Informal caregiving is demanding and stressful. This stress may exceed the caregiver's ability to adapt, and many eventually become care recipients themselves as years of stress and deferred self-care put them at increased risk for illness. Self-care refers to the behaviors undertaken to maintain health and manage illness. Engaging in self-care may improve health status, defined as physical functioning and mental well-being. Caregivers of adults with heart failure (HF) are an understudied group. HF is extremely common. Most HF patients remain in the community through the end of their lives, depending on informal caregivers to assist them. The trajectory of illness in HF is highly variable, which limits the use of palliative care and respite services. As a consequence, HF caregivers report significant stress and poor self-care. Health coaching, a support intervention, can improve self-care in patients, but studies evaluating HF caregivers are limited, as are studies of the cost-effectiveness of support interventions for caregivers. Even less is known about the effect of caregiver support interventions on HF patient outcomes. Caregiving duties often confine caregivers to the home and many are unable to attend in-person sessions, so we have developed and pilot tested a virtual support intervention (ViCCY ["Vicky"] – Virtual Caregiver Coach for You), that we propose to evaluate among HF caregivers. Using a randomized controlled trial (RCT) design, we will enroll informal HF caregivers with poor self-care (Health Self-Care Neglect scale score ≥2), randomizing them 1:1 to an intervention or control group. Both groups will receive standard care augmented with Health Information (HI) delivered through the Internet, but the ViCCY caregiver group will also receive 10 front-loaded coaching support sessions tailored to individual issues. The control group will have access to the same HI resources over the same interval, using the same Internet program, but without coaching support. At baseline and 3, 6, 9, and 12 months, we will collect self-reported data on self-care, stress, coping, and health status. At 6 months, we will compare ViCCY to HI alone to assess intervention efficacy using intent-to-treat analysis. Our pilot data suggest that addition of support provided by the health coach will make ViCCY more efficacious than HI alone. A sample of 250 caregivers (125/arm) will provide >90% power to detect significant differences between the groups on the primary outcome of self-care (Aim 1). We will collect quality adjusted life years (QALYs) and health care resource use in caregivers over 12 months to assess cost-effectiveness of ViCCY (Aim 2). To explore the effect of caregiver outcomes on HF patients' outcomes (hospitalization rates, hospital days, mortality rates, QALYs) over a 12-month period (Aim 3) and knowing that not all HF patients will participate, we will consent a subgroup of the HF patients cared for by these caregivers (at least 40 dyads). If shown to be efficacious and cost-effective, our virtual health coaching intervention can easily scaled to support millions of caregivers worldwide. This application addresses the NINR strategic plan and is directly responsive to PA-18-150.

SPECIFIC AIMS

Informal caregivers have been called the "hidden victim" of illness.[1] Caregiving is demanding and stressful for those who provide extraordinary, uncompensated care for loved ones, often daily for months and years.[2] This stress may exceed the caregiver's ability to adapt,[3] and many eventually become care recipients themselves as years of stress and deferred self-care put them at increased risk for illness.[4-8] Self-care refers to those behaviors a person undertakes to maintain health and manage illness.[9] Engaging in self-care may improve an individual's health status,[10] defined as physical functioning and mental well-being.

Caregivers of adults with heart failure (HF) are an understudied group. HF is extremely common (12% of US adults after age 65).[11] Most HF patients remain in the community through the end of their lives, depending on informal caregivers to assist them.[12] The trajectory of illness in HF is highly variable, which limits the use of palliative care and respite services.[13-15] As a consequence, caregivers of patients with HF (HF caregivers) report significant stress and poor self-care, [16-20] and there is a critical need to identify ways to improve self-care in HF caregivers. Without doing so, we risk losing these burdened caregivers to their own health issues.

Support interventions can encourage self-care by helping caregivers to focus on values, solve problems, and transform their goals into action.[21,22] We and others have shown that health coaching can improve self-care and outcomes in patients,[23-25] but studies of caregivers are limited, as are studies of the cost-effectiveness of support interventions for caregivers.[15,26,27] Even less is known about the effect of caregiver support on patient outcomes, although caregiver burden and stress have been shown to be associated with higher rates of hospitalization for patients with HF.[28,29] Although caregiving duties often confine caregivers to the home and many are unable to attend in-person sessions,[30] support interventions can be delivered by telephone[31] and the Internet.[24,32,33] Leveraging the growing availability and declining costs of – along with increasing receptivity of older adults to – technology,[34] we have developed and pilot tested a virtual support intervention (ViCCY ["Vicky"] – Virtual Caregiver Coach for You), that we propose to evaluate in HF caregivers.

Using a randomized controlled trial (RCT) design, we will enroll informal HF caregivers with poor self-care (Health Self-Care Neglect[35] scale score ≥2), randomizing them 1:1 to an intervention or control group. Both groups will receive standard care augmented with Health Information (HI) delivered through the Internet, but the ViCCY caregiver group will also receive 10 front-loaded coaching support sessions tailored to individual issues. The control group will have access to the same HI resources over the same interval, using the same Internet program, but without coaching support. At baseline and 3, 6, 9, and 12 months, we will collect self-reported data on self-care, stress, coping, and health status. At 6 months, we will compare the efficacy of ViCCY (HI plus coaching) to HI alone to assess intervention efficacy using intent-to-treat analysis. Our pilot data suggest that addition of support provided by the health coach will make ViCCY more efficacious than HI alone. A sample of 250 caregivers (125/arm) will provide >90% power to detect significant differences between the groups on the primary outcome of self-care (Aim 1). We will collect quality adjusted life years (QALYs) and health care resource use in caregivers over 12 months to assess cost-effectiveness of ViCCY (Aim 2). To explore the effect of caregiver outcomes on HF patients' outcomes over a 12-month period (Aim 3) and knowing that not all HF patients will participate, we will consent a subgroup of the HF patients cared for by these caregivers (at least 40 dyads). We have the following Specific Aims:

Aim 1: To compare the efficacy of ViCCY vs. HI alone in improving self-care. We hypothesize that, at 6 months after enrollment, caregivers randomized to ViCCY vs. HI alone will have **H1a:** Improved self-care measured with the Health Self-Care Neglect scale[35] (*primary outcome*); **H1b:** Less self-reported stress measured with the Perceived Stress Scale[36] *(secondary outcome);* **H1c:** Better coping measured with the Ways of Coping Questionnaire, short form[37,38] *(secondary outcome)*; and **H1d:** Better perceived mental and physical health status measured with the SF-36[39] *(secondary outcome).*

Aim 2: To estimate the cost and cost-effectiveness of ViCCY. We hypothesize that, at 12 months after enrollment, caregivers randomized to ViCCY vs. HI alone will have **H2a**: Higher QALYs measured with the SF-6D (short form six-dimension) derived from the SF-36[40] *(secondary outcome);* and **H2b:** Lower health care resource use *(secondary outcome)*.

Aim 3 (Exploratory): To explore the effect of caregiver outcomes on HF patient outcomes. We hypothesize that, at 12 months after enrollment, HF patients whose caregivers improve vs. not improve in self-care – regardless of group – will have **H3a:** Lower hospitalization rates; **H3b:** Fewer hospital days; **H3c:** Lower mortality rates; and **H3d:** Higher QALYs measured with the SF-6D.[40]

If shown to be efficacious and cost-effective, our virtual health coaching intervention can easily scaled to support millions of caregivers worldwide. This application addresses the NINR strategic plan and is directly responsive to PA-18-150.

RESEARCH STRATEGY

A. SIGNIFICANCE

A.1. Informal caregivers are stressed and their self-care is poor. Informal caregivers carry the bulk of the responsibility for the care of ill, disabled, and elderly individuals.[41] More than 42 million unpaid informal caregivers provide care to someone needing help because of a limitation in physical, mental, or cognitive functioning.[42] As a group, informal caregivers have more stress,[43,44] worse self-care,[10,45-48] poorer health status,[8,27,49,50] and higher mortality than non-caregivers.[48,51-55] Caregivers often feel left alone to cope with problems, which exacerbates their stress.[56] When stressed, caregivers are less vigilant and less motivated to engage in behaviors that will benefit themselves and their charges.[57,58] In a study of 121 mainly female caregivers (mean age 61±13.4 years) of older family members, healthy self-care behaviors were lowest in those with high stress scores.[59] In another study, after four years of follow-up, stressed caregivers were at 63% higher risk for mortality than non-caregiving controls.[7] Together these studies illustrate the risk that informal care providers face when they defer self-care in response to the stress of caregiving.

A.2. Informal caregivers of patients with heart failure (HF caregivers) are an understudied population. Although informal HF caregivers face many of the same issues as other caregivers, they also face unique challenges. HF caregivers are older than other caregivers (mean 55.7 vs 49.4 years; $p < 0.001$).[60] Both the patients and their caregivers often have multiple comorbid illnesses, making caregiving complicated. The trajectory of HF is highly variable with a gradual decline in function, so the need for caregiving lasts longer than for other populations.[61] Because of this unpredictability, neither palliative care to HF patients nor respite services to their caregivers are routinely offered.[13,20,60,62,63] HF is associated with poor physical capacity, depression, behavior problems, and cognitive impairment.[20,64-67] Caregivers report difficulty coping with these patient-symptoms,[68] with the most stressful daily duties being providing emotional support, structuring and planning activities, and managing patient behavior and mood.[69-71] Caregivers must supervise and monitor complex care regimens and coordinate frequent hospitalizations,[72,73] the latter being so stressful that well-being is lower in caregivers than in patients when HF patients are hospitalized.[74] HF caregiving is expensive, incurring lost-wages and out-of-pocket expenses; in a study of end-stage HF patients, 23% of families had lost all or most of their savings by the time the patient died.[75] These issues have a profound effect on caregivers' lives.[76,77] While caregivers of other populations often report satisfaction from caregiving, we see no evidence of caregiving satisfaction in HF caregivers. They are burdened, stressed, and poor in self-care.[30,69,71,78]

A.3. Effective interventions are needed for HF caregivers. Few randomized controlled trials (RCTs) of interventions for HF caregivers have been published, [79] and of those, most have focused on improving HF caregiver burden, stress, or health status – not ***caregiver self-care***.[76,80,81] The most common interventions involved psychoeducation facilitated by a registered nurse (RN), supplemented with face-to-face follow-up sessions, home visits, telephone calls and/or virtual monitoring.[82] Two studies focused on helping caregivers support ***patient self-care***,[81,83] but none focused on improving ***caregiver self-care***. Few interventions reported a significant effect on one or more primary outcomes, and many were resource-intensive. For example, in a *successful* study in the Veterans Affairs system,[84] team-managed, home-based primary care with a dedicated care manager, 24-hour contact for patients, prior approval of hospital readmissions, and team participation in discharge planning effectively reduced caregiver stress and improved health status, but ***patient care costs increased*** by 12% at 12 months due to increased staffing.[84] In an *unsuccessful* approach, a trial of a 12-week chair exercise program for HF patients hypothesized to decrease stress in caregivers[85] demonstrated ***increased caregiver stress*** after six months, perhaps due to increased caregiving demands. We believe that few interventions have been effective because of failure to include elements argued to be essential in caregiving interventions:[86] 1) a psychosocial rather than purely educational approach; 2) flexibility; 3) multidimensionality; and 4) sufficient intervention dose. We developed ViCCY to address these elements.

A.4. Internet-based virtual approaches can be used to support homebound caregivers. Successful implementation of potentially effective interventions is impeded when caregivers are homebound with caregiving duties.[30,87] Yet, such isolated individuals may be among the most stressed caregivers in need of support.[88,89] The home environment may be the best place to deliver an intervention, where distractions are predictable and privacy can be optimized.[90] Home interventions are perceived as convenient, requiring less time commitment, travel costs, and waiting times; duration and timing of sessions can be flexible and accommodate caregiver preferences. Support is important to the success of psychosocial interventions,[91] and virtual visual contact overcomes the challenges of lack of visual cues found in telephone-based interventions.[92] A 2015 review of virtual interventions to support family caregivers concluded that caregivers were satisfied and comfortable with virtual support.[93] Another review of eight open-label trials and 16 RCTs concluded that

Internet-based interventions were effective in reducing caregiver stress and improving their well-being.[94] According to the 2015 US Census, 77% of the US population has broadband Internet access at home.[95] Thus, live video-streaming is now possible for most people in the US at very low cost, making virtual support a potentially efficacious way to intervene with homebound caregivers.[96]

A.5. Little is known about the cost-effectiveness of interventions for caregivers. Few cost-effectiveness analyses of support interventions have been performed in any chronically ill population. One review suggested that psychological therapies and psychosocial interventions were potentially cost-effective in people with dementia and their family caregivers.[97] In a pragmatic RCT providing an 8-session coping intervention to family caregivers of people with dementia, the cost-effectiveness acceptability curve[98] indicated >99% chance of being cost-effective in the short and longer term.[99,100] There is also evidence that psychological therapies provided by Internet are cost-effective.[101] No economic analyses of support interventions have been conducted in the HF population, but the annual cost associated with informal caregiving of patients with HF in the US was estimated at $3 billion in 2010.[102] A Cochrane review examined the cost-effectiveness of home palliative care for adults with advanced illness, including HF, and their family caregivers,[15] but found inconclusive evidence and recommended more study.[15]

A.6. Dyadic processes influence outcomes. By definition, the caregiving relationship involves two people.[103] Several studies, including our own, have demonstrated that dyadic processes influence outcomes in both HF patients and their caregivers.[78,80,104-108] The vast majority of these studies are descriptive, and no one has tested the influence of an intervention for caregivers on HF patient outcomes. The mechanism by which dyadic processes influence outcomes appears to be related to the quality of the relationship.[105-108] Relationship quality influences burden,[109] emotional distress,[110] self-care behaviors,[14,105] decision-making,[111] and quality of life in both HF patients and caregivers.[112] It is plausible that the relationship influences HF patient hospitalizations and mortality, but there is little evidence on this topic.[28,29,113] Hospital readmissions within 30-days are especially high (20-25%) in HF patients,[114] with almost two thirds of readmissions occurring within 15 days of discharge.[115] Four of every five HF patients require hospitalization annually, and at least one-third are hospitalized repeatedly.[116] By 12 months, close to two-thirds of all HF patients have been readmitted.[117] Hospitalizations are costly,[118] and the annual total costs attributable to HF are so high[119] that HF is the primary contributor to the US Medicare budget.[120] More than half of those who develop HF die within five years of diagnosis.[11]

A.7. Theoretical Framework. The proposed study is based on the Transactional Model of Stress and Coping (**Figure 1**).[121] Stressful experiences such as caregiving demand – circumstances that give rise to real or perceived stress – are construed as person-environment transactions.[121] Primary appraisal of demand involves assessment of its significance, which results in perceived burden. Secondary appraisal involves assessment of the resources available to cope with it. These appraisals lead to the coping effort.[121] Without successful coping, self-care is poor, which decreases health status in caregivers. Our virtual support intervention [ViCCY ("Vicky") – Virtual Caregiver Coach for You] addresses both appraisal and coping. Because stress does not affect all people equally, the intervention is tailored to individual appraisals and the factors most likely to influence demand and perceived burden.[122] A key strength of the Transactional Model of Stress and Coping is its recognition that both individual and environmental variables respond to coping. See Section C.5 and Table 3 for details on how the theory is used in ViCCY.

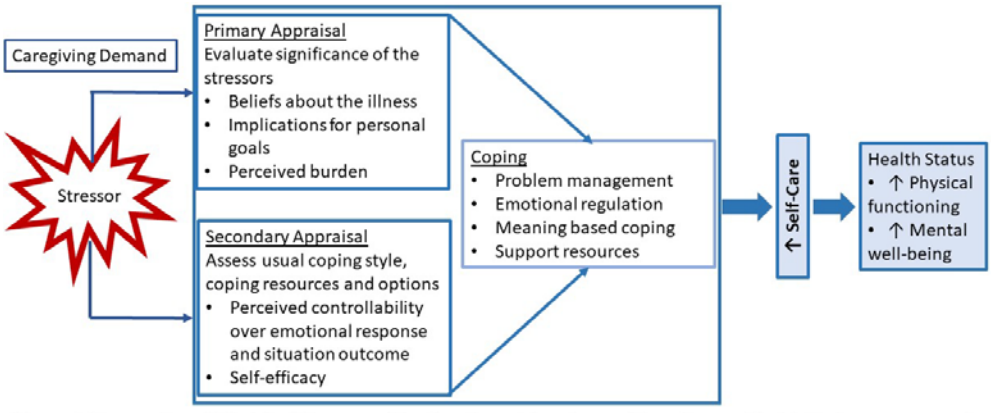

Figure 1. Transactional Model of Stress and Coping. Caregiving demand is a stressor that initiates a process of primary appraisal (e.g., perceived burden) and secondary appraisal (e.g. controllability) in caregivers. These appraisals lead to coping efforts, which are supported with our ViCCY intervention. ViCCY is anticipated to promote caregiver coping and improve self-care (e.g., eat better, sleep more, exercise), which will improve caregiver health status. An intervention that improves caregiver outcomes may improve heart failure patient outcomes, but patient outcomes are not shown here. (ViCCY = virtual caregiver coach for you)

Scientific premise. This study builds on a body of evidence that is strong in describing stress in HF caregivers but weak in linking that stress to poor caregiver self-care. We have demonstrated in HF ***patients*** that self-care improves health status,[123,124] but the relationship between self-care and health status has rarely been tested in HF ***caregivers***.[125] Health coaching has been shown to decrease perceived stress and improve

self-care and health status in other caregiver populations.[126] Some of these studies have provided virtual support to homebound caregivers, and a few included older caregivers such as those we anticipate enrolling. However, very few studies have addressed the cost-effectiveness of interventions targeting informal caregivers. Furthermore, in addition to our primary aims, we will explore the impact of caregiver outcomes on HF patient outcomes. Although a growing body of research illustrates the influence of caregivers on patients and vice versa, (i.e., dyadic processes), very few intervention studies have explored the influence of the caregiver experience on patient outcomes.

