QUERI

Effectiveness of Family and Caregiver Interventions on Patient Outcomes among Adults with Cancer or Memory-Related Disorders: A Systematic Review

EXECUTIVE SUMMARY

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) managers and policymakers, as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout VA.

QUERI provides funding for four ESP Centers and each Center has an active VA affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence,
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of QUERI Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at nicole.floyd@va.gov.

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EXECUTIVE SUMMARY

BACKGROUND

Two federal laws have been signed in the last five years that have expanded the Veterans Health Administration's (VHA) authority to provide services to families of Veterans. This expansion allows the VHA to provide a number of clinical and support services, training, and education to families and caregivers of patients with service connected and non-service connected injuries or conditions. The VHA has responded by initiating a set of support services, including counseling, a caregiver support line, and website, to support families and caregivers of Veterans. With this new authorization, there is now the potential to adopt or integrate additional family-involved interventions to improve Veterans' outcomes. This review's aim was to evaluate which interventions are efficacious in affecting patient outcomes for memory-related disorders or cancer.

Family and caregiver interventions, especially interventions targeted to caregivers caring for someone with a physical health condition, typically aim to develop caregiver skills to manage their caregiving tasks and to reduce caregiver burden. An often implicit assumption in these interventions is that by reducing caregiver burden and improving caregiver skills, the care recipient will also benefit. Reflecting this, the majority of family-focused intervention studies and reviews of these studies have concentrated only on family or caregiver outcomes.[1-4] We conducted a systematic review of interventions that explicitly tested this assumption. We evaluated the published evidence assessing whether family involved interventions improve patient outcomes (i.e., efficacy) and whether specific family involved interventions are better than alternative ones (i.e., specificity or comparative effectiveness). We specifically examined the effects of family-involved interventions on the patients, not on the family members. We assessed if there is evidence that interventions targeted at family members only or both family members and adult care recipients improve the patients' outcomes. We limited our focus to family members caring for those with cancer and memory-related conditions since the majority of studies examine one of these two conditions. This project was nominated by Sonja Batten, PhD, Office of Mental Health Services. The key questions and scope were refined with input from a technical expert panel.

We addressed the following key questions:

Key Question #1. What are the benefits of family and caregiver psychosocial interventions for adult patients with cancer or memory-related disorders compared to usual care or wait list?

a. What are the harms of these interventions?
b. Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?

Key Question #2. What are the benefits of one family or caregiver oriented psychosocial intervention compared to either: 1) a patient-directed intervention, or 2) another alternative family-oriented intervention in improving outcomes for adult patients with cancer or memory-related disorders?

a. What are the harms of these interventions?
b. Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?

METHODS

DATA SOURCES

We searched MEDLINE (Ovid) and PsycINFO for randomized controlled trials (RCTs) and systematic reviews published 1980 to December, 2012 using the following search terms: family, couples, home nursing, legal guardians, couple therapy, family therapy, or marital therapy. Because social and cultural norms and resources for family support vary across countries, we limited the search to studies conducted in the United States. We included only studies involving subjects over age 18 and published in the English language. Additional citations were identified from reference lists of retrieved articles. Titles, abstracts, and articles were reviewed by trained research personnel. We included studies published after 1995.

After the full-text review, we further refined the scope to include only studies that targeted patients with one of two conditions—cancer or memory-related disorders. These conditions made up the majority of the studies reviewed, providing the largest body of evidence from which we could synthesize the evidence.

DEFINITIONS OF KEY CONCEPTS OF FAMILY AND OUTCOMES

The literature uses a number of different terms to describe those who provide help and support to patients: family, caregivers, care partners, support network. For convenience sake, we use the term "family" to describe all those, related and non-related, who provide direct care and support to patients with cancer or memory disorders. Study settings often determine how the person with the condition is described (e.g., patient, resident, spouse). Since participants were included in trials based on their diagnosis, we use the term "patient" to describe the person with memory-related disorder or cancer.

We examined the effect of family-involved interventions on five outcomes: quality of life, depression/anxiety, symptom control, health care utilization, and relationship adjustment. Quality of life was defined as overall quality of life (i.e., global quality of life), and then further conceptualized to include functional status, including physical functioning (e.g., activities of daily living and instrumental activities of daily living); general psychological functioning that does not directly correspond with mental health conditions or diagnoses in the Diagnostic and Statistical Manual (DSM) (e.g., distress, psychological well-being); cognitive functioning (e.g., memory capacity, problem solving abilities); and social functioning (e.g., social and family well-being). Depression/anxiety included reports of depressive symptoms or anxiety using standardized assessments. Symptom control or management included reports of any physical symptoms associated with treatment or disease progression (e.g., for cancer: pain, sexual functioning; for memory-related disorders: agitation, wandering or other problem behaviors). Utilization included all types of health care utilization, including hospitalization, institutionalization, or emergency room visits, and relationship adjustment including family functioning and relationship quality.

CATEGORIZATION OF INTERVENTIONS

Disease symptoms, treatment side effects, and consequences of disease progression are often the targets of patient-centered interventions. Because both the interventions and the targets of the interventions are unique and differ by condition, we reviewed the cancer and memory-related disorders studies separately. To further understand whether certain types of interventions had more evidence than others, we first reviewed the study methods of all the selected trials and then grouped similar interventions into categories.

For cancer studies, each trial was grouped into one of five categories: 1) telephone or web-based counseling, where, in at least one intervention arm, telephone or web-based counseling was provided separately for family members and care recipient; 2) behavioral couples therapy or adaptations of cognitive behavior therapy (CBT); 3) training for family members to manage or control specific patient symptoms; 4) interventions that, in addition to training families to effectively manage care recipient symptoms or behaviors, also included family support or counseling; and 5) unique interventions with unique intervention targets.

Interventions for families of those with memory disorders were grouped into one of three categories: 1) training families to change or manage patient behavior, 2) interventions that provided support or counseling for family members and trained them to effectively manage patient symptoms or behaviors, and 3) unique interventions with unique intervention targets. We summarize results by intervention categories.

DATA EXTRACTION AND QUALITY ASSESSMENT

We extracted study characteristics, patient characteristics, and outcomes separately for cancer studies and memory-related studies. Data were extracted once by an investigator or trained research associate and then verified by another, all under the supervision of the Principal Investigator. We focused on the patient- and family-centered outcomes outlined above. For cancer, our outcomes of interest were: overall quality of life; the components of quality of life (physical, general psychological functioning, and social functioning), symptom control/management, depression/anxiety, utilization (including hospitalization and institutionalization), and relationship adjustment. For memory disorders, we assessed similar outcomes but included cognitive functioning instead of general psychological functioning.

Only outcomes that were assessed using previously published scales or measures or had clear end-points (e.g., death, hospitalization) were included. In order to determine both immediate and long-term benefits of the intervention, we captured, whenever possible, data at two time-points: post-intervention ($\pm$1 month) and at least 6 months post-intervention. For studies with multiple assessments at greater than 6 months post-intervention, the last available assessment was extracted.

