Strengths-building through life purpose, self-care goal setting and social support: Study protocol for Caregiver Support

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ABSTRACT

Background: For caregivers of people with heart failure, addressing a range of care recipient needs at home can potentially be burdensome, but caregivers may also gain meaning from caregiving. The Caregiver Support Program, a multicomponent strengths-based intervention, is designed to improve outcomes of heart failure caregivers.

Objectives: 1) Test the feasibility and gauge an initial effect size of the Caregiver Support Program to improve caregiver quality of life (primary outcome), and fatigue and burden (secondary outcomes) from baseline to 16 weeks, 2) test whether fatigue and caregiver burden are associated with objective measures of resilience (sweat inflammatory cytokines (Il-6 and IL-10) and self-reported resilience, 3) evaluate changes in heart rate variability, IL-6 and IL-10, pre- and post-intervention.

Methods: This is a single-blind, two group, waitlist control trial. Eligible caregivers are 1) ≥ 18 years, 2) English speaking, 3) live with the person with heart failure or visit them at least 3 days per week to provide care, 4) provide support for at least 1 instrumental activity of daily living (IADL), 5) live within a 1 h driving radius of the Johns Hopkins Hospital, and 6) the care-recipient has been hospitalized within the last 6 months. Trial participants are randomized into the immediate intervention (n = 24) or waitlist control group (n = 24). Data collection is at baseline, 16 weeks, and 32 weeks.

Conclusion: The Caregiver Support program has the potential to increase quality of life and decrease fatigue and caregiver burden for caregivers of people with heart failure and multiple co-morbidities.

1. Background

1.1. Heart failure caregivers: an essential role with unmet needs

Caregivers of persons managing heart failure (HF) make significant contributions to support the experience of living with a chronic illness [1]. Providing care requires focus on a wide range of needs of the person living with HF: assistance with everyday activities, healthcare activities such as transitions between settings of care, medication management and wound care [2]. As HF progresses, caregiving responsibilities often increase. Caregivers disproportionately affected by these increases include those struggling with financial strain, non-spousal caregivers and caregivers who are managing their own chronic conditions [1,3–5].

Previous studies of family caregivers of people with HF have identified worsening caregiver quality of life (QOL) over the course of the persons' illness [2,6,7]. For people with HF, being able to live at home as HF worsens provides a sense of security, freedom and normalcy [8]. However, many caregivers report increased distress, loneliness, and responsibility while supporting the care recipient in the home [9]. The chronic stress of caregiving may also influence physical health through physiological stress response pathways, creating increased inflammation and decreased heart rate variability (HRV) [10–12]. Caregiver fatigue and burden are prevalent and associated with decreased caregiver QOL, demonstrating the need to improve caregiver outcomes [10].

1.2. Improving HF Caregiver experience

Promoting caregiver recognition of their own needs and addressing their own self-care needs is a priority recommendation for caregiving research [1,13]. Most caregiving interventions focus on reducing burden through psychoeducational programs related to patient care, but few focus on encouraging self-care behaviors of the caregiver to promote their own health and well-being [14]. Flipping the paradigm of caregiver intervention away from a burden focus towards a strengths focus can highlight and develop caregivers' existing strengths, build new strengths, decrease stressors, and improve resilience. Evidence suggests that resilience, or positive adaptation when facing stressors [15], can be improved through a multiple approaches including, 1) [22–24]articulating individual purpose in life [16–18], 2) engaging caregivers in developing action plans to achieve self-care goals [19–21], and 3) engaging and improving social support [22–24]. Therefore, interventions focused on life purpose, self-care goal-setting and engaging social support are promising methods for improving caregiver-reported outcomes and biomarkers of physiological stress and resilience.

1.3. Caregiver Support Program and study purpose

We present the rationale and design of a feasibility study of a multicomponent intervention to improve outcomes for caregivers of persons with HF and multiple chronic conditions. The Caregiver Support Program includes 5 individualized, nurse-led synchronous sessions conducted using video conferencing over 10 weeks and uses evidence-based strategies to improve quality of life of caregivers. Strategies are centered on caregiver recognition of their own self-care needs and

sharing responsibilities of caregiving. We utilized human-centered design in intervention development to encourage person-centeredness of intervention components and delivery through co-creation, engaging the caregivers and study team as equal partners in development.

The specific aims of this study are to: 1) test the feasibility and gauge an initial effect size of the intervention to improve (primary outcome) QOL, (secondary outcomes) fatigue, and caregiver burden among caregivers from baseline to 16 weeks, 2) test whether fatigue and caregiver burden are associated with physiological measures of resilience (inflammatory cytokines (Il-6 and IL-10) detected in sweat patches) and self-reported resilience, 3) evaluate changes in heart rate variability (HRV), pre- and post-intervention. The protocol was developed in accordance with SPIRIT guidelines depicted in Fig. 1.

