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

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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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INTRODUCTION

BACKGROUND

Since 2008, two federal laws have been signed that have established or expanded the VA's authority to provide clinical and support services to families of Veterans. The first, signed into law on October 10, 2008, allows the VA to provide enhanced family mental health services, such as consultation, professional counseling, marriage and family counseling, and training to families of patients with Service Connected and Non-Service Connected injuries or conditions when: 1) no Veteran treatment would otherwise occur without the family member's involvement; 2) the Veteran's treatment would be less or not effective without family member's involvement; or 3) the treatment can be delivered most efficiently when the family member is included in treatment (Public Law 110-387: Veterans' Mental Health and Other Care Improvements Act of 2008, Section 301, amending title 38 of United States Code (U.S.C.) § 1701(5)(B) and 38 U.S.C. § 1782a and b). The second law, signed in May, 2010, allows the VA authority to provide these same services and comprehensive support services to family caregivers of Veterans and also directs the VA to provide additional benefits (e.g., financial stipends and health care benefits) to eligible caregivers who provide essential care to Veterans severely injured in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF) (Public Law 111-163: Caregivers and Veterans Omnibus Health Services Act). With this new authority to extend some services to family members, and the VA's adoption of a patient-centered medical home model in primary care, a model that, among other things, aims to integrate family involvement, the VA now has the potential to adopt or integrate efficacious family-involved interventions to improve Veterans' outcomes.

Our previous review[13] was a synthesis of evidence of family-involved interventions for improving Veterans' mental health outcomes. In this review we sought to synthesize the evidence of family-involved interventions aimed at improving adult patients' physical health outcomes, in particular, for cancer and memory-related conditions. We limited our focus to family members caring for those with cancer and memory-related conditions since the majority of studies fitting our criteria examined one of these two conditions.

To date, the majority of reviews on family interventions have concentrated on family or caregiver health and well-being[1-4] focusing on interventions developed to reduce the physical and psychosocial toll that is associated with providing care and support. A large proportion of these interventions are also targeted to parents of children with chronic disease, illness, or disabilities. The few reviews of family intervention effects on adult patient outcomes have had a narrow scope, including one with only couple-oriented interventions, thus excluding studies with non-spouse family or caregivers,[14] and one with family or couple therapy interventions compared to a "standard treatment" comparison group, thus excluding any comparative effectiveness of interventions.[6]

DEFINITIONS OF KEY CONCEPTS OF FAMILY AND OUTCOMES

Study settings often determine how the person with the condition is described (e.g., care recipient, resident, spouse). Since participants were included in trials based on their diagnosis, we use the term "patient" to describe the person with dementia or cancer.

The literature uses a number of different terms to describe those who provide unpaid help and support to patients: family, informal caregivers, care partners, and support network. For convenience, we use the term "family member" to describe all those, related and non-related, who provide direct care and support to patients with cancer or memory-related disorders. Given the broad range of care and support needed by those with cancer and memory-related conditions, we opted for this more general term, although we concede that not all participants were required to be related to the patient.

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 or side effects associated with treatment or disease progression (e.g., for cancer: pain and 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. Relationship adjustment included broad measures of general relationship adjustment, relationship quality, or relationship functioning.

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 types of interventions and targets of the intervention 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 similar categories by condition (cancer or memory-related conditions). The intervention categories are similar to categories conceptualized by Fisher,[15] although two additional categories (telephone or web-based counseling and unique interventions) were included.

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 patient; 2) behavioral couples therapy or adaptations of cognitive behavior therapy; 3) training for family members to manage or control specific

patient symptoms; 4) interventions that, in addition to training families to effectively manage patient 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.

OBJECTIVES

Using our analytic framework to guide our approach (Figure 1), we conducted a systematic review of the published randomized controlled trials (RCTs) evaluating whether family involved interventions improve patient outcomes (i.e., efficacy) and whether one specific family involved intervention is better than an alternative one (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 patients improve the patients' outcomes.

Given the previous work in this area, we focused our review only on those studies conducted after 1995. Several studies have shown social and cultural norms and resources for family support vary across countries;[16, 17] therefore, we limited the search to articles conducted in the United States and to articles published in English. To assure comparability to the adult population that the VA serves, we included only studies involving subjects over age 18 and limited our review to improvements in quality of life, depression/anxiety, symptom management/control, health care utilization and relationship adjustment. Our analytic framework, shown in Figure 1, outlines our target population, and our interventions, comparators, and outcomes of interest. We review the evidence on family involved interventions compared to usual care or wait list and also to individually-focused interventions or an alternative family-involved intervention.

Our key questions were:

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?