B. INNOVATION

Our proposed research is innovative for several reasons:

1. We focus on a patient population (those with HF) with unique issues – e.g., symptom burden, impaired cognition, frequent hospitalizations, multimorbidity, and complex regimens – that increase caregiver demand, burden, and stress. While dementia caregivers face many of these issues,[127] HF is different because palliative care is not offered routinely and respite services are rarely available.[8,63,128] Without support services, these caregivers are extraordinarily stressed.[20,129] High stress levels are associated with poor self-care.[130]
2. Few studies of caregivers have focused on their self-care, and those studied other populations. Most studies of HF emphasize the caregiver's role in promoting HF *patient* self-care. The proposed study will provide a robust description of HF *caregivers'* self-care and the manner in which it changes with intervention.
3. We have developed a unique approach to health coaching that targets stress and self-care concurrently. ViCCY is potentially more powerful than interventions addressing either issue alone because self-care is lower in stressed populations and self-care can potentiate stress reduction approaches.[131]
4. Using video technology to intervene with caregivers is *not* new but it is new in HF caregivers, who are a predominately older population. In spite of mounting evidence that older adults use technology regularly,[132-135] ageism persists and elders often are assumed to be unable to participate in research using technology.[136,137] Our proposed study will be one of the first adequately powered trials of a virtual intervention for predominately older caregivers. If efficacious, this approach to the delivery of ViCCY can easily be deployed in any location and with other populations.
5. Very few caregiver intervention studies have addressed cost-effectiveness. We include a formal cost effectiveness analysis in which caregivers are followed for 12 months.
6. We explore the influence of caregiver outcomes on HF patient outcomes. A growing body of research illustrates the powerful influence of individuals in a dyad or couple on each other.[106,108] But our study is unique and innovative in exploring the effect of a stress intervention for caregivers on outcomes in HF patients. Measuring QALYs in both caregivers and HF patients, we will be able to assess benefit in both.

C. APPROACH

C.1. Research Team (see Biographical Sketches and Letters of Support for details). Our multidisciplinary team based at the University of Pennsylvania (Penn) is well positioned to complete the proposed study. Team members, most of whom have worked together for the past decade,[138-145] bring unique but complementary perspectives that have informed all dimensions of the proposal: Barbara Riegel, PhD [Principal Investigator (PI)] HF, health coaching, motivational interviewing, caregivers, self-care]; Kathryn Bowles, PhD (Co-I) virtual technologies; Karen Hirschman, PhD (Co-I) interventions with older caregivers; Joyce Wald, DO (Co-I), heart failure; Norma B. Coe, PhD (Co-I) cost-effectiveness analysis; and Alexandra Hanlon, PhD (Co-I) biostatistics. Led by the PI, members will share responsibility for the conduct and integrity of the study. See Budget Narrative for specific responsibilities and contributions.

C.2. Preliminary Studies. We developed our intervention in patients and have modified it for caregivers. In the first study, we ***refined our tailored health coaching intervention in 15 HF patients*** (mean age 60 ± 13.3 years, 53% White, 60% female).[146] The intervention, provided by an RN during an average of 3 ± 1.5 home visits over 3 months, focused on improving self-care. Motivational interviewing was used to elicit beliefs about the illness, personal goals, and self-efficacy. Reflective listening and empathy were used to provide support, decrease barriers and build skill in self-care. There was evidence of improvement in self-care in 80% of HF patients after receiving the intervention.[146] In a second study, we tested health coaching vs. standard education in 100 HF patients (mean age 62 ± 12.8 years, 54% Black, 30% female) in an RCT.[147] The intervention was provided by an RN in 1 in-person session and 2-3 telephone sessions over the first month after hospital discharge. At 3 months, more improvement in self-care was seen on the Self-Care of HF Index[148]

in the intervention group than the control group (19.7 ± 16.0 vs. 12.1 ± 18.3 improvement in standardized scores), a clinically and statistically significant difference after adjusting for confounding variables.[149] The effect size was moderate (Cohen's d = 0.44). *Based on qualitative data collected in both studies, we learned that face-to-face sessions were more effective than telephone sessions, so we moved to using virtual technology.*

In preparation for this proposal, we conducted ***three pilot studies to adapt the intervention for caregivers***. We first enrolled seven homebound female spouse caregivers of HF patients and interviewed them to identify stressors associated with caregiving. When we described the planned program, all were receptive to the electronic intervention and five of the seven women wanted to participate *("I need help desperately")*.[71] In the second pilot study, we tested four methods of distance communication – telephone, tablet (iPad) with video, laptop computer with video and a detachable webcam, and touchscreen videophone. The iPad facilitated privacy by allowing the caregiver to move to a private place while conversing and was preferred over other devices *("the iPad is just less threatening")*. In the third study, we assessed feasibility of our planned methods and pilot-tested the ViCCY intervention.[150] We enrolled four HF caregivers (white female spouses, mean age 66 ± 8.5 years) and gave each an iPad. Health coaches engaged each caregiver in 8 support sessions over a 3-month period. Each session lasted approximately 1 hour. Data were collected at enrollment and three months later using most of the methods proposed below. Table 1 shows change in the main target variables. Technology problems were more common in coaches than caregivers and were quickly resolved with assistance. *Together these pilot studies illustrate that caregivers are interested in participating, they are comfortable with the tablet technology, and our proposed methods are feasible. We learned to hire coaches adept with technology and to ensure that participants have a strong Internet connection.*

Table 1. Results from Pilot Study of Four Caregivers	Baseline Score (SD)	3-Month Follow-up Score (SD)
Perceived Stress Scale (lower is better)	20.7 (4.3)	18.2 (0.96)
Health Self-Care Neglect Scale (1-10 possible range, lower is better)	3.2 (2.5)	1.2 (1.2)
SF-12 Health Status, Mental Component Score (higher is better)	52.1 (9.1)	55.6 (4.3)

We have used virtual technology to deliver numerous interventions, including some of the early work using virtual approaches with older adults.[138,140] In a field experiment funded by the Department of Commerce, we enrolled 174 elderly diabetic home health patients and provided a virtual intervention.[151] Of those who refused, only 12% said the technology was too complicated, in spite of the fact that we used first-generation technology that was far more complicated than that proposed in this study – a virtual technology approach with tablets. *Satisfaction with this delivery method was high. Our research staff has extensive experience in setting it up and instructing those having no knowledge of tablets to become proficient in its use.*[138,139,151-153]

C.3. Study Overview (Figure 2). We will use a RCT design to achieve robust and unbiased results, as detailed below. We will enroll 250 informal HF caregivers and, when possible, the HF patients for whom they care. After collecting baseline data, we will block randomize the caregivers 1:1 to the intervention or control group, stratifying randomization by caregiver sex and relationship to the patient (e.g., spouse, adult child) – factors known to influence caregiving burden, perceived stress, and receptivity to the intervention.[8,154] We will provide tablet devices with wireless network access and connect caregivers in both conditions to the Internet so they can access the Internet site providing Health Information (HI) content, which will be the only content provided to caregivers in the control group. In addition to HI, the intervention group will receive 10 front-loaded sessions of ViCCY over 6 months. Assessments of self-care, perceived stress, coping, and health status will be conducted at baseline (after enrollment but prior to randomization) and by phone at 3, 6, 9 and 12 months. Using contrasts within a mixed-effect modeling framework, we will assess intervention efficacy at 6 months using intention-to-treat analysis. We chose to provide 10 health coaching sessions based on our pilot data and literature demonstrating that a shorter duration of health coaching is not routinely effective.[21] We chose to assess the primary aim at 6 months based on prior psychosocial intervention studies,[83,125,155] but we will assess outcomes at 3-month intervals based on this rationale: *baseline (enrollment)*, to generate consistent profiles of all enrollees at a consistent point in time and prior to implementation of the new intervention; at *3-months*, very early effects, at *6-months,* short-term effects; and at *12-months*, the longer-term effects of ViCCY vs. HI. These 3-month intervals also will allow us to compare our results with others.[156,157] We chose a 12-

Figure 2. Illustration of the sequence of enrollment, randomization, and data collection over the 12 month period. Data collection time point months shown in **bold.** Primary outcome collected at 6-months. (R=randomization)

month follow-up interval for the cost-effectiveness analysis to allow for a full year of event accrual. We will pull resource use data from the electronic medical record (EMR) in 30 day increments and validated these data during routine follow-up calls with caregivers. We expect the proposed study to require 5 years for completion.

C.4. Sample.

C.4.a Recruitment. We will enroll a consecutive sample of informal HF caregivers identified from the Penn Heart and Vascular Center (PHVC), the largest out-patient HF clinic in the Philadelphia region and a site at which the PI has established relationships and success in past recruitment of participants. In 2017, there were 5344 HF patient visits (mean 445 visits per month). Of these, approximately 832 were new HF patients (mean 69 new patients per month). In a prior study at this site, we enrolled 139 HF patients over 18 months; 84% of the screened and eligible patients enrolled.[142] These 139 HF patients (45% female, 34% non-White, mostly Black) all lived at home with a family caregiver.

If recruitment is slower than expected, we will identify caregivers visiting HF patients hospitalized at one of three University of Pennsylvania Health System (UPHS) sites, all of which use a single, integrated EMR with the level of financial data needed to address our cost-effectiveness aim. The Hospital of the University of Pennsylvania (HUP) has 789 licensed acute care beds. Between July 2016 and July 2017, HUP admitted 1,859 HF patients. Presbyterian Medical Center (PMC) has 331 patient beds and admitted 1,621 HF patients in that year. Pennsylvania Hospital (PAH) has 496 licensed patient beds and admitted 716 HF patients that year. From these various sources, it is reasonable to project identifying **100 unique HF patients each month**, most of whom will have caregivers. Based on our prior research,[158-161] we anticipate that 90 will have caregivers and 70% of these (63 caregivers) will be eligible, and 15% will enroll. Thus, we estimate enrolling 10 caregivers per month. We will require a minimum of 25 months for enrollment, and have conservatively allowed 30 months for enrollment and five years to complete the study.

We will explore the relationship between HF caregiver and HF patient outcomes in a subgroup of at least 40 caregiver-patient dyads; 40 dyads is sufficient to provide reliable parameter estimates. HF patient participants will be asked to provide informed consent to allow us to access their EMR to collect clinical information and track events and, in the case that patients receive care outside the Penn health system, for the caregiver to report on patient health care resource use. HF patients will not receive an intervention. If a caregiver agrees to participate but the HF patient does not, we will still enroll the caregiver. It is not possible (or desirable) to exclude caregivers of patients with comorbid illnesses that may increase caregiving demand given the high prevalence of comorbid conditions in HF patients.[162-164] Thus, whenever possible we will also gather EMR data on patients' comorbid illnesses using the Charlson Index categories of mild, moderate, or severe[165] for use as a covariate in analyses.

Based on our prior studies, we anticipate enrolling a diverse sample, with many in vulnerable racial, socio-economic, and geographically disadvantaged groups.[160,166,167] Most caregivers will be spouses but some will be adult children. Although the sex distribution of HF patients is about equal,[11] female HF patients are typically older. See **Table 2** for caregiver inclusion and exclusion criteria. All willing HF patients cared for by an eligible and enrolled caregiver and capable of giving written informed consent will be eligible for inclusion.

Table 2. HF Caregiver Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
1. Informal caregiver providing care at least 8 hours/week	1. Cognitive impairment (Telephone Interview for Cognitive Status [TICS][168] < 25)
2. Reporting poor self-care on screening (Health Self-Care Neglect scale[35] score ≥2 based on our pilot data)	2. Participation in another support RCT
3. Able to complete the protocol, e.g., adequate vision and hearing, English speaking	3. Untreated major psychiatric illness (Use of anti-anxiety/anti-depressant medicines is acceptable and will be adjusted in analysis if group imbalance is identified.)
4. Living within 50 miles of the research office in case home visits are required for enrollment or Internet set-up	4. Plans to move out of the area imminently

C.4.b. Screening, Enrollment, and Baseline Assessment. We will have a study Research Assistant (RA) on site during PHVC clinic hours and anticipate that many informal caregivers will be screened and enrolled during a HF patient clinic visit because meeting in person is anticipated to maximize enrollment.[169] To obtain a consecutive sample we will seek a HIPAA waiver to screen the daily appointment schedule to identify every patient with a potentially eligible caregiver (e.g., living within 50 miles of the research office). Clinic staff will identify potential caregiver participants (e.g., speak English) and determine their interest in speaking with research staff about the study. If caregivers agree to speak with research staff, the RA will explain the study and screen the caregiver for inclusion and exclusion criteria with standardized testing (e.g., self-care) and interview (e.g., hearing). Fully eligible caregivers who provide informed consent (see Human Subjects) will complete the baseline assessment (Section C.9) before being randomized to study arm.

If we need to enroll from the hospital, an RA will be available in the hospital daily to give interested caregivers study information and conduct screening. We will obtain a HIPAA waiver to allow us to screen the daily admission log to identify every HF patient with a potentially eligible caregiver (e.g., living within 50 miles of the research office). Caregivers willing to speak with research staff will be screened as described above.

If the caregiver is not able to complete the baseline assessment at the time of the clinic visit or during the patient's hospitalization, a home visit will be scheduled to complete baseline data collection. After all baseline data are collection, the caregiver will be randomized to study arm. At that time, participants will be trained in tablet use and how to access the Health Information website. A research diary will be provided to aid tracking of health care resource use and cost.

C.4.c Consideration of Sex as a Biological Variable. In accordance with NIH guidance, we will include sex as a biological variable in study design (block randomization of men and women to each group), analyses, and reporting. We will report all primary and secondary outcomes separately by sex to enhance the rigor and transparency of our findings. We expect to enroll more female than male caregivers because most HF caregivers are female[55] and support interventions are more appealing to women.[170] Enrolling at least 50 men is a goal so that sex-related differences in intervention efficacy and outcomes can be identified. We will monitor enrollment weekly. If fewer than 15 male caregivers are enrolled in the first 3 months, we will conduct a focus group with male caregivers to identify specific elements that could be emphasized to make the intervention more attractive to them.[171-175]

C.4.d. Randomization and Blinding. Block randomization will be used to achieve equal distribution of key variables in each condition. We will block randomize on caregiver sex (male/female) and relationship to patient (e.g., spouse) – factors shown to influence perceived caregiving burden[176] and receptivity to intervention.[177] The randomization sequence will be generated *a priori* by a statistician independent of the study investigators using a randomly permuted blocks algorithm to ensure equal distribution of these variables in each study arm. The Project Manager will notify the study staff and participants of their group assignment (ViCCY or HI only) by telephone, email or message, as preferred by the individual. Although balance in sample size can be achieved with block randomization, the groups may not be fully comparable on other factors. Initial comparison of the groups will allow us to control for important covariates in the analyses.[178] Investigators and all staff involved in collecting assessment data will be blinded to group assignment until after the data are locked. The RN providing the intervention and the caregiver participants will not be blinded. All baseline data will be collected prior to randomizing. Timing of follow-up assessments will be based on day of randomization.

C.5. Augmented Standard Care – Health Information (HI). Caregivers in both the intervention and control arms will receive augmented standard care content (HI) through the Internet. Standard care typically involves unstructured, intermittent outreach by nurses staffing physicians' offices, but there is evidence that caregivers' needs are not met with this approach.[16,179] Augmented standard care (HI) in this study will be based on informational resources from the UK National Health Service (http://www.nhs.uk/pages/home.aspx). This rich Internet site (see Section C.7 for Internet availability) has educational pages on hundreds of conditions. The site offers self-help books and free self-help computer exercises designed for stress reduction and healthy self-care. For instance, one module, *Moodzone,* teaches stress management skills with an interactive game, anxiety assessment, a downloadable relaxation audio, workbook, and feedback assessment. Using flashed diagrams and online exercises, *Moodzone* illustrates the relationship between thoughts and emotions and works through the process of dealing with stress. Relaxation and meditation techniques are described. *Live Well* provides excellent, updated content on diet, exercise, substance abuse, immunizations, etc. If a participant wishes to use the self-help books—equivalent in content—instead of or in addition to the online materials or in addition, we will provide those materials. Participating caregivers in both study arms will be encouraged to spend at least 30 minutes weekly using the Internet modules or books for six months and will receive monthly reminder cards by mail. We will track participant use of the website using Google Analytics, and those who are not using the website will be telephoned and reminded to do so. Those who choose to use books rather than the website will be asked to keep track of the number of book chapters reviewed each month. Use of the website or book chapters will be used as a measure of fidelity in both arms (see Section C.8). After six months, we will pick up all tablet devices (both groups) to minimize bleeding of the intervention into the follow-up period, and we will continue to track use of the website to identify if bleeding occurs.