2. Methods

2.1. Conceptual framework

This study is guided by the Society to Cells Resilience Framework [15]. This framework posits that intervening on multiple socio-ecologic domains (in this case, physiologic, individual, and family) leads to more lasting effects on individual resilience compared to intervening on one domain. Further, resilience can be fostered at critical times in the life course, such as times of increased caregiving responsibilities. One mechanism for developing this resilience may be the encouragement of self-care behaviors that promote health and well-being such as stress management, attending to healthcare needs and improving social connections. Guided by this framework, the proposed study will test

		Baseline	Week 1-10	Week 16	Week 18-28	Week 32
Enrollment	Eligibility Screening	■				
	Informed Consent	■				
	Randomization	■				
Intervention	Immediate Intervention		■			
	Waitlist Control				■	
Assessments	Caregiver Demographics Social Determinants of Health	■				
	Primary Outcome: Quality of Life: - 36-Item Short Form Health Survey[54] **Secondary Outcomes:** Fatigue: - PROMIS Fatigue Short Form[47] Caregiver Burden: - Oberst Caregiver Burden Scale[48] - Modified Caregiver Strain Index[49] Social Support: - ENRICHD Social Support[50] - Global Family Functioning Scale[51] Depression: - Patient Health Questionnaire 8[55] Resilience: - Coping Self-Efficacy Scale[52] - Brief Resilience Scale[53] - IL-6 & IL-10 - Sweat Patch - Heartrate Variability	■		■		■

Fig. 1. Schedule of enrollment, intervention and assessments
Legend: Eligibility screening is via provider referral and EMR screening. Eligible participants provide informed consent via phone and electronic methods. Participants complete the assessments electronically or by phone with support from a research assistant.

whether Caregiver Support influences both individual and physiological level factors (Fig. 2).

2.2. Human-centered design

This intervention was developed utilizing human-centered design principles. Human-centered design is a collaborative, creative process dedicated to understanding people's needs and designing interventions that better serve people's needs. The methodology includes ideation, the generation of innovative approaches to problems, and prototyping followed by iterative implementation and improvement [25]. Although each proposed component of the intervention is evidence-based, we did not identify an existing intervention which included these components that could be adapted. Therefore, the human-centered design process was extensive to develop this intervention.

Key stakeholders, such as providers, community partners and related healthcare specialists were critically important to the human-centered design process. In addition, end users (i.e., caregivers) were engaged throughout the design process. First, we held regular meetings with advanced HF clinic nurse practitioners and physicians to build on ongoing collaborations and gain clinic staff trust. Second, we explored unmet needs of caregivers and existing strategies that promote resilience among caregivers. During this phase, we piloted quantitative surveys and conducted semi-structured interviews with care recipients and caregivers.

Key findings from this early work included high levels of fatigue among caregivers (approaching that of care recipients with advanced HF) and less perceived social support by caregivers than care recipients (manuscript in development). In addition, caregivers found it difficult to prioritize their own self-care or ask for help with caregiving. Third, as we developed materials for study participants including the activity worksheets and flyers, we engaged the multi-disciplinary HF care team (social workers, palliative care physicians and nurse practitioners, the Community Research Advisory Council, community caregiving experts) to evaluate materials and suggest community resources. Fourth, although originally proposed as an intervention with in-home visits, research restrictions related to COVID-19 required a protocol revision to include a robust plan for virtual interactions. We adapted our materials and intervention delivery for a virtual approach and re-engaged stakeholders for feedback. Fifth, we trialed intervention delivery in an open label pilot.

2.3. Nurse interventionist training

Nurse interventionists are selected based on their expertise in heart failure and palliative care and skills in therapeutic communication. Nurse interventionists are trained for 2 months prior to the study; they attend weekly meetings with the study team to review the intervention protocol and role play interactions. They also practice therapeutic communication skills such as mirroring, reflection and synthesis. Interventionists also attend meetings with community partners to increase knowledge of community resources. Finally interventionists are trained to use all technology for intervention visits and prepare for basic trouble-shooting.