We assessed the risk of bias for each trial and used this assessment as the basis for rating the trial's quality. Using established criteria for RCTs to evaluate for risk of bias, we considered whether the intervention allocation was concealed; participants, interventionists, and health care providers were blinded to treatment allocation; intention-to-treat (ITT) analyses were used; withdrawals and dropouts by group assignment were adequately described; and if the treatment was monitored

for quality and consistency (i.e., treatment integrity). We rated trials as good, fair, or poor quality and considered allocation concealment and blinding (of outcome assessment at a minimum) as critical elements for a good quality trial. We based our evaluations for risk of bias and strength of evidence on criteria used by the Agency for Healthcare Research and Quality and the Cochrane Collaboration. A good quality trial (low risk of bias) indicated that the trial reported adequate allocation concealment, a minimum of single blinding (participants or investigators or assessors are blinded), and that either intent-to-treat analysis was conducted or clear reasons for dropouts/attrition by group were provided. A fair quality trial (moderate risk of bias) was one in which allocation concealment and blinding criteria were either met or unclear and no more than one of the remaining criterion (ITT, withdrawals) were unmet. A trial with adequate allocation concealment that did not meet other domains, or did not make clear whether other domains were met, was rated as fair. Trials were rated poor quality (high risk of bias) if the trial had inadequate allocation concealment or no blinding and/or clearly met only one of the established risk of bias domains.

We determined the strength of evidence for each outcome based on all the studies that assessed that outcome. We rated the strength of evidence for each outcome using the following grades: 1) high confidence – further research is very unlikely to change the confidence in the estimate of effect, meaning that the evidence reflects the true effect; 2) moderate confidence – further research may change our confidence in the estimate of effect and may change the estimate; 3) low confidence – further research is very likely to have an important impact on the confidence in the estimate of effect and is likely to change the estimate, meaning that there is low confidence that the evidence reflects the true effect; and 4) insufficient – the evidence was unavailable or did not permit a conclusion.

DATA SYNTHESIS

We analyzed studies by comparing their characteristics, methods, and findings. Few pooled analyses of data were possible due to heterogeneity of populations, interventions and outcomes across studies; therefore, most findings were summarized narratively.

When reported, intervention effect sizes from trials were extracted. If effect sizes in a trial were not reported but sample size, standard deviation, and mean scores were, we calculated intervention effect sizes for each outcome in order to compare across studies. If the effect size was significant (the confidence interval did not include 0), we considered this a significant effect in our summary, even if the authors report null findings. We considered Cohen's guide for interpreting effect sizes (i.e., d of 0.2 = small effect, 0.5 = medium effect, 0.8 = large effect) when evaluating outcome data.

We compiled a summary of findings by condition for each question, and then summarized findings across intervention categories.

PEER REVIEW

A draft version of this report was reviewed by technical experts, as well as clinical leadership. Reviewer comments (see Appendix C) were addressed and our responses were incorporated in the final report.

RESULTS

OVERVIEW OF ALL STUDIES

We reviewed 2,771 titles and abstracts from the electronic search. After excluding 1,990 abstracts that did not meet our inclusion criteria, we retrieved 781 full-text articles for further review. We excluded another 736 references that did not fit our criteria, leaving 45 to review. We identified an additional 14 articles by reviewing citations of previously identified articles. In total, we identified 59 references for inclusion in the current review, representing 56 unique trials. We found 29 papers representing 27 unique trials that specified that the intervention was targeted to cancer patients and their families and 30 papers representing 29 trials targeted to patients with memory disorders and their families.

STUDY DESIGN AND QUALITY

All included studies were RCTs, with the majority being fair or poor methodological quality (9 good, 32 fair, 15 poor). Most studies reported multiple outcomes, though few reported data on most of our outcomes. The duration of the intervention and follow up periods varied. Many studies reported a large number of comparisons, including findings from multiple subscales, few of which showed significant differences between treatment groups. Some of the significant intervention effects were found in single trials, subscales from larger quality of life, depression, or symptom indices, and may be due to chance or reporting bias. The reproducibility and broader applicability should be viewed with caution.

CANCER

Description of Cancer Studies

A wide range of patients and family members participated in the studies. Nearly all studies examined either women with breast cancer, men with prostate cancer, or men and women with any type of cancer. The patients were, on average, 60 years old (range: 46-71 years) and family members were 56 years old (range: 49-62 years). Over half the patients were men (51%) and over 61% of the family members were female. Twenty-one percent of patients were of non-white race. One study assessed U.S. Veterans. Across all trials, sixteen reported including patients with cancer stages 0-3, ten trials included patients with late stage cancer (stages 4 and 5), and three included patients at the end of life. Studies ranged in size from 12 to 476 participants, with a median 120 dyads per trial. Interventions were, on average, 6 weeks long, but some were as short as one session, while one was 25 months.

Key Question #1: What are the benefits of family and caregiver psychosocial interventions for adult patients with cancer compared to usual care or wait list?

a. **What are the harms of these interventions?**
b. **Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?**

We identified 18 cancer trials and 20 papers that addressed Key Question #1 (KQ1), most assessing patients with either prostate or breast cancer. The large majority were rated as fair quality (15/18, 83%). The rest were poor quality (3/18, 17%). Fourteen compared a family involved intervention to a standard treatment control, typically a wait list or usual care. The remaining 4 trials had multiple conditions, including a family involved intervention, a standard treatment control condition, and either another family involved intervention or a patient-only intervention. We further categorized studies by their intervention subgroups: telephone or web-based counseling provided to patient and family member separately (4 trials), adaptations of couples CBT (5 trials), family assisted approaches to patient care (4 trials), family focused CBT interventions that include family coping and problem solving (4 trials), or unique interventions (1 trial). Studies ranged in size from 14 participants to 476, with a median of 126 per trial. Interventions were, on average, 6 sessions over 6 weeks, but ranged from 3 to 12 sessions over the course of one week to 5 months.

We summarize findings between the intervention group and the control group and address comparative effectiveness between family or family and patient interventions in Key Question #2 (KQ2).

Benefits

Overall, the available data indicated that compared to usual or standard care, family involved interventions did not consistently improve global quality of life; mental, physical, or social functioning; depression/anxiety; or symptom control among patients with cancer. None of the studies reported on hospitalization or institutionalization. Few studies reported statistically significant effects on any outcome and non-significant effect sizes were typically small to moderate effects. As shown in Executive Summary Table 1, the overall strength of evidence for intervention effectiveness was low for all outcomes due to moderate risk of bias (poor methodological quality) and imprecision of the effect size. Many studies had small sample sizes and outcome data between conditions were not always reported post-intervention. We also found limited reporting of outcomes within each intervention category. This precluded us from calculating more reliable estimates to determine the strength of evidence of each intervention on particular outcomes. We do describe the number of studies within each category that report each outcome (and the details of an intervention if the difference between conditions on an outcome was significant).

The variability in study populations and interventions made pooling of data problematic and the generalization of findings from any single study for broader conclusions difficult. However, while the specific strategies in these interventions to control or manage symptoms varied across intervention categories, we did find that most included a problem-solving component where family members were "coached" to identify symptoms and potential solutions to reduce the symptoms. We found a greater proportion of interventions that focused on the family member, instead of the couple, were effective. The exception was couples who were in relatively new relationships or couples who at baseline were in less supportive relationships. These couples showed improvements in quality of life due to couples therapy compared to usual care.