C.6. Intervention - ViCCY. In addition to augmented standard care HI, caregivers randomized to ViCCY will receive 10 front-loaded sessions of virtual health coaching by trained RNs (Section C.6.a) over 6 months with content based on the theoretical framework and our prior research (**Table 3, next page**). As shown in **Figure**

3, sessions are weekly initially and decrease in frequency over time. ViCCY incorporates the factors essential in caregiver interventions;[86] it is a psychosocial approach that is personalized and tailored to be flexible; is multidimensional, providing support for coping with perceived stress while fostering self-care; and is sufficient in dose, based on our pilot work. We refined our approach based on caregiver input to focus on *relieving* stress rather than intensifying demand and burden,[71] thereby promoting caregivers' ability to respond to stressors with adaptive coping. We aim to build motivation to gain the knowledge and skills needed to achieve self-identified health goals.[180] We focus on identifying personal values, solving problems, and transforming goals into action using a combination of psychological and behavioral interventions.[181]

Figure 3. Intervention sequence in Virtual Caregiver Coach for You (ViCCY) Treatment Arm. A total of 10 sessions are planned with booster sessions provided if requested by the caregiver. Between sessions, caregivers will complete "homework" (i.e. strategies to use and practice), which will be reviewed by the RN to monitor how these activities worked for the caregiver. At the end of the 6-month intervention period the RN will sever the virtual relationship, referring the caregiver to the HI website for further support.

We use motivational interviewing in all ViCCY sessions.[182] Observations are presented to the caregiver in a way that builds confidence, motivates action, and enhances self-care by breaking the cycle of negative self-perception and emotions with the knowledge, skills, and beliefs needed to engage in healthy behaviors.[183-186] We discuss goal-setting and action-planning in early sessions. Consistent with motivational interviewing, information (e.g., reasons for specific patient behavior) is given only if and when the caregiver is receptive to it.

A series of sessions is provided with the goal of achieving a lasting effect.[187] In preliminary studies, we found a direct relationship between the number of sessions provided and the effect obtained,[166,188] with 10 sessions of health coaching typically being a sufficient dose.[21] Because maintaining contact is important to the success of stress reduction interventions,[91] the assigned RN will check in with caregivers between intervention sessions. We will offer booster sessions to any caregiver in the ViCCY arm who wishes to receive additional support during the 6-month intervention interval.[21] We will track the number of sessions and test for differential effectiveness based on the dose received. If a brief check-in call becomes an intervention session, it will be tracked for use in analysis. We will mail monthly newsletters to maximize retention (see Recruitment and Retention Plan). Because we found that early and intense contact with the coach builds the relationship, engages the participant in the treatment program,[189] and maximizes outcomes,[190] we will front-load the intervention sessions (**Figure 3**). Consistency is important for trust building, behavioral change, and growth,[191] so one RN health coach will be assigned to work with each caregiver for the full 6-month period. Intervention content is carefully standardized, guided by a manual with session agendas and checklist of specific content to be covered in each call, but also tailored to allow the coach to focus on caregiver needs, addressing unique and varying individual characteristics, preferences, and goals.[192,193]

Table 3. Intervention Content Derived from the Transactional Model of Stress and Coping

Theoretical Dimension	Intervention Actions by the RN Health Coach
Caregiving demand	Assess caregiving demand (e.g., patient behaviors, communicating with providers, feeling isolated).[12,18,194] Provide "mutual education" and cross-learning—caregivers educate the RN about the nature of their problems and the RN educates the caregiver about the purpose of health coaching and how self-care can help the caregiver.
Primary appraisal (significance of the stressor)	Assess beliefs about HF and personal goals to determine how caregiving demand impacts caregiving burden and personal goals.
Secondary appraisal (assess coping resources and options)	Assess perceptions of controllability and self-efficacy in dealing with specific situations. Use goal setting to set up discussions of the discrepancy between goals and self-care behavior, ambivalence about self-care, and action planning.
Coping: Problem management	Assess structural and contextual factors influencing coping (e.g., social determinants of health). Identify resources needed. Teach practical skills to activate self-care and encourage a sense of health ownership (e.g., self-monitoring of thoughts and behavior). Introduce problem solving.[195,196] Emphasize self-care as a pleasurable and healthy method of coping. Discuss action planning, emphasizing skills that can help deal with problems (e.g., brainstorming about potential solutions when problems seem insurmountable). Teach how to itemize and prioritize questions before meetings with providers. Focus on building confidence.
Coping: Emotional regulation	Teach that avoidant coping styles (e.g., denial) are not helpful.[197] Encourage perceptions of controllability and self-efficacy as they are associated with engaged coping (e.g. problem-solving). Teach relaxation exercises (e.g., guided imagery, controlled diaphragmatic breathing, and meditation) early and reinforce throughout to promote emotional regulation.
Coping: Meaning-based coping	Encourage gratitude to decrease stress and improve wellbeing.[198-200] Encourage spiritual beliefs and engagement in positive events. Focus on ways to find satisfaction with caregiving.
Support resources	Identify interpersonal and community resources available to provide respite and support.

C.6.a. Health coaches. We will hire two baccalaureate-level RNs who have at least three years of clinical

experience in cardiac nursing, excellent interpersonal communication skills, and comfort with technology.[201] RNs will receive two days of initial training in health coaching from Dr. Riegel and then complete a 7-hour online training program in motivational interviewing provided by the University of Colorado, College of Nursing. Thereafter, weekly training and supervision will be conducted by Drs. Riegel and Hirschman as the RNs begin coaching caregiver participants. As part of this supervision, audio-recordings of coaching sessions will be reviewed by independent raters using the Behavior Change Technique taxonomy.[202] Two trained raters will judge three randomly selected session recordings for each coach. Raters will assess completeness and thoroughness of the therapeutic techniques used, calculating intraclass correlation coefficients as a measure of interrater reliability. RNs who receive less than moderate ratings will receive individual session supervision. If an RN receives a low rating on any session, s/he will be required to undergo additional training and will be suspended from coaching study participants until the deficiencies are remedied. We have had success in this approach for recruiting, training, and retaining health coaches engaged in prior trials.[23,149,153]

C.7. Internet Access. We will offer a variety of Internet options to participating caregivers. We will offer tablet devices, which are versatile for allowing privacy, to all participants. The tablet uses an embedded computer camera capable of full 2-way duplex video and audio transmissions for real-time communication. Existing broadband Internet connection is not required because we supply devices with mobile connectivity. Technology experts (Caryl Technologies, with whom we have worked in the past) will train research staff to set up Internet service and devices during an in-person visit and ensure that the system is functioning well before research procedures begin. Caregivers will be left with a step-by-step manual and the research office phone number in case technology issues occur. If they wish to use their own computer, we will locate the site on their computers and ensure that it functions properly. We will provide a camera for anyone in the ViCCY arm who wishes to use her/his own computer. If their personal technology proves to be inadequate, we will offer a tablet to ensure access to the website and the intervention.

ViCCY sessions will be provided entirely by video-conferencing technology. A secure cloud account will be set up for the ViCCY sessions, which will begin within one week of set-up. As described previously, we have conducted several funded clinical trials using virtual technology that illustrate our experience with installing, teaching, trouble shooting, using, and evaluating such applications in participants' homes.[139,203-208] Almost all of these studies involved older adults. This experience taught us that the devices are easy to install and use. In one typical study with older adults, average use (number of days the equipment was used divided by number of days available) was 81% (range 6%-100%).[138]

C.8. Process evaluation. Treatment fidelity will be monitored as detailed in **Table 4**.[209-211] To examine whether caregivers' expectations are influencing outcomes, caregivers in both groups will complete the Outcome Expectancy and Treatment Credibility Scale[212] at baseline and 6 months to facilitate data interpretation. This scale has good internal consistency (α=0.85) and has been used in numerous prior studies, including trials in which an intervention is delivered by Internet.[213,214]

Table 4. Methods of Process Evaluation to Ensure Treatment Fidelity

Goal	Strategies
Study Design Ensure that the treatment dose (number, frequency, length of contact) is adequately described and the same for each participant	• Provide all participants with consistent access to HI • Provide all intervention group participants with 10 doses of ViCCY over six months • Use a detailed treatment manual with session agendas and checklist of points to cover to enhance treatment quality and consistency • Use a software program to monitor use of the HI website
Plan for Implementation Setbacks (e.g. coach drops out)	• Hire 2 RNs, maintain a pool of qualified RNs so that new ones can be trained as needed • Track attrition (Research Assistants (RAs), RNs, participants) and reasons for dropout
Coach Training Standardize training to ensure that it is conducted similarly for all RNs. Train RNs to well-defined performance criteria	• Train RNs together using standardized training manuals and the same instructor • Design training to accommodate individual styles while assuring standardization • Specify performance criteria *a priori* • Provide remedial training immediately when problems are detected
Treatment Delivery Monitor and control for treatment differences	• Monitor all encounters, with deviations from protocol addressed quickly • Assure that a single RN is assigned to provide ViCCY for each caregiver for continuity • Randomly choose 3 early ViCCY sessions per RN to audio-record and rate for fidelity • Provide routine supervisory oversight using fidelity ratings to minimize decay or drift • Assure that RNs self-monitor, completing an intervention log after each contact
Treatment Enactment Monitor and control for participant perceptions of RN differences (e.g., warmth, credibility)	• Assess participant perceptions of RNs' characteristics through intermittent phone calls • Give feedback to RNs and mentor them to rectify complaints • Analyze treatment enactment data after 50%, 75%, and 100% of participants are recruited and compare by group (ViCCY and HI)[215]

C.9. Caregiver Characteristics and Outcomes. *On enrollment*, the RA will collect self-report data from caregivers using encrypted laptop computers. Data will be entered directly into the REDCap database as collected, with data entry screens designed to incorporate range checks and concurrent checks to minimize errors. Caregiver burden[216] will be measured using the Dutch Objective Burden Inventory (alpha coefficient 0.81-0.84, construct validity), which measures the full range of activities required to care for HF patients (demand) as well as the burden associated with these demands.[217,218] Quality of the relationship with the patient; social determinants of health; and demographic, caregiving, and clinical characteristics will be gathered from caregivers at enrollment only. *At 3, 6, 9 and 12-months* post randomization we will telephone caregivers and collect self-report data on self-care, stress, coping, and health status (**Table 5**). At 12 months we will measure QALYs. These data will be obtained by interview and entered directly into REDCap using encrypted laptop computers. Self-report instruments with demonstrated cultural-sensitivity and prior validity testing in caregiving samples were chosen, and measures are as brief as possible to minimize burden.

C.10. HF Patient Characteristics. With patient consent, HF patient demographic and clinical characteristics will be abstracted from the medical record at enrollment. Duration of HF will be measured in months. All comorbid conditions will be noted and classified using the Charlson Index.[165] Physician ratings of New York Heart Association functional class as noted in the EMR at enrollment will be used to describe HF patients. The SF-6D will be administered to HF patients at baseline and 12 months to obtain QALYs.[40]

Table 5. Caregiver Outcome Variables and Measurement

Definition and Measure	Items	Item responses	Reliability	Validity	Comments
Self-care (behaviors undertaken to maintain health). Health Self-Care Neglect (HSCN) scale[35] and the short Health-promoting lifestyle profile (HPLP) II.[219]	10 30	HSCN dichotomous. HPLP 4-point Likert scale; higher score = more healthy behavior.	0.76 0.90	Content Criterion Convergent Divergent Construct	The HSCN has not been widely tested so we augment this measure with the widely-used Health-promoting lifestyle profile II. To minimize burden, we will use the short form.
Stress (demands exceed ability to cope). Perceived Stress Scale (PSS).[36]	10	5-point scale (0=never to 4=very often).	0.84-0.86	Concurrent Predictive Construct	Gold standard for assessing stress.[220] Norms are available for comparison.
Coping (ability to respond to stressors with appropriate adaptive coping resources).[121] Ways of Coping Questionnaire, short form.[38]	30	4-point Likert-scale response format (0 = not used to 3 = used a great deal); higher scores indicate greater coping.	0.95	Construct	The original scale has been used widely since developed by Lazarus in 1985. This short version has been used numerous times in studies with older adult caregivers.[221-225]
Health status (physical and mental health). Medical Outcomes Study Short form (SF)-36.[136,137]	36	Varied (3-, 5- and 6-pt scale and dichotomous [yes/no]); each component score is standardized 0-100 point scale.	>0.80	Convergent Divergent	Standardized scores and national norms for comparison. SF-36 valid in many populations,[39,226] and caregivers.[227,228] One of the common data elements.
Quality of the relationship scale[229] measures giving and receiving support.	10	4-point Likert scale (never to always).	0.85	Predictive	Adapted to be used with couple or parent–child relationships.[109]
Demographic characteristics and social determinants of health influence self-care.[230-234]		Collected with the Protocol for Response to and Assessing Patient Assets, Risks, and Experiences (PRAPARE).[235]	Standardized measure of individual level data		Age, race, sex, education etc. (common data elements), money, resources (food, housing), social and emotional health, support (transportation, safety)
Caregiving characteristics assessed in HF studies.[236-240]		To be collected at baseline in sociodemographic survey			Relationship to the patient, time spent caregiving (historical, daily)
Chronic conditions and medications. Interview format of the Charlson Comorbidity Index.[241]	11	Chronic conditions (most scored 1 point. Scores range from 0 to 34).[241] Self-report of medicines.	--	Predictive	Caregiver Health Characteristics: • All medications including over-the-counter and herbals, by interview. • All chronic conditions
Work performance [lost productivity due to time away from work (absenteeism) and reduced efficiency at work (presenteeism).[242] 7-day work performance questionnaire.[243]	13	Interview format. Varied (10-pt scale and dichotomous [yes/no] and number hours spent per-forming paid and unpaid work	0.73	Predictive Concurrent Construct	Caregivers will be interviewed at baseline, 3-, 6-, 9-, and 12-months to assess lost productivity.

C.11. Health care utilization outcomes: Caregivers and patients. Health care utilization of both caregivers and consenting HF patients will be obtained from the EMR for 12 months before and 12 months after randomization using a process of active surveillance **(Table 6**). The Penn Data Store will monitor inpatient and outpatient activity and generate automated reports for tracking of mortality. As EMR data may be incomplete if a person is hospitalized outside the Penn health system, caregivers will be asked about their health care use when they are telephoned at 3, 6, 9, and 12 months. If the patient in their care has provided consent, we will also ask the caregiver about HF patient hospitalizations outside the Penn health system. We will ask about all major categories of use including provider visits, hospitalizations, emergency department (ED) visits,

diagnostic and therapeutic procedures, ambulance services, and home care services received. RAs blinded to study group will perform these assessments.

Table 6. Cost Effectiveness Data to be Collected on Caregivers and HF Patients

Variable	Definition and Comment	Measures
QALYs	QALYs are derived from the SF-36 because the SF-6D based on the SF-36 is more discriminative than that derived from the SF-12.[244]	SF-36
Hospital readmission rates	Risk-standardized all-cause readmission rates (RSRR) endorsed by the National Quality Forum[245] as a measure of hospital performance and aligns with published standards for statistical models used for calculation and public reporting of health outcomes and efficiency measures.[246]	EMR
Days in the hospital	Captures the natural history of the multimorbid HF patient experience.[247] Used to describe the burden of disease from the individual and healthcare system perspectives[248] and in previous trials.[249-251] Maximal exposure of 365 days.	EMR
Resources used	Provider visits, hospitalizations, ED visits, diagnostic and therapeutic procedures, ambulance services, and home care services	EMR
Death	If we suspect that the patient is dead, we will use family, then local, then national resources to confirm.	EMR

C.12. Database Set-up and Management. REDCap (Research Electronic Data Capture) will be used as a central resource for data processing and management. REDCap is a web application and back-end database model designed to support data capture for research.[252] REDCap was developed around HIPAA-security guidelines with features such as data encryption. It provides an intuitive interface for data entry with data validation, audit trails for tracking data manipulation and export procedures, automated export procedures for seamless data downloads to common statistical packages, and procedures for importing data from external sources. We will use standard operating procedures to guide all data management activities, such as the naming of variables, data cleaning and handling of missing data. Missing fields will not be allowed except in certain pre-specified cases (e.g., income).

C.13. Power. We will enroll 250 caregivers (125 caregivers per study arm) to achieve over 90% power to detect significant overall differences in longitudinal profiles between the groups on the primary outcome of Health Self-Care Neglect Scale.[35] Assuming estimates similar to those in our pilot data, and extrapolating through 6 months, along with control group scores that also decline over time (due to interaction that comes with participation in a clinical trial) but at a slower rate than the intervention, it is assumed that ViCCY caregivers will demonstrate mean Health Self-Care Neglect scores of 3.2, 1.25, 1.1 while HI caregivers will demonstrate mean scores of 3.2, 3.0, 2.7 at baseline, 3, and 6 months, respectively. Combining the two data sets, this translates to mean scores of 1.85 and 2.97 (D=1.12) overall for intervention and control group caregivers, respectively—in line with a clinically meaningful difference equal to 0.4*SD (SD 2.8)=1.12 units.[253] We conservatively assumed that standard deviations (pilot estimates 2.5 and 1.3 at baseline and 3 months) are constant over time, equal to 2.8, and that the variance-covariance matrix pattern is generated using a mixed effects model design (congruent with the primary analytic plan) with a first-order auto-correlation parameter equal to 0.3. A design with three assessment points and 100 participants per group (200 total) achieves 99% power to test the overall between-group effect (intervention vs. control without regard to changes over time), 99% power to test the overall time effect, and 90% power to test the group x time interaction effect. All tests are based on simulations with 100 iterations, a 5% significance level, mean vectors and variance-covariance as described above. We anticipate 20% attrition based on our prior experience with the intervention, which was found to be helpful, supportive, and stress relieving rather than burdensome. Further, we will remunerate caregivers for their time and effort (see Human Subjects).