2.4. Intervention components

A summary of intervention components and literature supporting each component is provided in Table 1. The intervention consists of 5 virtual visits (using HIPAA compliant Zoom video calls with screen-sharing capabilities) with five interim phone (call or text) or email contacts to evaluate goal attainment progress (Table 2). All participants
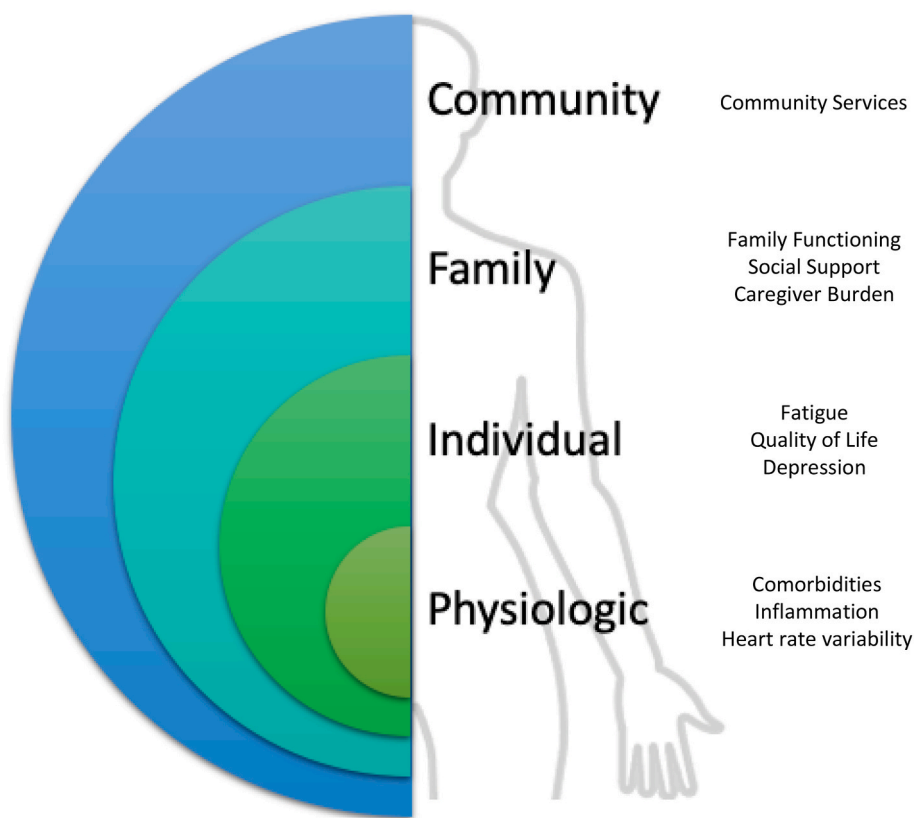

Fig. 2. Society to Cells Conceptual Framework (adapted)
Caption: Adapted from Szanton and Gill's Society to Cells framework, we show multiple levels of contextual factors that contribute to the resilience of a person. The Caregiver Support Program was designed to intervene on multiple levels to improve the outcomes of caregivers of persons with heart failure.

Table 1
Intervention Components and evidence basis for component selection.

Nurse-led Intervention Components	Evidence Basis for Component
Self-care goal-setting Goals are discussed each visit with action plans focused on a single behavior over the 2 weeks between visits and reinforced during phone calls.	- Drives behavior change by encouraging the caregiver to set their own priorities, based on their own free choice within each intervention component topic [44]. - The sharing of the action plan with the interventionist helps to reinforce the personal commitment and has been highly successful in multiple trials [21,44,45].
Whole-person Assessment Guided interaction with multiple domains such as finances, hobbies, caregiving, etc. Goal-setting is focused on domains discussed.	- Involving the caregiver in assessment and encouraging them to set their own goals is person-centered, builds rapport and increases participation [46–48]. - Caregiver physical and psychosocial assessment is suggested by HF guidelines, but not commonly used in practice [1,28,49,50]
Life purpose Discussion prompts are selected using a card game-style activity. Worksheet uses discussion to help draft a purpose statement. Goal-setting is focused on activities related to fulfilling life purpose.	- Life purpose was associated with lower mortality and CVD [51], stroke [52], MI [53], better preventive health behaviors [54], lower allostatic load [55] - Life purpose can be improved through intervention [56–58] and is linked to down-regulation of pro-inflammatory genes [59]
Social Support Mapping activity encourages caregivers to map their social connections and relate their self-care and caregiving needs to people in their social network. Goal-setting is focused on making a social connection.	- Perceived social support can be enhanced through interventions [60] - Helping the caregiver identify ways they are already supported may increase a sense of perceived support [13] - Setting goals to engage the existing social network may increase self-efficacy for future needs and engagement [61]
Instrumental Support Curated list of instrumental supports available in the local community (e. g., provision of transportation or support with medication management) is discussed with the caregiver. Goal-setting is focused on accessing available resources.	- Instrumental support may enhance emotionally supportive interventions [60,62,63] - Addressing needs to support instrumental activities of daily living may improve retention from participants [64] - Interventions that provide instrumental support while equipping community members are more sustainable and impactful than providing the support without considering social support/ network [65,66,67].

Table 2
Study visit timeline for immediate intervention group[a].