In total, 5 of 18 trials showed any significant intervention effects. Of these five trials, only three showed significant effects across multiple outcomes. These three studies, two of fair and one of

poor quality, accounted for 73% of the significant findings for KQ1, but had little in common with each other, targeting different cancer patients and families and using different intervention strategies. Significant intervention effects in single trials may be due to chance or reporting bias, and making conclusions about common elements that are effective is difficult. The broader applicability of these interventions should also be viewed with caution.

Four of 11 studies reporting symptom control found significant improvements with a family-involved intervention, and two of nine studies showed reductions in depressive symptoms and anxiety. Six studies reported on global quality of life, but none found a statistically significant effect. Physical, general psychological, and social functioning were reported in 9, 10, and 5 studies, respectively, with almost all studies reporting no significant effect. Relationship adjustment was assessed in five studies, but trials either did not report significant differences or reported insufficient evidence to assess the significance of an effect. Therefore, while family-involved interventions did improve symptom management and depression for cancer patients in some trials, there is insufficient evidence that these intervention strategies affect other outcomes.

Harms

For the cancer trials, studies did not report on harms to patients. Two trials, however, reported family outcomes that were worse for those in the family/couple intervention conditions than in comparator conditions. Authors suggested that these negative effects were due to the effect of increased awareness of their own problems, the patient's problems, the implications of the patient's medical problems, and/or the effect of merely directly talking about cancer and surgery.

Intervention Categories

Below we summarize findings by intervention category.

Telephone or Web-Based Counseling for Family and Patients (4 Trials)

- Among patients with cancer, telephone or web-based counseling for family members did not improve physical functioning or depression more than usual care. Of three trials assessing general psychological functioning and symptom control, only one showed significant improvements. Few studies assessed social functioning, global quality of life, and no studies assessed relationship adjustment; therefore, little evidence exists to assess whether interventions have an effect on these outcomes.
- One study among men with prostate cancer found that weekly nurse telephone calls to manage uncertainty and patient concerns reduced symptoms in white, but not black men.
- One study, following breast cancer patients through different stages of care, found that telephone counseling and psychoeducation, compared to usual care, improved general psychological functioning from post-surgery to adjuvant treatment. However, this effect reversed from adjuvant treatment to ongoing recovery, with general psychological functioning in the telephone counseling group significantly lower than those in usual care.

Adaptations of Couples CBT (5 Trials)

- With one possible exception (described below), adaptations of CBT did not improve physical functioning, general psychological functioning, or symptom control compared to usual care. Few studies assessed the impact of this type of intervention on global quality of life,

depression/anxiety, or relationship adjustment but those that did showed no improvements compared to usual care conditions. No studies assessed the effect of couples CBT on social functioning.
- One small study (n=14) reported low to moderate effects on physical functioning, symptom management, and relationship adjustment, but measures of statistical significance were not reported.
- Couple therapy improved quality of life among patients in less supportive intimate relationships and for patients in newer relationships. Likewise, in a second study, those who endorsed emotional processing as a coping strategy at baseline and received couples therapy had fewer depressive symptoms than those in usual care.

Family Assisted Approaches to Patient Care (4 Trials)

- Few studies assessed outcomes of interest. Of four trials addressing KQ1, three of poor quality and one of fair quality, only one trial assessed each of the following outcomes: physical functioning, general psychological functioning, social functioning, global quality of life, and relationship adjustment.
- One study found significant differences in several measures of patient depression, general psychological functioning, and symptom control; however, two other studies found no differences in measures of depression. One study of pain in advanced cancer patients reported a non-significant treatment effect but lower ratings of pain in the intervention group than in the usual care group.

Family Focused CBT Interventions that Include Skill Building, Family Coping, and Problem Solving to Address Patient Behaviors and Family Issues (4 Trials)

- Family focused interventions did not consistently improve patient symptoms. One adaptation of CBT for family members aimed to help caregivers manage patients' symptoms and reduce emotional distress improved physical and social functioning and depression, but another similar study showed no effect.
- Compared to usual care, a family directed intervention that included supportive telephone calls, problem-solving instruction, and demonstrations on how to use the problem-solving strategies, reduced overall symptoms associated with cancer among hospice patients, but, global quality of life or specific symptoms, such as pain, dyspnea or constipation did not improve. Another study that did not include hospice patients showed no effect on these same outcomes.

Unique Interventions (1 Trial)

- No significant differences in functioning, depression, symptom control or relationship adjustment were found in a unique trial that compared usual care to a problem-solving intervention for couples. The intervention utilized a monthly nurse-administered needs assessment to identify quality of life problems and provide amenable suggestions for addressing the problems, but did not show a significant effect on outcomes.

Executive Summary Table 1. KQ1 – Cancer: Strength of Evidence for Trials Comparing Therapy with Family Component to Usual Care or Wait List Control

Outcome	# studies (n*) # studies of each intervention category	Risk of bias	Directness	Precision	Consistency	Evidence rating
Physical functioning	9 (1266) Phone=3;CBT=2;FAA=1; FFSM=2;Misc=1	Moderate: all trials rated fair quality	Direct	Imprecise. One trial reported a statistically significant difference versus usual care. Non-significant effect sizes ranged from small to large with wide confidence intervals (seven trials). One trial reported a non-significant difference (point estimate could not be calculated).	Consistent	Low
General psychological functioning	10 (1410) Phone=3;CBT=4;FAA=1; FFSM=1;Misc=1	Moderate: nine trials rated fair quality; one rated poor	Direct	Imprecise. Two trials reported statistically significant differences versus usual care. Non-significant effect sizes were small with wide confidence intervals (seven trials). One trial reported a non-significant difference (point estimate could not be calculated).	Consistent	Low
Social functioning	5 (749) Phone=1;CBT=0; FAA=1;FFSM=2;Misc=1	Moderate: all trials rated fair quality	Direct	Imprecise. One trial reported a statistically significant difference versus usual care. Non-significant effect sizes were small with wide confidence intervals (three trials). One trial reported a non-significant difference (point estimate could not be calculated).	Consistent	Low
Global quality of life	6 (1367) Phone=1;PAA=1; FAA=1; FFSM=3; Misc=0	Moderate: five trials rated fair quality; one rated poor	Direct	Imprecise. No trial reported a statistically significant difference versus usual care. Non-significant effect sizes ranged were small with wide confidence intervals (four trials). One trial reported a non-significant difference (point estimate could not be calculated). Significance could not be determined for another trial.	Consistent	Low
Depression/ anxiety	9 (1519) Phone=2;CBT=1;FAA=3; FFSM=2;Misc=1	Moderate: six trials rated fair quality; three rated poor	Direct	Imprecise. Two trials reported statistically significant differences versus usual care. Non-significant effect sizes were small with wide confidence intervals (seven trials).	Consistent	Low
Symptom control/ management	11** (1673) Phone=3;CBT=2;FAA=3; FFSM=2;Misc=1	Moderate: nine trials rated fair quality; two rated poor	Direct	Imprecise. Four trials reported statistically significant differences versus usual care. One trial reported intervention was “superior” with medium to large effect sizes. Non-significant effect sizes were small (five trials). Significance could not be determined in one trial.	Consistent	Low

*Number of subjects randomized

**Some studies had multiple outcome measures

Intervention Category: Phone=Telephone or Web-based; CBT=Couples cognitive behavior therapy; FAA=Family assisted approaches to patient care; FFSM=Family focused CBT with coping and problem solving; Misc=Unique intervention

Key Question #2. What are the benefits of one family or caregiver oriented psychosocial intervention compared to either: 1) a patient-directed intervention or 2) another alternative family-oriented intervention in improving outcomes for adult patients with cancer?

a. **What are the harms of these interventions?**
b. **Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?**

Thirteen cancer trials met inclusion criteria for KQ2. Four trials included men with prostate cancer and two included women with breast cancer. Two studies included men and women with lung cancer and one with gastrointestinal (GI) cancers. Four studies included men and women with any cancer source. Two studies were rated good quality, nine as fair, and two as poor quality. Studies ranged in size from 12 to 329, with a median 130 dyads per trial. Four studies included long-term follow up.