C.14. Data Analysis Plan. All analyses will use an intent-to-treat approach. Descriptive statistics will be used to characterize the sample, with measures of central tendency and variation for continuous measures, and frequencies and percentages for categorical variables. Distributional properties will be examined to determine if variance stabilizing or normalizing transformations should be applied. Non-inferential interim analyses will be performed to ensure data collection and archiving procedures are operating correctly. Outliers will be assessed by visual inspection and checked for accuracy. Once the database is locked, comparisons by group will assess for balance and identify multi-collinearity and areas requiring statistical adjustment. For comparisons involving continuous variables, homoscedasticity will be evaluated using Levine's tests. Normality will be assessed using Shapiro-Wilk tests. Should violations emerge, transformations will be applied or non-parametric tests used.

While every effort will be made to obtain complete data on every participant, some missing data are inevitable.[254] The underlying mechanism—missing completely at random (MCAR), nonignorable or not missing at random (NMAR)—will be evaluated prior to adjusting to minimize bias from missing data.[255-257] We expect most missing data to be MCAR (e.g., finding data collection burdensome). However, systematic bias may exist for those who withdraw so baseline characteristics will be compared among those with and without complete

follow-up data. To assess potential biases, we will compare withdrawal rates and time to withdrawal.[258,259] If the number lost to follow-up is small (< 5%) and the missing observations can be considered MCAR, then the primary hypotheses will be tested using the complete observed data. If missing observations cannot be assumed to be MCAR, more complex approaches will be considered such as shared parameter models[260] or random pattern-mixture models.[261-263] Sensitivity analyses for these models will be performed.[264] These approaches assume that participants dropped out for either informative (e.g., illness exacerbation) or non-informative reasons (e.g., withdrawing consent). If dropouts are informative, we will adjust for this potential bias by introducing a covariate(s) into the analysis to help to explain why participants dropped out early.

To assess changes in each of the primary and secondary outcomes over time, separate mixed effects regression models will be generated with SAS Proc Mixed.[265] We are not powered for secondary outcomes (e.g., stress, coping, health status), but we will examine effect sizes and confidence intervals (CIs) to determine if lack of power is driving nonsignificant results. Mixed models can account for correlation between repeated measures and handle non-excessive MAR or MCAR data better than traditional models and allow for use of time-independent and time-dependent covariates.[266] Both random slopes and random intercepts will be modeled to represent deviations from the average, or fixed-effect, slope over time and intercept, respectively. REML will be used for parameter estimation and the most appropriate covariance structure will be examined. Scores will be analyzed as repeated observations, with mean-centered baseline outcome scores serving as a covariate. Other predictor variables will include group, assessment time, and the interaction of group time (primary effect of interest). Baseline measures and group will be analyzed as time-independent covariates. The evaluation of differences in outcome profiles over time according to group will rely on the group x time interaction terms, while differences by the balancing variables will rely on the mixed-effects modeling of higher order interaction terms.[267-270] Statistical significance for individual intervention contrasts will be evaluated for each outcome, applying the Benjamini & Hochberg[271] method to control for the type I error rate at 5%. The Akaike information criterion (AIC)[272] will be used to evaluate overall model fit and to select the best-fitting longitudinal change pattern. We expect the groups to be balanced on baseline characteristics due to randomization; however, imbalances that occur by chance will be adjusted for in all analyses. Time-dependent covariates of perceived stress and potential moderating effects of natural support or an intervening hospitalization will be examined in exploratory models. Using methods described above, time-specific contrasts will be estimated to evaluate differences in outcome within groups at 9 and 12 months.

C.14.2. Aim 2: To estimate the cost and cost-effectiveness of ViCCY over 12 months. We hypothesize that caregivers randomized to ViCCY vs. HI only will have **H2a:** Higher QALYs measured with the SF-6D derived from the SF-36;[40] and **H2b:** Lower health care resource use. The primary outcomes of this analysis include the difference in costs (intervention cost minus cost offsets), the difference in QALYs measured with the SF-6D,[40] and the incremental cost effectiveness ratio (the difference in costs divided by the difference in QALYs). Costs will include both the costs of intervention implementation (number and length of intervention contacts, RN time to assess need for and delivery of the intervention, technology expenses, supervision time, and initial training). Cost offsets include the costs of health care (detailed below) and the difference in workplace productivity collected for both study groups. QALYs will be used to assess effectiveness. We hypothesize that compared to HI, ViCCY will require more resources for intervention implementation, but will reduce use of other health care resources. It is unclear if the changes in health care resource use or labor productivity will fully offset the intervention implementation costs (leading to a finding of dominance: lower cost and greater effect) or if net costs will be positive (leading to a finding of cost-effectiveness). We will follow a micro-costing approach in which all clinically relevant resources used in the study groups will be tracked and converted to costs using appropriate price weights.

We will obtain and summarize all health care use and convert it to payer costs (i.e., a payer's perspective) by use of Medicare fees. Many, if not most, of the anticipated participants will be over 65 years old, which makes Medicare fees appropriate for the analysis. Fees will be derived from the last study year, so there will be no need to adjust for inflation. Because follow-up will be for a year, at most, there will be no need to discount costs. Medication costs will be based on average wholesale prices adjusted to average sales prices as reported by the U.S. Office of the Inspector General.[273] We will evaluate the effect of a reasonable range of private sector cost estimates in sensitivity analyses. Costing methods will adhere to standards proposed by the US Public Health Service-sponsored Panel on Cost-Effectiveness in Health and Medicine.[98] Resources and costs associated with research and data collection will be excluded from analyses. Sensitivity analyses will be performed using self-reported information on key variables (e.g., exploring alternative outcomes across a range of outcome CIs). We have used these procedures successfully in prior studies.[8,274,275]

Resource utilization and cost comparisons will be examined overall and by resource category over four

time periods (0-3 months, 3-6 months, 6-9 months; and 9-12 months), with the main outcome at one year. Statistical comparisons will be performed using generalized estimating equations (GEE) with links selected using the Pearson correlation test, the Pregibon link test, and the modified Hosmer and Lemeshow test, and families selected using the modified Park test.[276] Estimates of average total treatment costs and QALYs will be generated separately for each group. Non-parametric 95% CIs will be determined for group differences in mean total costs using empirical sampling distributions (1,000 iterations) generated with bootstrapping methodology with replacement.[277,278] We will compute a non-parametric two-sided p-value based on the empirical sampling distribution. Differences in cost and QALYs will be used to calculate the incremental cost-effectiveness ratio. Reported measures of sampling uncertainty for this ratio will include 1) the plot of the joint distribution of the difference in cost and effect on the cost-effectiveness plane, 2) the confidence interval for the cost-effectiveness ratio calculated by use of the Fieller's theorem method, and 3) the acceptability curve.[98] Sensitivity analysis is a critical component of an economic evaluation since all assumptions and parameter estimates have uncertain precision.[98] As more than one approach is often available to monetize outcomes, we will calculate a lower and upper bound estimate, as relevant, for the benefit (QALYs) and cost calculations. We will combine this series of sensitivity analyses to form a lower and upper bound estimate for preliminary ICER.

C.14.3. Aim 3 (Exploratory): To explore the effect of caregiver outcomes (self-care, stress, coping, health status) on HF patient outcomes. We hypothesize that at 12 months, HF patients whose caregivers improve vs. not improve in self-care (regardless of group) will have **H3a:** Lower hospitalization rates; **H3b:** Fewer hospital days; **H3c:** Lower mortality rates; and **H3d:** Higher QALYs measured with the SF-6D.[40] We will analyze number of hospitalizations and days in the hospital using GEE regression models with the Poisson distribution as the working outcome distribution. GEE allows for modeling of the marginal distribution of each outcome variable as a function of the caregiver predictor of interest over time, and accounts for the likely correlations of the repeated outcome measures for each participant. An approach similar to that described for Aim 1 will be used within the GEE framework (different correlation structures will be examined, baseline outcomes will be included as a covariate).

We will measure time to death from date of the caregiver's enrollment in the study to the date of patient death. Patients remaining free from an event will be censored at their last follow-up. Kaplan-Meier estimates will be plotted to provide a visual demonstration of time to death by group (categorized caregiver outcomes), and the log-rank test will be used for comparisons. GEE and frailty type multivariable modeling will be applied to time-to-event data within the context of equally spaced time intervals.[279-281] This approach allows for the addition of a random effect to a general Cox proportional hazards model to account for the likely correlation of repeated measures for each study participant while also accounting for censoring.

QALYs will be analyzed using mixed effects regression modeling. As described above, scores will be analyzed as repeated observations, with mean-centered baseline outcome scores serving as a covariate. Other predictor variables will include time-dependent caregiver variables, assessment time, and the corresponding two-way interaction term (primary effect of interest). Statistically significant findings will be concluded on the basis of a two-sided 0.05 level of significance, recognizing these analyses are exploratory in nature and findings will be used to generate hypotheses. Finally, we will examine the effect of caregiver outcome on HF patient outcomes in patient-caregiver dyads using the Actor-Partner Interdependence Model.[282]

C.15. Methodological challenges. We have considered the following methodological challenges:

1. There is the possibility of differential compliance with the protocol – for instance, if the HF patient has an exacerbation that distracts the caregiver and interferes with the intervention or assessments. We will allow some flexibility in the timing of ViCCY sessions to accommodate such events and increase the generalizability of study results. Caregivers in the ViCCY arm will be able to schedule calls with the RN coach during day, evening, and weekend hours to limit stress from study participation. For both arms, we will allow data collection calls to be completed up to two weeks before or after the planned contact date to accommodate schedules. We will collect data on cancelled and delayed events for later analysis and adjust for delays and the dose of intervention received in analyses.
2. A threat to validity includes the potential for the control group to receive a level of natural support sufficient to interfere with our ability to detect treatment effects from ViCCY.[283] We will interview participants about naturally occurring support so that we can adjust for this in the analysis if needed.
3. We may have difficulty enrolling the most stressed and burdened caregivers who may see the trial as one more demand; however, in pilot testing we found that caregivers were grateful for the support.
4. It is possible that the patient could die during the year in the study; half of all HF patients die within 5 years.[11] Should this occur, the caregiver will be dropped from the study.

LITERATURE CITED

1. Lindqvist G, Hakansson A, Petersson K. Informal home caregiving in a gender perspective: A selected literature review. *VÅRD I NORDEN.* 2004;24(4):26-30.
2. Family Caregiver Alliance. Definitions. 2014.
3. Wallhagen MI. Caregiving demands: their difficulty and effects on the well-being of elderly caregivers. *Scholarly inquiry for nursing practice.* 1992;6(2):111-127; discussion 129-133.
4. Haley WE, Roth DL, Howard G, Safford MM. Caregiving strain and estimated risk for stroke and coronary heart disease among spouse caregivers: differential effects by race and sex. *Stroke.* 2010;41(2):331-336.
5. Lee S, Colditz GA, Berkman LF, Kawachi I. Caregiving and risk of coronary heart disease in U.S. women: a prospective study. *Am J Prev Med.* 2003;24(2):113-119.
6. Mausbach BT, von Kanel R, Aschbacher K, et al. Spousal caregivers of patients with Alzheimer's disease show longitudinal increases in plasma level of tissue-type plasminogen activator antigen. *Psychosom Med.* 2007;69(8):816-822.
7. Schulz R, Beach SR. Caregiving as a risk factor for mortality: the Caregiver Health Effects Study. *JAMA.* 1999;282(23):2215-2219.
8. Coe NB, Van Houtven CH. Caring for mom and neglecting yourself? The health effects of caring for an elderly parent. *Health economics.* 2009;18(9):991-1010.
9. Riegel B, Jaarsma T, Stromberg A. A middle-range theory of self-care of chronic illness. *ANS Adv Nurs Sci.* 2012;35(3):194-204.
10. Acton GJ. Health-promoting self-care in family caregivers. *West J Nurs Res.* 2002;24(1):73-86.
11. Benjamin EJ, Blaha MJ, Chiuve SE, et al. Heart Disease and Stroke Statistics-2017 Update: A Report From the American Heart Association. *Circulation.* 2017;135(10):e146-e603.
12. Pressler SJ, Gradus-Pizlo I, Chubinski SD, et al. Family caregiver outcomes in heart failure. *Am J Crit Care.* 2009;18(2):149-159.
13. Stromberg A, Luttik ML. Burden of caring: risks and consequences imposed on caregivers of those living and dying with advanced heart failure. *Curr Opin Support Palliat Care.* 2015;9(1):26-30.
14. Buck HG, Mogle J, Riegel B, McMillan S, Bakitas M. Exploring the Relationship of Patient and Informal Caregiver Characteristics with Heart Failure Self-Care Using the Actor-Partner Interdependence Model: Implications for Outpatient Palliative Care. *J Palliat Med.* 2015;18(12):1026-1032.
15. Gomes B, Calanzani N, Curiale V, McCrone P, Higginson IJ. Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers. *Cochrane Database Syst Rev.* 2013(6):Cd007760.
16. Saunders MM. Family caregivers need support with heart failure patients. *Holist Nurs Pract.* 2003;17(3):136-142.
17. Luttik ML, Jaarsma T, Veeger N, Tijssen J, Sanderman R, van Veldhuisen DJ. Caregiver burden in partners of Heart Failure patients; limited influence of disease severity. *Eur J Heart Fail.* 2007;9(6-7):695-701.
18. Molloy GJ, Johnston DW, Witham MD. Family caregiving and congestive heart failure. Review and analysis. *Eur J Heart Fail.* 2005;7(4):592-603.
19. Usher BM, Cammarata K. Heart failure and family caregiver burden: an update. *Progress in Cardiovascular Nursing.* 2009;24(3):113-114.
20. McIlfatrick S, Doherty LC, Murphy M, et al. 'The importance of planning for the future': Burden and unmet needs of caregivers' in advanced heart failure: A mixed methods study. *Palliat Med.* 2017:269216317743958.
21. Olsen JM, Nesbitt BJ. Health coaching to improve healthy lifestyle behaviors: an integrative review. *Am J Health Promot.* 2010;25(1):e1-e12.
22. Chen HM, Huang MF, Yeh YC, Huang WH, Chen CS. Effectiveness of coping strategies intervention on caregiver burden among caregivers of elderly patients with dementia. *Psychogeriatrics.* 2015;15(1):20-25.
23. Dickson VV, Melkus GD, Katz S, et al. Building skill in heart failure self-care among community dwelling older adults: results of a pilot study. *Patient Educ Couns.* 2014;96(2):188-196.
24. Wayne N, Perez DF, Kaplan DM, Ritvo P. Health Coaching Reduces HbA1c in Type 2 Diabetic Patients From a Lower-Socioeconomic Status Community: A Randomized Controlled Trial. *J Med Internet Res.* 2015;17(10):e224.

25. Sathe A, Flowers E, Mathur A, et al. A culturally specific health coaching program targeting cardiovascular disease risk in South Asians: rationale, design, and baseline data. *Ethn Dis.* 2013;23(3):304-309.
26. Hale R, Giese J. Cost-Effectiveness of Health Coaching: An Integrative Review. *Professional case management.* 2017;22(5):228-238.
27. Van Houtven CH, Smith VA, Stechuchak KM, et al. Comprehensive Support for Family Caregivers: Impact on Veteran Health Care Utilization and Costs. *Med Care Res Rev.* 2017:1077558717697015.
28. Schwarz KA, Elman CS. Identification of factors predictive of hospital readmissions for patients with heart failure. *Heart Lung.* 2003;32(2):88-99.
29. Bidwell JT, Vellone E, Lyons KS, et al. Caregiver determinants of patient clinical event risk in heart failure. *Eur J Cardiovasc Nurs.* 2017;16(8):707-714.
30. Saunders MM. Perspectives from family caregivers receiving home nursing support: findings from a qualitative study of home care patients with heart failure. *Home Healthc Nurse.* 2012;30(2):82-90.
31. O'Neil A, Hawkes AL, Atherton JJ, et al. Telephone-delivered health coaching improves anxiety outcomes after myocardial infarction: the 'ProActive Heart' trial. *Eur J Prev Cardiol.* 2014;21(1):30-38.
32. Leveille SG, Huang A, Tsai SB, Allen M, Weingart SN, Iezzoni LI. Health coaching via an internet portal for primary care patients with chronic conditions: a randomized controlled trial. *Medical care.* 2009;47(1):41-47.
33. Glasgow RE, Nutting PA, Toobert DJ, et al. Effects of a brief computer-assisted diabetes self-management intervention on dietary, biological and quality-of-life outcomes. *Chronic illness.* 2006;2(1):27-38.
34. Hilty DM, Ferrer DC, Parish MB, Johnston B, Callahan EJ, Yellowlees PM. The effectiveness of telemental health: a 2013 review. *Telemedicine Journal & E-Health.* 2013;19(6):444-454.
35. Boise L. Health Self-Care Neglect Scale. *Empowering family caregivers: The powerful tools for caregiving program. Educational Gerontology, 31, 573-586.*2005.
36. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav.* 1983;24(4):385-396.
37. Folkman S, Lazarus R. Manual for the Ways of Coping questionnaire *Research Edition*. Palo Alto, CA: Consulting Psychologists; 1988.
38. Sherer RF, Weibe FA, Luther DC, Adams JS. Dimensionality of coping: Factor stability using the Ways of Coping Questionnaire. . *Psychological Reports.* 1988;62:763-700.
39. McHorney CA, Ware JE, Jr., Raczek AE. The MOS 36-Item Short-Form Health Survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Medical care.* 1993;31(3):247-263.
40. Sayah FA, Qiu W, Xie F, Johnson JA. Comparative performance of the EQ-5D-5L and SF-6D index scores in adults with type 2 diabetes. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2017;26(8):2057-2066.
41. Hoefman RJ, Meulenkamp TM, De Jong JD. Who is responsible for providing care? Investigating the role of care tasks and past experiences in a cross-sectional survey in the Netherlands. *BMC health services research.* 2017;17(1):477.
42. Reinhard SC, Feinberg LS, Choula R, Houser A, Institute APP. *Valuing the invaluable: 2015 update: Undeniable progress, but big gaps remain.* 2015.
43. Davis LL, Gilliss CL, Deshefy-Longhi T, Chestnutt DH, Molloy M. The nature and scope of stressful spousal caregiving relationships. *Journal of family nursing.* 2011;17(2):224-240.
44. Ostwald SK, Bernal MP, Cron SG, Godwin KM. Stress experienced by stroke survivors and spousal caregivers during the first year after discharge from inpatient rehabilitation. *Top Stroke Rehabil.* 2009;16(2):93-104.
45. Furlong KE, Wuest J. Self-care behaviors of spouses caring for significant others with Alzheimer's disease: the emergence of self-care worthiness as a salient condition. *Qual Health Res.* 2008;18(12):1662-1672.
46. Lu YF, Wykle M. Relationships between caregiver stress and self-care behaviors in response to symptoms. *Clin Nurs Res.* 2007;16(1):29-43.
47. Ortiz N, Lamdan R, Johnson S, Korbage A. Caregiver status: a potential risk factor for extreme self-neglect. *Psychosomatics.*50(2):166-168.
48. Gallant MP, Connell CM. Predictors of decreased self-care among spouse caregivers of older adults with dementing illnesses. *J Aging Health.* 1997;9(3):373-395.