Format and timing of visits	Key activities
Baseline Data Collection	Sweat patch application
	Survey
	72 h post-application, remove sweat patch and deliver for storage and analysis
	Heartrate Variability Measurement
Randomization	Mail randomization results
Visit Week 1	Whole Person Assessment
	Set goal #1 and discuss strategies to achieve goal
Phone Check-in Week 2	Assess goal #1 attainment and strategies to achieve goal
Visit Week 3	Life purpose card activity
	Social Support activity
	Assess goal attainment and revisit strategies
	Set goal #2 and discuss strategies to achieve goal
Phone Check-in Week 4	Assess goal #2 attainment and strategies to achieve goal
Visit Week 5	Review/edit purpose statement
	Instrumental Support Activity
	Assess goal attainment and strategies to achieve goal
	Follow-up re: social support
	Set goal #3 and discuss strategies to achieve goal
Phone Check-in Week 6	Review/edit purpose statement
	Assess goal #3 attainment and strategies to achieve goal
Visit Week 7	Assess goal attainment and strategies to achieve goal
	Follow-up re: instrumental and social support
	Set goal #4 and discuss strategies to achieve goal
Phone Check-in Week 8	Review/edit purpose statement
	Assess goal #4 attainment and strategies to achieve goal
Visit Week 9	Review of progress, goals and purpose
	Discuss how caregiver will involve social support in next goals
	Wrap-up activity with summary of values, purpose and next goal
Phone Check-in Week 10	Provide summary statement from wrap-up activity and instructions for next steps
Data Collection Visit Week 16	Sweat patch application
	Survey
	Sweat patch Pickup 72 h post application
	Heartrate Variability Measurement
Data Collection Visit Week 32	Sweat patch application
	Survey
	Sweat patch Pickup 72 h post application
	Heartrate Variability Measurement

[a] Waitlist control group will begin intervention at week 16.

receive each intervention component, tailored to participants' life purpose and self-care goals. Exemplars of self-care goal-setting are listed in Table 3. The rationale for timing of intervention visits and duration of the study was based on key stakeholder input.

2.4.1. Whole Person Assessment

The first visit consists of the Whole Person Assessment, a guided conversation between the nurse interventionist and caregiver exploring 8 domains of the caregiver's life including: education, employment, resources, health, fun, community, culture, spirituality, caregiving and household. (See Supplementary Materials) These domains are based on the National Consensus Project's Clinical Practice Guidelines including eight domains palliative care [26] and adapted through our iterative human-centered design process. The purpose of this component is to understand the caregivers' life context and develop rapport with the nurse interventionist. Caregivers select a domain and the nurse uses prompts to explore each domain. After all domains are addressed, the caregiver selects a priority domain, sets a goal to promote self-care related to the domain and collaborates with the interventionist to develop an action plan to achieve the goal. For instance, if the caregiver

selects the spirituality domain, they may choose to spend 10 min per day listening to calming music or praying.

2.4.2. Life purpose

Caregivers are presented with 4 categories of cards that contain discussion prompts. The categories include Caring for Yourself, Experience as a Caregiver, Purpose, and Emotions. Because the visits are conducted virtually, the cards are presented on PowerPoint slides via shared video conference, in which the caregiver selects the initial card category to begin the discussion. The caregiver selects a card category to begin the discussion. During the discussion, the interventionist uses a worksheet to record information shared by the caregiver. Following the visit, the interventionist synthesizes key stories, feelings, and observations (Fig. 3). At the subsequent visit, the interventionist shares the synthesis and asks the caregiver to provide additional information or feedback. Then, the interventionist and caregiver co-create a list of important values. The caregiver is encouraged to select their top three values to develop and draft their purpose statement. Finally, the interventionist and caregiver discuss and set an achievable self-care goal that connects to their life purpose.

2.4.3. Social support

The social support component is based on work by Boissevain (1974)

Table 3
Exemplars of self-care goal-setting and intervention approaches.

Example Goals	Intervention Approaches
Physical activity: Increase physical activity by 10% or 1 day per week	1) RN will assess current physical activities, weekly duration and intensity. 2) RN will assess safety of physical activity with Physical Activity Readiness assessment with final evaluation by nurse practitioner 3) RN implements NIA Go4Life physical activities, with emphasis on variety, strength training and cardio in a safe environment. 3) RN will assess interest in group activities or engaging social support to increase accountability and help participant get connected.
Stress management: Decrease exposure to stressors, increase use of coping strategies	1) RN will assess stressors with focus on caregiving-related stress 2) RN will work with caregiver to draft a list of caregiving concerns to be addressed at the next visit with the patient's cardiologist 3) Participant will identify coping strategies such as positive self-talk, ways to defuse stressful situations and prevent stress through restorative activities focused on purpose in life.
Advance Care Planning: Use Prepare your care to have a guided discussion and document plans.	1) RN will assess advance care planning needs 2) RN will review the Prepare for your Care (https://prepareforyourcare.org) website and 5 steps to prepare an advance directive 3) Participant will engage in shared decision making with care recipient and share challenges with RN for next steps.
Rest: Improve nighttime sleep quality	1) RN to assess for duration, quality and sleep hygiene 2) RN will help caregiver identify modifications to sleep environment and bedtime routine 3) RN will assess for daytime fatigue and sleepiness.

which visually depicts concentric circles as a way to describe level of intimacy or connectedness in a relationship [27]. Participants are asked to reflect on and map existing social connections (Fig. 2), from closest social connections to distant but reliable social connections, who can help meet emotional and practical needs. Goal-setting for this domain is focused on making a social connection to promote self-care and life purpose.