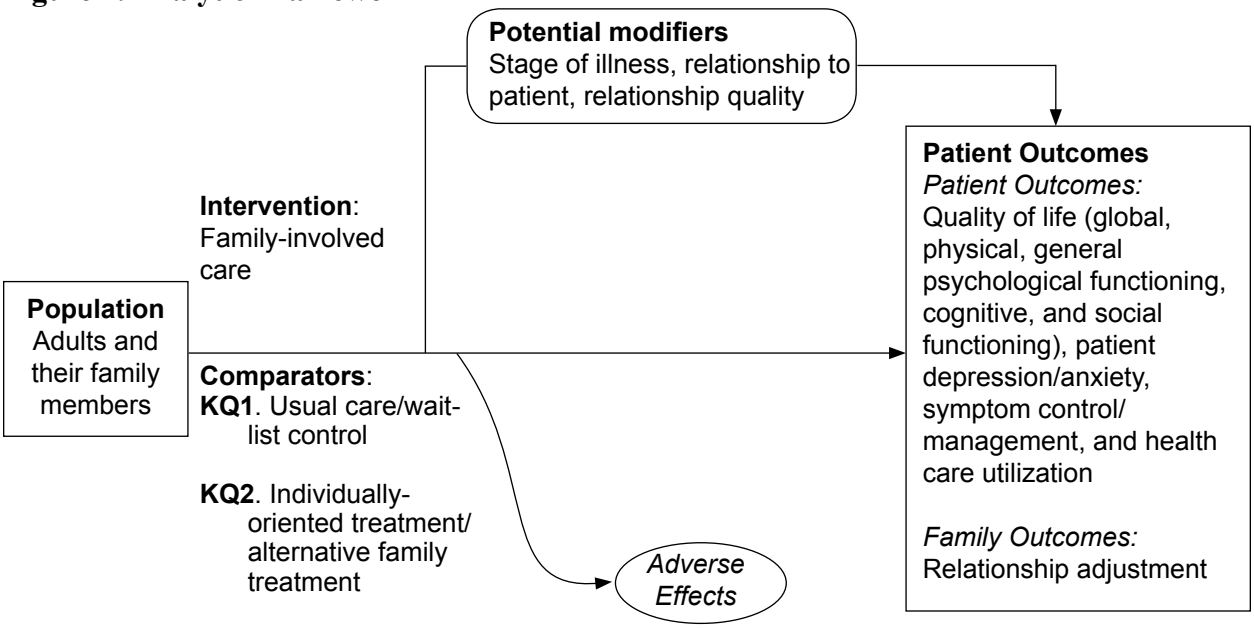
a. What are the harms of these interventions?
b. Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?

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?

We anticipated that this review will be of interest to clinicians, researchers, and policy makers. Our intention was to review the evidence on interventions that could potentially provide a benefit or clearly provide no benefit on patient-centered outcomes for those with cancer and memory-related conditions and have organized and then analyzed the review in different ways to meet the needs of stakeholders. The evidence is first divided by condition (cancer and memory-related disorders). Within each condition, our two key questions, based on type of trial and comparators (efficacy trials in Key Question #1 and comparative effectiveness in Key Question #2), are reviewed. Within each key question, we summarize the effects on each identified outcome across all interventions, and then the effects of trials in each intervention category (e.g., telephone and web-based counseling, couple counseling, etc.) on each outcome. In our summaries, we take into consideration disease stage and the relationship of the patient to the family member in order to determine if specific groups or sub-groups benefit from the intervention.

Figure 1. Analytic Framework



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METHODS

TOPIC DEVELOPMENT

Sonja Batten, PhD, and the Office of Mental Health Services nominated this topic to learn what the benefits to a Veteran's medical outcomes are if their family members are included in treatment or care and if there is any evidence that providing support services to a family member improves outcomes or effectiveness of the treatment that is being provided to a Veteran who is receiving care for a medical condition.

SEARCH STRATEGY

Trained research personnel 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. The complete search strategy is presented in Appendix A. Additional citations were identified from systematic reviews, reference lists of retrieved articles, and suggestions made by our technical expert panel members and peer reviewers.

STUDY SELECTION

Titles, abstracts, and articles were reviewed by researchers trained in the critical analysis of literature. Full text versions of potentially eligible articles were retrieved for review. Although our search identified studies of patients with both mental health and physical health conditions published from 1980 to the present, due to the volume of eligible articles identified by our search and previous work in this area, we narrowed our primary inclusion criteria at the time of full-text review to include RCTs or systematic reviews or meta-analyses of RCTs meeting the following criteria:

- Conducted in the United States,
- Involved patients at least 18 years old with a physical health condition,
- Included an intervention that involves family members or caregivers of the adult patient (patient may or may not be present for the intervention),
- Reported patient outcomes of interest, as outlined in the analytic framework (Figure 1),
- Included a control group; control group may be usual care/wait list control or an alternative active treatment (e.g., individually-oriented treatment or another family/couple-oriented intervention), and
- Published in a peer-reviewed publication after 1995.

After the full-text review, we applied a secondary exclusion criterion to further refine the scope and narrow the search. This criterion included only studies that targeted patients with one of two conditions – cancer or memory-related conditions. These conditions made up the majority of the studies reviewed, providing the largest body of evidence from which we could synthesize the evidence.

DATA ABSTRACTION

We abstracted study characteristics, patient characteristics, and outcomes separately for cancer studies and memory-related studies. Data were abstracted by one study team member (investigators or trained research associates) and verified by another, all under the supervision of the Principal Investigator.

We abstracted the following study characteristics for each included study: author, date of publication, funding source, patient characteristics (gender, age, race/ethnicity, marital status, education, Veteran status), family member characteristics (gender, age, race/ethnicity, marital status, education, relationship to patient), recruitment method, inclusion and exclusion criteria (physical health condition, how the condition was assessed, family/caregivers involvement, and other specific inclusion and exclusion criteria), treatment groups, intervention characteristics (format, whether a specific protocol was used, number of sessions, treatment length, approach, and treatment integrity), outcomes assessed, and study quality (reports of allocation concealment, blinding, analysis approach, description of withdrawals).

We focused on the patient- and family-centered outcomes outlined above. For cancer, our primary outcomes of interest were: overall quality of life; the components of quality of life (physical, mental health, and social functioning); and symptom control/management. Secondary outcomes included depression/anxiety, utilization (including hospitalization and institutionalization), and relationship adjustment. For memory disorders, we assessed similar outcomes as for cancer 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 more than 6 months post intervention, the last available assessment was abstracted.