Four trials had three or more intervention arms, including a family involved intervention, a usual care or wait list control group, and another family or patient intervention. Three trials compared a family intervention to an individual intervention. All other trials included comparisons of at least two family-involved interventions. The comparison conditions in these trials were either: 1) a unique attention control condition that included a low intensity family-involved intervention where families were minimally engaged, such as providing families with health education only; 2) a less-intense or structured version of the family-involved intervention being tested; or 3) the same intervention, but using two different modes of delivery.

Benefits

Overall, as shown in Executive Summary Table 2, we found either low or insufficient evidence regarding the effectiveness of family-involved interventions versus other active controls, or alternative family or patient interventions. The overall strength of evidence for intervention effectiveness was low for general psychological functioning, depression/anxiety, and symptom control/management due to the moderate risk of bias, imprecision of the effect size, and poor methodological quality, including small sample sizes. There was insufficient evidence on the comparative effectiveness of family-involved interventions for physical functioning, social functioning, and global quality of life due to few trials reporting these outcomes and inadequate reporting of outcomes between conditions post-intervention. What evidence we found generally indicates that interventions with a family component were not more effective compared to an active control or an alternative family or individual intervention. Some evidence exists to suggest that interventions that actively involved families did improve general psychological functioning, depression/anxiety, and symptom control or management. Few interventions had significant group effects on relationship adjustment. There were no data on health care utilization, including hospitalizations or institutionalization.

Few studies reported statistically significant effects on any outcome. A number of studies provided inadequate outcome data to assess an effect between interventions. The variability in study populations and interventions made pooling of data problematic and generalizing findings from any single study difficult.

In total, eight of thirteen trials reported at least one significant intervention effect on an outcome of interest. Of these, only three showed more than one outcome with significant intervention effects and, as we found in KQ1, these interventions had little in common with each other, limiting our ability to make generalizations.

We did find some important findings among the trials. Three trials comparing individual treatment to family or couple treatment found both interventions were equally effective at improving outcomes at post-intervention. One of these trials, however, did eventually show that couples counseling significantly improved general psychological functioning and symptom control. In this trial, post-intervention outcomes were not significant, but outcomes at six months post-intervention were. It may be that benefits of counseling do not emerge immediately and require longer follow up to determine an effect.

Results from trials that directly compared different family involved interventions varied. One study showed that, compared to psychoeducation, telephone counseling provided a significant benefit for improving patient depression and compared to a self-managed exercise program, telephone counseling significantly improved patient anxiety. In another trial, web-based counseling was as effective as face-to-face counseling in improving patient general psychological functioning, symptom control, and relationship adjustment.

Other interventions also showed mixed results. In the four trials that compared family-involved interventions to health- or psycho-education only, family involved interventions were no better at improving outcomes, except for one trial, in which relationship adjustment was better for those receiving partner-assisted emotional disclosure therapy. Another trial showed an unanticipated effect, with the health education only intervention significantly improving general psychological functioning, depression, and symptom control compared to the family-involved intervention.

We expect that some of the significant intervention effects found in single trials may be due to chance or reporting bias, and making conclusions about common elements that are effective is difficult. While family-involved interventions did improve symptom management, depression/anxiety, general psychological functioning, and relationship adjustment for cancer patients in some trials, there is insufficient evidence that any one type of intervention is superior to another at improving outcomes. We emphasize caution about the broader applicability of any intervention benefits, because of the potential that the benefits may be due to chance.

Harms

No studies addressing KQ2 reported harms to patients or family members.

Intervention Categories

Below we summarize findings by intervention category.

<u>Telephone or Web-Based Counseling for Family and Patients (5 Trials)</u>

- Telephone counseling for cancer patients and family members had mixed results, showing both improvements and worsening of depression and general psychological function. Counseling had little effect on physical or social functioning, symptom control, or relationship adjustment.

- Both face-to-face counseling and internet-based counseling for patients with localized prostate cancer and their family member had similar improvements in general psychological functioning, symptom control, and relationship adjustment suggesting that the web-based counseling was equally as effective as face-to-face counseling.

Adaptations of Couples CBT (2 Trials)

- One good quality and one poor quality trial compared couple therapy to an alternative treatment.
- In one trial, patients with prostate cancer who received sex therapy as part of couple therapy reported similar changes in general psychological functioning, symptom control, and relationship adjustment as patients who received the same intervention content in individual therapy.
- In the other trial, couples who received CBT compared to a less intensive health education intervention for spouses showed significant improvements in relationship adjustment. Patients who at baseline "held back" from discussing cancer-related concerns with their spouses showed the most improvement in relationship quality compared to the health education group.

Family Assisted Approaches, Including Skill Training, to Improve Patient Outcomes (2 Trials)

- Two studies tested the impact of training family members to be problem solving "coaches" for patients and found that training family members was equally effective as training only patients or providing only education and support.

Family Focused CBT Interventions that Include Skill Building, Family Coping, and Problem Solving to Address Patient Behaviors and Family Issues (1 Trial)

- One trial that involved training family members of hospice patients with cancer in cognitive behavior therapy-based problem solving reported a significant group by time interaction for overall symptom distress but did not report on the significance of the difference between the two active intervention arms. The group by time interaction was not significant for quality of life or three targeted symptoms (control of pain, dyspnea, and constipation).

Unique Interventions (3 Trials)

- Compared to providing internet access and online resources for supporting cancer patients, those who received internet access and access to a web-based program that included communication and support from peers, experts, and clinicians, coaching, and tools to improve the caregiving experience reported improvement in symptom control (i.e., symptom distress).
- Foot reflexology significantly reduced anxiety more than "special attention" after adjusting for baseline anxiety levels in patients with metastatic cancer, especially among patients with moderate to severe baseline anxiety.
- Native Hawaiian cancer patients and families who received a culturally specific adaptation of CBT reported significant changes in general psychological functioning post-intervention compared to non-specific CBT.

