














SYSTEMATIC REVIEW AND META-ANALYSIS

# Clinicians for CARE: A Systematic Review and Meta-Analysis of Interventions to Support Caregivers of Patients With Heart Disease

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**BACKGROUND:** Caregivers provide critical support for patients with chronic diseases, including heart disease, but often experience caregiver stress that negatively impacts their health, quality of life, and patient outcomes. We aimed to inform health care teams on an evidence-based approach to supporting the caregivers of patients with heart disease.

**METHODS AND RESULTS:** We conducted a systematic review and meta-analysis of randomized controlled trials written in English that evaluated interventions to support caregivers of patients with heart disease. We identified 15,561 articles as of April 2, 2020 from 6 databases; of which 20 unique randomized controlled trials were evaluated, representing a total of 1570 patients and 1776 caregivers. Most interventions focused on improving quality of life, and reducing burden, depression, and anxiety; 85% (17 of 20) of the randomized controlled trials provided psychoeducation for caregivers. Interventions had mixed results, with moderate non-significant effects observed for depression (Hedges'  $g = -0.64$ ; 95% CI,  $-1.34$  to  $0.06$ ) and burden (Hedges'  $g = -0.51$ ; 95% CI,  $-2.71$  to  $1.70$ ) at 2 to 4 months postintervention and small non-significant effects observed for quality of life and anxiety. These results were limited by the heterogeneity of outcome measures and intervention delivery methods. A qualitative synthesis of major themes of the interventions resulted in clinical recommendations represented with the acronym "CARE" (Caregiver-Centered, Active engagement, Reinforcement, Education).

**CONCLUSIONS:** This systematic review highlights the need for greater understanding of the challenges faced by caregivers and the development of guidelines to help clinicians address those challenges. More research is necessary to develop clinical interventions that consistently improve caregiver outcomes.

**Key Words:** anxiety ■ burden ■ cardiovascular disease ■ caregiver ■ depression ■ heart disease

Family and other caregivers play a vital role in the long-term health maintenance and care of patients with chronic illnesses such as heart disease, a leading cause of hospital admission, death, and economic burden in the United States.<sup>1-4</sup> In a report

published by the National Alliance on Caregiving and the American Association of Retired Persons, there are about 41.8 million Americans providing care to adults aged >50 years.<sup>5</sup> These caregivers perform important roles, including supporting patients in their activities

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## CLINICAL PERSPECTIVE

### What Is New?

- Recently, more attention has been given to the physical and emotional challenges faced by the family members and friends that support the health care needs of patients with chronic diseases, including cardiovascular disease; these caregivers play a crucial role in the health care maintenance of our patients which can lead to stress, depression, anxiety, and decreased quality of life.
- Little is known about the best ways the clinical team can support caregivers of patients with cardiovascular disease.
- Our systematic review highlights and attempts to address the need for evidence-based guidelines to help the clinical team better engage and support caregivers of patients with cardiovascular disease.

### What Are the Clinical Implications?

- The clinical team has a role in addressing caregiver burden by finding ways to better support the caregivers of our patients.
- Based CARE (Caregiver centered, Active engagement, Reinforcement, Education) to help clinicians better support the caregivers of their patients.
- Caregiver-centered health care delivery will identify caregivers at risk of burnout, engage them as part of the team, provide educational resources to help empower them in their roles, and reinforce skills or knowledge taught.

## Nonstandard Abbreviations and Acronyms

<b>CARE</b>	Caregiver-Centered, Active Engagement, Reinforcement, Education
<b>NIH</b>	National Institutes of Health
<b>QoL</b>	quality of life

of daily living and instrumental activities of daily living, providing transportation to medical appointments, and aiding in medication adherence. The overall economic value of unpaid caregivers in the United States in 2017 was estimated to be 470 billion dollars.<sup>6</sup>

Caregiver involvement in the care of patients with heart disease has shown benefit in patient outcomes through improvement in dietary adherence, medication adherence, and patient attendance at follow-up visits.<sup>1,7</sup> However, the caregiver role has also been associated with added stress and burden.<sup>8-13</sup> Aiding patients

in adhering to a diet that is within heart disease guidelines was noted to be particularly challenging by caregivers.<sup>14</sup> Other common challenges that heart disease caregivers face include increased mental and physical stress, fear of the unknown, uncertainty of appropriate grocery shopping, challenges of meal preparation, and lack of acknowledgment and validation from the patient's health care team.<sup>14-19</sup> As a result of the additional stress and less healthy lifestyles that occur from these challenges, caregivers of patients with heart disease were found to be at higher risk for CVD morbidity and mental health disorders.<sup>15,20</sup>

While caregivers play a crucial role in supporting our patients, their contributions and the challenges they face have not been addressed effectively by clinicians.<sup>21,22</sup> Consequently, to address these adverse effects, there is a need for evidence-based recommendations to guide the clinical team in supporting caregivers of patients with heart disease. In recent years, there has been increased awareness of the importance of engaging caregivers as partners in patient care; this is reflected by new policies and practices that promote caregiver support and engagement by the clinical team.<sup>21,23,24,25,26,27,28</sup> However, there remains a deficit in uniform evidence-based guidelines for clinicians.

This systematic review aimed to examine the literature for interventions to inform the health care team on evidence-based approaches to support the caregivers of patients with heart disease. We reviewed randomized controlled trials (RCTs) of caregiver interventions in populations of patients with heart disease. We performed a meta-analysis of the results. We also conducted a qualitative synthesis of major themes of the interventions, informed by our literature review, to develop a framework to guide clinicians in recognizing, engaging, and supporting caregivers.

## METHODS

### Study Search Strategy and Data Sources

This study did not use experimental animals, medications, biologics, or devices. This study is not human subjects research, and thus Institutional Review Board review is not required. The data that support the findings of this study are available from the corresponding author (S.S.M.) upon reasonable request. The search was developed and executed by the informationist (J. N.), in collaboration with the study team. All searches were run on June 21, 2019 and updated on April 2, 2020 in the following databases: Medline (PubMed), Embase (Embase.com), The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials, Cochrane Methodology Register), PsycINFO (EbscoHost), CINAHL (EbscoHOST), and Web of Science (Science and Social Science Citation

Index). For the search strategies designed for Medline (PubMed), the Cochrane Library, PsycINFO, Embase, and CINAHL, controlled vocabulary terms for each concept were identified and combined with keyword synonyms. Web of Science was searched using keyword terms only. A Boolean search strategy was created and summarized here: (caregiver OR spouse OR family, etc) AND (cardiovascular disease OR heart disease OR myocardial infarction OR heart failure, etc) AND (intervention OR education OR support OR psychoeducation, etc). The entire search strategy can be found in Tables S1 through S6. Additional studies were identified by searching the references of review articles and included studies.

### Eligibility Criteria

Studies were considered eligible for inclusion if they (1) used an RCT design, (2) were written in the English language, (3) evaluated interventions for caregivers of patients with heart disease, and (4) reported caregiver outcomes. There was no time frame restriction included in the criteria. The interventions considered targeted caregivers alone or caregivers and patients together. Outcomes of interest included caregiver burden, depression, anxiety, quality of life (QoL), and knowledge of heart disease (ie, causes, strategies for risk reduction, symptoms, and medications), though no restrictions were placed on the type of caregiver outcome evaluated. If patient outcomes were reported, these data points were also included and evaluated as an exploratory outcome. Caregivers were defined as adults (aged  $\geq 18$  years) who contributed to the health care needs and daily activities of the patient and included friends or family members. We excluded studies involving: (1) health care workers as the caregivers, since the goal of this systematic review was to understand the impact of interventions on informal caregivers (family and friends), (2) caregivers of patients with stroke, because of additional challenges of caring for patients with cognitive and motor deficits, (3) palliative care or end-stage heart failure requiring mechanical assist devices, attributable to ethical and decision-making roles of caregivers confounding standard care, (4) pediatric or adolescent patients, because of our focus on care for adult patients (aged  $\geq 18$  years). We also excluded conference abstracts and protocol papers.