QUALITY ASSESSMENT

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 evaluating risk of bias in RCTs, we considered whether: the intervention allocation was concealed; participants, interventionists, or 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 assessors at a minimum) as critical elements for a good quality trial.[18]

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.

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. We compiled a summary of findings by condition for each question, and then summarized findings across intervention categories. 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.[19]

STRENGTH OF EVIDENCE

We determined the strength of evidence for each outcome based on all studies that assessed that outcome. Using criteria outlined by Owens et al.,[20] (see Appendix B), we rated the strength of evidence for each outcome using the following grades: 1) high confidence indicated that 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 denoted that further research may change our confidence in the estimate of effect and may change the estimate; 3) low confidence indicated that 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, indicating that the evidence was unavailable or did not permit a conclusion.

PEER REVIEW

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

RESULTS

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

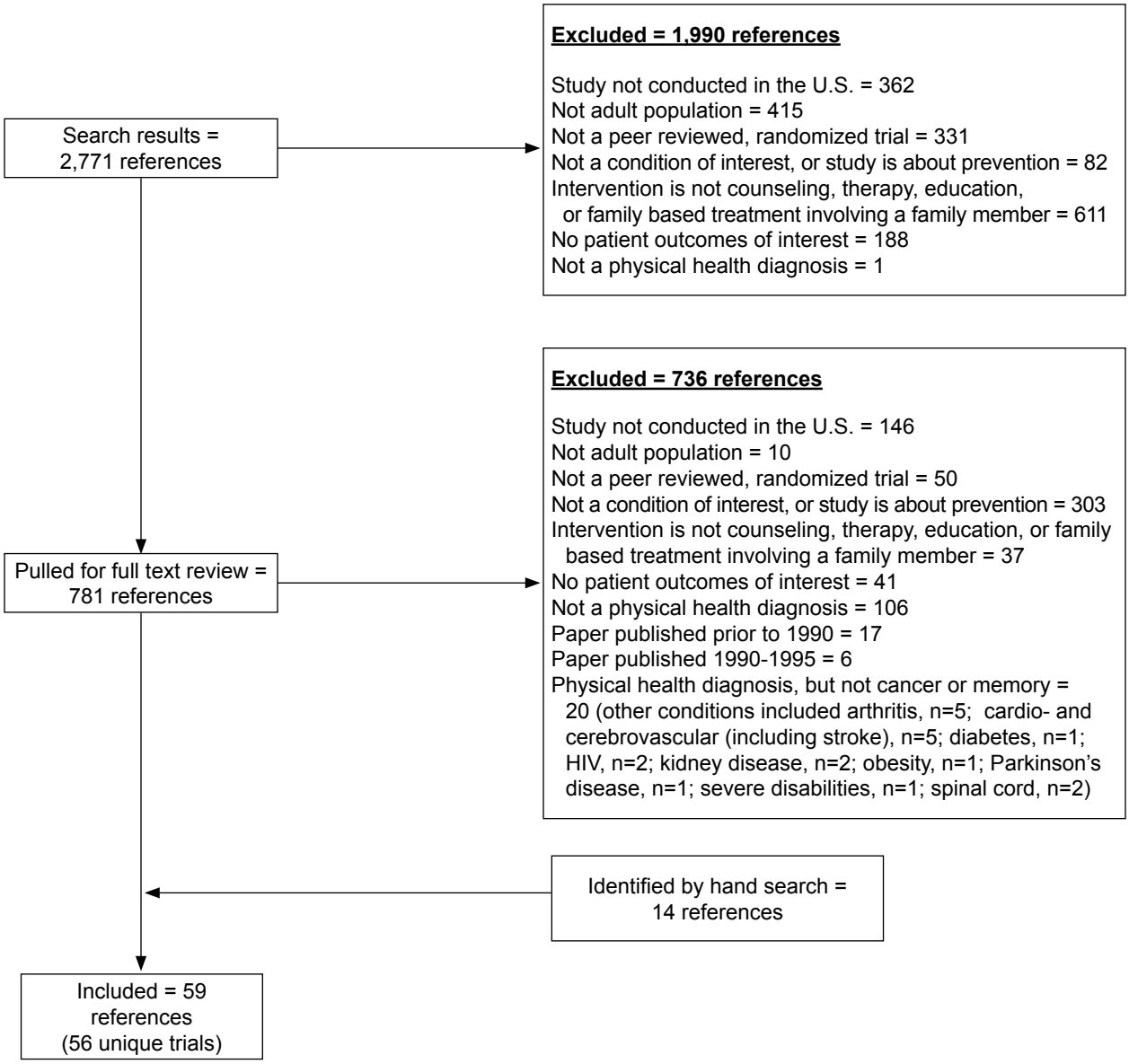
LITERATURE FLOW

As shown in our literature flow diagram (Figure 2), we reviewed 2,771 titles and abstracts from the electronic search. After excluding 1,990 abstracts that did not meet our inclusion criteria, we then retrieved 781 full-text articles for further review. Using our inclusion/exclusion criteria we excluded another 736 references, leaving 45 eligible for inclusion. We identified an additional 14 articles by hand search (e.g., review of citations in previously identified articles, suggestions from reviewers). In total, we identified 59 references for inclusion in the current review, representing 56 unique trials. We grouped the studies by cancer or memory disorders and addressed the key questions for each condition. 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 or in 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.