Executive Summary Table 2. KQ2 – Cancer: Strength of Evidence for Trials Comparing Therapy with Family Component to Alternative Interventions

Outcome	# studies (n*) # studies each intervention category	Risk of bias	Directness	Precision	Consistency	Evidence rating
Physical functioning	4 (637) Phone=2; FAA=1;Misc=1	Moderate: one trial rated good quality; three rated fair	Direct	Precision indeterminate. Four trials reported no significant differences versus active control. Point estimate of effect not reported and could not be calculated for three of the four trials.	Unknown	Insufficient
General psychological functioning	7** (811) Phone=3; CBT=2; FAA=1;Misc=1	Moderate: one trial rated good quality; four rated fair; two rated poor	Direct	Imprecise. Two trials reported a significant difference versus active control (point estimates could not be calculated). One trial reported active control significantly better than intervention. Non-significant differences reported for four trials; effect sizes were small with wide confidence intervals (two trials) or could not be calculated (two trials).	Inconsistent	Low
Social functioning	2 (482) Phone=1;FAA=1	Moderate: one trial rated good quality; one rated fair	Direct	Precision indeterminate. No trial reported statistically significant differences versus active control. Point estimate of effect not reported and could not be calculated for either trial.	Unknown	Insufficient
Quality of life-global	2 (482) FAA=1;FFSM=1	High: one trial rated fair quality; one rated poor	Direct	Imprecise. One poor quality trial reported no significant difference versus active control with wide confidence intervals. Point estimate of effect not reported and could not be calculated for other trial.	Unknown	Insufficient
Depression/ anxiety	5** (641) Phone=2;FAA=2; Misc=1	Moderate: one trial rated good quality; three rated fair; one rated poor	Direct	Imprecise. Two trials reported significant differences versus active control. Another trial reported active control significantly better than intervention. Non-significant effect sizes were small with wide confidence intervals (one trial). Point estimate of effect not reported and could not be calculated for one trial.	Consistent	Low
Symptom control/ management	10 (1845) Phone=4; CBT=1;FAA=2; FFSM=1;Misc=2	Moderate: one trial rated good quality; seven rated fair; two rated poor	Direct	Imprecise. Two trials reported statistically significant differences versus active control. One trial reported active control significantly better than intervention. Non-significant effect sizes were small with wide confidence intervals (two trials). Point estimate of effect not reported and could not be calculated for five trials; significance could not be determined for two of these trials.	Consistent	Low

*Number of subjects randomized

**Some studies had multiple outcomes measures

Intervention Category: Phone=Telephone or Web-based; CBT=Couples cognitive behavior therapy; FAA=Family assisted approaches to patient care; FFSM=Family focused CBT with coping and problem solving; Misc=Unique intervention

MEMORY-RELATED DISORDERS

Description of Memory Studies

Studies ranged in size from 36 to 642 dyads, with a median of 117 per trial. In total, over 4,600 (n=4,631) patients/family dyads were randomized into the 29 memory-related disorder trials, with 4,108 dyads analyzed. Interventions ranged in duration from one session to multiple sessions over two years, but on average, were 16 weeks long. One study, however, is a long, ongoing trial, initiated 18 years prior to the paper's publication. Five trials required the family member to be a spouse or intimate partner (17%), while all the others included any family member or unpaid caregiver involved in care.

Patients in these trials were older than those in the cancer studies, averaging 78 years (range: 73-86 years). Family members were also slightly older in the memory trials, compared to family members in cancer trials, averaging 65 years (range: 48-74 years).

All studies enrolled both men and women. More women than men were patients (55% vs. 45%), but 73% of family members were women (range: 54-100%). Nineteen percent of patients were of non-white race. One of the trials reported the veteran status of the participants and two studies reported recruiting from VA clinics.

Participants also varied in the severity of their memory loss and cognitive function. Although 6 trials did not require that patients meet a specific score on a cognition test like the Mini-Mental State Exam (MMSE) or Global Deterioration Scale (GDS) to be enrolled in a trial, the remainder did. Four trials included patients with mild to moderate cognitive impairment, seven included patients with moderate to severe cognitive impairment, and twelve trials included patients with mild to severe impairment.

Key Question #1: What are the benefits of family and caregiver psychosocial interventions for adult patients with memory-related disorders compared to usual care or wait list?

a. **What are the harms of these interventions?**
b. **Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?**

We identified 19 trials on memory-related conditions that met criteria for KQ1. Three were rated as good, eight as fair, and eight as poor quality trials. Studies ranged in size from 47 to 406 dyads with a median of 103 per trial. Four trials required the family member to be a spouse while the others included any family member involved in care. Interventions ranged from one to twelve sessions, typically lasting 12-16 weeks long. Manuals or standardized protocols were used in about 60% of trials.

Twelve studies compared a family involved intervention to usual care and six to a wait list control condition. One included a cross-over design. Fifteen trials compared a single family-involved intervention to a control condition and four included multiple family-involved interventions and a control condition. We further categorized studies by intervention type: family assisted approaches, including skill training, to improve patient care (7 trials), family focused CBT interventions to address patient behaviors and family issues (6 trials), and unique interventions (6 trials).

Benefits

Compared to usual care or wait list, family involved interventions did not consistently improve physical or cognitive functioning, hospitalizations, or institutionalization for patients with memory-related disorders. Few studies reported statistically significant effects on any outcome, and the non-significant effect sizes were typically small to moderate in magnitude. Some interventions either minimally or modestly improved quality of life, symptom control, and depression or anxiety compared to the control condition.

We found that the strength of evidence for intervention effectiveness was low for all outcomes due to moderate risk of bias and imprecision of the effect size, as shown in Executive Summary Table 3. The variability in study populations and interventions made pooling of data problematic and the generalization of findings from any single study difficult. We also found limited reporting of some outcomes within each intervention category. This precluded us from calculating more reliable estimates to determine the strength of evidence for each intervention on particular outcomes.

We found suggestive evidence that targeted interventions to specific groups of patients or family members may be more effective than more general interventions in managing and controlling symptoms and reducing depression. Five of eleven interventions showed significant improvements in symptom control/management. Two of these studies were unique interventions that included targeted strategies to help families control or manage specific symptoms (e.g., agitation, affect). The other three specifically targeted family members who reported either significant distress about patient problem behaviors and patients who needed a great deal of assistance with daily tasks. Evidence does not show that either general or targeted interventions improved other important outcomes, such as physical and cognitive functioning, quality of life, and utilization compared to usual care or wait list.

Harms

Most studies did not report on patient harms. Of the studies that also measured family outcomes, no study reported poorer outcomes among family members in family or couple interventions compared to those in comparator conditions.

Intervention Categories

Below we summarize findings for each outcome by intervention category. We attempt to make summary statements about the patterns of findings and highlight interventions and populations that may yield potential benefit. We do, however, emphasize caution about any intervention benefits because of the potential that the benefits may be due to chance.

<u>Family Assisted Approaches, Including Skill Training, to Improve Patient Outcomes (7 Trials)</u>

- Most studies reported either physical functioning (4 trials) or symptom control/management (5 trials). Three each reported cognitive function and global quality of life and 1 each reported on depression and utilization. No studies reported relationship adjustment.
- Interventions generally did not improve outcomes over usual care or wait list control.
    - Exceptions included:
        - An in-home problem-solving intervention aimed at teaching family members methods to improve patient behavior and effective communication skills did not

produce a significant effect post-intervention, but over time both quality of life and cognitive function improved for Alzheimer's disease patients with agitation behaviors or depression compared to usual care.
    - An in-home intervention that included teaching family members environmental modifications, problem-solving, and coaching skills resulted in improvements in patient physical functioning and reductions in disruptive behaviors.
    - A tailored activity program designed to teach family members to reduce the mood and behavior disturbances of patients with dementia reduced the frequency of patients' problem behaviors.

