used to enjoy (or if their partner is experiencing these symptoms), and if they have a partner/spouse who is willing to participate as well. Cognitive functioning will be evaluated using the Telephone Interview for Cognitive Status (TICS), which is a brief, standardized test of cognitive function that can be administered over the phone or in person. If minimum criteria are met, participants will be enrolled.

Following screening, eligible dyads will be adaptively randomized into PPI and waitlist control groups based on sex of the stroke survivor. PPI dyads will partake in 3 in-person study sessions at the Occupational Therapy's Life Skills Clinic: pre- (T1:baseline), post- (T2), and 3-months post-intervention (T3). Waitlisted dyads will complete a waitlist baseline assessment (T0), followed by T1, T2, and T3 assessments.

T1 session: Dyads will complete baseline surveys (see Appendix). In order to reduce burden and fatigue, we split the survey packet into two packets: one that is mailed ahead that participants complete at home and bring to their session, and a second packet that is completed at the clinic. The latter survey packet contains the more sensitive questionnaires (e.g. mood measures, asking about relationship quality) and participants complete these in separate rooms to allow for privacy in answering potentially sensitive questions. We will also collect observational data on the couple's interaction dynamics. Participants will engage in two dyadic interaction tasks (together in the same room), which will be digitally recorded: (1) a structured discussion task and (2) a collaborative problem-solving task. Both of the dyadic tasks we are using are widely used among couples' researchers (37-40). The first task consists of two prompted 5 minute discussions on a) a neutral (baseline) topic such as a television program they watch and b) a negative topic. We are interested in learning how a couple handles discussing a stressful topic. Topics for the stressful discussions will be chosen from a list of common areas of disagreement for couples (e.g., household responsibilities, communication, health and exercise) based on dyad match (i.e. both participants in a couple nominate the topic) and valence (topic is rated as appropriately stressful). The second dyadic task consists of a collaborative cognitive task in which the couple is asked to imagine that they need to run a list of errands for a trip (e.g., pick up medication, withdraw money at the bank) (38). They are provided a map of a fictitious community with locations for stops for their errands list. The couple then generates a plan that specifies the 5 most important errands they plan to complete, the order in which they complete them, and the route they plan to take. We selected this task because we are interested to learn how the couple collaborates during problem-solving on a task that mirrors the types of everyday decisions couples make. Following each dyadic task, we will administer a brief affect measure as a manipulation check (the stressful discussion task, for example, should have evoked more negative emotion than the neutral task), and a measure to assess perception of the task and their partner during the task.

Intervention: The PI or a trained RA will train participants in the activity exercises. We selected PPI activities on empirically supported evidence for efficacy in improving depressive

symptoms and/or increasing well-being (26, 31, 32). We have adapted them to be completed individually and together as a couple. Based on existing research suggesting that practicing a variety of self-selected PPI activities produces more sustained increases in well-being (44), participants are instructed to select PPI's from a menu (Table 1) and to complete at least two PPI activities alone and two together each week for 8 weeks. They are encouraged to perform the activities especially on "bad" days (feeling down). They will each be given a booklet containing descriptions of these activities (with examples) and a tracking calendar to help complete activities at home.

Table 1. Positive psychology activities

Expressing gratitude	Counting blessings, appreciation of life circumstances and gratitude to (thanking someone) by writing or expressing gratitude directly to anot
Practicing acts of kindness	Performing good deeds for other people, whether friends or strangers, or anonymously, either spontaneously or planned.
Fostering relationships	Strengthening and enjoying relationships by making time for people, e appreciation, and affection, and being supportive.
Focusing on the positive	Replaying positive experiences and self-monitoring instances of well- listing three good things that happened that day).
Savoring	Taking delight, and replaying life's momentary pleasures and wonder to finding beauty, relishing ordinary experiences, and savoring those e with others.
Working towards a goal	Picking one or two significant goals that are meaningful and devoting to pursuing them.
Spirituality	Becoming more involved in religion or spirituality by, for example, se and purpose, finding the sacred in ordinary life, and meditating.

The RA will call participants weekly to collect data on mood and remind participants to complete and mail in their weekly check-in surveys. These check-in surveys include the tracking calendar page for that week and a series of questions about mood and other changes in behavior for that week (see appendix). Participants also have an opportunity to ask questions at these check-in calls.

Post-intervention and 3-month follow-up sessions: At post-intervention (T2) and 3-month follow-up (T3), participant dyads will return to the Life Skills Clinic to complete study measures. At T2, the dyads will complete surveys and engage again in the two dyadic interaction tasks. The dyads will also complete a post-program feedback questionnaire and semi-structured interview. Feedback will be incorporated into future intervention protocols. At T3, dyads will complete a final set of surveys and a final brief interview to assess whether they continue to engage in the PPI activities and to discuss barriers and/or supports for continuing these activities. Dyads will be compensated for their time at each testing session and weekly check-in surveys they complete.

Procedures performed for research purposes only:

Statistical Methods, Data Analysis and Interpretation

Study data will be maintained in REDCap (Research Electronic Data Capture tools), a highly secure, web-based application designed to support data capture. The **University of Utah Study Design and Biostatistics Center will guide statistical analyses.** We will calculate response, recruitment, and attrition rates. PPI acceptability will be assessed post-treatment using a satisfaction survey and a feedback interview. Participants will indicate overall benefit, negative effects, and intervention satisfaction.