### Study Selection and Data Collection

The Covidence platform was used to identify and select relevant studies following Preferred Reporting Items for Systematic reviews and Meta-Analyses guidelines.<sup>29</sup> Titles and abstracts, followed by full-text articles, were screened independently by at least 2 authors (K. K., H. X., A. S., S. J., S. P., R. S., N. O., A. D.) with a third author resolving conflicts (D. W., K. K., H. X.).

Data for eligible studies were extracted by a single author (C.N.) using a pre-made form including (1) title, (2) year, (3) journal, (4) type of journal, (5) country, (6) number of patients, (7) type of patient heart disease (8) number of caregivers, (9) type of intervention, (10) follow-up time, (11) caregiver outcomes, and (12) patient outcomes. The extracted data were validated by a second author (A.D.) to ensure consistency, and discrepancies were resolved by a third author (K.K.). We used deductive analysis to identify repeated intervention themes that were associated with improved caregiver outcomes. Each intervention's themes were evaluated and summarized by at least 2 independent authors (K. K., A. S., H. X.); discrepancies were resolved by discussion. Themes were then categorized and organized by discussion (K. K., A. S., H. X.).

### Study Quality Assessment

Quality of the articles was assessed using an NIH (National Institutes of Health) study quality assessment tool<sup>30</sup> by 2 reviewers (C. N., N. O.), with resolution of conflicts by a third author (S. J.). The NIH quality assessment tool allowed answers of yes, no, or cannot determine, for 14 questions evaluating each study's internal validity. Final assessment of study quality was determined independently by 2 reviewers (C. N., N. O.) with resolution of conflicts by a third author (S. J.) and is included in Table S7.

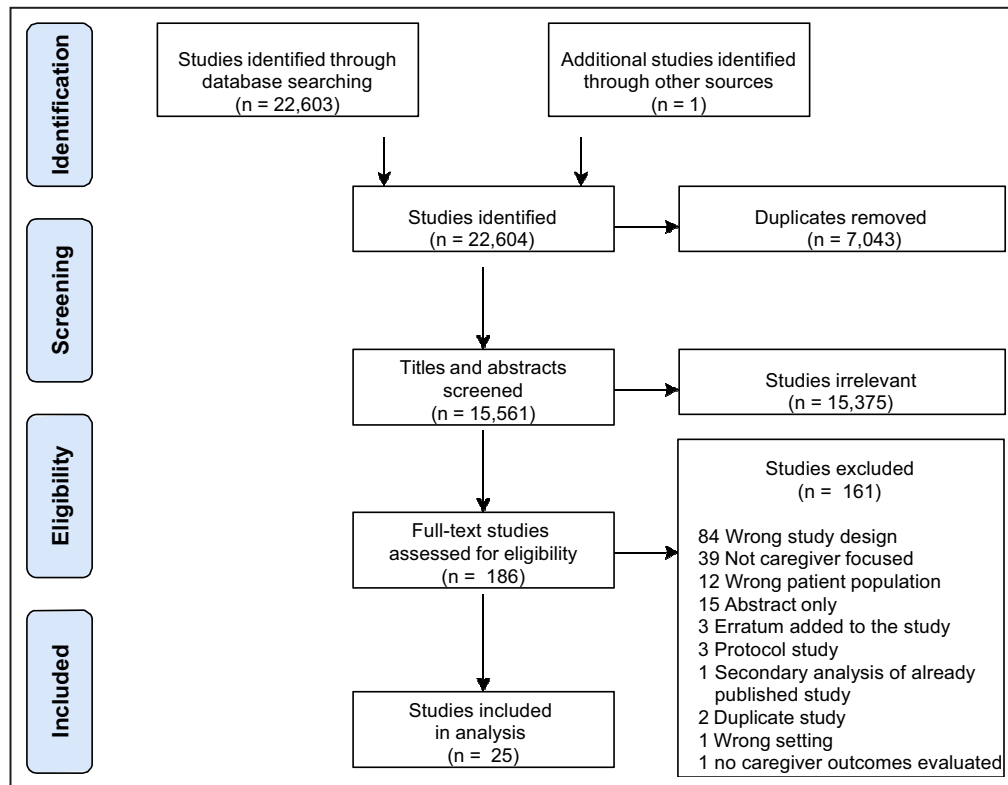
### Statistical Analysis

A random-effects meta-analysis was performed for the primary outcomes of QoL, anxiety, depression, and caregiver burden. To evaluate outcomes from the heterogeneous assessment tools used across the studies, we calculated a standardized mean difference, Hedges'  $g$ ,<sup>31</sup> as a measure of intervention effect. It was calculated using the means and SDs of the outcome measures in the study groups at the timepoint falling within 2 to 4 months postintervention. When postintervention SDs were not available, we assumed the postintervention SD was equal to the SD at baseline. Based on the magnitude of Hedges'  $g$ , we interpreted effects as small (0.2), medium (0.5), and large (0.8). Meta-analysis was performed using Stata 16 (StatCorp. 2019. *Stata Statistical Software: Release 16*. College Station, TX: StataCorp LLC).

## RESULTS

### Study Characteristics

A total of 15,561 articles were screened, which resulted in 25 studies that met inclusion criteria, representing 20 distinct RCTs that were included in our review (Figure 1). The additional 5 articles<sup>32-36</sup> assessed additional



**Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses flow diagram.**

outcomes from 4 of the distinct RCTs.<sup>35,37,38,40</sup> Some studies defined caregivers as family caregivers.<sup>40-47</sup> Five studies focused specifically on partners who lived with and cared for patients.<sup>32,38,48,49,50</sup> Only 2 studies broadly specified caregivers as an unpaid person who helped the patient on a daily basis or as an individual identified as a caregiver by the patient.<sup>51,52</sup> The ratio of male to female caregivers was not reported in most studies. A summary of the included studies, which consisted of a total of 1570 patients and 1776 caregivers, is shown in Table 1.<sup>32-56</sup>

Of the 20 distinct RCTs, 5 studies were conducted in the United States, 1 in Canada, 6 in Europe, 4 in the Middle East, 3 in Asia, and 1 in New Zealand. Thirteen RCTs were conducted among patients with heart failure, 2 among patients with myocardial infarction, 2 in patients post coronary artery bypass graft surgery, 2 in mixed patient populations simply defined as having ischemic heart disease or cardiovascular disease, and 1 in patients with implantable cardioverter defibrillators for sudden cardiac arrest (Table 1). Of the 20 RCTs, 9 were published in medical journals, 6 in nursing journals, 4 in psychology journals, and 1 in a religious journal.

### Intervention Characteristics

There was considerable heterogeneity among the interventions tested, but the majority (n=17, out of 20)

of the RCTs provided psychoeducation for caregivers (Table 1). The goal of psychoeducation therapeutic interventions is to enhance understanding of the disease and provide support to cope with illness. With regard to intervention targets, 12 of the 20 (60%) RCTs targeted patients and caregivers together, while the remaining 8 (40%) targeted caregivers alone. Intervention duration ranged from a single 30-minute session on the day of hospital discharge up to an entire year. The majority of interventions lasted between 4 to 12 weeks (n=11, out of 20). Intervention modalities varied and consisted of  $\geq 1$  of the following: hard copy resources such as pamphlets and books, one-on-one counseling telephone coaching, and both large and small group sessions led by nurses, trained research personnel, therapists/psychologists, or other medical professionals.