Figure 2. Literature Flow Diagram



CANCER

Population Studied

A wide range of patients and family members participated in the studies. Details of baseline characteristics are found in Table 1. 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 (range: 49-62 years). Half the patients were men (51%), but 61% of the family members were female. Twenty-one percent of patients were of non-white race. Only one study[21] explicitly assessed outcomes of U.S. Veterans, although one study reported recruiting from VA hospitals and clinics.[22]

Table 1. Cancer - Summary of Baseline Characteristics (27 trials)

Characteristics	Number/mean (range)	Number of trials reporting
Total number of patient/family dyads randomized	4195	27
Total number of patients from dyads analyzed	3345	26
Age of patients, years	60 (46-71)	26
Age of family members, years	56 (49-62)	21
Participant marital status, % married	80 (49-100)	19
Patient gender, % male	51 (0-100)	26
Family member gender, % female	61 (0-100)	18
Race, % non-white patients	21 (2-100)	21
Veterans, %	100	1

Overall, as summarized in Table 2, cancer trials were heterogeneous in patient, disease, intervention, and comparator characteristics. Trials primarily enrolled participants with early stage cancers. 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. Nearly all (23/27 trials) reported using a specific manual or protocol for the intervention. Studies ranged in size from 12 to 476 participants, with a median of 120 dyads per trial. Interventions were, on average, 6 weeks long, but varied in length from one session to 25 months. For KQ1, the majority of the trials compared family-involved interventions to usual care (17/18 trials) instead of wait list (1/18 trials). For KQ2, more interventions were compared to other family treatments (11/13 trials), typically health education or psychoeducation, than to individual treatments (2/13 trials).

Table 2. Cancer - Summary of Heterogeneity

Trial characteristic		Number of trials reporting
Stage of diagnosis*	Early (stage 0-1)	16
	Mid (stage 2-3)	16
	Late (stage 4-5)	10
	End of life	3
Manualized intervention	Yes	23
	Not reported	4
Family intervention with	Wife/female intimate partner	3
	Husband/male intimate partner	1
	Husband/wife or male/female intimate partner	7
	Any identified family member	16
Family intervention compared to**	Wait list (KQ1)	1
	Usual care (KQ1)	17
	Individual treatment (KQ2)	2
	Other family treatment(s) (KQ2)	11
Patient gender	Men	9
	Women	7
	Both men and women	11

*Groups are not mutually exclusive.
**Four trials included multiple arms and comparators for both KQ1 and KQ2 are included.

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?**

Description of Study Design and Quality

We identified 18 cancer trials and 20 papers that fit criteria for KQ1. Details of study characteristics for each included study are found in Appendix D, Table 1.

Most trials addressing KQ1 enrolled either men with prostate cancer (n=6),[22-28] women with breast cancer (n=5),[8, 29-33] or either men or women with any type of cancer (n=7).[34-40] The majority of studies were of fair quality (15 fair, 3 poor). Studies ranged in size from 14 to 476 participants, with a median 126 per trial, and included an average of 6 sessions per intervention (range: 3-10 sessions). Six trials included follow up periods 6-8 months after the completion of the intervention[8, 22, 23, 31-33, 37] and one followed participants 12 months post-intervention.[36]

Description of Interventions and Comparators

We categorized studies into one of five different types of intervention: telephone or web-based counseling; adaptations of couples cognitive behavior therapy (CBT); family assisted approaches to patient care; family focused CBT interventions that include family coping and problem

solving; and unique interventions. Intervention groups were compared to either wait list (n=1)[36] or usual care (n=17) groups. One other trial[41] reported having a wait list control group in addition to two family-involved treatment groups, but did not report any information or data on the wait list group. This trial, therefore, is reviewed under KQ2. Four trials had multiple conditions, including a family involved intervention, a control condition, and either another family-involved intervention or a patient-only intervention.[24, 30, 36, 40] We summarize findings between the intervention group and the control group here and address comparative effectiveness between family or family and patient interventions in KQ2.

Four trials included telephone or web-based interventions providing counseling separately to the patient and family member either over the telephone or over the internet.[23, 24, 29, 30] Two of these trials compared usual care to either additional interventions, including combinations of different family-involved interventions,[30] or individual patient counseling and family member counseling.[24]

Five trials compared an adaptation of behavioral couples therapy to usual care.[8, 25-27, 31-33] Interventions were focused on relationship enhancement,[27, 31] coping skills,[25, 26, 32] or stress management and communication.[8, 33] The number of sessions ranged from five[27] to nine[32] and all were in-person and with individual dyads, with the exceptions of one telephone-based couples intervention[25, 26] and one group intervention.[8, 33]

Four trials tested interventions that targeted family assisted approaches to patient care. Interventions included training patients and family members to control symptoms and exploit or mobilize existing resources. Three trials compared the intervention to usual care[28, 34, 35] and one compared a wait list control group to training patients and family members and training patients only.[36]

Four trials compared multi-component interventions to usual care. The interventions offered training for symptom management and also included components targeted at family coping and problem solving.[37-40] Therefore, both the patient and family member were targets in these interventions. Two trials[38, 40] implemented the COPE (Creativity, Optimism, Planning, and Expert information) intervention to aid family members with patient symptom management and problem solving. Another targeted couples, teaching them to manage patient symptoms related to chemotherapy through CBT.[39] The fourth compared usual care to individual counseling for family members and intended to provide support and problem solving training.[37]

The one unique trial compared usual care to an intervention for family members to eliminate or reduce symptoms. The intervention tested the efficacy of a computer program targeted at counselors or therapists working on problem solving strategies either in-person or over the telephone with family members of prostate cancer patients.