For **Aim 1**, mixed effects linear regression models will be fitted to the primary outcomes (mood, well-being). The survivor and caregiver will be nested within dyads, with the mixed effects approach accounting for lack of independence. The repeated measurements will be included in separate models, as immediate efficacy (post-intervention) and sustained efficacy (3-month follow-up) are two separate questions. In both models, the pre-intervention outcome will be included as a covariate to adjust for any baseline difference. This approach is more statistically powerful than a change analysis (e.g., change = post minus baseline) and avoids regression toward the mean bias[45, 46]. PPI will be the primary predictor variable (1=PPI, 0=Control). For the ***H1b hypothesis***, the significance test for the PPI predictor variable tests this hypothesis. While controlling for baseline differences, this "analysis of covariance" approach tests a group difference in improvement from baseline[45, 46]. For the ***H1a hypothesis***, if the effect is positive, the H1b test is also a test of the H1a and demonstrates that outcome. It would be incorrect to test the change from pre- to post-intervention using only the PPI subgroup, as that simple pre-post contrast cannot rule out that the change would have happened anyway without the PPI. To assess whether PPI works for either survivors or caregivers, a separate model will be fitted to each PPI or survivor subgroup, while making the comparison to the control group. The p values will be adjusted for two comparisons using Hochberg's multiple comparison procedure[47] while adjusting for the survivor-caregiver correlation to improve statistical power[48].

Both the PPI and control groups will have a sample size of 12 dyads (12 survivors and 12 caregivers; total 24 dyads). It is advised that pilot studies have a sample size n=12, as the standard error and 95% confidence interval narrow rapidly up until n=12 and then improvement levels off dramatically as samples increase[49]. Using a Stata/14 software power analysis formula specific to our analysis of covariance approach, while assuming the Pearson correlation between the baseline and follow-up outcome is r=0.70, and using a two-sided comparison alpha = 0.027 to allow for a Sankoh adjustment to the Hochberg procedure that assumes r=0.50 between the outcomes of the two comparisons, so that both multiple comparisons are sufficiently powered, this sample size provides 80% power to detect a 0.89 standard deviation (SD) mean difference between the PPI and control groups. This represents a large effect by Cohen's criteria (small effect, 0.2 SD, medium, 0.5 SD, large, 0.8 SD difference)[50]. Thus, if the PPI intervention has a large effect, this pilot study has sufficient statistical power to arrive at a confirmatory conclusion for Aim 1. Even if statistical significance is not achieved, if the study effect is in the expected direction, proof of concept will be demonstrated. Likewise, the study will provide estimates that

can be used in a sample size determination for a later larger study.

Aim 2: To determine if the PPI improves quality of interactions in couples during stressful discussion and collaborative problem-solving tasks we will analyze the dyadic tasks. Trained coders will code recordings using the Rapid Marital Interaction Coding System, v.2 (RMICS-2)[51, 52], a valid and reliable observational coding system for quantitative communication coding, using 6 hierarchical codes to describe dyadic behavior at a macro category level, focusing on positive and negative aspects of communication (e.g. laughter, hostility) and problem-solving. The unit of analysis is speaker turn and both spouses' communication is coded. This coding system allows for both verbal and nonverbal cues to be assessed. Audio/video data from the study will be downloaded and trained coders will assess for quality. Using Noldus Observer software, they will document how much time overall (total number of turns) each participant spent talking to his/her spouse/partner in each task and code these conversations using RMICS. Per standard guidelines[52], 25% of audio will be assessed for reliability and drift between the 2 coders throughout the study using Cohen's kappa. Coders will be blind to which tapes are reliability coded, with kappa expected to be 0.6 for codes with adequate representation.

Coded data will be imported into SPSS for further analysis. Ratios of talk for each individual code will be created for both survivor and spouse (e.g. spouse problem discussion/total spouse talk). These ratios provide a more standardized measure for comparison and control for differences in how frequently participants speak (total talk). Coded communication will be analyzed using descriptive statistics to determine proportions of positive and negative talk. Given that these two variables represent a continuous score between 0 and 1 for each person, the pre to post comparison will be made with a paired sample t-test to test the Aim 2 ***H2*** hypothesis. A sample size of 24 couples provides 80% power to detect a 0.59 SD mean change from pre to post, which represents a medium-large effect size by Cohen's criteria. Realistically, we expect only a medium effect in the expected direction, so proof of concept will be demonstrated. Likewise, the study will provide estimates that can be used in a sample size determination for a later larger study.

Aim 3: To determine whether increases in mood in one partner are associated with improved mood in the other partner over time, we will analyze survivor and spouse PANAS scores using the Actor-Partner Interdependence Model (APIM) framework. In APIM models, the couple is the unit of analysis[53, 54]. In this model, the predictor variables are a survivor's and spouse's positive and negative affect scores at weekly intervals. The outcome variables are a survivor and spouse's weekly affect. As seen in *Figure 2*, this analysis can determine the correlation between couples' scores at each time point (interdependence effects), so a specific growth-curve structure does not need to be specified. The model examines how one's own score predicts one's following week score (actor effects), and how one's weekly score predicts the following week's score of the other spouse (partner effects). These analyses are run simultaneously in a structural equation model with repeated measurements, using as many weeks as are available for each couple, so drop-outs are not an issue. The statistical power of Aim 3 is larger than Aims 1 or 2 because we have 8 repeated measurements. To determine the actual power, we would have to specify a value for the intraclass correlation coefficient (ICC) of the repeated measurements, and then apply a design effect. We suspect that even after doing that, however, we would only have sufficient

power to demonstrate feasibility. So, like Aims 1 and 2, Aim 3 will be a feasibility hypothesis.