### Timing of Interventions

Timing of the interventions and time points when teams assessed caregiver outcomes are represented in a temporal Gantt chart (Figure 2). The majority of RCTs (n=19, out of 20) assessed baseline measurements of outcomes and most (n=17) used once weekly intervention protocols. Thirteen of the RCTs assessed outcomes at time points of 6 months and beyond, and 17 of the RCTs had at least 1 assessment of outcomes within the first month. Interventions were delivered over various time

**Table 1. Summary Table of RCTs Evaluating Interventions for Caregivers of Patients With Heart Disease**

Author	Y	Heart disease	Target population	Number of patients	Number of caregivers	Intervention summary (1. type of intervention, 2. delivery mode, 3. facilitators, 4. number of intervention sessions)	Timeline of assessment
Ågren et al. <sup>32</sup> , Ågren et al. <sup>37</sup>	2015, 2015	CHF	Caregiver and patient	42	42	(1) Psychoeducation (2) in person (3) thoracic surgeon, thoracic anesthetist and a nurse (4) 3 sessions, 30–60 mins, over 24 wk	Baseline, postintervention, 12 mo
Ågren et al. <sup>38</sup> , Lijeroos et al. <sup>33</sup> , Lijeroos et al. <sup>34</sup>	2012, 2015, 2017	CHF	Caregiver and patient	155	155	(1) Psychoeducation (2) in person (3) nurse (4) 3 sessions in 12 wk	Baseline, 3 mo, 12 mo
Borji et al. <sup>41</sup>	2018	CHF	Caregiver only	Not reported	71	(1) Spiritual intervention (2) in person (3) nurses (4) 6 45-min sessions during a period of 2 wk	Baseline, 6 wk
Broadbent et al. <sup>39</sup>	2009	MI	Caregiver and patient	103	57	(1) Psychoeducation (2) in person (3) psychologist (4) 4 sessions	1 wk
Etemadifar et al. <sup>40</sup> , Etemadifar et al. <sup>36</sup>	2014, 2017	CHF	Caregiver only	87	87	(1) Psychoeducation (2) in person (3) cardiologist, a psychiatric nurse, a cardiac care nurse, and a clergyman (4) 2 h/wk for 4 wk	Baseline, postintervention, 4 mo
Far et al. <sup>42</sup>	2016	Mixed heart disease population	Caregiver only	Not reported	64	Not reported	Baseline, postintervention, 1 mo
Fathani et al. <sup>43</sup>	2016	CHF	Caregiver only	Not reported	120	(1) Psychoeducation, health coaching (2) in person (3) therapist (4) 1–4 sessions, 30–60 mins each	Baseline, 1 mo
Gary et al. <sup>44</sup>	2018	CHF	Caregiver only	Not reported	127	(1) Psychoeducation, exercise (2) in person, telephone follow-up (3) therapist (4) 4 sessions over 12 wk	Baseline, 6 mo
Hartford et al. <sup>49</sup>	2002	CABG	Caregiver and patient	131	131	(1) Psychoeducation (2) in person, telephone follow-up (3) nurse (4) 6 calls in 7 wk	Baseline, week 4, week 8
Hu et al. <sup>45</sup>	2016	CHF	Caregiver only	118	118	(1) Psychoeducation, support group (2) in person (3) therapist (4) 30 min sessions over 3 mo	Baseline, postintervention, 6 mo
Johnston et al. <sup>48</sup>	1999	MI	Caregiver and patient	100	100	(1) Psychoeducation (2) in person (3) nurse (4) 6 wk	Baseline, 2 wk after discharge, 2, 6, and 12 mo
Kim et al. <sup>46</sup>	2016	Mixed heart disease population	Caregiver only	54	54	(1) Cardiopulmonary resuscitation training, psychoeducation (2) in person, telephone nurses (4) a 30 min session	Baseline, postintervention, 4 wk
Lang et al. <sup>54</sup>	2018	HFpEF	Caregiver and patient	50	21	(1) Psychoeducation (2) in person, telephone follow-up (3) cardiac nurses (4) at least 3 sessions over 12 wk	Baseline, 3 mo, 6 mo
Mahler and Kulik <sup>50</sup>	2002	CABG	Caregiver and patient	296	296	(1) Psychoeducation (2) video, no follow-up (3) cardiothoracic nurse, couples who have had CABG (4) 1 video session	Baseline, 1 mo, 3 mo, 6 mo
Molloy et al. <sup>53</sup>	2005	CHF	Caregiver only	60	42	(1) Exercise (2) in person (3) therapist (4) 12 wk	Baseline, 3 mo, 6 mo
Piamjariyakul et al. <sup>51</sup>	2015	CHF	Caregiver and patient	Not reported	20	(1) Psychoeducation and coaching (2) in person, telephone (3) nurse (4) 60–90 min session weekly for 4 wk	Baseline, 6 mo

(Continued)



**Table 1. Continued**

Author	Y	Heart disease	Target population	Number of patients	Number of caregivers	Intervention summary (1. type of intervention, 2. delivery mode, 3. facilitators, 4. number of intervention sessions)	Timeline of assessment
Sneed et al <sup>56</sup>	1997	SCA/ICD placement	Caregiver and patient	34	31	(1) Psychoeducation, support group (2) telephone, in-person support group (3) cardiovascular case manager (4) weekly for 8 wk with 2 in-person support groups over 4 mo	Baseline, 5-6 days post-operatively, 4 mo
Srisuk et al <sup>47</sup>	2016	CHF	Caregiver and patient	200	100	(1) Psychoeducation (2) in person, telephone support (3) nurses (4) not reported	Baseline, 3 mo, 6 mo
Wingham et al <sup>62</sup>	2019	CHF	Caregiver and patient	97	97	(1) Psychoeducation (2) in person, telephone follow-up, (3) nurses, therapists (4) 4-6 sessions over 12 wk	Baseline, 4 mo, 6 mo, 12 mo
Wu et al <sup>55</sup>	2019	CHF	Caregiver and patient	43	43	(1) Psychoeducation (2) in person, telephone follow-up (3) therapist (4) bi-weekly	Baseline, 3 mo, 6 mo

CABG indicates coronary artery bypass graft; CHF, congestive heart failure; HFpEF, heart failure with preserved ejection fraction; ICD, implantable cardiac defibrillator; MI, myocardial infarction; and SCA, sudden cardiac arrest.

points and in various intervals, so it was difficult to draw conclusions about the optimal timings of interventions for caregivers. Time points at which studies measured and assessed impact of intervention on caregiver outcomes were recorded and reported in the Gantt chart.

### Outcomes Measurement

Outcome assessment tools were heterogeneous across the studies. For instance, 2 out of 5 studies that measured QoL in caregivers and patients used Short form-36,<sup>43,45</sup> and 1 study used the comparable shortened version, Short form-12.<sup>47</sup> Depression and/or anxiety of caregivers were assessed as outcomes in 12 studies: 4 studies used the Hospital Anxiety and Depression Scale<sup>48,52,53,54</sup> 2 studies used the Center for Epidemiologic Studies Depression Scale,<sup>45,51</sup> 2 studies used the Beck Anxiety Inventory,<sup>41,49</sup> and the remaining studies used various other metrics. Caregiver burden was evaluated in 9 studies using various metrics including Zarit Burden Inventory,<sup>36,45</sup> Caregiver Burden Scale,<sup>32,38</sup> and Caregiver Burden Questionnaire—Heart Failure.<sup>52,54</sup> Caregiver knowledge was evaluated in only 2 studies using different metrics.<sup>48,55</sup>

### Effects of Interventions on Caregiver Health and Behavioral Outcomes

Across studies, we estimate small increases in physical QoL (Hedges' g=0.178; 95% CI, -0.09 to 0.45) and mental QoL (Hedges' g=0.22; 95% CI, -0.04 to 0.48), and small reductions in anxiety (Hedges' g=-0.48; 95% CI, -1.08 to 0.12) (Table 2). For each of the small effect sizes on QoL and anxiety, the CI included the null value which suggests that the intervention may not have had an effect on these outcomes. We noted moderate reductions in caregiver depression (Hedges' g=-0.64; 95% CI, -1.34 to 0.06) and caregiver burden (Hedges' g=-0.51; 95% CI, -2.71 to 1.70) (Table 2). Similarly, given the wide CIs for these effect sizes that crossed null, there is a possibility that the interventions had no effect on these outcomes. Forest plots of the individual study effects show heterogeneity across studies for each caregiver outcome (Figure 3). Both caregiver depression and caregiver burden showed considerable heterogeneity across studies (I<sup>2</sup>=91.54% and I<sup>2</sup>=98.72%, respectively), suggesting the combined effect size for these outcomes should not be interpreted as an average intervention effect.