2.4.4. Instrumental support

Working closely with key stakeholders, we identified 6 categories of instrumental support caregivers were interested in and community resources relevant to each category: food, healthcare, medication organization, household help, home evaluation and healthcare decision-making. Based on the Whole Person Assessment and Life purpose activities, the nurse interventionist presents a curated list of instrumental supports available in their community (e.g., grocery or meal delivery or support with medication management) (Fig. 2). The caregiver selects one to two supports to explore with the interventionist. This process aims to address both informational and instrumental components of social support. Goal-setting for this domain is focused on accessing selected resources and considering how the caregiver's social support could be engaged to provide needed instrumental support. *Open-label pilot.*

We conducted an open label pilot (n = 3) with our prototype intervention to refine intervention components and improve delivery, again using the human-centered design process. Recruitment was identical to the randomized trial, however all participants were enrolled in the intervention instead of being randomized. The participants were interviewed after program completion to elicit feedback on surveys, intervention content, number of visits, user-friendliness of intervention components (e.g. life purpose activity), and satisfaction with the overall program. This feedback was used to modify the intervention for the waitlist control trial resulting in several important changes. First, we re-ordered the social support discussion earlier in the intervention to allow for a better connection between the Whole Person Assessment and an understanding of the caregiver's broader social connections. Second, interventionists identified a concern about lack of closure with participants and participants expressed feeling a strong connection to interventionists and were not ready to end visits. We therefore created a transitional closing activity to help the caregiver set goals with someone in their identified social circles. We also added some debriefing questions to explore acceptability of the intervention. Third, we discovered that participants highly valued the opportunity to meet virtually/remotely and mentioned they would have felt the home visit approach to be slightly invasive. Based on this we plan to continue remote visits for the intervention in the trial.

2.5. Waitlist randomized control trial

This single-blind, two group, waitlist control trial tests the feasibility and gauges an initial effect size of the Caregiver Support intervention to improve QOL. With a target sample size of 40 and to account for estimated 20% attrition, our recruitment goal is 48 participants. Trial
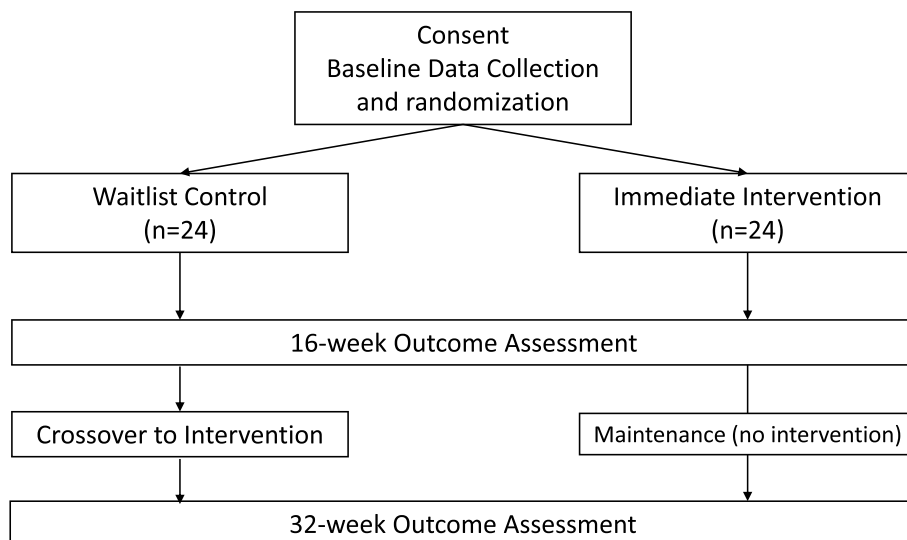
Fig. 3. Flowchart of study design.

participants who enroll are randomized into the immediate intervention or waitlist control group. The immediate intervention group (n = 24) receives the intervention during weeks 0–16. The waitlist control group (n = 24) is provided usual care for caregivers during the first 16 weeks, then begins the intervention at 16-weeks. Waitlist control design is used to provide an untreated comparison and allow wait-listed participants an opportunity to receive the intervention at a later date [26,27]. A flow chart summarizing study design is presented in Fig. 3 and a timeline for study visits is provided in Table 2.