Family Focused CBT Interventions that Include Skill Building, Family Coping, and Problem Solving to Address Patient Behaviors and Family Issues (6 Trials)

- One fair quality trial found that compared to usual care, advanced caregiver training that included occupational therapy to reduce home environment hazards and nursing sessions to reduce stress and improve self-care significantly reduced patient problem behavior.
- One good quality trial found that compared to usual care, counseling and support groups for caregivers and other family members had persistent and long term effect on increasing time to nursing home placement.
- One fair quality trial found that compared to usual care or wait list, behavioral therapy that included training on increasing pleasant events significantly reduced depression. In this same trial behavioral therapy that included a problem solving component also significantly reduced depression.

Unique Interventions (6 Trials)

- These interventions tested unique strategies to improve outcomes, including: individualized plans of care developed by families and patients, family visit training, support groups, communication training, exercise promotion, and audiotapes of loved ones. No studies assessed cognitive functioning or relationship adjustment. Three studies assessed symptom management/control and depression/anxiety and two assessed physical functioning. One trial assessed addressed global quality of life and two assessed utilization.
- Two of three interventions assessing symptom management showed significant effects on the targeted behaviors, though the magnitude of effect was small to moderate.
- All three interventions assessing depression showed significant reductions in depressive symptoms, though the magnitude of effect was small to moderate.
- An intervention using support groups for both patients with early stage dementia and their family member also significantly improved quality of life.
- These trials were typically specialized interventions to specifically address a certain behavior or symptom. While findings could not be pooled, the consistency of findings suggests that family-involved interventions, where the family has a clear and unique role to address a specific behavior, may have stronger effects than those interventions that target a broader array of behaviors.

Executive Summary Table 3. KQ1 – Memory-Related Disorders: Strength of Evidence for Trials Comparing Therapy with Family Component to Usual Care or Wait List Control

Outcome	# studies (n*) # studies of each intervention category	Risk of bias	Directness	Precision	Consistency	Evidence rating
Physical functioning	8** (1149) FAA=4;FFSM=2;Misc=2	High: one trial rated good quality; one rated fair; six rated poor	Direct	Imprecise. Two trials reported statistically significant differences versus usual care. Non-significant effect sizes were small to medium with wide confidence intervals (two trials); two other trials reported non-significant differences (point estimates could not be calculated). Significance could not be determined for two trials.	Inconsistent	Low
Cognitive functioning	5** (434) FAA=3;FFSM=2;Misc=0	Moderate: one trial rated good quality; two rated fair; two rated poor	Direct	Imprecise. Two trials reported statistically significant differences versus usual care. Effect sizes were small to large. Three trials reported no significant differences; point estimates could not be calculated for one of these trials.	Inconsistent	Low
Quality of life	4 (390) FAA=3;FFSM=0;Misc=1	Moderate: one trial rated good quality; 1 rated fair; two rated poor	Direct	Imprecise. Two trials reported statistically significant differences versus usual care (small to medium effect sizes). One trial reported non-significant differences (point estimates could not be calculated). Significance could not be determined for one trial.	Inconsistent	Low
Symptom control/ management	11** (1815) FAA=5;FFSM=3;Misc=3	Moderate: three trials rated good quality; three rated fair; five rated poor	Direct	Imprecise. Five trials reported statistically significant differences versus usual care (effect sizes small to medium in three trials, not reported in two trials). Non-significant effect sizes were mostly small with wide confidence intervals (two trials). Three trials reported non-significant differences (point estimates could not be calculated). Significance not reported or could not be determined in one trial.	Inconsistent	Low
Depression/ anxiety	5** (493) FAA=1;FFSM=1;Misc=3	Moderate: one trial rated good quality; three rated fair; 1 rated poor	Direct	Imprecise. Four trials reported statistically significant differences versus usual care (effect sizes small to large). One trial reported non-significant differences (point estimate could not be calculated)	Consistent	Low
Utilization	6** (1044) FAA=1;FFSM=3;Misc=2	Moderate: one trial rated good quality; three rated fair; two rated poor	Direct	Imprecise. One trial reported statistically significant differences versus usual care for utilization outcomes. Five trials reported non-significant differences (point estimates could not be calculated for two trials).	Inconsistent	Low

*Number of subjects randomized

**Some studies had multiple outcome measures

Intervention Category: FAA=Family assisted approaches to patient care; FFSM=Family focused CBT with coping and problem solving; Misc=Unique intervention

Key Question #2. What are the benefits of one family or caregiver oriented psychosocial intervention compared to either: 1) a patient-directed intervention or 2) another alternative family-oriented intervention in improving outcomes for adult patients with memory-related disorders?

a. **What are the harms of these interventions?**
b. **Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?**

Fourteen memory-related disorder trials met inclusion criteria. Six were rated as poor, five as fair, and three as good quality trials. Trials ranged in size from 36 to 518 dyads, with a median of 97 per trial. A total of 2,198 dyads were included in these studies and 1,817 were included in analyses.

Nine of the 14 trials included only two conditions, where a family involved intervention was directly compared to either an attention control condition (typically an education component with or without a supportive phone call) or another unique family intervention. Five trials had multiple experimental conditions and compared at least two family interventions.

Benefits

As shown in Executive Summary Table 4, we rated the strength of evidence for the effectiveness of family-involved interventions for memory-related disorders as low. Overall, few studies showed significant differences across outcomes. Studies comparing a family-involved intervention to an attention control condition showed few improvements on outcomes. Evidence is not strong enough to suggest that interventions beyond providing education and minimal support to family members are more beneficial to patients. Likewise, data were insufficient to suggest that one type of intervention is superior to another at improving patient outcomes.

Three of the twelve studies that assessed symptom control did show improvements. All were narrowly focused interventions intended to change specific symptoms. These findings suggest that tailoring an intervention to fit the very specific symptoms and needs of the patients may be more advantageous than general psychosocial interventions in improving symptom control. Beyond these findings, there was little consistency in findings on intervention effects for physical functioning or quality of life and no trials reported significant findings in cognitive functioning, depression, or utilization.

Harms

Few studies reported potential harms caused by the interventions and of those, no harms were reported to patients or family members in the interventions.

Intervention Categories

Below we summarize findings by intervention category.

Family Assisted Approaches, Including Skill Training, to Improve Patient Outcomes (5 Trials)

- Five trials targeting family skills training to change patient behavior met eligibility criteria. One of these was of good quality, one was fair, and three were of poor quality.
- One study showed a significant effect on improving patient problem behaviors. In the other studies, interventions did not significantly improve outcomes.
- Two trials reported assessing patient physical functioning and symptom control but did not report post-intervention data.