49. Kim Y, Wellisch DK, Spillers RL, Crammer C. Psychological distress of female cancer caregivers: effects of type of cancer and caregivers' spirituality. *Support Care Cancer.* 2007;15(12):1367-1374.
50. Eriksson M, Svedlund M. 'The intruder': spouses' narratives about life with a chronically ill partner. *J Clin Nurs.* 2006;15(3):324-333.
51. Baumgarten M. The health of persons giving care to the demented elderly: a critical review of the literature. *J Clin Epidemiol.* 1989;42(12):1137-1148.
52. Bergman-Evans B. A health profile of spousal Alzheimer's caregivers. Depression and physical health characteristics. *J Psychosoc Nurs Ment Health Serv.* 1994;32(9):25-30.
53. Wykle ML. The physical and mental health of women caregivers of older adults. *J Gerontol Nurs.* 1994;20(3):48-49.
54. Jutras S, Lavoie JP. Living with an impaired elderly person: the informal caregiver's physical and mental health. *J Aging Health.* 1995;7(1):46-73.
55. National Academies of Sciences E, and Medicine,. *Families Caring for an Aging America.* Washington, DC: The National Academies Press; 2016.
56. Wiener L, Viola A, Kearney J, et al. Impact of Caregiving for a Child With Cancer on Parental Health Behaviors, Relationship Quality, and Spiritual Faith: Do Lone Parents Fare Worse? *J Pediatr Oncol Nurs.* 2015.
57. von Kanel R, von Kanel R. Psychological distress and cardiovascular risk: what are the links? *J Am Coll Cardiol.* 2008;52(25):2163-2165.
58. Wang X, Robinson KM, Hardin HK. The Impact of Caregiving on Caregivers' Medication Adherence and Appointment Keeping. *West J Nurs Res.* 2015;37(12):1548-1562.
59. Sisk RJ. Caregiver burden and health promotion. *Int J Nurs Stud.* 2000;37(1):37-43.
60. Davidson PM, Abernethy AP, Newton PJ, Clark K, Currow DC. The caregiving perspective in heart failure: a population based study. *BMC health services research.* 2013;13:342.
61. Alosco ML, Spitznagel MB, Cohen R, et al. Reduced cognitive function predicts functional decline in patients with heart failure over 12 months. *Eur J Cardiovasc Nurs.* 2014;13(4):304-310.
62. Dionne-Odom JN, Kono A, Frost J, et al. Translating and testing the ENABLE: CHF-PC concurrent palliative care model for older adults with heart failure and their family caregivers. *J Palliat Med.* 2014;17(9):995-1004.
63. Collins LG, Swartz K. Caregiver care. *Am Fam Physician.* 2011;83(11):1309-1317.
64. Opasich C, Gualco A, De Feo S, et al. Physical and emotional symptom burden of patients with end-stage heart failure: what to measure, how and why. *J Cardiovasc Med (Hagerstown).* 2008;9(11):1104-1108.
65. Zambroski CH, Moser DK, Bhat G, Ziegler C. Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. *Eur J Cardiovasc Nurs.* 2005;4(3):198-206.
66. Pressler SJ, Subramanian U, Kareken D, et al. Cognitive deficits in chronic heart failure. *Nurs Res.* 2010;59(2):127-139.
67. Chung ML, Lennie TA, Mudd-Martin G, Dunbar SB, Pressler SJ, Moser DK. Depressive symptoms in patients with heart failure negatively affect family caregiver outcomes and quality of life. *Eur J Cardiovasc Nurs.* 2016;15(1):30-38.
68. Wingham J, Frost J, Britten N, et al. Needs of caregivers in heart failure management: A qualitative study. *Chronic illness.* 2015;11(4):304-319.
69. Sagerian M, Riegel B, Burt S, Yamada A. Caregiver Burden in Hispanic and Non-Hispanic Whites with Heart Failure. Paper presented at: Heart Failure Society of America; September, 2002, 2002; Boca Raton, FL.
70. Hupcey JE, Fenstermacher K, Kitko L, Penrod J. Achieving medical stability: Wives' experiences with heart failure. *Clinical Nursing Research.* 2010;19(3):211-229.
71. Sigafus M, Riegel B. Riding the Roller-Coaster: Experiences of Caregivers of Adults with Heart Failure. Penn-ICOWHI 18th International Congress on Women's Health; "Cities and Women's Health: Global Perspectives"; April 7- 10, 2010, 2010; University of Pennsylvania, Philadelphia, PA, USA.
72. Freydberg N, Strain L, Tsuyuki RT, McAlister FA, Clark AM. "If he gives in, he will be gone...": the influence of work and place on experiences, reactions and self-care of heart failure in rural Canada. *Social Science & Medicine.* 2010;70(7):1077-1083.
73. Buck HG, Harkness K, Wion R, et al. Caregivers' contributions to heart failure self-care: a systematic review. *Eur J Cardiovasc Nurs.* 2015;14(1):79-89.

74. Luttik ML, Jaarsma T, Veeger NJGM, van Veldhuisen DJ. For better and for worse: Quality of life impaired in HF patients as well as in their partners. *Eur J Cardiovasc Nurs.* 2005;4(1):11-14.
75. Levenson JW, McCarthy EP, Lynn J, Davis RB, Phillips RS. The last six months of life for patients with congestive heart failure. *Journal of the American Geriatrics Society.* 2000;48(5 Suppl):S101-109.
76. Evangelista LS, Stromberg A, Dionne-Odom JN. An integrated review of interventions to improve psychological outcomes in caregivers of patients with heart failure. *Curr Opin Support Palliat Care.* 2015.
77. Malik FA, Gysels M, Higginson IJ. Living with breathlessness: a survey of caregivers of breathless patients with lung cancer or heart failure. *Palliat Med.* 2013;27(7):647-656.
78. Vellone E, Chung ML, Cocchieri A, Rocco G, Alvaro R, Riegel B. Effects of Self-Care on Quality of Life in Adults with Heart Failure and Their Spousal Caregivers: Testing Dyadic Dynamics using the Actor-Partner Interdependence Model. *Journal of family nursing.* 2014;20(1):120-141.
79. Pressler SJ, Jung M, Friedman J. Heart failure and debilitating cardiovascular problems In: Burgio LD, Gaugler JE, Hilgeman MM, eds. *The spectrum of family caregiving for adults and elders with chronic illness*. New York, NY: Oxford University Press; 2016.
80. Liljeroos M, Agren S, Jaarsma T, Arestedt K, Stromberg A. Long-term effects of a dyadic psycho-educational intervention on caregiver burden and morbidity in partners of patients with heart failure: a randomized controlled trial. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2017;26(2):367-379.
81. Srisuk N, Cameron J, Ski CF, Thompson DR. Randomized controlled trial of family-based education for patients with heart failure and their carers. *Journal of advanced nursing.* 2017;73(4):857-870.
82. Evangelista LS, Stromberg A, Dionne-Odom JN. An integrated review of interventions to improve psychological outcomes in caregivers of patients with heart failure. *Curr Opin Support Palliat Care.* 2016;10(1):24-31.
83. Piette JD, Striplin D, Marinec N, Chen J, Aikens JE. A randomized trial of mobile health support for heart failure patients and their informal caregivers: impacts on caregiver-reported outcomes. *Medical care.* 2015;53(8):692-699.
84. Hughes SL, Weaver FM, Giobbie-Hurder A, et al. Effectiveness of team-managed home-based primary care: a randomized multicenter trial. *Journal of the American Medical Association.* 2000;284(22):2877-2885.
85. Molloy GJ, Johnston DW, Gao C, et al. Effects of an exercise intervention for older heart failure patients on caregiver burden and emotional distress. *European Journal of Cardiovascular Prevention & Rehabilitation.* 2006;13(3):381-387.
86. Zarit S, Femia E. Behavioral and psychosocial interventions for family caregivers. *Am J Nurs.* 2008;108(9 Suppl):47-53; quiz 53.
87. Grant I, McKibbin CL, Taylor MJ, et al. In-home respite intervention reduces plasma epinephrine in stressed Alzheimer caregivers. *Am J Geriatr Psychiatry.* 2003;11(1):62-72.
88. Hardy VL, Riffle KL. Support for caregivers of dependent elderly. A support group can help a dependent elderly person by helping a caregiver overcome feelings of social isolation. *Geriatr Nurs.* 1993;14(3):161-164.
89. Hayes L, Hawthorne G, Farhall J, O'Hanlon B, Harvey C. Quality of Life and Social Isolation Among Caregivers of Adults with Schizophrenia: Policy and Outcomes. *Community mental health journal.* 2015;51(5):591-597.
90. Dunbar SB, Jacobson LH, Deaton C. Heart failure: strategies to enhance patient self-management. *AACN clinical issues.* 1998;9(2):244-256.
91. Dennis CL, Dowswell T. Psychosocial and psychological interventions for preventing postpartum depression. *Cochrane Database Syst Rev.* 2013;2(2):CD001134.
92. Thrasher S, Power M, Morant N, Marks I, Dalgleish T. Social support moderates outcome in a randomized controlled trial of exposure therapy and (or) cognitive restructuring for chronic posttraumatic stress disorder. *Canadian journal of psychiatry Revue canadienne de psychiatrie.* 2010;55(3):187-190.
93. Chi NC, Demiris G. A systematic review of telehealth tools and interventions to support family caregivers. *Journal of telemedicine and telecare.* 2015;21(1):37-44.
94. Hu C, Kung S, Rummans TA, Clark MM, Lapid MI. Reducing caregiver stress with internet-based interventions: a systematic review of open-label and randomized controlled trials. *J Am Med Inform Assoc.* 2015;22(e1):e194-209.

95. Ryan C, Lewis JM. *Computer and Internet Use in the United States: 2015 American Community Survey Reports.* U.S. Department of Commerce Economics and Statistics Administration; September 2017.
96. Finkelstein SM, Ratner E. Managing chronic disease through home telehealth. *Minn Med.* 2006;89(11):42-45.
97. Olazaran J, Reisberg B, Clare L, et al. Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy. *Dement Geriatr Cogn Disord.* 2010;30(2):161-178.
98. Gold M, Siegel J, Russell L, Weinstein M, eds. *Cost-effectiveness in health and medicine.* New York, NY: Oxford University Press; 1996.
99. Livingston G, Barber J, Rapaport P, et al. START (STrAtegies for RelaTives) study: a pragmatic randomised controlled trial to determine the clinical effectiveness and cost-effectiveness of a manual-based coping strategy programme in promoting the mental health of carers of people with dementia. *Health technology assessment.* 2014;18(61):1-242.
100. Knapp M, King D, Romeo R, et al. Cost effectiveness of a manual based coping strategy programme in promoting the mental health of family carers of people with dementia (the START (STrAtegies for RelaTives) study): a pragmatic randomised controlled trial. *Bmj.* 2013;347:f6342.
101. Warmerdam L, Smit F, van Straten A, Riper H, Cuijpers P. Cost-utility and cost-effectiveness of internet-based treatment for adults with depressive symptoms: randomized trial. *J Med Internet Res.* 2010;12(5):e53.
102. Joo H, Fang J, Losby JL, Wang G. Cost of informal caregiving for patients with heart failure. *Am Heart J.* 2015;169(1):142-148.e142.
103. Lyons KS, Zarit SH, Sayer AG, Whitlatch CJ. Caregiving as a dyadic process: perspectives from caregiver and receiver. *The journals of gerontology Series B, Psychological sciences and social sciences.* 2002;57(3):P195-204.
104. Al-Rawashdeh SY, Lennie TA, Chung ML. Sleep Disturbance Association With Quality of Life in Heart Failure Patients-Caregivers Dyads. *West J Nurs Res.* 2016.
105. Bidwell JT, Vellone E, Lyons KS, et al. Determinants of Heart Failure Self-Care Maintenance and Management in Patients and Caregivers: A Dyadic Analysis. *Res Nurs Health.* 2015;38(5):392-402.
106. Lee CS, Vellone E, Lyons KS, et al. Patterns and predictors of patient and caregiver engagement in heart failure care: a multi-level dyadic study. *Int J Nurs Stud.* 2015;52(2):588-597.
107. Retrum JH, Nowels CT, Bekelman DB. Patient and caregiver congruence: the importance of dyads in heart failure care. *J Cardiovasc Nurs.* 2013;28(2):129-136.
108. Agren S, Evangelista LS, Hjelm C, Stromberg A. Dyads affected by chronic heart failure: a randomized study evaluating effects of education and psychosocial support to patients with heart failure and their partners. *Journal of cardiac failure.* 2012;18(5):359-366.
109. Winter L, Moriarty HJ. Quality of relationship between veterans with traumatic brain injury and their family members. *Brain Inj.* 2017;31(4):493-501.
110. Kitko LA, Hupcey JE, Pinto C, Palese M. Patient and Caregiver Incongruence in Advanced Heart Failure. *Clin Nurs Res.* 2015;24(4):388-400.
111. Hopp FP, Marsack C, Camp JK, Thomas S. Go to the hospital or stay at home? A qualitative study of expected hospital decision making among older African Americans with advanced heart failure. *Journal of gerontological social work.* 2014;57(1):4-23.
112. Vellone E, Chung ML, Cocchieri A, Rocco G, Alvaro R, Riegel B. Effects of self-care on quality of life in adults with heart failure and their spousal caregivers: testing dyadic dynamics using the actor-partner interdependence model. *Journal of family nursing.* 2014;20(1):120-141.
113. Hooker SA, Grigsby ME, Riegel B, Bekelman DB. The Impact of Relationship Quality on Health-Related Outcomes in Heart Failure Patients and Informal Family Caregivers: An Integrative Review. *J Cardiovasc Nurs.* 2015;30(4 Suppl 1):S52-63.
114. Kociol RD, Liang L, Hernandez AF, et al. Are we targeting the right metric for heart failure? Comparison of hospital 30-day readmission rates and total episode of care inpatient days. *Am Heart J.* 2013;165(6):987-994 e981.
115. Dharmarajan K, Hsieh AF, Lin Z, et al. Diagnoses and timing of 30-day readmissions after hospitalization for heart failure, acute myocardial infarction, or pneumonia. *JAMA.* 2013;309(4):355-363.
116. Dunlay SM, Redfield MM, Weston SA, et al. Hospitalizations after heart failure diagnosis a community perspective. *J Am Coll Cardiol.* 2009;54(18):1695-1702.