### Effects of Interventions on Patient Health and Behavioral Outcomes

As an exploratory aim, we evaluated the patient outcomes of medication adherence and hospital



**Figure 2. Temporal Gantt chart characterizing timing of implementation of interventions for caregivers, and points at which caregiver outcomes were assessed.**

Studies are listed based on overall caregiver outcomes: positive outcomes, neutral or no change studies, and negative or adverse effect studies. Number of interventions per week (ie, once a week, twice a week, or ≥3 times a week) is color-coded. Time points at which patients are assessed for outcomes, for instance, by phone call or electronic survey, is marked with check marks.

readmission in the RCTs that targeted caregivers and patients together. Patient medication adherence was only studied by Wu and colleagues<sup>55</sup>; they reported a statistically significant improvement in adherence. Three studies measured rehospitalization with mixed outcomes.<sup>50,51,54</sup> Because of the limited number of reports, no additional statistical analysis was performed.

**CARE Model and Themes of Interventions**

We summarized and evaluated key themes from the psychoeducational interventions. When themes were organized, 4 central ones arose, which were subsequently organized under a framework, represented by Caregiver-Centered, Active Engagement, Reinforcement, and Education (CARE) (Figure 4). The 4 thematic categories of “CARE” are: (1) Caregiver-centered approaches that assess the unique needs of caregivers, and promote convenient and culturally appropriate responses to their needs, (2) Active engagement of the caregiver by the patient care team using a variety of resources and tools, (3) Reinforcement of knowledge and shared goals, and (4) Continued

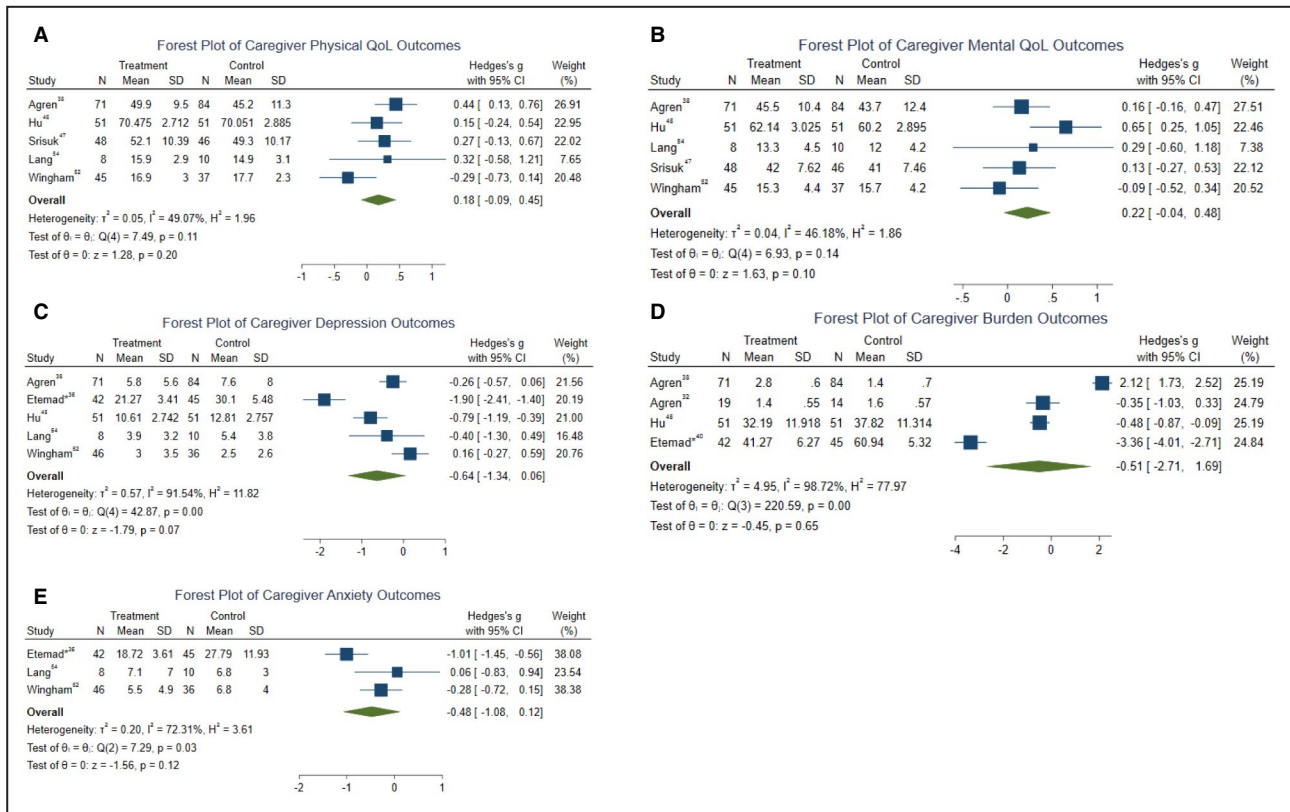
education of caregivers after assessing for gaps in knowledge to empower them to confidently provide care to patients.

**Quality of Evidence**

Our quality review (Table S7) found 13 studies (65%) of good quality, 6 studies (30%) of fair quality, and 1 study (5%) of poor quality. The details of the interventions, such as the frequency and length, total duration of the intervention period, and material content were reported in most studies. Of note, 1 study by Far and colleagues<sup>42</sup> did not report details of the intervention,

**Table 2. Hedges’ g Effect Size of Psychoeducational Interventions and CIs**

Caregiver outcome	No. of studies	Hedges’ g (95% CI)
Physical quality of life	5	0.18 (–0.09 to 0.45)
Mental quality of life	5	0.22 (–0.04 to 0.48)
Depression	5	–0.64 (–1.34 to 0.06)
Anxiety	3	–0.48 (–1.08 to 0.12)
Burden	4	–0.51 (–2.71 to 1.70)



**Figure 3. Forest plots representing effect size (Hedges' g) distribution for the outcomes. A, Physical quality of life (Hedges' g=0.178; 95% CI, -0.09 to 0.45). B, Mental quality of life (Hedges' g=0.22; 95% CI, -0.04 to 0.48). C, Depression (Hedges' g=-0.64; 95% CI, -1.34 to 0.06). D, Burden (Hedges' g=-0.51; 95% CI, -2.71 to 1.70). E, Anxiety (Hedges' g=-0.48; 95% CI, -1.08 to 0.12).**

and 2 studies,<sup>32,51</sup> were pilot studies that were mainly hypothesis-generating.

There was also a high degree of heterogeneity in the tools used for outcome assessment and in the outcomes that were measured for patients and caregivers. Similarly, we found a lack of standardization in defining the inclusion criteria for the caregiver as aforementioned.