2.5.1. Study population

We enroll caregivers of persons with HF and at least one other chronic condition. The Caregivers must be: 1) 18 years or older, 2) English speaking, 3) live with the person with HF or visit them ≥3 days per week to provide care or support, 4) provide assistance with ≥1 instrumental activity of daily living (IADL), and 5) live within a 1 h driving radius of the Johns Hopkins Hospital. Although the care recipient is not included in the study, they must be an established patient at the Johns Hopkins HF Bridge Clinic and have been hospitalized within the last 6 months to capture the caregiver at a potential time of increased caregiving needs. We are characterizing these care recipients as persons with 'advanced HF' because they were hospitalized for HF symptoms and require ongoing specialty cardiology care, with stage C-D (advanced stages) HF [28].

2.5.2. Recruitment

Participants are recruited through clinician referral and distribution of a recruitment flyer in the Johns Hopkins HF Bridge Clinic (early post-hospitalization follow-up HF care clinic) and other relevant areas of the Johns Hopkins Hospital. We screen interested participants for eligibility and explain study procedures either by phone or in-person.

2.5.3. Informed consent

A survey is sent to the participant's email - using the REDCap e-consent module - where they can view the consent form and provide electronic consent signature. Over the phone, the research assistant reviews the informed consent with the participant while the participant reads along on their device. The participant answers 3 questions to assess their understanding of the research study and provides an electronic signature to submit the survey. The participant is provided a PDF of the signed consent form.

2.5.4. Baseline data collection

After informed consent, the participant completes the baseline data collection survey (instruments detailed in Table 4). The sweat patch is applied (details below). Heart rate variability is measured on the day of sweat patch pick-up, 72 h after application. After baseline data collection, the participant is randomized to the immediate intervention or waitlist group.

2.5.5. Randomization and blinding

Within 48 h of the baseline data collection, we randomize the participant using block randomization (block sizes of 4) stratified on the relationship of the caregiver to the care recipient (spousal or non-spousal). Block randomization was used to not only reduce confounding and opportunities for bias, but to balance the composition of the treatment groups. Stratification by relationship was used because non-spousal caregivers may have higher burden and different needs than spousal caregivers [1,3]. Randomization is performed in the REDCap randomization module. Assignment is communicated to the participant by letter. The immediate intervention group is sent the study materials and contacted to begin the intervention within 1 week of randomization. The data collector is blinded to study assignment. At both data collection visits after randomization (16 and 32 weeks), data collectors use standardized language to instruct participants not to discuss their group assignment to maintain blinding.

Table 4
Constructs, instruments and reliability.

Theoretical Construct	Instruments and variables	Number of Items	Cronbach's alpha
Caregiver demographics and characteristics	Demographics, caregiving physical and supportive tasks description, employment Physical Activity Readiness Assessment	23	–
Fatigue	PROMIS-Fatigue Short form Score ranges from 0 to 35 with higher scores indicating higher levels of fatigue.	7	0.9 [47]
Caregiver Burden	Oberst Caregiver Burden Scale 2 domains: time caregiving and task difficulty Scores range from 15 to 75. Higher scores indicate greater task difficulty and more time spent on each task, higher burden.	15	0.90 [48]
	Modified Caregiver Strain Index Scores range from 0 to 48 with higher scores indicating higher feelings of burden.	13	0.86 [49]
Social Support	ENRICHD Social Support Scores range from 0 to 25 Higher scores indicate higher levels of social support	7	0.89 [50]
	Family Functioning – Family Assessment Device Questionnaire: Global Family Functioning Scale (only) Scores range from 12 to 48 Higher scores indicate higher levels of family functioning	12	0.9 [51]
Resilience	Sweat patch (IL6, IL10)	–	–
	Heart Rate Variability	–	–
	Coping Self-Efficacy Scale Scores range from 0 to 130. Higher scores indicate higher coping self-efficacy.	13	0.91 [52]
	Brief Resilience Scale Scores range from 6 to 30 Higher scores indicate higher levels of resilience	8	0.91 [53]
Quality of Life	36-Item Short Form Health Survey (SF-36) Items are scored on a 0–100 range, with total scores averaged for each subscale. The eight domains are also averaged to create an overall score from 0 to 100. Higher scores indicate a more favorable health state.	36	0.85 [54]
Depression	PHQ-8 Scores range from 0 to 24 Higher scores indicate higher levels of depressive symptoms	8	0.82 [55]

2.5.6. Waitlist control condition

The waitlist group receives usual care for caregivers for the first 16 weeks. Usual care involves inclusion of the caregiver in the patient visit at the Johns Hopkins HF Bridge Clinic, if the caregiver is present. Teaching is provided to both patients and caregivers by clinic providers on an as needed basis and written resources regarding HF management are provided. Waitlist participants receive monthly study postcards to encourage retention. The post cards are a brief one-page document mailed to participants with an encouraging quote, gratitude message for involvement in the study, and a reminder of upcoming steps.