117. Ross JS, Chen J, Lin Z, et al. Recent national trends in readmission rates after heart failure hospitalization. *Circ Heart Fail.* 2010;3(1):97-103.
118. Kazi DS, Mark DB. The economics of heart failure. *Heart Fail Clin.* 2013;9(1):93-106.
119. Heidenreich PA, Albert NM, Allen LA, et al. Forecasting the Impact of Heart Failure in the United States: A Policy Statement From the American Heart Association. *Circ Heart Fail.* 2013.
120. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. *NEnglJMed.* 2009;360(14):1418-1428.
121. Lazarus R, Folkman S. *Stress, appraisal and coping.* New York: Springer; 1984.
122. Glanz K, Schwartz MD. Stress, coping, and health behavior. In: Glanz K, Rimer BK, Viswanath K, eds. *Health Behavior and Health Education: Theory, Research, and Practice*. 4th ed. San Francisco, CA: Jossey-Bass; 2008.
123. Clark AP, McDougall G, Riegel B, et al. Health Status and Self-care Outcomes After an Education-Support Intervention for People With Chronic Heart Failure. *J Cardiovasc Nurs.* 2015;30(4 Suppl 1):S3-13.
124. Lee CS, Suwanno J, Riegel B. The relationship between self-care and health status domains in Thai patients with heart failure. *Eur J Cardiovasc Nurs.* 2009;8(4):259-266.
125. Piette JD, Striplin D, Marinec N, et al. A Mobile Health Intervention Supporting Heart Failure Patients and Their Informal Caregivers: A Randomized Comparative Effectiveness Trial. *J Med Internet Res.* 2015;17(6):e142.
126. Williams VP, Bishop-Fitzpatrick L, Lane JD, et al. Video-based coping skills to reduce health risk and improve psychological and physical well-being in Alzheimer's disease family caregivers. *Psychosom Med.* 2010;72(9):897-904.
127. Schulz R, Sherwood PR. Physical and mental health effects of family caregiving. *Am J Nurs.* 2008;108(9 Suppl):23-27; quiz 27.
128. Saunders MM. Factors associated with caregiver burden in heart failure family caregivers. *West J Nurs Res.* 2008;30(8):943-959.
129. Schwarz KA, Dunphy G. An examination of perceived stress in family caregivers of older adults with heart failure. *Experimental aging research.* 2003;29(2):221-235.
130. Ogbera A, Adeyemi-Doro A. Emotional distress is associated with poor self care in type 2 diabetes mellitus. *J Diabetes.* 2011;3(4):348-352.
131. Epel ES. Psychological and metabolic stress: a recipe for accelerated cellular aging? *Hormones (Athens).* 2009;8(1):7-22.
132. Olson KE, O'Brien MA, Rogers WA, Charness N. Diffusion of Technology: Frequency of Use for Younger and Older Adults. *Ageing international.* 2011;36(1):123-145.
133. Mitzner TL, Boron JB, Fausset CB, et al. Older Adults Talk Technology: Technology Usage and Attitudes. *Computers in human behavior.* 2010;26(6):1710-1721.
134. Hall AK, Stellefson M, Bernhardt JM. Healthy Aging 2.0: the potential of new media and technology. *Prev Chronic Dis.* 2012;9:E67.
135. Schulz R, Wahl HW, Matthews JT, De Vito Dabbs A, Beach SR, Czaja SJ. Advancing the Aging and Technology Agenda in Gerontology. *Gerontologist.* 2015;55(5):724-734.
136. Joyce K, Loe M. A sociological approach to ageing, technology and health. *Sociology of health & illness.* 2010;32(2):171-180.
137. Harris J, Regmi S. Ageism and equality. *J Med Ethics.* 2012;38(5):263-266.
138. Bowles K, Hanlon A, Glick HA, et al. Clinical Effectiveness, Access to and Satisfaction with Care using a Telehomecare Substitution Intervention: A Randomized Controlled Trial. *International Journal of Telemedicine and Applications.* 2011:1-13.
139. Bowles KH, Riegel B, Weiner MG, Glick H, Naylor MD. The effect of telehomecare on heart failure self care. *AMIA Annu Symp Proc.* 2010;2010:71-75.
140. Bowles KH, Riegel B, Weiner MG, Glick H, Naylor MD. The Effect of Telehealth on Heart Failure Self Care. *American Medical Informatics Association Annual Symposium Proceedings* 2010:71-75.
141. Dickson VV, Knafl GJ, Wald J, Riegel B. Racial Differences in Clinical Treatment and Self-Care Behaviors of Adults With Chronic Heart Failure. *J Am Heart Assoc.* 2015;4(4).
142. Riegel BB, Dickson VV, Knafl GJ, Wald J. Racial differences in clinical treatment and self-care behaviors of adults with chronic heart failure. *European Journal of Heart Failure.* 2015;17:168-168.
143. Riegel B, Hanlon AL, Zhang X, et al. What is the Best Measure of Daytime Sleepiness in Adults with Heart Failure? *J Amer Acad Nurs Pract.* 2013;25(5):272-279.

144. Tkacs NC, Pien G, Hanlon AL, et al. Assessing the interaction between sleep, stress, and catecholamines - a home-based feasibility study. 2011.
145. Brewster G, Hirschman K, Riegel B, et al. Association of Health-Related Quality of Life Domains with Daytime Sleepiness among Older Adult Recipients of Long-Term Services and Supports. under review.
146. Riegel B, Dickson VV, Hoke L, McMahon JP, Reis BF, Sayers S. A motivational counseling approach to improving heart failure self-care: mechanisms of effectiveness. *J Cardiovasc Nurs.* 2006;21(3):232-241.
147. Masterson Creber R, Patey M, Dickson VV, DeCesaris M, Riegel B. Motivational Interviewing Tailored Interventions for Heart Failure (MITI-HF): study design and methods. *Contemp Clin Trials.* 2015;41:62-68.
148. Riegel B, Lee CS, Dickson VV, Carlson B. An update on the self-care of heart failure index. *J Cardiovasc Nurs.* 2009;24(6):485-497.
149. Masterson Creber R, Patey M, Lee CS, Kuan A, Riegel B. Motivational Interviewing Tailored Interventions for Heart Failure (MITI-HF): Randomized Controlled Trial. *Patient Educ Couns.* 2015.
150. Riegel B, Christiansen K, Fontana S, et al. Cognitive Behavioral Therapy by iPad for Caregivers: A Pilot Study. 2013; Heart Failure Society of America.
151. Bowles KH, Dansky KH. Teaching self-management of diabetes via telehomecare. *Home Healthc Nurse.* 2002;20(1):36-42.
152. Bowles KH, Baugh AC. Applying research evidence to optimize telehomecare. *J Cardiovasc Nurs.* 2007;22(1):5-15.
153. Bowles KH, Hanlon AL, Glick HA, et al. Clinical effectiveness, access to, and satisfaction with care using a telehomecare substitution intervention: a randomized controlled trial. *Int J Telemed Appl.* 2011;2011:540138.
154. Schrank B, Ebert-Vogel A, Amering M, et al. Gender differences in caregiver burden and its determinants in family members of terminally ill cancer patients. *Psychooncology.* 2016;25(7):808-814.
155. Eyre V, Lang CC, Smith K, et al. Rehabilitation Enablement in Chronic Heart Failure-a facilitated self-care rehabilitation intervention in patients with heart failure with preserved ejection fraction (REACH-HFpEF) and their caregivers: rationale and protocol for a single-centre pilot randomised controlled trial. *BMJ Open.* 2016;6(10):e012853.
156. Baldwin BA, Kleeman KM, Stevens GL, Rasin J. Family caregiver stress: clinical assessment and management. *International psychogeriatrics / IPA.* 1989;1(2):185-194.
157. Schulz CH, Godwin KM, Hersch GI, Hyde LK, Irabor JJ, Ostwald SK. Return to work predictors of stroke survivors and their spousal caregivers. *Work.* 2017;57(1):111-124.
158. Riegel B, Glaser D, Richards K, et al. Modifiable factors associated with sleep dysfunction in adults with heart failure. *Eur J Cardiovasc Nurs.* 2012;11(4):402-409.
159. Riegel B, Lee CS, Ratcliffe SJ, et al. Predictors of objectively measured medication nonadherence in adults with heart failure. *Circ Heart Fail.* 2012;5(4):430-436.
160. Riegel B, Moelter ST, Ratcliffe SJ, et al. Excessive daytime sleepiness is associated with poor medication adherence in adults with heart failure. *Journal of cardiac failure.* 2011;17(4):340-348.
161. Riegel B, Ratcliffe SJ, Weintraub WS, et al. Double jeopardy: the influence of excessive daytime sleepiness and impaired cognition on health-related quality of life in adults with heart failure. *European Journal of Heart Failure.* 2012;14(7):730-736.
162. Braunstein JB, Anderson GF, Gerstenblith G, al. e. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. *J Am College Cardiology.* 2003;42(7):1226-1233.
163. Ceia F, Fonseca C, Mota T, et al. Aetiology, comorbidity and drug therapy of chronic heart failure in the real world: the EPICA substudy. *European Journal of Heart Failure.* 2004;6(6):801-806.
164. Page RL, 2nd, Lindenfeld J. The comorbidity conundrum: a focus on the role of noncardiovascular chronic conditions in the heart failure patient. *Current cardiology reports.* 2012;14(3):276-284.
165. Charlson M, Pompei P, Ales K, MacKenzie C. A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *J Chronic Dis.* 1987;40:373-383.
166. Riegel B, Dickson VV, Garcia LE, Masterson Creber R, Streur M. Mechanisms of change in self-care in adults with heart failure receiving a tailored, motivational interviewing intervention. *Patient Educ Couns.* 2016.
167. Riegel B, Masterson Creber R, Hill J, Chittams J, Hoke L. Effectiveness of Motivational Interviewing in Decreasing Hospital Readmission in Adults With Heart Failure and Multimorbidity. *Clin Nurs Res.* 2016;25(4):362-377.

168. Brandt J, Folstein MF. Telephone Interview for Cognitive Status. Psychological Assessment Resources, Inc.; 2003.
169. Cossette S, Frasure-Smith N, Dupuis J, Juneau M, Guertin MC. Randomized controlled trial of tailored nursing interventions to improve cardiac rehabilitation enrollment. *Nurs Res.* 2012;61(2):111-120.
170. Pinquart M, Sorensen S. Helping caregivers of persons with dementia: which interventions work and how large are their effects? *International Psychogeriatrics.* 2006;18(4):577-595.
171. Buchanan RJ, Radin D, Huang C. Burden among male caregivers assisting people with multiple sclerosis. *Gend Med.* 2010;7(6):637-646.
172. Coe M, Neufeld A. Male caregivers' use of formal support. *West J Nurs Res.* 1999;21(4):568-588.
173. Hubbell L, Hubbell K. The burnout risk for male caregivers in providing care to spouses afflicted with Alzheimer's disease. *J Health Hum Serv Adm.* 2002;25(1):115-132.
174. Pierce LL, Steiner V. What are male caregivers talking about? *Top Stroke Rehabil.* 2004;11(2):77-83.
175. Sanders S. Experiences of rural male caregivers of older adults with their informal support networks. *Journal of gerontological social work.* 2007;49(4):97-115.
176. Duggleby W, Williams A, Ghosh S, et al. Factors influencing changes in health related quality of life of caregivers of persons with multiple chronic conditions. *Health Qual Life Outcomes.* 2016;14:81.
177. Zivin K, Kales HC. Adherence to depression treatment in older adults: a narrative review. *Drugs Aging.* 2008;25(7):559-571.
178. Pocock SJ, Simon R. Sequential treatment assignment with balancing for prognostic factors in the controlled clinical trial. *Biometrics.* 1975;31(1):103-115.
179. Rausch SM, Baker K, Boonmee J. Sleep disturbances in caregivers of patients with end-stage congestive heart failure: Part I--The problem. *Prog Cardiovasc Nurs.* 2007;22(1):38-40.
180. Bennett HD, Coleman EA, Parry C, Bodenheimer T, Chen EH. Health coaching for patients with chronic illness. *Fam Pract Manag.* 2010;17(5):24-29.
181. Olsen JM. Health coaching: a concept analysis. *Nurs Forum.* 2014;49(1):18-29.
182. Huffman M. Using motivational interviewing: through evidence-based health coaching. *Home Healthc Nurse.* 2014;32(9):543-548.
183. Hibbard JH, Mahoney E. Toward a theory of patient and consumer activation. *Patient Educ Couns.* 2010;78(3):377-381.
184. Lauver DR, Ward SE, Heidrich SM, et al. Patient-centered interventions. *Res Nurs Health.* 2002;25(4):246-255.
185. Resnicow K, McMaster F, Rollnick S. Action reflections: a client-centered technique to bridge the WHY-HOW transition in Motivational Interviewing. *Behav Cogn Psychother.* 2012;40(4):474-480.
186. Hibbard JH, Mahoney ER, Stock R, Tusler M. Do increases in patient activation result in improved self-management behaviors? *Health Serv Res.* 2007;42(4):1443-1463.
187. Demonceau J, Ruppar T, Kristanto P, et al. Identification and assessment of adherence-enhancing interventions in studies assessing medication adherence through electronically compiled drug dosing histories: a systematic literature review and meta-analysis. *Drugs.* 2013;73(6):545-562.
188. Masterson Creber R, Patey M, Lee CS, Kuan A, Jurgens C, Riegel B. Motivational interviewing to improve self-care for patients with chronic heart failure: MITI-HF randomized controlled trial. *Patient Educ Couns.* 2016;99(2):256-264.
189. Sefcik JS, Petrovsky D, Streur M, et al. "In our corner": A qualitative descriptive study of patient engagement in a community-based care coordination program. *Clinical Nursing Research.* 2016:1-20.
190. Murtaugh CM, Deb P, Zhu C, et al. Reducing Readmissions among Heart Failure Patients Discharged to Home Health Care: Effectiveness of Early and Intensive Nursing Services and Early Physician Follow-Up. *Health Serv Res.* 2016.
191. Sidhu MS, Daley A, Jordan R, et al. Patient self-management in primary care patients with mild COPD - protocol of a randomised controlled trial of telephone health coaching. *BMC Pulm Med.* 2015;15:16.
192. Ryan P, Lauver DR. The efficacy of tailored interventions. *J Nurs Scholarsh.* 2002;34(4):331-337.
193. Brodaty H, Green A, Koschera A. Meta-analysis of psychosocial interventions for caregivers of people with dementia. *J Am Geriatr Soc.* 2003;51(5):657-664.
194. Doherty LC, Fitzsimons D, McIlfatrick SJ. Carers' needs in advanced heart failure: A systematic narrative review. *Eur J Cardiovasc Nurs.* 2015.
195. Mauldon M, Melkus G, Cagganello M. Tomando Control: a culturally appropriate diabetes education program for spanish-speaking indviduals with type 2 diabetes mellitus- evaluation of a pilot project. *The Diabetes Educator.* 2006;32(5):751-760.

196. Steinhardt M, Mamerow M, Brown S, Jolly C. A reslience intervention in African American adults with type 2 diabetes: A pilot study of efficacy. *The Diabetes Educator.* 2009;35(2):274-284.
197. Taylor BJ, Irish LA, Martire LM, et al. Avoidant Coping and Poor Sleep Efficiency in Dementia Caregivers. *Psychosom Med.* 2015;77(9):1050-1057.
198. Ghandeharioun A, Azaria A, Taylor S, Picard RW. "Kind and Grateful": A Context-Sensitive Smartphone App Utilizing Inspirational Content to Promote Gratitude. *Psychology of well-being.* 2016;6:9.
199. O'Leary K, Dockray S. The effects of two novel gratitude and mindfulness interventions on well-being. *Journal of alternative and complementary medicine (New York, NY).* 2015;21(4):243-245.
200. Kini P, Wong J, McInnis S, Gabana N, Brown JW. The effects of gratitude expression on neural activity. *NeuroImage.* 2016;128:1-10.
201. Newman CF, Beck JS. Selecting, Training, and Supervising Therapists. In: Nezu AM, Nezu CM, eds. *Evidence-based outcome research: A practical guide to conducting randomized controlled trials for psychosocial interventions*. Oxford, UK: Oxford University Press; 2008:245-262.
202. Michie S, Ashford S, Sniehotta FF, Dombrowski SU, Bishop A, French DP. A refined taxonomy of behaviour change techniques to help people change their physical activity and healthy eating behaviours: the CALO-RE taxonomy. *Psychol Health.* 2011;26(11):1479-1498.
203. Dansky KH, Palmer L, Shea D, Bowles KH. Cost analysis of telehomecare. *Telemedicine journal and e-health : the official journal of the American Telemedicine Association.* 2001;7(3):225-232.
204. Dansky KH, Bowles KH. Lessons learned from a telehomecare project. *Caring.* 2002;21(4):18-22.
205. Dansky KH, Bowles KH, Palmer L. Clinical outcomes of telehomecare for diabetic patients receiving home care. *The journal on information technology in healthcare.* 2003;1(1):61-74.
206. Dansky KH, Vasey J, Bowles K. Impact of telehealth on clinical outcomes in patients with heart failure. *Clin Nurs Res.* 2008;17(3):182-199.
207. Dansky KH, Vasey J, Bowles K. Use of telehealth by older adults to manage heart failure. *Res Gerontol Nurs.* 2008;1(1):25-32.
208. Dansky KH, Bowles KH. Impact of telehealth on heart failure outcomes. *Circulation.* 2007;113(21):794.
209. Bellg AJ, Borrelli B, Resnick B, et al. Enhancing treatment fidelity in health behavior change studies: best practices and recommendations from the NIH Behavior Change Consortium. *Health Psychol.* 2004;23(5):443-451.
210. Resnick B, Bellg AJ, Borrelli B, et al. Examples of Implementation and Evaluation of Treatment Fidelity in the BCC Studies: Where We Are and Where We Need to Go. *Ann Behav Med.* 2005;29(2 Suppl):46-54.
211. Spillane V, Byrne MC, Byrne M, Leathem CS, O'Malley M, Cupples ME. Monitoring treatment fidelity in a randomized controlled trial of a complex intervention. *Journal of advanced nursing.* 2007;60(3):343-352.
212. Devilly GJ, Borkovec TD. Psychometric properties of the credibility/expectancy questionnaire. *Journal of behavior therapy and experimental psychiatry.* 2000;31(2):73-86.
213. Vos-Vromans DC, Smeets RJ, Rijnders LJ, et al. Cognitive behavioural therapy versus multidisciplinary rehabilitation treatment for patients with chronic fatigue syndrome: study protocol for a randomised controlled trial (FatiGo). *Trials.* 2012;13:71.
214. Ljotsson B, Hedman E, Andersson E, et al. Internet-delivered exposure-based treatment vs. stress management for irritable bowel syndrome: a randomized trial. *The American journal of gastroenterology.* 2011;106(8):1481-1491.
215. Bova C, Jaffarian C, Crawford S, Quintos JB, Lee M, Sullivan-Bolyai S. Intervention Fidelity: Monitoring Drift, Providing Feedback, and Assessing the Control Condition. *Nurs Res.* 2017;66(1):54-59.
216. Luttik ML, Jaarsma T, Tijssen JG, et al. The objective burden in partners of heart failure patients; development and initial validation of the Dutch Objective Burden Inventory. *Eur J Cardiovasc Nurs.* 2008;7(1):3-9.
217. Makdessi A, Harkness K, Luttik ML, McKelvie RS. The Dutch Objective Burden Inventory: validity and reliability in a Canadian population of caregivers for people with heart failure. *Eur J Cardiovasc Nurs.* 2011;10(4):234-240.
218. Hwang B, Fleischmann KE, Howie-Esquivel J, Stotts NA, Dracup K. Caregiving for patients with heart failure: impact on patients' families. *American journal of critical care : an official publication, American Association of Critical-Care Nurses.* 2011;20(6):431-442.