Family Focused CBT Interventions that Include Skill Building, Family Coping, and Problem Solving to Address Patient Behaviors and Family Issues (3 Trials)

- Six trials included CBT-based interventions. One was of good, three of fair, and two of poor quality.
- An intervention for patients with Alzheimer's disease and family members that included a biobehavioral home-based intervention for functional independence, quality of life, and problem behaviors showed a small statistically significant effect on overall functional independence post-intervention compared to the attention control group, a moderate effect on Instrumental Activities of Daily Living (IADL) dependence, and a small effect on activity engagement.
- The REACH II intervention, targeting five elements of caregiving, had a significant effect on patient quality of life compared to an attention control group.
- None of the trials showed significant differences across conditions in post-intervention cognitive functioning, symptom control/management, depression, or health care utilization.

Unique Interventions (3 Trials)

- Three trials, one rated as good, one as fair, and one as poor quality, reported on unique interventions. Trials included testing the use of audiotapes recorded by loved ones to reduce agitation, sleep education to improve sleep quality and problem behaviors related to dementia (e.g., social engagement and depression), and scheduled toileting, communication training, and exercise promotion to reduce urinary incontinence.
- There was no difference in agitation for nursing home patients with Alzheimer's disease who received a personalized audiotape made by a family member recalling positive memories of the patient compared to those receiving an audio tape of someone reading an emotionally neutral article.
- Among patients with Alzheimer's disease, a sleep education intervention for family members decreased patient night wake time compared to the attention control group.
- The toileting training program for family members significantly decreased patient incontinence versus attention control. The study was initially designed to compare two intervention groups (with identical intervention content, but one with home visits every two months and one with home visits every six months), however, both groups were later combined for analysis purposes and no differences were reported.

Executive Summary Table 4. KQ2 – Memory-Related Disorders: Strength of Evidence for Trials Comparing Therapy with Family Component to Alternative Interventions

Outcome	# studies (n*) # studies of each intervention category	Risk of bias	Directness	Precision	Consistency	Evidence rating
Physical functioning	5** (852) FAA=3;FFSM=2	Moderate: one trial rated good quality; two fair, two poor	Direct	Imprecise. One trial reported statistically significant difference versus alternative interventions. Two trials reported non-significant differences (small effect sizes or effect sizes not reported). Significance not reported or could not be determined in two trials.	Unknown	Low
Cognitive functioning	6** (675) FAA=1;FFSM=3; Misc=2	Moderate: one trial rated good quality; two fair; three poor	Direct	Imprecise. No trial reported a statistically significant difference versus alternative interventions. Effect sizes were small to medium with wide confidence intervals.	Consistent	Low
Quality of life	2** (755) FFSM=2	Moderate: one trial rated good quality; one fair	Direct	Imprecise. One trial reported a statistically significant difference versus attention control. One trial reported a small, non-significant effect.	Unknown	Low
Symptom control/ management	12** (1820) FAA=5;FFSM=4; Misc=3	Moderate: three trials rated good quality; four fair; five poor	Direct	Imprecise. Three trials reported statistically significant differences versus alternative interventions. Non-significant effect sizes were small with wide confidence intervals (five trials). Two trials reported non-significant differences (effect sizes could not be calculated). Significance not reported or could not be determined in two trials.	Consistent	Low
Depression/ anxiety	2** (108) FFSM=1; Misc=1	Moderate: one trial rated good quality; one fair	Direct	Imprecise. One trial reported a significant difference in change from baseline on one depression outcome compared to attention control. Another depression outcome did not differ significantly between groups. The second trial reported non-significant differences with small effect sizes.	Consistent	Low

*Number of subjects randomized

**Some studies had multiple outcomes measures

Intervention Category: Phone=Telephone or Web-based; CBT=Couples cognitive behavior therapy; FAA=Family assisted approaches to patient care; FFSM=Family focused CBT with coping and problem solving; Misc=Unique intervention

SUMMARY AND DISCUSSION

In this review we assess the evidence of family-involved interventions for improving outcomes in adult patients with cancer and memory-related conditions. Overall, we find that evidence does not favor family-involved interventions over usual cancer care or over usual care for memory disorders. Nor do we find that, for either condition, family-involved interventions are superior to ones that are patient-focused or provide only health education or psychoeducation. The evidence does suggest, however, that family involved interventions designed for a specific sub-group (e.g., cancer patients with late stage cancer, couples in newer relationships, hospice patients) or for a specific symptom or problem (e.g., incontinence, sleep hygiene) may be more effective at improving symptom control/management, including depression and anxiety symptoms, and for cancer, general psychological functioning. Many of these studies, however, were of poor or fair quality, with small sample sizes, and multiple comparisons, and should be viewed with some caution. Interventions designed to improve general functional status (e.g., physical functioning, cognitive functioning) across stages of disease, however, do not have a strong evidence base. For cancer, the evidence about whether telephone or web-based counseling is as effective as other forms of counseling is inconclusive, but given the potential benefit to rural or home-bound family and patients, will be important to pursue in future research.

The disease courses for cancer and memory-related conditions are often different and the family's potential role in helping to improve outcomes reflects these differences. In addition to the side effects and consequences of treatment, cancer patients and their families are often faced with significant changes and challenges in their relationships and the uncertainties of how the disease and their lives will progress. Family-involved interventions, therefore, focus on reducing distress, depression, and anxiety; improving relationship quality; and managing symptoms. Family roles can also be significantly disrupted when a family member with a memory disorder begins to show signs of disease progression, but, sadly, there is little ambiguity about the unalterable course of these diseases. Families know that patient functioning will decline over time and not improve. Family interventions, therefore, tend to concentrate more on maintaining or improving patient quality of life and managing problem behaviors as they evolve. Our findings are unfortunate in that they highlight the limits of what families can do and do not provide clear answers to how families can improve patient outcomes.

Our findings echo a previous review that used similar criteria to ours.[5] Martire reports that studies were very heterogeneous and that the evidence suggests that family interventions improved depression but had little effect on anxiety and no effect on physical disability. It is rather disappointing that our review, conducted 10 years after the Martire review, has similar conclusions as it casts doubt on whether any progress has been made at improving patient outcomes in spite of the increasingly important role families are taking in patient care. A recent review by Hartmann[6] is more heartening. Compared to usual care, family psychoeducation or family or couple therapy had small, but significant effects on the physical and mental health of patients with cardiovascular disease/stroke and HIV/AIDS and on mental health for cancer patients. It is possible, therefore, that our conclusions are specific only to cancer and memory-related disorders and cannot be generalized to other conditions. Some have suggested that family psychosocial interventions of any kind may lessen patient psychological distress,[7, 8] but our findings comparing usual care or wait list controls to family-involved interventions suggest

this is not the case. Others have suggested that time alone may be a factor in reducing some negative outcomes or improving positive outcomes among patients.[9] Given the lack of long-term outcome data, we cannot determine if this is true, but a number of our studies reported that even if differences were not significant, those in the intervention group improved, while those in the control group declined.[10-12]

Our review has a number of limitations. First, we included only RCTs in our review. Although we had a large number of RCTs to review, it is possible that evidence from rigorous observational evidence would lead to different conclusions, although they would likely also introduce different biases. Second, a number of studies in our review were primarily designed to improve family member outcomes (e.g., reducing caregiver burden), not patient outcomes. This may have affected how the data were reported and the strength of the evidence for single trials. Third, we limited our review to two conditions: cancer and memory-related disorders. Expanding our review to include other conditions may affect our conclusions as well, although we expect it would not, given the number of studies with other conditions we identified in our original search and consistent findings in the review by Martire,[5] who included multiple conditions. Fourth, our review did not include any large-scale interventions or program evaluations of family involved interventions that are comparable to caregiver programs that VHA has recently implemented (e.g., Caregiver Hotline, Operation Enduring Freedom/Operation Iraqi Freedom [OEF/OIF] Caregiver Stipend Program, etc.). Therefore, we have insufficient evidence to determine if current programs targeting caregivers will, in fact, affect short- or long-term patient outcomes. This is an area that needs further study.