## DISCUSSION

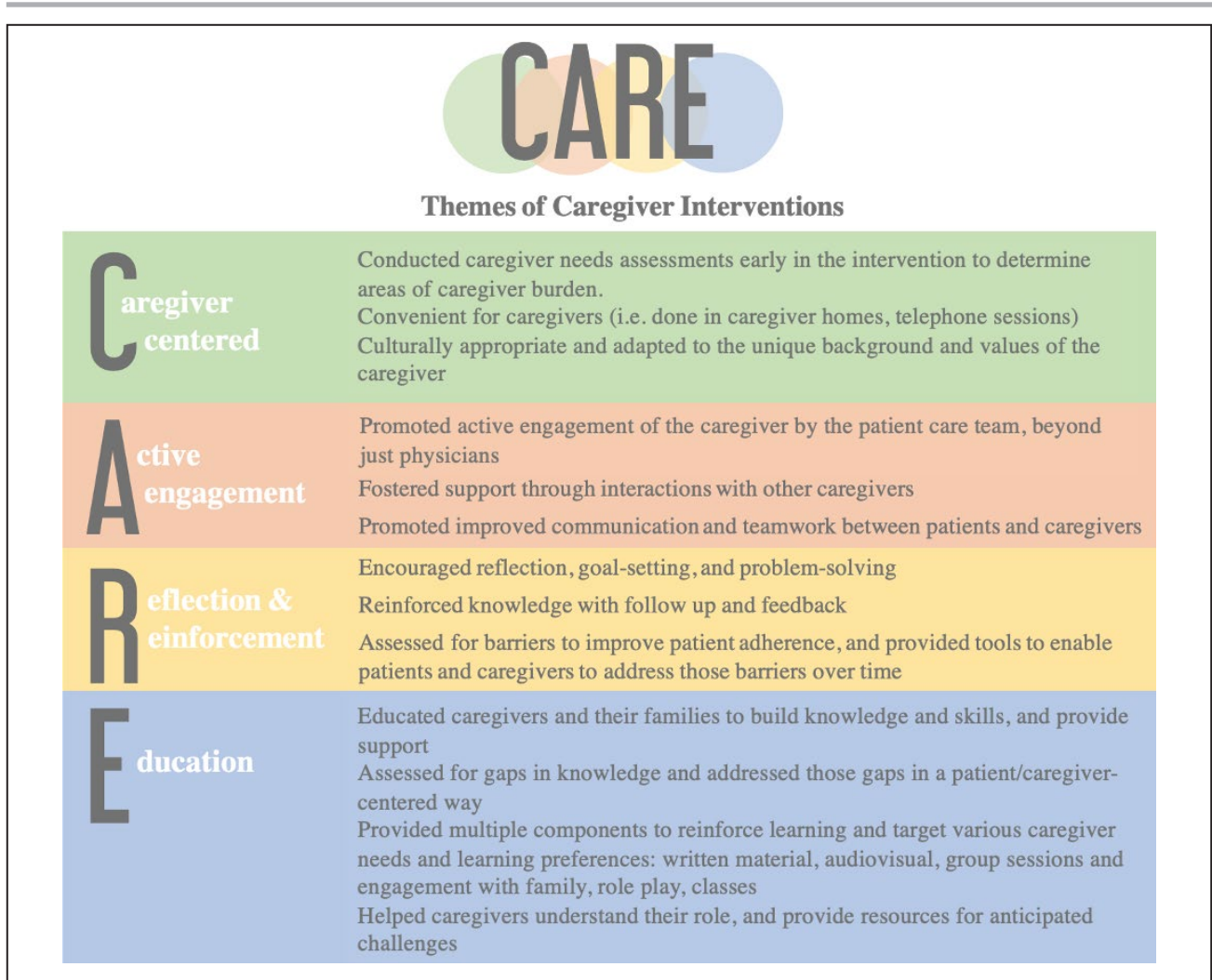
Caregivers play a vital role in supporting patients with heart disease, but experience significant burden while performing this role, emphasizing the need for greater support from the clinical team. However, it is still not always clear to the clinical teams who a patient's caregivers are and how to best support them. Prior systematic reviews have focused on evaluating and understanding the caregiver experience and caregiver burden.<sup>20,22,57</sup> We build upon this knowledge by investigating RCTs of interventions designed to educate and support caregivers of patients with heart disease. The goal was to identify interventions with statistically significant outcomes to help provide

guidelines for clinical teams to better engage the caregivers of their patients.

Our systematic review found that most interventions were designed to focus on psychoeducation, were delivered over multiple weeks, and had at least 1 in-person meeting. In summary, meta-analysis across studies showed no change compared with control in caregiver burden, anxiety, depression, physical quality of life or mental quality of life. However, it is important to note that some individual RCTs did demonstrate statistically significant improvement in at least 1 caregiver health or behavioral outcome. It may be reasonable to assume that these specific interventions have scalable potential, but the limited number of studies and heterogeneity of interventions and outcomes measured in this meta-analysis possibly resulted in a type II error.

As an exploratory aim we also evaluated the medication adherence and rehospitalization of patients in the RCTs that targeted both caregivers and their patients. It is interesting to note that none of the patient health and behavioral outcomes evaluated in these studies was negatively impacted. Two studies showed significant improvements in patient medication adherence<sup>55</sup> and rehospitalization.<sup>51</sup> Similarly, while the





**Figure 4.** Evidence-based themes and framework to aid clinical team support of caregivers.

meta-analysis was limited by the number of studies, these optimistic findings warrant additional investigation utilizing standardized methodologies.

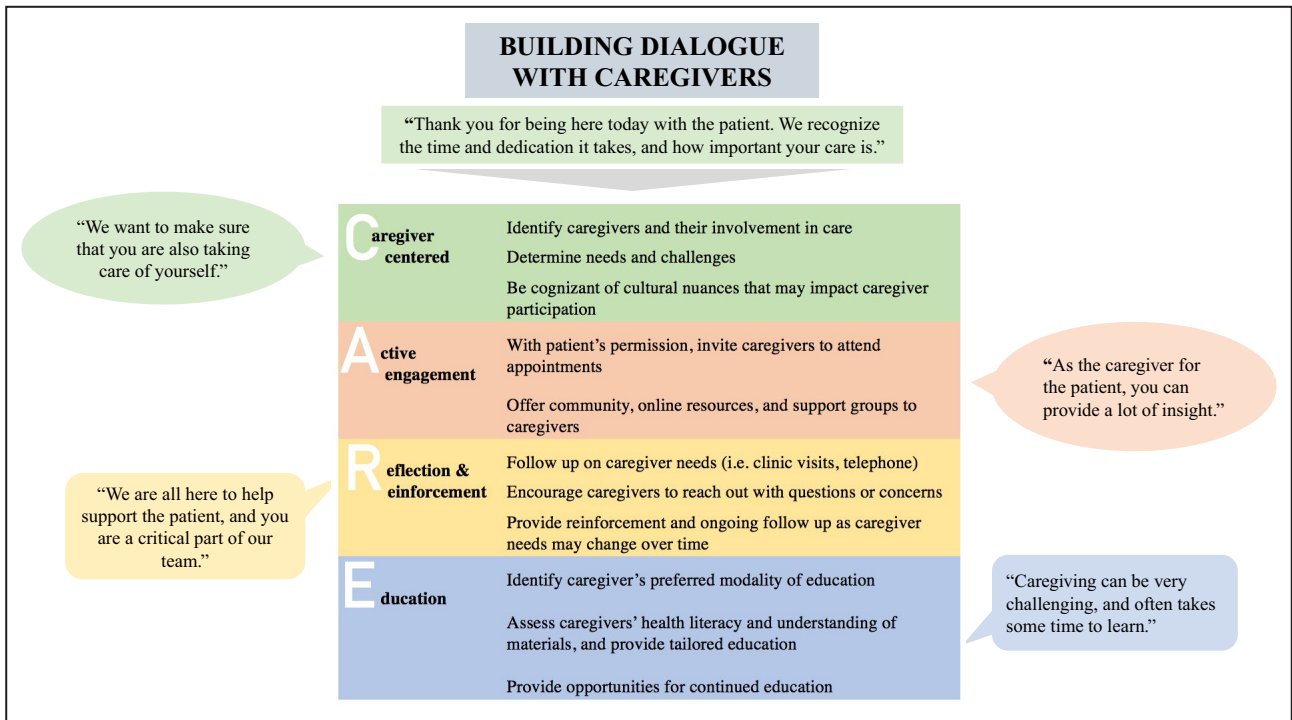
Given the variation in study intervention design, implementation, and outcome measures, direct comparison between studies was challenging. However, during our review, we noted multiple themes that were key for effective caregiver interventions. Using a qualitative approach, we organized the recurring themes and developed the CARE model (Figure 4) to highlight strategies and tools for the clinical team to better engage and support caregivers and to provide a foundation for the design of future interventions. Using the CARE model, we developed scripts and strategies that health care professionals can use to better engage and navigate the caregiver relationship (Figure 5).

While our review focused on caregivers of patients with heart disease because of its prevalence and lack of representation in the caregiver literature, we believe

that the guidelines presented are generalizable to the patient-caregiver dyad in other chronic diseases. The aspects of the CARE model highlighted by the interventions in this review are also well supported in the existing caregiver literature.