Treatment Adherence

All studies reported some indicator of treatment adherence, however, the level of detail on adherence varied greatly and differences across treatment conditions, when applicable, were not always reported. Two studies reported the proportion of participants completing the intervention,[26, 36] while others reported the proportion of sessions not completed[8, 27, 33] or retention throughout the trial.[39] Dropouts were another way of reporting adherence in a number of trials.[32, 38] The majority

of studies, however, reported the proportion of participants who completed the final outcome measures[8, 31, 33, 37, 40] or did not report final outcomes.[28, 34-36]

Treatment adherence varied by the study sample's cancer stage. Two studies of prostate cancer patients with early stage disease reported that the proportion completing the intervention ranged from 78%[26] to 96%.[36] Likewise, Kurtz[39] found that overall study retention rates ranged from 83% at week 10 and 67% at week 20 for the intervention arm and 79% and 71%, respectively, for the control arm, but rates of attrition were significantly higher at 10 weeks for the patients with late-stage disease. Studies reporting high rates of dropouts or low rates of participants completing final outcome assessments were also more likely to be studies of patients with more advanced cancer. In Meyers,[38] 65% and 67% of the intervention and control dyads, respectively, dropped out, mostly due to the patient's death. In Kayser,[32] 33% and 15% of the intervention and control group participants, respectively, all with early stage breast cancer, dropped out. Similarly, the proportion of participants who completed the final outcome measures ranged from the upper end of 70% and 66% of the intervention and control group, respectively, in a study of early-stage breast cancer[8, 33] to only 28% and 37% of the intervention and control group, respectively, in a study of hospice patients.[40]

Outcomes Assessed

Of the 18 trials, 12 included primary outcomes for patients[8, 22-24, 26, 31-36, 38, 40] and 4 had primary outcomes that included both patient and family members.[27-30] Two trials[37, 39] targeted the intervention to family members or patient/family member dyads, but included individual patient outcomes of interest as secondary outcomes. The primary outcomes for these two studies were caregiver outcomes.

The most frequently assessed outcomes were symptom control/management (11/18 trials);[22-24, 26, 28, 30, 31, 34, 36, 37, 40] general psychological functioning (10/18 trials);[8, 22, 23, 26, 27, 29-31, 33, 36, 37] physical functioning (9/18 trials);[22, 23, 26, 29-31, 34, 37, 39] and depression/anxiety (9/18 trials).[8, 22, 23, 28, 29, 33, 35-37, 39] Six of eighteen trials assessed global quality of life[23, 32, 36-38, 40] and five of eighteen trials assessed each social functioning[22, 30, 34, 37, 39] and/or relationship adjustment.[22, 27, 28, 31, 37] None of the eighteen trials reported on health care utilization. Specific information about cancer trials, including instruments used to assess each outcome and abstracted outcome data, can be found in Appendix D, Tables 2-8.

Findings

Overall Benefits

The available data indicated that family involved interventions versus usual care or wait list did not consistently improve outcomes among patients with cancer for global quality of life, mental, physical or social functioning, or depression/anxiety. Some interventions to improve symptoms reported significant improvements compared to usual care, however, improvements were found across a broad range of symptoms. No one symptom associated with cancer or cancer treatment consistently improved across trials. 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 in magnitude. As shown in Table

3, the overall strength of evidence for intervention effectiveness was low for all outcomes, due to the moderate risk of bias, imprecision of the effect size and poor methodological quality, including underpowered analyses, and inadequate reporting of outcomes between conditions post-intervention. The variability in study populations and interventions made pooling of data problematic and generalizing findings from any single study difficult.

A summary of all study outcomes is presented in Table 4. Of the 11 trials assessing symptom control/management, including physical effects of cancer like pain, dyspnea, and reduced sexual functioning, four showed significant improvements in symptom control. Two of these were poor[28, 36] and two were fair quality.[22, 30, 40] The significant differences found in these trials are reviewed below. In Nezu,[36] problem solving training for family members showed a large effect on recently diagnosed cancer patients' symptom scores compared to the wait list group. However, the poor quality of the study tempers the findings. McMillan et al.[40] reported that, over time, the COPE intervention significantly reduced overall symptoms but not three targeted symptoms (intensity of pain, dyspnea, and constipation) compared to the controls. Effect sizes could not be calculated because mean values post-intervention were not provided. In Budin[30] side-effect distress and severity improved during on-going recovery following treatment for breast cancer, but this effect was only observed when the intervention groups in this multiple-arm trial were pooled and compared to usual care. Regarding sexual functioning, in McCorkle,[28] a poor quality study, patients with prostate cancer undergoing radical prostatectomy who, along with their spouses received a standardized nursing protocol, reported significantly better sexual functioning than those in usual care.

Two of ten trials, one of fair[30] and one of poor[36] quality, showed significant improvements in general psychological functioning. In one,[30] the intervention significantly improved psychological well-being in patients with breast cancer, showing that well-being in one of the treatment groups, standard care plus telephone counseling, between post-surgery and adjuvant therapy, significantly improved compared to usual care. However, this improvement was followed by a significant decrease during ongoing recovery, with the mean score for the standard care plus telephone counseling group falling below those in all other conditions, including the standard care only condition. The authors suggest that the telephone counseling may have helped patients appraise in realistic terms their circumstances and normalize reactions and feelings to them, thus providing them with freedom over time to more freely and articulately report their well-being.

In the second trial,[36] a trial that included family members of someone who had recently been diagnosed with cancer and also screened positive for psychological distress, the intervention, which included training in problem solving, significantly reduced patient psychiatric symptom (BSI, ES=-4.39 [-5.18, -3.60]) and improved patient mood (POMS, ES -2.01 [-2.53, -1.49]) and distress (Omega, ES -1.97 [-2.48, -1.45]) compared to those in a wait list control group.