219. Walker SN, Sechrist KR, Pender NJ. The Health-Promoting Lifestyle Profile: development and psychometric characteristics. *Nurs Res.* 1987;36(2):76-81.
220. Sheldon Cohen: award for distinguished scientific contributions. *The American psychologist.* 2004;59(8):673-675.
221. Anderson MI, Simpson GK, Daher M, Matheson L. Chapter 7 the relationship between coping and psychological adjustment in family caregivers of individuals with traumatic brain injury: a systematic review. *Annual review of nursing research.* 2015;33:219-247.
222. Aschbacher K, Patterson TL, von Kanel R, et al. Coping processes and hemostatic reactivity to acute stress in dementia caregivers. *Psychosom Med.* 2005;67(6):964-971.
223. Papastavrou E, Tsangari H, Karayiannis G, Papacostas S, Efstathiou G, Sourtzi P. Caring and coping: the dementia caregivers. *Aging & mental health.* 2011;15(6):702-711.
224. Sander AM, Davis LC, Struchen MA, et al. Relationship of race/ethnicity to caregivers' coping, appraisals, and distress after traumatic brain injury. *NeuroRehabilitation.* 2007;22(1):9-17.
225. Washington KT, Rakes CR. Coping Responses Among Hospice Family Caregivers: A Confirmatory Factor Analysis. *J Pain Symptom Manage.* 2015;50(6):867-873.
226. Gandek B, Sinclair SJ, Kosinski M, Ware JE, Jr. Psychometric evaluation of the SF-36 health survey in Medicare managed care. *Health Care Financ Rev.* 2004;25(4):5-25.
227. Griva K, Goh CS, Kang WC, et al. Quality of life and emotional distress in patients and burden in caregivers: a comparison between assisted peritoneal dialysis and self-care peritoneal dialysis. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation.* 2015.
228. Martin J, Padierna A, Aguirre U, Gonzalez N, Munoz P, Quintana JM. Predictors of quality of life and caregiver burden among maternal and paternal caregivers of patients with eating disorders. *Psychiatry Res.* 2013;210(3):1107-1115.
229. Lawrence RH, Tennstedt SL, Assmann SF. Quality of the caregiver--care recipient relationship: does it offset negative consequences of caregiving for family caregivers? *Psychol Aging.* 1998;13(1):150-158.
230. Gold R, Cottrell E, Bunce A, et al. Developing Electronic Health Record (EHR) Strategies Related to Health Center Patients' Social Determinants of Health. *J Am Board Fam Med.* 2017;30(4):428-447.
231. Walker RJ, Gebregziabher M, Martin-Harris B, Egede LE. Understanding the influence of psychological and socioeconomic factors on diabetes self-care using structured equation modeling. *Patient Educ Couns.* 2015;98(1):34-40.
232. Walker RJ, Smalls BL, Egede LE. Social determinants of health in adults with type 2 diabetes--Contribution of mutable and immutable factors. *Diabetes Res Clin Pract.* 2015;110(2):193-201.
233. Patel MR, Piette JD, Resnicow K, Kowalski-Dobson T, Heisler M. Social Determinants of Health, Cost-related Nonadherence, and Cost-reducing Behaviors Among Adults With Diabetes: Findings From the National Health Interview Survey. *Medical care.* 2016;54(8):796-803.
234. Hill KE, Gleadle JM, Pulvirenti M, McNaughton DA. The social determinants of health for people with type 1 diabetes that progress to end-stage renal disease. *Health Expect.* 2015;18(6):2513-2521.
235. Centers NAoCH. PRAPARE Implementation and Action Toolkit. 2017. Accessed Jan 11, 2018.
236. Brazil K, Kaasalainen S, Williams A, Rodriguez C. Comparing the experiences of rural and urban family caregivers of the terminally ill. *Rural and remote health.* 2013;13(1):2250.
237. Wong SY, Wong CK, Chan FW, et al. Chronic psychosocial stress: does it modulate immunity to the influenza vaccine in Hong Kong Chinese elderly caregivers? *Age.* 2012.
238. Rokach A, Findler L, Chin J, Lev S, Kollender Y. Cancer patients, their caregivers and coping with loneliness. *Psychology, health & medicine.* 2012.
239. Davis LC, Sander AM, Struchen MA, Sherer M, Nakase-Richardson R, Malec JF. Medical and psychosocial predictors of caregiver distress and perceived burden following traumatic brain injury. *The Journal of head trauma rehabilitation.* 2009;24(3):145-154.
240. Sander AM, Sherer M, Malec JF, et al. Preinjury emotional and family functioning in caregivers of persons with traumatic brain injury. *Archives of physical medicine and rehabilitation.* 2003;84(2):197-203.
241. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Medical care.* 1996;34(1):73-84.
242. Organization. WH. World Health Organization Health and Performance Questionnaire (HPQ): Clinical Trials Baseline Version. 2002.

243. Kessler RC, Ames M, Hymel PA, et al. Using the World Health Organization Health and Work Performance Questionnaire (HPQ) to evaluate the indirect workplace costs of illness. *J Occup Environ Med.* 2004;46(6 Suppl):S23-37.
244. Luo N, Wang P, Fu AZ, Johnson JA, Coons SJ. Preference-based SF-6D scores derived from the SF-36 and SF-12 have different discriminative power in a population health survey. *Medical care.* 2012;50(7):627-632.
245. (NQF) NQF. *Preferred Practices and Performance Measures for Measuring and Reporting Care Coordination: A Consensus Report.* Washington, DC2010.
246. Krumholz HM, Keenan PS, Brush JE, Jr., et al. Standards for measures used for public reporting of efficiency in health care: a scientific statement from the American Heart Association Interdisciplinary Council on Quality of Care and Outcomes Research and the American College of Cardiology Foundation. *Circulation.* 2008;118(18):1885-1893.
247. Goodlin SJ. Palliative care in congestive heart failure. *J Am Coll Cardiol.* 2009;54(5):386-396.
248. Wasywich CA, Gamble GD, Whalley GA, Doughty RN. Understanding changing patterns of survival and hospitalization for heart failure over two decades in New Zealand: utility of 'days alive and out of hospital' from epidemiological data. *Eur J Heart Fail.* 2010;12(5):462-468.
249. Binanay C, Califf RM, Hasselblad V, et al. Evaluation study of congestive heart failure and pulmonary artery catheterization effectiveness: the ESCAPE trial. *JAMA.* 2005;294(13):1625-1633.
250. Ariti CA, Cleland JG, Pocock SJ, et al. Days alive and out of hospital and the patient journey in patients with heart failure: Insights from the candesartan in heart failure: assessment of reduction in mortality and morbidity (CHARM) program. *Am Heart J.* 2011;162(5):900-906.
251. Stewart S, Ball J, Horowitz JD, et al. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic, multicentre, randomised controlled trial. *Lancet.* 2014;385:775-784.
252. Harris PA, Taylor, R. , Thielke, R., Payne, J., Gonzalez, N., & Conde, J.G. Research electronic data capture (REDCap)-A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics.* 2009;42(2):377-381.
253. Falissard B, Lukasiewicz M, Corruble E. The MDP75: a new approach in the determination of the minimal clinically meaningful difference in a scale or a questionnaire. *J Clin Epidemiol.* 2003;56(7):618-621.
254. Gleason TC, Staelin R. Proposal for Handling Missing Data. *Psychometrika.* 1975;40(2):229-252.
255. Little RJA, Rubin DB. *Statistical analysis with missing data.* 2nd ed. New Jersey: Wiley & Sons, Inc.; 2002.
256. Roth PL. Missing data: A conceptual review for applied psychologists. *Personnel Psychology.* 1994;47:537-560.
257. Schafer JL, Graham JW. Missing data: Our view of the state of the art. *Psychological Methods.* 2002;7(2):147-177.
258. Lavori PW, Dawson R, Shera D. A multiple imputation strategy for clinical trials with truncation of patient data. *Statistics in Medicine.* 1995;14:1913-1925.
259. Crawford SL, Tennstedt SL, McKinlay JB. A comparison of analytic methods for non-random missingness of outcome data. *Journal of Clinical Epidemiology.* 1995;48(2):209-219.
260. Little RJA. Modeling the drop-out rate mechanism in repeated measures studies. *Journal of American Statistical Association.* 1995;90:1112-1121.
261. Laird NM. Missing data in longitudinal studies. *Statistics in Medicine.* 1988;7:305-315.
262. Little RJA. A class of pattern-mixture models for normal incomplete data. *Biometrika.* 1994(81):471-483.
263. Molenberghs G, Thijs H JI, Beunckens C, Kenward MG, Mallinckrodt C, Carroll RJ. Analyzing incomplete longitudinal clinical trial data. *Biostatistics.* 2004;5:445-464.
264. Verbeke G, Molenberghs G, Thijs H, Lesaffre E, Kenward MG. Sensitivity analysis for nonrandom dropout: a local influence approach. *Biometrics.* 2001;57(1):7-14.
265. Littell RC, Milliken GA, Stroup WW, Wolfinger RD. *SAS System for Mixed Models.* Cary, NC: SAS Institute; 1996.
266. Gueorguieva R, Krystal JH. Move over ANOVA: progress in analyzing repeated-measures data and its reflection in papers published in the Archives of General Psychiatry. *Arch Gen Psychiatry.* 2004;61(3):310-317.
267. Aiken L, West S. *Multiple regression: Testing and interpreting interactions.* Newbury Park: Sage; 1991.

268. Bryk AS, & Raudenbush, S.W. . *Hierarchical linear models: Applications and data analysis methods.* Newbury Park, CA: Sage; 1992.
269. Laird NM, Ware JH. Random-effects models for longitudinal data. *Biometrics.* 1982;38(4):963-974.
270. Dunton GF, Tscherne J, Rodriguez D. Factorial validity and gender invariance of the physical activity enjoyment scale (PACES) in older adolescents. *Res Q Exerc Sport.* 2009;80(1):117-121.
271. Benjamini Y, Drai D, Elmer G, Kafkafi N, Golani I. Controlling the false discovery rate in behavior genetics research. *Behavioural brain research.* 2001;125(1-2):279-284.
272. Akaike H. A new look at statistical model identification. *IEEE Transactions on Automatic Control.* 1974;19:716-723.
273. Office of the Inspector General. Medicaid Drug Price Comparison: Average Sales Price To Average Wholesale Price, . Department of Health & Human Services (DHHS); 2005.
274. Khandelwal N, Benkeser DC, Coe NB, Curtis JR. Potential Influence of Advance Care Planning and Palliative Care Consultation on ICU Costs for Patients With Chronic and Serious Illness. *Crit Care Med.* 2016;44(8):1474-1481.
275. Khandelwal N, Engelberg RA, Benkeser DC, Coe NB, Curtis JR. End-of-life expenditure in the ICU and perceived quality of dying. *Chest.* 2014;146(6):1594-1603.
276. Glick HA, Doshi JA, Sonnad SS, Polsky D. *Economic Evaluation in Clinical Trials.* 2nd ed. Oxford: Oxford University Press; 2015.
277. Efron B, Tibshirani RJ. *An Introduction to the Bootstrap.* Vol 57. New York, NY: Chapman Hall; 1993.
278. Mooney CZ, Duval RD. *Bootstrapping: A Nonparametric Approach to Statistical Inference.* Vol 95. Newbury Park, CA: Sage; 1993.
279. Vaida F, Xu R. Proportional hazards model with random effects. *Stat Med.* 2000;19(24):3309-3324.
280. Yau KK, McGilchrist CA. ML and REML estimation in survival analysis with time dependent correlated frailty. *Stat Med.* 1998;17(11):1201-1213.
281. Zeger SL, Liang K. Longitudinal data analysis using generalized linear models. *Biometrics.* 1986;73(1):13-22.
282. Rayens MK, Svavarsdottir EK. A new methodological approach in nursing research: an actor, partner, and interaction effect model for family outcomes. *Res Nurs Health.* 2003;26(5):409-419.
283. Freedland KE, Mohr DC, Davidson KW, Schwartz JE. Usual and unusual care: existing practice control groups in randomized controlled trials of behavioral interventions. *Psychosomatic Medicine.* 2011;73(4):323-335.

Recruitment and Retention Plan

We plan to enroll a consecutive sample of 250 informal caregivers (125/arm) of heart failure (HF) patients (HF caregivers). The main enrolment site is the Penn Heart and Vascular Center (PHVC), the largest outpatient HF clinic in the Philadelphia region and a site at which the Principal Investigator (PI) has established relationships and success in past recruitment of participants. If recruitment is slower than expected, we will identify caregivers visiting HF patients hospitalized at one of three University of Pennsylvania Health System (UPHS) sites.

We anticipate identifying 100 unique HF patients each month, most of whom will have caregivers. Based on our prior research, we anticipate that 90 will have caregivers and 70% of these (63 caregivers) will be eligible, and 15% will enroll. Thus, we estimate enrolling 10 caregivers per month. Using this number, we anticipating needing at least 25 months for enrollment, but we have conservatively allowed 30 months for enrollment and five years to complete the study.

In addition to caregivers, we want to enroll at least 40 caregiver-patient dyads. We understand the challenges of enrolling dyads, but 40 dyads is sufficient to provide reliable parameter estimates for this exploratory aim. The effort of HF patient participants is minimal. They will not receive an intervention. They will be asked to provide informed consent to allow us to access their electronic medical record (EMR) to collect clinical information and track events and, in the case that patients receive care outside the Penn health system, for the caregiver to report on patient health care resource use. At the end of the study period (12 months), the HF patients will be asked to provide data on quality adjusted life years (QALYs).

We will have a study Research Assistant (RA) on site during PHVC clinic hours so that the RA can meet the informal caregiver in person because we anticipate that a face-to-face meeting will maximize enrollment. We plan to seek a HIPAA waiver to screen the daily appointment schedule to identify every patient with a potentially eligible caregiver (e.g., living within 50 miles of the research office). Dr. Wald, a co-investigator on the study, will ask clinic staff to identify potential caregiver participants (e.g., speak English) and determine their willingness to speak with research staff about the study.

To facilitate the engagement of clinic staff, we will meet with them before the study begins to tell them about the study. We will bring lunch to compensate their time in talking with us. We will use that forum to build enthusiasm about the study. We will hold similar events throughout the enrollment period to assure that engagement of staff in enrollment does not wane. During these subsequent events, we will update the clinic staff on our progress.

We will prepare informational materials for the clinic staff to use to engage the interest of informal caregivers. These materials will use clear and simple language with graphics that portray caregivers of different ages and races. We will place these materials in the waiting rooms, at the front desk, and in all the examination rooms. Research staff will make sure that these materials are consistently available.

If we need to enroll from the hospital because enrollment is not sufficiently brisk in the clinic, an RA will be available in the hospital daily to give interested caregivers study information and conduct screening. We will obtain a HIPAA waiver to allow us to screen the daily admission log to identify every HF patient with a potentially eligible caregiver (e.g., living within 50 miles of the research office). We will engage hospital staff in a manner to that described above for clinic staff.

We recognize that some caregivers will learn about the study in the clinic or hospital but not decide to participate until after they are home. For these situations, we will have a dedicated telephone number and email address for potential participants to learn more about the study. Anyone who contacts us in this manner will receive a response within 48 hours.

If we find that we are unable to recruit a diverse racial/ethnic sample, we will identify additional community agencies and other clinics that serve different racial and ethnic populations. We will work with staff at those clinics to facilitate successfully on-site recruitment. Recruitment flyers will reflect images and language that speak to a diverse population.

Our training of staff will emphasize good clinical practice in working with study participants. Staff training will include developing cultural competency (cultural awareness, knowledge, and skills) in working with diverse populations, participant recruitment, and follow-up activities. Our goal is to minimize language and communication problems to support retention and engagement. For example, we will make sure that the reading materials are written at a basic reading level. Print will be sufficiently large to accommodate age-related vision changes. Regular staff meetings will provide further opportunity for continued cultural competency training and discussion.

From experience, we recognize that identifying the ideal way to recruit participants is challenging. Issues that impede enrolment include lack of staff engagement, resistance from unexpected sources, and RA staff turnover. We will meet with research staff at least weekly to monitor these issues and any others that arise. We will monitor our processes intensely until we have identified a successful method of enrolling caregivers. Thereafter, we will continue to monitor our processes regularly.

Retention

Once enrolled, it is important that we keep participants in the study for the full 12 months. We will monitor retention regularly and discuss retention trends at monthly meetings of the full study team. Our plans to accomplish this goal address contact frequency, tokens of appreciation, newsletters, and remuneration.