2.5.6.1. 16-Week crossover to intervention and maintenance. After 16 weeks, the waitlist group begins the intervention and the immediate intervention group begins a maintenance phase in which they receive the monthly study postcards but no interventionist interactions. The 32-week assessment measures whether 1) immediate intervention participants continue intervention strategies independently and maintain improvement on the self-report scales and 2) waitlist participants improve following the intervention.

2.6. Sample size

As a feasibility study, the analyses will likely not have adequate power to detect significant differences. Therefore, effect sizes, rather than statistical significance will be examined for evidence of the effectiveness of the intervention. With a target sample size of 40 after attrition, we will be able to estimate stable effect sizes associated with the intervention [29]. This effect size will be compared to the literature for similar interventions and used to estimate the needed sample size for a fully powered effectiveness trial.

2.7. Data collection and management

2.7.1. Survey data

After recruitment, the primary method for survey completion is via email. Alternatively, in the event of lack of access to email or other technology challenges, a trained research assistant can verbally elicit questionnaire data from participants over the phone or in person.

2.7.2. Sweat patch

Sweat samples are collected via a non-occlusive adhesive patch which remains in place on the caregivers' skin for 72 h. It consists of a white absorbent pad surrounds by a semi-permeable adhesive allowing water to escape but trapping proteins and electrolytes. This non-invasive collection method has been used successfully in the past to collect IL-6 and IL-10 [30]. It has also been found to correlate with plasma inflammatory markers [31,32]. A contactless protocol was developed to maintain safety of the participants and study team during COVID-19. Written instructions are provided and the participant places the sweat patch on their abdomen. Participants then remove the sweat patch after 72 h and place it in a provided plastic specimen bag for contactless pick up. The sweat patches are transported on dry ice and stored in a $-80\,°C$ freezer. At the time of study completion, the patches will be analyzed for levels of the cytokines IL-6 and IL-10 using the Sweat Patch Extraction Protocol analyzed using a 3-step digital immunoassay [30,33].

2.7.3. Heart rate variability

A 5 min two-lead tracing is captured using the KardiaMobile ECG device (AliveCor, San Francisco, CA, USA) and analyzed with Kubios HRV software (Kubios, Inc. Kuopio, Eastern Finland). Participants place their forefingers on the touch pad while seated and resting. The device automatically saves the ECG rhythm strip on the password protected AliveCor app and study personnel send the de-identified ECG file to the University of Oklahoma HRV Laboratory where it is analyzed for HRV and counts of abnormal beats. This capture method has been successful in other studies [34,35]. If any suspected abnormality is seen on the analysis, the PI is notified the subject is subsequently notified to contact their provider.

2.8. Measures and outcomes

We chose measures (Table 4) based on previous RCT experience as well as those that met the following criteria: 1) possess known reliability and validity with ethnically diverse samples; 2) are sensitive to change from an intervention; 3) have clinical relevance to QOL; 4) Common Data Elements to connect this work with the broader literature and 5) represent objective as well as subjective indicators of the domains we

seek to impact. Finally, we sought to achieve a balance between psychometric quality and practical considerations such as respondent burden. All instruments with the exception of demographics are measured at baseline, 16 and 32 weeks post-intervention.

2.9. Fidelity plan

Our fidelity plan is based on the NIH Behavior Change consortium developed by national leaders [36]. We enhance fidelity through design elements (intervention is distinct and based on theory); training (intervention manual); delivery (reminder calls before intervention sessions; records of home sessions (by date and duration); checklists, direct observations and discussions concerning intervention engagement, and enactment. Ten percent of sessions are audio taped and reviewed by the research coordinator using *a priori* monitoring checklists developed for this study. Evaluation includes periodic assessments of data quality, participant recruitment, accrual, and retention.

2.10. Analysis

Exploratory and descriptive analysis will be completed for all study variables. Variables will be examined for normality and described with means and standard deviations or medians and interquartile ranges accordingly. Baseline characteristics comparing the two groups (usual care vs. intervention) will be assessed to determine if randomization achieved balance between arms. If differences are found we will conduct unadjusted and adjusted analysis controlling for variables on which the two groups differ and compare the pattern of results. Statistical significance will be set at 0.05.