For depression/anxiety, two of the nine interventions, one of fair[39] and one of poor quality,[36] showed significant improvements over usual care or wait list. One demonstrated a medium effect on improving depressive symptoms (ES=-0.39 [-0.64, -0.13])[39] compared to usual care. The other showed a significant improvement post-treatment in depression (HAM-D, ES=-4.30 [-5.08, -3.53]).[36]

Only one of nine trials assessing physical functioning showed a significant improvement (SF-36 physical functioning sub-scale, ES=0.38 [0.12, 0.64]).[39] This same study was the only study of five assessing social functioning to show an improvement (SF-36 social functioning sub-scale, ES=0.35 [0.10, 0.61]). In this fair-quality trial, men and women undergoing a first course of chemotherapy (primarily for breast or lung cancer) received either usual care or, with a family member, a cognitive behavioral-based training program to address specific patient symptoms.

None of six trials assessing global quality of life and none of five assessing relationship functioning showed any intervention effect.

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. In total, five of the 18 trials showed any significant intervention effects.[22, 28, 30, 36, 39, 40] Of these only three showed significant effects across multiple outcomes.[30, 36, 39] These three interventions had little in common with each other, targeting different cancer patients and families and using different intervention strategies. 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, therefore, is difficult. The broader applicability of these interventions should also be viewed with caution.

Overall Harms

For the cancer trials, studies did not report that any patients were harmed. Two trials, however, reported worse outcomes for family members or couples in the intervention conditions than in comparator conditions. Specifically, McCorkle and colleagues[28] found that spouses in the intervention group reported significantly worse sexual functioning and greater marital interaction distress after the intervention than those in treatment as usual. Manne and colleagues[27] found an interaction effect with family baseline scores on some variables, such that family members with better self-reported adjustment at baseline, that is, experiencing lower than average cancer-related distress and greater than average relationship adjustment and intimacy, actually reported poorer scores on these variables after treatment if they were assigned to the couple intervention rather than treatment as usual. In both of these trials, authors' suggested these negative effects were due to family members' 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. The authors suggested the intervention helped couples better talk about and understand these issues.

Table 3. 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

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Table 4. KQ1 – Cancer: Outcomes Reported in Trials Comparing Therapy with Family Component to Usual Care or Wait List Control

Author, year	Type?	N#	Study quality+	Quality of Life				Depression/ anxiety	Symptom control/ Management	Relationship adjustment
				Physical functioning	General psychological functioning*	Social functioning	Global QoL			
CANCER: Telephone or web-based counseling for family and patients (n=4)										
Budin 2008[30]	breast	249	fair	↔	↑	↔			↑	
Mishel 2002[24]	prostate	239	fair						↔/±	
Northouse 2005[29]	breast	200	fair	↔	↔			↔		
Northouse 2007[23]	prostate	263	fair	↔	↔		↔	↔	↔	
CANCER: Adaptations of couples CBT (n=5)										
Baucom 2009[31]	breast	14	fair	↔[a]	↔				↔[a]	↔[a]
Campbell 2004,[25] 2007[26]	prostate	40	fair	↔	↔				↔	
Kayser 2010[32]	breast	63	fair				↔			
Manne 2005,[8] 2007[33]	breast	238	fair		↔			↔		
Manne 2011[27]	prostate	71	fair		↔					↔
CANCER: Family assisted approaches to patient care (n=4)										
Keefe 2005[34]	any	78	fair	↔		↔			↔	
Kozachik 2001[35]	any	120	poor					↔		
McCorkle 2007[28]	prostate	126	poor					↔	↑/↔	↔
Nezu 2003[36]	any	150	poor		↑		↔	↑	↑	
CANCER: Family focused CBT interventions that include family coping and problem solving (n=4)										
Blanchard 1996[37]	any	86	fair	↔	↔	↔	↔	↔	↔	↔
Kurtz 2005[39]	any	237	fair	↑		↑		↑		
McMillan 2007[40]	any	329	fair				↔		↔/↑	
Meyers 2011[38]	any	476	fair				±			
CANCER: Unique intervention (n=1)										
Giesler 2005[22]	prostate	99	fair	↔	↔	↔		↔	↔	↔

RATINGS: ↑ Tx significantly better than comparator; ↔ No significant difference between intervention and comparator; ↓ Treatment significantly worse than comparator; ± Significance not reported or could not be determined

#Number randomized

+Good (low risk of bias): 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. Fair (moderate risk of bias): The trial met or was unclear for allocation concealment and blinding with no more than one of the remaining domains (ITT, withdrawals) unmet. A trial with adequate allocation concealment that did not meet other domains was rated fair. Poor (high risk of bias): The trial had inadequate allocation concealment or blinding and/or clearly met only one of the established risks of bias domains.

*Includes broad measures of general psychological functioning or psychological or emotional distress that do not directly correspond with conditions or diagnoses in the Diagnostic and Statistical Manual (DSM)

[a]Authors report intervention was "superior" to usual care for physical function, symptom control, and relationship adjustment based on medium to large effect sizes; no confidence intervals or p values reported

Intervention Categories

Below we summarize study findings by intervention category. We use semi-quantitative descriptions of individual study results, 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.