### Caregiver-Centered Approach

Wolff and colleagues, and others have highlighted the spectrum of caregiver needs, arguing for a more tailored approach to care that has the caregiver in focus.<sup>21,34,42,43</sup> At baseline some caregivers are at higher risk of incurring the negative health effects of being a caregiver and require more immediate intervention to prevent harm.<sup>21,58</sup> Some of these risk factors include poor health, lack of choice in being a caregiver, and low-wage jobs without flexibility.<sup>21</sup> Several of the studies in the review included caregiver needs assessment in the form of questionnaires or interviews, allowing the interventions to be more aligned with the



**Figure 5. Building dialogue with caregivers.**

We use the Caregiver-Centered, Active Engagement, Reinforcement, Education (CARE) model to develop scripts for health care professionals to build dialogue with caregivers. We provide statements that recognize the important role caregivers play, engage the caregiver in conversation, and follow-up questions to navigate caregiver interactions.

identified caregiver needs instead of a one size fits all approach.<sup>40,42,43,52</sup>

**Active Engagement**

Caregivers support patients in various ways, including assisting with activities of daily living, instrumental activities of daily living, and health care-related activities such as medication administration, organizing appointments, and providing transportation. Buck and colleagues and others have underscored the importance of caregiver engagement by the medical team as co-providers of care.<sup>21,22,27,57,59,60</sup> Caregivers want to be treated as part of the care team and are often frustrated by their health care teams’ lack of acknowledgment and support.<sup>27,59</sup> As supported by our review, successful interventions used various methods to actively engage caregivers. These included the use of multimedia resources,<sup>40,44,46,47</sup> role play,<sup>55</sup> teach back,<sup>44,47,51,55</sup> peer support groups,<sup>45</sup> small group activities,<sup>45</sup> and workbooks/manuals.<sup>46,47,51,52,54</sup> Engagement by the health care team should be multidisciplinary, extending to physicians, pharmacists, nurses, dieticians, physical therapists, social workers, and more.

**Reinforcement**

Most studies in this review, apart from a select few,<sup>35,53</sup> provided ongoing training, follow-up, or booster

sessions to reinforce and build on skills or knowledge gained. Because of knowledge attrition and ongoing needs, follow-up and reinforcement is likely important for improved outcomes. What is less clear in the literature is intervals at which reinforcement is required, and frequency, though it will likely be driven by the unique needs of the caregiver and patient.

**Education**

Caregivers often feel ill-prepared to deliver care, and lack understanding and knowledge about the patient’s disease process and their role in supporting patients, which results in increased uncertainty and distress.<sup>22,27,35,61,62,63,64</sup> This highlights the value placed by caregivers in understanding their loved ones disease and how they can effectively support them. In a study of an intervention for caregivers of patients who had a heart attack, caregivers had increased understanding, less anxiety, and more positive expectations when they attended 1 half-hour patient-and-spouse session with a psychologist, focused on illness perception, in addition to standard of care.<sup>35</sup> All interventions in our review offered some form of education covering illness perception, clinical knowledge base, or psychosocial components of care. Topics for education are diverse and should be guided by the disease process and by caregiver and patient needs.

We acknowledge that while these best practices may be identified, the level of support that can be offered to caregivers of patients may be limited, because of time constraints in busy practices and the patient-centered focus of our reimbursement system. Consequently, initial caregiver interventions should be designed to be cost and resource effective. For example, in their study, Lang and colleagues, discuss the societal, health care utilization, and intervention costs associated with their positive caregiver and patient outcomes.<sup>54</sup> In a recent article, Wolff and colleagues outlined strategies at a clinical and policy level to begin addressing this inequity of care.<sup>21</sup> They argue that the clinical team has a responsibility for identification of at-risk caregivers, assessment of caregiver burden, and provision of tailored support to caregivers.<sup>21</sup> However, Wolff and colleagues also acknowledged that the clinical team needs to be better educated to engage and support caregivers, and reimbursement strategies must change to hold the entire clinical team accountable in the support of caregivers.<sup>21</sup> As we await continued policy shifts, we propose the CARE model as a way to enable clinicians to identify and engage caregivers most at risk and to provide a framework for continued research. The CARE model provides themes in which clinicians may engage, build dialogue with, and identify needs of caregivers. While it is our hope that this model provides strategies that will reduce caregiver stress and improve their quality of life, we must acknowledge that there are inherent qualities of the caregiver such as age, comorbidities, resilience, and existing social support that are not as easily impacted and can also have an important effect on caregiver outcomes. Consequently, further translational studies are necessary to identify effective interventions for caregivers that are resource-efficient, and adaptable to the workflow of members of the health care team.

### Strengths and Limitations

To build upon prior caregiver intervention literature, we categorized the themes and outcomes of the included studies and created the CARE model. The model highlights specific areas for future caregiver interventions to target. We also analyzed and reported outcomes among both patients and caregivers, highlighting the dynamic and complex interactions that exist in chronic disease management. The studies also included a wide spectrum of demographics and countries.

There are a few limitations of this study. Given the scope of our topic and a lack of clearly established search terms in the literature to encompass for example, family and other unpaid caregivers, we used broad search terms that resulted in thousands of returned articles. The low specificity led to many unrelated search returns, which had to be manually filtered. We also

discovered a lack of consistency in who was considered a caregiver across studies. Since, for example, the needs of spousal caregivers may differ from the needs of caregivers who live outside the home, making direct comparisons between studies is more challenging. The heterogeneity of caregiver interventions and reported outcomes and small sample sizes may have resulted in an error of omission, potentially masking significant findings. The considerable heterogeneity across studies means that the combined effect sizes may not be meaningful as an average intervention effect. Further, the small number of studies do not allow for exploration of the causes of such heterogeneity. Future work should focus on developing standardized approaches with common metrics to reduce the potential for a type II error.

We recognize that another limitation of our systematic review is that it does not capture unpublished, institutionalized support for caregivers. For example, Called to Care at Johns Hopkins Bayview Medical Center (Baltimore, MD) provides supportive services, education, and access to community resources for caregivers of patients at our institution, that is separate from assistance by the clinical team. Additionally, organizations like the American Heart Association and American College of Cardiology provide resources to support caregivers of patients with CVD. There are a myriad of other national and smaller local programs that exist to support caregivers. Our findings and evidence-based recommendations must be contextualized within these existing infrastructures to collaboratively promote improved caregiver support and engagement.

### FUTURE DIRECTIONS

There is a need for better designed clinical trials to help establish evidence-based clinical practices for supporting caregivers. Additionally, establishing a clear relationship between caregiver support and patient outcomes may be valuable to help promote changes in policy and clinical practice. Using heart disease as an index case, our model's reliability and validity should be further studied. Thereafter, it can serve as a model for other chronic diseases that require extensive caregiver involvement.

We note that in our systematic review, there was also a high degree of heterogeneity in what outcomes were measured, and how they were assessed for both caregivers and patients. This reflects a need for more standardization of caregiver interventions and outcomes assessment. Similarly, we found a lack of standardization in defining "caregiver", such as "who is a caregiver?" and "what roles do they play?". This is important to note because moving forward, we must

agree on a standard definition of “caregiver”, in order to better represent the caregiver population, recognize them and their role in the health of the patient, and develop practices that help them maintain their health and quality of life. We also acknowledge that in practice, the terminology “caregiver” may not be universally accepted. For example, while a spouse or adult child may support a loved one with their health care decisions and needs, they may not consider themselves to be a caregiver.

In our review, we also noted a high degree of heterogeneity in the timing of interventions and the intervals over which they were delivered. This made drawing conclusions about optimal timing challenging. We hypothesize that the timing of the intervention may be an important factor. For example, during transitions from hospital to home or after a new or worsening diagnosis, an intervention may have a greater impact on caregiver outcomes. Furthermore, in our study, evaluation of outcomes occurred periodically throughout and immediately following interventions. We hypothesize that timing of follow-up impacts the magnitude of detected outcomes. Consequently, the timing of interventions is a potentially important factor that warrants further investigation.