Based on our findings, we have a number of recommendations to consider. First, our review does suggest that general interventions for families may not improve patient outcomes, and when resources are limited, exclusive family interventions targeting specific conditions, behaviors, or symptoms will likely be more effective. Second, other studies have shown that family interventions can reduce burden[3] but it remains unclear if, by reducing family burden, families can provide better care which, in turn, can improve patient outcomes. Future research that can rigorously test this question is needed. Understanding the link between family health and patient health is critical for understanding whether separate interventions should address family issues and patient issues, or if investing in family interventions will provide downstream improvements in patient outcomes. Third, given the increasing role that Veterans' families and families, in general, have in the treatment of chronic disease, it is critical that future research is undertaken to fill the gaps that our review has highlighted and build on the promising strengths we have identified. We, therefore, have a number of recommendations for future research. First, researchers should attend to issues of study quality, including blinding, allocation concealment, descriptions of dropouts, and intent to treat analyses. Second, outcome data should be reported post-treatment for each condition and, when feasible, longer term outcomes should be included to assess intervention sustainability. Third, researchers should report study subgroups, including relationship of family member to patient and disease stage. Finally, researchers should consider either reducing the number of comparisons or conditions to preserve statistical power or increasing sample size as much as is feasible.

CONCLUSIONS

VHA has taken broad and important steps to integrate families into the care of Veterans and to support them in their role. Research examining the effects of family interventions on outcomes of patients with cancer and memory-related disorders is underdeveloped. There is both little and weak evidence to suggest that general family interventions improve outcomes for these patients; sub-groups of family members and patients with specific needs may benefit more than others. Customizing and targeting family-involved interventions to specific sub-groups may be the most efficient way to improve patient outcomes.

ABBREVIATIONS TABLE

ABID	Agitated Behavior in Dementia
AD	Alzheimer's disease
A-DAS	Abbreviated Dyadic Adjustment Scale
ADAS-Cog	Alzheimer's Disease Assessment Scale – cognitive subscale
ADCS-ADL	Alzheimer's Disease Cooperative Study – Activities of Daily Living
ADL	Activities of Daily Living
BANS	Bedford Alzheimer's Nursing Scale
BCTRI	Breast Cancer Treatment Response Inventory
BDI	Beck Depression Inventory
BFI	Brief Fatigue Inventory
BMI	Body Mass Index
BPI	Brief Pain Inventory
BSI	Brief Symptom Inventory
CARES	Cancer Rehabilitation Evaluation System
CBT	Cognitive Behavior Therapy
CPR	Cardio Pulmonary Resuscitation
CES-D	Center for Epidemiologic Studies-Depression
CCI	Cancer Care Intervention
CI	Confidence Interval
CKD	Chronic Kidney Disease
CMAI	Cohen-Mansfield Agitation Inventory
COH QOL	City of Hope Quality of Life Instruments for Patients or Caregivers
COPE (Gitlin)	Care of Persons with Dementia in Their Environments
COPE	Creativity, Optimism, Planning and Expert Information
CSDD	Cornell Scale for Depression in Dementia
DAS	Dyadic Adjustment Scale
DSM	Diagnostic and Statistical Manual of Mental Disorders
ECOG	Eastern Cooperative Oncology Group
EPIC	Expanded Prostate Cancer Index Composite
ESML	Early Stage Memory Loss
FAA	Family assisted approaches to symptom management
FACT-B	Functional Assessment of Cancer Therapy-Breast
FACT-G	Functional Assessment of Cancer Therapy-General
FF	Face-to-Face Counseling
FFSM	Family focused symptom management
FLIC	Functional Living Index - Cancer
FVEP	Family Visit Education Program
GDS	Global Deterioration Scale
GIPB	Geriatric Indices of Positive Behavior
GSI	Global Symptom Inventory
HEAC	Health Education Attention Condition
HQLI	Hospice Quality of Life Index
HDRS	Hamilton Depression Rating Scale
HR	Hazard Ratio
IADL	Instrumental Activities of Daily Living
IET	Intimacy-Enhancing Therapy
IIEF	International Index of Erectile Function
IPT	Interpersonal Psychotherapy
ITT	Intention To Treat
KQ	Key Question
MOS	Medical Outcomes Survey

MBPC	Memory and Behavior Problem Checklist - original
MFI	Multidimensional Fatigue Inventory
MFW	Minnesota Family Workshop
MHI	Mental Health Inventory
MISC	Unique intervention
MMSE	Mini-Mental State Exam
MOSES	Multidimensional Observation Scale for Elderly Subjects
MPB	Management of Problem Behaviors
MSAS	Memorial Symptom Assessment Scale
NA	Not Applicable
NH	Nursing Home
NPI	Neuropsychiatric Inventory
NR	Not Reported
NS	Not Significant
NYU-ADRC	New York University Aging and Dementia Research Center
OARS	Older Americans Resources and Services
OEF/OIF	Operation Enduring Freedom/Operation Iraqi Freedom
PAIS	Psychosocial Adjustment to Illness Scale
PAL-C	Profile of Adaptation to Life Clinical Scale
PANAS	Positive and Negative Affect Schedule
PC-ACP	Patient Centered Advance Care Planning
PHONE	Telephone or web-based intervention
PICP	Partners in Coping Program
POMS	Profile of Mood States (also POMS-SF Short Form)
PR	Proxy Report
PSS	Perceived Stress Scale
PSS-FA	Perceived Social Support - Family
QMI	Quality of Marriage Index
RCT	Randomized Control Trial
RMBPC	Revised Memory and Behavior Problem Checklist
RSC	Rotterdam Symptom Checklist
SCS	Social Competence Scale
SIMPRES	Simulated Presence
SF-36	SF-36 Health Survey (also SF-12 and SF-20 versions)
SO	Significant Other
SPIRIT	Sharing Patients' Illness Representations to Increase Trust
S-PRT	Self-Perception and Relationship Tool
SR	Self-Report
SRHS	Self-rated Health Subscale
STAI	State Trait Anxiety Index
SW	Social Worker
SSWS	Standard Social Work Services
TNM	Tumor-lymph Node-Metastases
TIP-C	Telephone Interpersonal Counseling
TSI	Test for Severe Impairment
TX	Treatment
US	United States
UMD	Uncertainty Management Direct
UMS	Uncertainty Management Supplemented
VA	Veterans Affairs
VHA	Veterans Health Administration
VS	versus