Overview of Trials of Telephone or Web-Based Counseling for Family and Patients

Four studies, all of fair quality, examined interventions where at least one condition in each study included a telephone or web-based counseling component that was compared to a usual care condition.[23, 24, 29, 30] In these studies, patients and family members received individually focused counseling (not relationship counseling). In two of the studies,[23, 29] the intervention was delivered to the patient/family member dyad whenever possible. In the other two studies,[24, 30] the intervention was delivered individually to the patient and their family member. Calculated effect sizes for each trial and outcome are shown in Table 5. In one study,[30] four conditions were compared: 1) usual care (standard disease management), 2) usual care plus four phase-specific psychoeducation sessions delivered via videotape (viewed separately by patients and partners), 3) usual care plus four phase-specific manualized telephone counseling sessions individualized for patients and partners, and 4) usual care plus the psychoeducation and telephone counseling interventions. The timing of the intervention sessions was linked to generally recognized phases of the cancer experience: diagnosis, post-surgery, adjuvant therapy, and ongoing recovery. In a second study, patients and their partners were assigned to: 1) usual care, 2) an eight-week nurse-delivered telephone intervention for patients (including interventions for cognitive reframing of disease or treatment-related problems, problem solving, and communication skill development), or 3) same intervention supplemented with an identical intervention for the patient's support person, but delivered separately for each.[24] In the two trials by Northouse,[23, 29] patients and family members were randomized either into usual standard care or standard care plus the FOCUS program. The FOCUS program included a supportive-education intervention that targeted family involvement, optimistic attitude, coping effectiveness, uncertainty reduction, and symptom management. Telephone counseling, however, was only one part of the intervention. Over a four month period, the intervention group received three home visits from a study nurse followed by two pre-arranged telephone calls to the patient and two calls to the family member.

Across the four studies, an average of 238 patient dyads was enrolled (range: 200-263 dyads). Patients were, on average, 58 years old and white (72%). Two studies recruited female patients with breast cancer[23, 30] and the others recruited patients with prostate cancer.[23, 24] Three studies included patients with either recent diagnoses[23, 30] or localized cancer.[24] The fourth study recruited women with recurrent or progressing cancer, analyzing only those with Stage 3 or 4 breast cancer.[23] None of the studies reported that the participants were Veterans, although one study reported that some patients were recruited from a VA medical center.[24]

Family members recruited to participate, were, on average, 54 years old and 77% were white. In two studies the overall proportion of family member participants by gender was not reported,[24, 29] and likewise, two studies did not report the exact relationship between the patient and family member participant.[24, 30] In the studies that reported a relationship to the patient, one reported the

majority of family members recruited were husbands (62%), but also included siblings (9%), adult daughters (13%), adult sons (3%), and other friends and relatives (13%)[29] while in the other, all family members were spouses.[23]

Aside from the type or stage of cancer and availability of a family member or support person, there were few additional inclusion and exclusion criteria. One study excluded patients with any ongoing chronic disease, psychiatric diagnosis, including drug abuse, or prior cancer diagnosis[30] and another excluded those who were being treated for another malignancy.[24] One study included only patients with a life expectancy greater than 6 months[29] and another included only patients with a life expectancy greater than 12 months.[23]

Findings from Trials of Telephone or Web-based Counseling for Family and Patients

As shown in Table 4, only one of the four trials had intervention effects on our outcomes of interest.[30] In this trial, the intervention significantly improved both symptom control/management and general psychological functioning compared to usual care.

One study did report significant sub-group differences, but as with the overall results, generalizations based on these results should be done with caution.[24] In this trial of prostate cancer patients and their families, white men in the family-involved intervention group had a significant (p=0.02) decrease in the number of symptoms reported from baseline to post-treatment compared to white men in the control group. There was no significant difference between treatment groups for African American men during that time period. For sexual functioning, African American men in the family-involved intervention reported more satisfaction with sexual functioning compared with those in the control group (p=0.01), but there were no differences among African Americans or whites in either group in their ability to have an erection.

Overall, with one of four trials reporting significant intervention effects, there is little evidence to suggest that, compared to usual care, interventions that include telephone or web-based counseling to patients or family members significantly improve quality of life, patient depression/anxiety, or symptom management in patients with breast cancer or prostate cancer. There is a lack of evidence available to make conclusions about how family-involved interventions affect relationship adjustment.

Summary from Trials of Telephone or Web-based Counseling for Family and Patients

- 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.[30] Few studies assessed social functioning or global quality of life. No studies assessed relationship adjustment; therefore, little evidence exists to assess the effect on these outcomes.
- One study among men with prostate cancer found that, compared to usual care, weekly nurse telephone calls to manage uncertainty and patient concerns reduced symptoms in white, but not black men.[24]
- 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.[23]

Overview of Trials of Couple Therapy Interventions

Seven papers representing five trials compared couple therapy with cognitive behavioral or similar components to usual care.[8, 25-27, 31-33] Interventions were focused on relationship enhancement,[27, 31] coping skills,[26, 32] or stress management and communication.[8, 33]

All trials were of fair quality. Of the five, three trials were of women with breast cancer[8, 31-33] and two trials studied men with prostate cancer.[25-27] Each of the breast and prostate cancer studies included only early or early to mid-stage cancer patients.[8, 25-27, 31-33] Sample sizes ranged from 14[31] to 238.[8] Patients averaged in age from 46[32] to 61 years old;[25, 26] one study did not report age.[8] Most had received education beyond their high school diploma (48-89%);[25, 26, 33] one reported a median of 16 years of education,[31] and two trials did not report patient education.[8, 32] Two trials were comprised of mostly white patients (86-88%);[27, 31] and one trial included only African American patients.[25, 26] The remaining two trials did not report the racial background of the patient participants.[8, 32] No trials reported the Veteran status of the patients or their included family members. No studies reported excluding participants for relationship distress or co-occurring mental health conditions, including substance use, or relationship distress. Only Baucom and colleagues[31] explicitly excluded participants with a history of other breast cancer or other cancer in the past 5 years.