## CONCLUSIONS

The vital role that caregivers play in supporting the care of patients with heart disease and the resulting burden experienced by performing this role highlights the need for greater support from the clinical team. Many of the caregivers in the intervention groups did not exhibit a significant improvement from control groups. However, statistically significant improvements in some outcomes were demonstrated and rarely did the interventions worsen caregiver outcomes. Our systematic review highlighted themes on engaging and supporting caregivers (CARE) based on the RCTs. There remains a need for evidence-based recommendations to guide the health care team in best practices for engaging and aiding caregivers of patients with heart disease.

## ARTICLE INFORMATION

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## Disclosures

Under a license agreement between Corrie Health and the Johns Hopkins University, the University owns equity in Corrie Health and the University and Drs Marvel, Lee, and Martin are entitled to royalty distributions related to technology described in the study discussed in this publication. Additionally, Drs Marvel, Lee, and Martin are cofounders of and hold equity in Corrie Health. This arrangement has been reviewed and approved by the Johns Hopkins University in accordance with its conflict of interest policies. Dr Martin has served as a consultant to Akcea, Amgen, AstraZeneca, Esperion, Kaneka, Novo Nordisk, Quest Diagnostics, Regeneron, REGENXBIO, Sanofi, and 89bio. He is a coinventor on a system to estimate low-density lipoprotein cholesterol levels, patent application pending. The remaining authors have no disclosures to report.

## Supplementary Material

Tables S1–S7

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# **Supplemental Material**

**Table S1. PubMed Search terms (Limited to English).**

#1	<p>(<b>"Heart Failure"</b>[Mesh:NoExp] OR <b>"Myocardial Infarction"</b>[Mesh:NoExp] OR <b>"Arrhythmias, Cardiac"</b>[Mesh:NoExp] OR <b>"Heart Diseases"</b>[Mesh:NoExp] OR <b>"Cardiovascular Diseases"</b>[Mesh:NoExp] OR <b>"coronary artery disease"</b>[tiab] OR <b>"ischemic heart disease"</b>[tiab] OR <b>"heart failure"</b>[tiab] OR <b>"myocardial infarction"</b>[tiab] OR <b>"ventricular dysfunction"</b>[tiab] OR <b>heart attack*</b>[tiab] OR <b>"acute coronary syndrome"</b>[tiab] OR <b>"coronary heart disease"</b>[tiab] OR <b>"postmyocardial infarction"</b>[tiab] OR <b>cardiomyopath*</b>[tiab] OR <b>arrhythmia*</b>[tiab] OR <b>"heart valve disease"</b>[tiab] OR <b>"pulmonary heart disease"</b>[tiab] OR <b>"hypertensive heart disease"</b>[tiab] OR <b>cardiovascular disease*</b>[tiab] OR <b>heart disease*</b>[tiab])</p>
#2	<p>(<b>"Caregivers"</b>[Mesh] OR <b>"Spouses"</b>[Mesh] OR <b>caregiver*</b>[tiab] OR <b>"caring intervention"</b>[tiab] OR <b>"care giver"</b>[tiab] OR <b>"care givers"</b>[tiab] OR <b>"care giving"</b>[tiab] OR <b>spouse*</b>[tiab] OR <b>significant other*</b>[tiab] OR <b>"family caring"</b>[tiab] OR <b>family caregiver*</b>[tiab] OR <b>family partner*</b>[tiab] OR <b>"partner support"</b>[tiab] OR <b>husband*</b>[tiab] OR <b>wives</b>[tiab] OR <b>wife</b>[tiab] OR <b>partner</b>[tiab] OR <b>"adult children"</b>[tiab] OR <b>"relatives"</b>[tiab] OR <b>sibling*</b>[tiab] OR <b>spouse*</b>[tiab] OR <b>carers</b>[tiab])</p>
#3	<p>(<b>intervention*</b>[tiab] OR <b>"Counseling"</b>[Mesh] OR <b>"Social Support"</b>[Mesh] OR <b>"education"</b>[Subheading] OR <b>"Education"</b>[Mesh] OR <b>"Mentoring"</b>[Mesh] OR <b>mentor*</b>[tiab] OR <b>educat*</b>[tiab] OR <b>counsel*</b>[tiab] OR <b>coach*</b>[tiab] OR <b>train*</b>[tiab] OR <b>teach*</b>[tiab] OR <b>instruct*</b>[tiab] OR <b>support*</b> OR <b>"self care"</b>[tiab] OR <b>"self</b></p>

	management"[tiab] OR psychoeducation[tiab] OR "Telemedicine"[Mesh] OR mHealth[tiab] OR "mobile health"[tiab] OR telemedicine[tiab] OR telemonitoring[tiab] OR "e health"[tiab] OR ((text messag*[tiab] Or mobile application*[tiab] OR mobile phone*[tiab] OR cell phone*[tiab] or smartphon*[tiab] Or smart phone*[tiab]) AND health[tiab]))
#4	#1 AND #2 AND #3
#5	(Animals[mesh] NOT humans[mesh])
#6	#4 NOT #5

**Table S2. Embase search terms (Limited to English, journal articles).**

#1	<p>( 'heart failure'/de OR 'heart infarction'/exp OR 'heart arrhythmia'/exp OR 'heart disease'/exp OR 'cardiovascular disease'/exp) OR (“coronary artery disease” OR “ischemic heart disease” OR “heart failure” OR “myocardial infarction” OR “ventricular dysfunction” OR “heart attack*” OR “acute coronary syndrome” OR “coronary heart disease” OR “postmyocardial infarction” OR cardiomyopath* OR arrhythmia* OR “heart valve disease” OR “pulmonary heart disease” OR “hypertensive heart disease” OR “cardiovascular disease*” OR “heart disease*”):ti,ab</p>
#2	<p>( 'caregiver'/exp OR 'spouse'/exp ) OR (caregiver* OR “caring intervention” OR “care giver” OR “care givers” OR “care giving” OR spouse* OR “significant other*” OR “family caring” OR “family caregiver*” OR “family partner*” OR “partner support” OR husband* OR wives OR wife OR partner OR “adult children” OR relatives OR sibling* OR spouse* OR carers):ti,ab</p>
#3	<p>( 'counseling'/exp OR 'social support'/exp OR 'education'/exp OR 'telemedicine'/exp) OR (mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR “self care” OR “self management” OR psychoeducation OR mHealth OR “mobile health” OR telemedicine OR telemonitoring OR “e health”):ti,ab OR ((“text messag*”:ti,ab Or “mobile application*”:ti,ab OR “mobile phone*” OR “cell phone*”:ti,ab or smartphon*:ti,ab Or “smart phone*”:ti,ab) AND (health:ti,ab))</p>



#4	#1 AND #2 AND #3
#5	(Animals/exp or invertebrate/exp or 'animal experiment'/exp or 'animal tissue'/exp or 'animal cell'/exp or nonhuman/exp) NOT (humans/exp)
#6	#4 NOT #5

**Table S3. CINAHL search terms (Limited to English, journal articles).**

<p>#1</p>	<p>(MH "Heart Failure") OR (MH "Myocardial Infarction") OR (MH "Heart Diseases") OR (MH "Cardiovascular Diseases") OR TI (“coronary artery disease” OR “ischemic heart disease” OR “heart failure” OR “myocardial infarction” OR “ventricular dysfunction” OR “heart attack*” OR “acute coronary syndrome” OR “coronary heart disease” OR “postmyocardial infarction” OR cardiomyopath* OR arrhythmia* OR “heart valve disease” OR “pulmonary heart disease” OR “hypertensive heart disease” OR “cardiovascular disease*” OR “heart disease*”)  OR AB (“coronary artery disease” OR “ischemic heart disease” OR “heart failure” OR “myocardial infarction” OR “ventricular dysfunction” OR “heart attack*” OR “acute coronary syndrome” OR “coronary heart disease” OR “postmyocardial infarction” OR cardiomyopath* OR arrhythmia* OR “heart valve disease” OR “pulmonary heart disease” OR “hypertensive heart disease” OR “cardiovascular disease*” OR “heart disease*”))</p>
<p>#2</p>	<p>(MH "Caregivers") OR (MH "Spouses") OR TI (caregiver* OR “caring intervention” OR “care giver” OR “care givers” OR “care giving” OR spouse* OR “significant other*” OR “family caring” OR “family caregiver*” OR “family partner*” OR “partner support” OR husband* OR wives OR wife OR partner OR “adult children” OR relatives OR sibling* OR spouse* OR carers) OR AB (caregiver* OR “caring intervention” OR “care giver” OR “care givers” OR “care giving” OR spouse* OR “significant other*” OR “family caring” OR “family caregiver*” OR “family partner*” OR “partner support” OR husband* OR wives</p>