Generalized estimating equations (GEE) will be used to examine the difference between intervention and usual care groups in change from baseline to 16 weeks for QOL (primary outcome). Time, group, and the group-by-time interaction will be included in the model. We will also examine differences between groups on fatigue and caregiver burden (secondary outcomes) using GEE. Cohen's d' effect sizes for the difference in change over time from baseline to 16 weeks between the two groups will be computed for the primary and secondary outcomes. To test whether fatigue and caregiver burden are associated with physiological measures of resilience, Il-6 and IL-10, we will use multiple regression models regressing cytokines on fatigue and caregiver burden. We will adjust for age in the model because of the known relationship of age and heart rate variability [37]. To evaluate changes in heart rate variability, IL-6 and IL-10, potential indicators of physiologic resilience, pre- and post-intervention, GEE and Cohen's d' effect sizes will be used as described above with heart rate variability, IL-6 and IL-10 as the dependent variables. We will also examine the relationship between fatigue and caregiver burden with HRV using multiple regression, with age as a covariate. Analysis of waitlist group improvement in the intervention from 16 to 32 weeks will be analyzed separately using the non-parametric Wilcoxon signed rank to test for improvement in primary and secondary outcomes. Similarly, the maintenance of improvements from 16 to 32 weeks will be analyzed separately for the immediate intervention group using the non-parametric Wilcoxon signed rank to test for maintenance of improvements in primary and secondary outcomes.

3. Discussion

The Caregiver Support program integrates evidence-based strategies using human-centered design to improve participant-researcher connection and person-centeredness of the intervention components. Delivery was informed and enhanced through a mixed methods study, involvement of key stakeholders and an open label pilot. The purpose of this feasibility study is to develop a strong foundation of evidence to support a larger definitive trial.

The Caregiver Support program is different from other caregiving

interventions in HF which have largely focused on patient self-care needs and providing education to increase caregiver involvement in medication adherence and symptom monitoring. These interventions may place more responsibilities on the caregiver, but few have focused solely on the well-being of the caregiver [1,38]. Trialed interventions for HF caregivers have had modest impact on emotional health outcomes such as caregiver depression and caregiver burden [39–43]. The Caregiver Support program builds on this previous work by increasing attention to holistic understanding of caregiver's lives and is strongly based in a tailored approach to meeting caregiver needs. This approach may lead to highly tailored self-care goals and engagement of instrumental and social supports. Through these approaches, the Caregiver Support program has the potential to increase QOL and decrease fatigue and caregiver burden for caregivers of people with HF and multiple co-morbidities, filling a large gap in current HF care delivery models.

3.1. Limitations & strengths

This study uses a conceptually driven intervention with pragmatism in undertaking a clinical trial in a complex clinical population. This intervention was originally designed to be implemented in-person with the interventionist and the participant both in the participant's home. However, with the advent of the COVID-19 pandemic, we adapted the intervention for virtual implementation. The evidence guiding the development and implementation of person-centered, interactive interventions in a virtual format is limited. In contrast, this presents a valuable opportunity for the development of novel interventions with flexible implementations strategies to accommodate individual and societal context (eg. safety during pandemic).

Also, because of the individualized tailoring of goal-setting, it may be difficult to establish which aspect of the intervention is influencing outcomes of interest. On the other hand, the ability to tailor the intervention components to the individual participant allows person-centeredness to take center stage in the implementation. Having a standard group of intervention components each of which can be tailored to fit the individual caregiver's context may allow for a more powerful, engaging intervention. Finally, this intervention was developed within a single-site. This will likely mean for broader implementation, additional work will be needed to understand the context of care and to identify instrumental supports within other communities.

4. Conclusion

Assessing the feasibility of the Caregiver Support Program in caregivers of people with HF serves as a foundation for future HF caregiving intervention research. This intervention is novel in its use of human-centered design for its development and the focus on individualization and flexibility of standard intervention components to address the specific context of the caregiver receiving it. Placing our focus on person-centeredness, while developing an understanding of the caregiver's social context, incorporating human-centered design in intervention development, and providing for individual tailoring of intervention components may provide for a more engaging and personalized intervention to support caregivers of people with HF.

Protocol version and trial status

The protocol is version number 1. We started recruitment in August of 2020 and will end data collection in Fall of 2021. The trial was registered at ClinicalTrials.gov on September 16, 2019, identifier NCT04090749.

Trial registration

ClinicalTrials.gov, NCT04090749, First posted on September 16, 2019, Current status: recruiting.

Ethics approval and consent

The Johns Hopkins Medicine Institutional Review Board has approved this study (IRB00277814). All participants provide consent as described in the manuscript.

Availability of data

Data will be submitted to clinical trials.gov and to the NIH Common Data Elements (CDE) Repository.

Competing interests

The authors have no conflicts of interest.

Authors' contributions

MAS and SS conceived of the study. *MAS, NP, JW, PMD, and SS* initiated the study design and *NVP, LG, AJ* and *MH* helped with implementation. *MAS, PMD and SS* are grant holders. *NP* provided statistical expertise in clinical trial design and *MAS* is conducting the primary statistical analysis. All authors contributed to refinement of the study protocol and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available when collected.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.conctc.2022.100917.

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