We will contact all participants at 3 month intervals by telephone for data collection. We will use these calls as a method to keep participants engaged. On enrollment, we will clearly explain the requirements of the study to all participants. We will specify that we need to speak with them every 3 months, asking “What is the best way for me to contact you?” We will obtain several phone numbers (home, work, and cell) and an email address whenever possible so that we can follow up with them easily. We will be flexible when scheduling appointments. We will carefully train the RAs to be polite, thoughtful, and sensitive to the stresses these informal caregivers are experiencing.

We will mail a regular newsletter that reports the progress of the study to keep the participants engaged. We will write this newsletter it in such a way that it can be distributed to participants in both the intervention and the control groups.

We will send participants small tokens of appreciation that will remind them of the study: birthday cards, refrigerator magnets and pens with the study logo, etc. For remuneration, we chose a market model of payment where the amount serves as an incentive rather than a reward. The advantage is more rapid recruitment and avoidance of subject financial sacrifice. Further, a completion bonus encourages subject retention. Using this model, caregivers will receive $25 at enrollment, $50 after the 6-month data are provided, $25 after the 9-month data

are provided, and $100 when they complete the study for a total remuneration of $200 for a 12-month commitment.

We have procedures planned and itemized in the research strategy for monitoring intervention fidelity. We anticipate that many of these procedures (e.g. health coach consistency for each participant in the intervention) will facilitate retention of participants.

At the end of the study, we will distribute research results to all participants in formats that are useful to the different communities involved (e.g., participants, families of participants, and referring practitioners). For participants, we will explain how the findings may ultimately improve their health. For health care practitioners, we will summarizes the findings succinctly to accommodate their busy schedules.

Estimated Timeline for Major Study Activities	YEAR 1				YEAR 2				YEAR 3				YEAR 4				YEAR 5			
Activity	Quarters																			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Hire and train the Project Manager																				
Develop databases, refine study materials																				
Obtain IRB approval																				
Hire, orient, train research and clinical (health coaches) staff																				
Prepare for sample enrollment with clinic staff meetings																				
Sample enrollment and data collection																				
Data entry and data cleaning																				
Provide intervention, actively monitoring treatment fidelity																				
Data collection finishes, final cleaning of all data																				
Complete data analysis																				
Disseminate results																				

HUMAN SUBJECTS

This Human Subjects Research meets the definition of 'Clinical Research'.

Protection of Human Subjects

Human Subjects Involvement, Characteristics, and Design. In the proposed RCT we will enroll adults who are informal caregivers of adults with heart failure (HF) and the HF patients they care for. The study focuses on the caregivers, but we will also enroll all willing HF patients to address our exploratory aim. We will seek HF patient consent to review their medical records for factors anticipated to add to the demand of caregiving (e.g., number of comorbid conditions) and health care resource use. QALYs will be collected from consenting HF patients.

The informal caregivers and the HF patients are anticipated to be primarily older adults because HF is a condition affecting primarily elders. In our most recent study of this population, the mean age of HF patient participants was 62 ± 12.5 years and most of their caregivers were spouses of a similar age. Considering the age group, most caregivers will have one or more chronic conditions.

The sampling plan involves enrolling a consecutive sample of adult caregivers and patients with chronic HF, whenever possible. We will focus enrolment on caregivers, approaching them after staff obtain permission during a clinic visit or during a hospitalization of the HF patient. Caregivers must be informal caregivers of patients with a confirmed diagnosis of HF. They will be screened with the 10-item Health Self-Care Neglect scale;[1] we will enroll only those who are poor in self-care using a cut-point of ≥2 based on our pilot study. Caregivers must be able to provide informed consent (speak English, see, hear, cognitively intact) and complete the protocol. We recognize that we may need to make a home visit to complete enrollment and/or set up tablets, so caregivers must live within 50 miles of the research office. We will exclude caregivers with cognitive impairment because we anticipate that they would have difficulty completing the intervention. We will exclude anyone with untreated major psychiatric illness such as psychosis. Anyone who is planning to move out of the area will not be enrolled. Anyone in a competing trial testing a support intervention also will be excluded. In this way, we anticipate enrolling only caregivers who are able to provide true informed consent and those who will potentially benefit from the intervention. Any HF patient cared for by an enrolled caregiver will be consented, if willing. We anticipate, however, that some patients will refuse. In this case, we will enroll only the caregiver.

The PI, Dr. Riegel will oversee the recruitment and enrollment of caregivers. We anticipate enrolling a diverse sample of participants, with many in vulnerable racial, socio-economic, and geographically disadvantaged groups. We acknowledge that there will be too few Asians and Hispanics to analyze in a meaningful way but we will include these caregivers and analyze their data in an exploratory fashion. We expect to enroll women more easily than men because most caregivers are women and this type of intervention is more appealing to women.[2] Recruitment efforts will focus on enrolling a sufficient number of men so that we can analyze sex-based differences in response to the intervention. We will balance sex and the nature of the relationship through block randomization to groups as we enroll. We will not include caregivers of children with HF; HF in a child is unusual. No caregivers who are < 18 years of age will be included because their stresses may be unique. No vulnerable populations will be enrolled.

The randomization sequence will be generated *a priori* by a statistician unassociated with the study. Study nurses and caregiver participants will be notified of their group assignment by the Project Manager. Both groups will receive Health Information (HI) delivered by the Internet (http://www.nhs.uk/pages/home.aspx) in addition to standard care. The intervention group will receive virtual health coaching (ViCCY) by video conferencing, with 10 front-loaded health coaching contacts over six months. This dose is based on published data demonstrating that six months of health coaching is needed to be effective.

No other collaborating sites are involved.

Sources of materials. The research material obtained from caregivers will be primarily self-report surveys (e.g., self-care, stress, health status) and clinical information such as names of medications. The self-report measures will be collected five times over the course of 12-months (baseline and 3, 6, 9, and 12 months). On enrollment, illness-related information and caregiver burden will be measured. [3,4] Quality of the relationship with the patient; social determinants of health; and demographic, caregiving, and clinical characteristics will be gathered from caregivers at enrollment only. Three randomly selected ViCCY sessions delivered by each health coach will be audiotaped, reviewed and rated for fidelity.

We will enroll HF patients whenever possible so that we can review their medical records to obtain information

to describe their HF illness severity, HF duration and comorbid conditions. If comorbidity of the patients differs between the groups we will use comorbidity as a covariate in analyses. We will also track hospitalizations, emergency department visits, and mortality in HF patients over the 12 months of the study to test our exploratory aim.

Because study participants are to be followed for 12-months, a central data file with subject name, phone number, email address if available, and address (needed to arrange data collection if no clinic visit is scheduled) will be kept by the PI and Project Manager. The research staff directly involved in data collection will have access to these data, but in the electronic file all identifying information will be removed and participants will be identified only by numbers. Only the PI and the Project Manager will be able to link the participant with his or her identification number.

Potential Risks. Participants will be monitored continually for the occurrence of adverse events defined as any untoward or unfavorable occurrence. Potential risks for caregivers include fatigue from data collection, stress in response to data collection or some element of the intervention, and loss of confidentiality. The most likely risk is fatigue, discussed further below. Patients are at risk for loss of confidentiality because we will be reviewing their medical records. Although the risk of a loss of confidentiality is possible for both caregivers and patients, it is judged to be unlikely as we are experienced in systems of protecting private information. All data are stored behind multiple firewalls. It is monitored regularly, and is accessible only to key personnel who receive private network/firewall, server/password, and data directory access rights. Thus, the risk of unlawful penetration is not a significant data safeguard concern.

Fatigue is anticipated in this study; some caregivers will be fatigued by data collection on top of their usual caregiving responsibilities. Survey data collection will take place five times and is anticipated to require less than one hour. We have streamlined data collection significantly by choosing short measures and those that can be administered by telephone. We will accommodate any request to break up the data collection into two separate sessions that can be scheduled up to two weeks apart.

Stress from data collection and/or the intervention is possible as the topics covered (e.g. demand of caregiving) may cause emotional distress. Empathy will be emphasized in the training of health coaches as a way to minimize distress. All RAs will be trained on how to approach the topics in a non-suggestive yet supportive and empathetic way to minimize distress.

Adequacy of Protection Against Risks

Recruitment and Informed Consent. After approval by the Institutional Review Board (IRB) at Penn, the research staff will work with staff from the HF clinic to identify eligible caregivers for referral to us. If enrollment from the clinic is slow we will also look for hospitalized HF patients. Once identified, those caregivers will be contacted by the providers to ask about their willingness to speak with the study team. Those agreeing to speak with us will have the study carefully explained to them by the research staff. Potential participants will be fully informed regarding the interventions and the schedule of the data collection. Those willing to be screened will undergo preliminary screening to assess inclusion and exclusion criteria.

Written informed consent will be obtained from caregivers and HF patients. Those who agree to participate will be asked to read and sign the consent form with integrated HIPAA authorization information (i.e., specifics about data elements to be collected and use of the private information). The consent form will specify that some intervention sessions will be audiotaped to ensure the quality of the intervention and judge treatment fidelity. We will explain that these audiotapes will be transcribed for analysis and then destroyed. The RAs will answer questions and make sure that the procedures that are to be used are fully understood.

As stress from study participation is the most concerning risk to caregivers, we will systematically monitor to assure that we identify it. We anticipate that stress may result in early withdrawal so we will monitor withdrawal rates methodically in each group. If a participant withdraws, reasons will be carefully noted.

As data collection is anticipated to require significant commitment and effort on the part of subjects, remuneration will be provided. We carefully considered the amount to pay participants using the guidelines from Dickert and Grady.[5] Because of the potential burden of data collection, we chose a market model of payment where the amount serves as an incentive rather than a reward. The advantage is more rapid recruitment and avoidance of subject financial sacrifice. Further, a completion bonus encourages subject retention. Using this model, caregivers will receive $25 at enrollment, $50 after the 6-month data are provided, $25 after the 9-month data are provided, and $100 when they complete the study for a total remuneration of

$200 for a 12-month commitment. This amount is not anticipated to be undue inducement, considering the effort and commitment required of participants.

Protection Against Risk. *Fatigue*. To minimize the most likely risk of fatigue during data collection, we selected surveys that are as short as possible. Completion of the self-report survey packet requires less than one hour. Testing will be scheduled at a time that is convenient for subjects. If participants are too fatigued to complete all measures, sociodemographic and clinical data will be administered at enrollment and the baseline surveys will be gathered in a subsequent telephone call (but before randomization). All delayed data collection will occur within a two-week interval. The RAs will be trained to be sensitive to signals from participants that a break is needed during testing. All participants will be informed that they can stop their participation in the study at any time. For subjects who find data collection too fatiguing, we will offer the option of providing only the most essential data reflecting the key outcome variables (e.g., health self-care neglect).

Stress. To minimize the risk of stress during data collection the RAs will be trained to be supportive and helpful to participants with questions about data collection. If a participant becomes stressed during data collection because of the questions asked, the burden of data collection, or for other personal reasons, data collection will be terminated, delayed, or abbreviated to only the most essential items (e.g. primary outcome variable). Significant stress will be reported to the Project Manager who will contact the caregiver to discuss the issue if indicated (the PI is blinded). The RAs will be trained to detect any signals that the participant is becoming upset before stress escalates. In a prior study we hired nursing and psychology students as RAs, which facilitated the assessment and management of participant stress during data collection.

RAs will be required to have sufficient maturity and background to interact appropriately with ill, aging, stressed individuals. The protocol for training of RAs, detailed in our operations manual, addresses enrollment methods and the collection of data in a uniform manner.[6] Training for RAs in data collection will occur during a two-day period prior to beginning subject enrollment. Training will begin with classroom instruction, including the purpose and background on each measure, importance of strict adherence to the standardized protocol, step-by-step instruction for survey administration, criteria for aborting testing and the procedure for audiotaping sessions and transmitting data. RAs will be trained to ensure that they do not prompt subjects with verbal or nonverbal cues. Training will include practice administering all tests. Consistency in data collection procedures will be assessed and reinforced during routine staff meetings. Retraining and retesting will be done immediately if a new RA is hired and annually thereafter. The PI and the Project Manager will meet weekly or bi-weekly with staff (in-person or by video) to discuss issues of enrollment and data collection. All decisions will be logged and filed for future reference. All issues will be reported immediately to the IRB and the Data Safety Monitoring Board, as discussed in that plan.

We will be enrolling a sample of stressed individuals and it is possible that we will identify someone with severe distress. We have a previously tested detailed safety plan (Riegel R01HL084394), which has been refined for use in this study. This safety plan addresses the concerns associated with severe stress that need to be handled in order to ensure that the research participants' needs are addressed. This plan includes the requirement that research staff undergo training in this safety protocol and participate in ongoing regular supervision by Dr. Riegel on these procedures. In addition, for participants randomized to the ViCCY group, specific rules to ensure privacy and safety will be discussed in the first session, such as being in a private place during sessions and not engaging in discussions while driving.

Confidentiality. To protect against any risk to subject confidentiality, all printed data forms will be coded with unique identifiers. The unique identification number will be kept separate from the files with protected health information (PHI) to protect subject confidentiality. Every effort will be made to prevent anyone who is not on the research team from knowing what information was collected from a particular subject. As part of the consent process, subjects will be made aware of the fact that there are some circumstances where the research team may have to provide subject information to other people (regulatory or legal circumstances). In addition, as we are unable to ensure total Internet security, this limitation of privacy will be noted in the informed consent. In this manner caregivers will be informed that although it is highly unlikely that anyone would access an audiotaped session, the prevention of such intrusions cannot be guaranteed. The content of the intervention sessions is not anticipated to be confidential in nature.

Data Storage. Since this data storage system is behind multiple firewalls, is monitored regularly, and is accessible only to key personnel who receive private network/firewall, server/password, and data directory access rights, the risk of unlawful penetration is not a significant data safeguard concern. Individually identifiable or deducible data will not be transmitted by unsecured telecommunications, which include the

Internet, email, and electronic File Transfer Protocol (FTP). Further, the data will not be physically moved or transmitted in any way from the server without written approval from the project manager. All output containing individual identifiable information is treated as confidential data. This information is never transferred electronically via email or other protocols.

All data will be backed up daily and system backups will be done weekly. Batch validity checks will be run on the database at periodic intervals to identify data that violate predefined rules. Data will be de-identified and stored on the database server with strong access controls, software firewall, secure file transfer protocols, network-wide virus protection software, and daily back-ups. The computers will be password-protected and maintained in a secure, locked location at the School of Nursing. Interim checks will be conducted regularly to ensure that data collection and archiving procedures are operating correctly and security and confidentiality are not compromised. All information obtained on paper (e.g., consent forms) will be numerically coded and locked in a secure location, as described further below.

Signed consent forms and other subject-specific information containing names will be kept separate from the subject identification numbers. The master list and subject information will be stored in different locked file cabinets in the PI's research offices at the University of Pennsylvania, School of Nursing. Access to these master files will be limited to those directly involved in the study.

Data will be compiled from all of the subjects in the study and aggregated for analysis and publication. All identifying data will be eliminated from files before data are electronically transferred to the biostatistician. As a result of aggregation, no individual subjects will be identifiable from the written materials. Audiotaped interviews will be assigned a unique identifier; any identifiable information in the interviews will be deleted during the transcription process.

Potential Benefits of the Proposed Research to Human Subjects and Others

We cannot guarantee that any participant will benefit by participating in this study, although all of the caregivers will receive health information. We acknowledge that subject burden may be an issue for these already-burdened caregivers. However, we believe that the benefits of the knowledge gained will outweigh the burden and the risks to participants. A Data and Safety Monitoring Board will be used to ensure the validity and integrity of the data. We anticipate that the results of this study will benefit society most, by helping to improve the support provided to caregivers of HF patients. It is our judgment that benefits outweigh the risk to study participants.

Importance of the knowledge to be gained

Heart failure is extremely common in the aging population worldwide. The vast majority of these patients are limited functionally and living at home with care provided to them by their loved ones. Little attention has been given to these caregivers. This study has the potential to address this underserved and distressed segment of the population by improving their abilities to cope with the stress of providing daily care to a loved one with a severe, debilitating, and chronic illness and refocus their attentions onto themselves (self-care). If perceived stress decreases in caregivers and they are able to care for themselves more effectively, this study will provide a new and innovative way to increase the support available for these caregivers.

ClinicalTrials.gov Requirement

We will register the trial with Clinical Trials.gov Protocol Registration System no later than 21 days after the first subject is enrolled.

CITATIONS

1. Boise L. Health Self-Care Neglect Scale. *Empowering family caregivers: The powerful tools for caregiving program. Educational Gerontology, 31, 573-586.*2005.
2. National Academies of Sciences E, and Medicine,. *Families Caring for an Aging America.* Washington, DC: The National Academies Press; 2016.
3. Luttik ML, Jaarsma T, Tijssen JG, et al. The objective burden in partners of heart failure patients; development and initial validation of the Dutch Objective Burden Inventory. *Eur J Cardiovasc Nurs.* 2008;7(1):3-9.
4. Makdessi A, Harkness K, Luttik ML, McKelvie RS. The Dutch Objective Burden Inventory: validity and reliability in a Canadian population of caregivers for people with heart failure. *Eur J Cardiovasc Nurs.* 2011;10(4):234-240.

5. Dickert N, Grady C. What's the price of a research subject? Approaches to payment for research participation. *N Engl J Med.* 1999;341(3):198-203.
6. Bowman A, Wyman JF, Peters J. The operations manual: a mechanism for improving the research process. *Nurs Res.* 2002;51(2):134-138.