	<p>OR wife OR partner OR “adult children” OR relatives OR sibling* OR spouse* OR carers))</p>
#3	<p>(MH "Counseling") OR (MH "Caregiver Support") OR (MH "Education") OR (MH "Mentorship") OR (MH "Telemedicine") OR TI (intervention* OR mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR “self care” OR “self management” OR psychoeducation OR mHealth OR “mobile health” OR telemedicine OR telemonitoring OR “e health” OR ((“text messag*” Or “mobile application*” OR “mobile phone*” OR “cell phone*” or smartphon* Or “smart phone*”) AND health)) OR AB (intervention* OR mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR “self care” OR “self management” OR psychoeducation OR mHealth OR “mobile health” OR telemedicine OR telemonitoring OR “e health” OR ((“text messag*” OR “mobile application*” OR “mobile phone*” OR “cell phone*” or smartphon* OR “smart phone*”) AND health))</p>
#4	<p>#1 AND #2 AND #3</p>

**Table S4.** PsycINFO (Limited to English, journal articles).

#1	<p>(DE "Cardiovascular Disorders" OR DE "Heart Disorders" OR DE "Myocardial Infarctions") OR TI ("coronary artery disease" OR "ischemic heart disease" OR "heart failure" OR "myocardial infarction" OR "ventricular dysfunction" OR "heart attack*" OR "acute coronary syndrome" OR "coronary heart disease" OR "postmyocardial infarction" OR cardiomyopath* OR arrhythmia* OR "heart valve disease" OR "pulmonary heart disease" OR "hypertensive heart disease" OR "cardiovascular disease*" OR "heart disease*") OR AB ("coronary artery disease" OR "ischemic heart disease" OR "heart failure" OR "myocardial infarction" OR "ventricular dysfunction" OR "heart attack*" OR "acute coronary syndrome" OR "coronary heart disease" OR "postmyocardial infarction" OR cardiomyopath* OR arrhythmia* OR "heart valve disease" OR "pulmonary heart disease" OR "hypertensive heart disease" OR "cardiovascular disease*" OR "heart disease*"))</p>
#2	<p>((DE "Caregivers") OR (DE "Spouses")) OR TI (caregiver* OR "caring intervention" OR "care giver" OR "care givers" OR "care giving" OR spouse* OR "significant other*" OR "family caring" OR "family caregiver*" OR "family partner*" OR "partner support" OR husband* OR wives OR wife OR partner OR "adult children" OR relatives OR sibling* OR spouse* OR carers) OR AB (caregiver* OR "caring intervention" OR "care giver" OR "care givers" OR "care giving" OR spouse* OR "significant other*" OR "family caring" OR "family caregiver*" OR "family partner*" OR "partner support" OR husband* OR wives</p>

	OR wife OR partner OR “adult children” OR relatives OR sibling* OR spouse* OR carers))
#3	<p>((DE "Social Support") OR (DE "Education") OR (DE "Mentor") OR (DE "Telemedicine")) OR</p> <p>OR TI (intervention* OR mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR “self care” OR “self management” OR psychoeducation OR mHealth OR “mobile health” OR telemedicine OR telemonitoring OR “e health” OR ((“text messag*” Or “mobile application*” OR “mobile phone*” OR “cell phone*” or smartphon* Or “smart phone*”) AND health)) OR AB (intervention* OR mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR “self care” OR “self management” OR psychoeducation OR mHealth OR “mobile health” OR telemedicine OR telemonitoring OR “e health” OR ((“text messag*” OR “mobile application*” OR “mobile phone*” OR “cell phone*” or smartphon* OR “smart phone*”) AND health))</p>
#4	#1 AND #2 AND #3



**Table S5. Web of Science Search Terms (English).**

#1	<p>TS=(“coronary artery disease” OR “ischemic heart disease” OR “heart failure” OR “myocardial infarction” OR “ventricular dysfunction” OR “heart attack*” OR “acute coronary syndrome” OR “coronary heart disease” OR “postmyocardial infarction” OR cardiomyopath* OR arrhythmia* OR “heart valve disease” OR “pulmonary heart disease” OR “hypertensive heart disease” OR “cardiovascular disease*” OR “heart disease*”)</p>
#2	<p>TS=(caregiver* OR “caring intervention” OR “care giver” OR “care givers” OR “care giving” OR spouse* OR “significant other*” OR “family caring” OR “family caregiver*” OR “partner support” OR husband* OR wives OR wife OR partner OR “adult children” OR relatives OR sibling* OR spouse* OR carers)</p>
#3	<p>TS=(mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR “self care” OR “self management” OR psychoeducation OR mHealth OR “mobile health” OR telemedicine OR telemonitoring OR “e health” OR (“text messag*” Or “mobile application*” OR “mobile phone*” OR “cell phone*” or smartphon* Or “smart phone*”) AND health))</p>
#4	<p>#1 AND #2 AND #3</p>

**Table S6. Cochrane Search Terms.**

#1	<p>[mh "Heart Failure"] OR [mh "Myocardial Infarction"] OR [mh "Arrhythmias, Cardiac"] OR [mh "Heart Diseases"] OR [mh "Cardiovascular Diseases"] OR "coronary artery disease" OR "ischemic heart disease" OR "heart failure" OR "myocardial infarction" OR "ventricular dysfunction" OR "heart attack*" OR "acute coronary syndrome" OR "coronary heart disease" OR "postmyocardial infarction" OR cardiomyopath* OR arrhythmia* OR "heart valve disease" OR "pulmonary heart disease" OR "hypertensive heart disease" OR "cardiovascular disease*" OR "heart disease*")</p>
#2	<p>([mh Caregivers] OR [mh Spouses] OR caregiver* OR "caring intervention" OR "care giver" OR "care givers" OR "care giving" OR spouse* OR "significant other*" OR "family caring" OR "family caregiver*" OR "family partner*" OR "partner support" OR husband* OR wives OR wife OR partner OR "adult children" OR "relatives" OR sibling* OR spouse* OR carers)</p>
#3	<p>(intervention* OR [mh Counseling] OR [mh "Social Support"] OR [mh Education] OR [mh Mentoring] OR mentor* OR educat* OR counsel* OR coach* OR train* Or teach* Or instruct* OR support* OR "self care" OR "self management" OR psychoeducation OR [mh Telemedicine] OR mHealth OR "mobile health" OR telemedicine OR telemonitoring OR "e health" OR ("text messag*" Or "mobile application*" OR "mobile phone*" OR "cell phone*" or smartphon* Or "smart phone*") AND health))</p>

#4	#1 AND #2 AND #3
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**Table S7. Quality assessment of articles using the NIH quality assessment tool.**

<b>Author name</b>	<b>Quality Rating</b>
Agren, 2015	Good
Agren, 2012	Fair
Borji	Good
Broadbent	Good
Etemadifar	Good
Far (Iran)	Poor
Fathani (Iran)	Fair
Gary	Good
Hartford	Fair
Hu	Good
Johnston	Fair
Kim	Fair
Lang	Good
Mahler	Fair
Molloy	Good
Piamjariyakul	Good
Sneed	Good
Srisuk	Good
Wingham	Good
Wu	Good