Family members were, on average, 49[32] to 58 years old.[25, 26] The proportion of family members with any post-high school education ranged from 38%[25, 26] to 89%,[32] with one study[31] reporting median years of education (16 years). Each study included only family members who were intimate partners. Only two trials, both by Manne, clearly reported family members' race. In these two, 83%[27] and 89%[8] of family members were white, with two trials not reporting race of family members.[25, 26, 32]

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Table 5. KQ1 – Cancer: Outcomes at Post-Treatment – Trials Comparing Telephone or Web-based Counseling to Usual Care

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Budin 2008[30] *1) Psycho-education (SE) 2)Telephone counseling (TC) 3) SE+TC+DM 4) Disease management (DM)*	249	breast	all stages	Physical functioning	SRHS, subscale	Data NR*, group x time interaction p=NS
				General psychological functioning	Psych. well-being, PAL-C subscale	**Data NR*, group x time interaction p=0.01**
				Social functioning	PAIS, domestic environment	Data NR*, group x time interaction p=NS
					PAIS, social environment	Data NR*, group x time interaction p=0.63
					PAIS, vocational environment	Data NR*, group x time interaction p=0.37
				Symptom mgmt - Side Effects	BCTRI, severity subscale	**TC+SE+DM vs. DM -0.55 [-0.92, -0.18]**
					BCTRI, distress subscale	**TC+SE+DM vs. DM -0.52 [-0.89, -0.15]**
Mishel 2002[24] *1) Uncertainty management direct 2) Uncertainty management supplemented 3) Usual care*	252	prostate	localized	Symptom mgmt	Control over urine flow	Data NR* NOTE: Active control groups showed trend toward more control over urine flow vs. usual care
					# of symptoms	Data NR*
					Symptom intensity	Data NR*
					Urine flow	Data NR*
					Ability for erection	Data NR*
					Sexual function	Data NR*
Northouse 2005[29] *1) Couples intervention (FOCUS) 2) Usual care*	200	breast	advanced	Physical functioning	FACT-B/SF 36	0.09 [-0.25, 0.43]
				General psychological functioning	FACT-B/SF 36	0.23 [-0.11, 0.57]
				Depression and anxiety	Beck Hopelessness Scale	0.16 [-0.18, 0.49]
Northouse 2007[23] *1) Couples intervention (FOCUS) 2) Usual care*	263	prostate	all stages	Physical functioning	SF 12	-0.02 [-0.27, 0.24]
				General psychological functioning	SF 12	0.08 [-0.18, 0.33]
					Omega	-0.06, p=0.60 [CI NR]
				QoL - Global	FACT-G	0.16, p=0.10 [CI NR]
				Depression and anxiety	Beck Hopelessness Scale	0.17, p=0.07 [CI NR]
				Symptom mgmt	Urinary, bowel, sexual, hormone	Range -0.10 to 0.19 p=NS (all) [CIs NR]

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; QoL=quality of life; NR=not reported; NS=not statistically significant; See Abbreviations Table for assessment tools

Findings from Trials of Couple Therapy Interventions

A summary of results is shown in Table 4 and calculated effect sizes for each trial and outcome are shown in Table 6. None of the trials reported significant intervention effects on outcomes. As with the telephone/web counseling interventions, however, significant sub-group differences were reported. In one trial by Manne and colleagues the authors found at 6 months post-treatment that couple therapy was more effective than usual care in improving well-being (quality of life) and loss of behavioral and emotional control for patients whose partners were the least supportive,[8] and that those who were more likely to endorse use of emotional processing, emotional expression, and acceptance to cope at baseline benefited more from couple therapy than usual care in reducing symptoms of depression,[33] although these findings were not found in a later trial.[27] In another study,[32] results suggested that the intervention was more beneficial for those in shorter-term relationships. One potential harm, noted by Manne et al.,[33] was that for patients with higher adjustment, that is lower levels of pre-intervention cancer specific distress or higher levels of marital satisfaction, couples therapy may increase distress or decrease relationship satisfaction. As previously noted, this may be a result of the intervention teaching patients to effectively discuss their worries or problems.

Summary of Trials of Couple Therapy Interventions

- 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 social functioning, global quality of life, or depression/anxiety, but of those that did, they showed no improvements compared to usual care conditions. No studies assessed the effect of couples CBT on relationship adjustment.
- 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.[31]
- Couple therapy improved quality of life among patients in less supportive intimate relationships and for patients in newer relationships.[8] Likewise, those who endorsed emotional processing as a coping strategy at baseline and received couples therapy had fewer depressive symptoms than those in usual care.[33]

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Table 6. KQ1 – Cancer: Outcomes at Post-Treatment – Trials Comparing Adaptations of Couples Cognitive Behavioral Therapy to Usual Care

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Baucom 2009[31] *1) Couple-based relationship enhancement* *2) Usual care*	14	breast	localized	Physical functioning	FACT-B	0.97 [CI NR]
				General psychological functioning	BSI	-0.07 [CI NR]
				Symptom mgmt	BFI	1.67 [CI NR]
					BPI	0.59 [CI NR]
					RSC	0.86 [CI NR]
				Relationship adj	QMI	0.48 [CI NR]
Campbell 2007[26] *1) Coping skills training* *2) Usual care*	40	prostate	Karnofsky score ≥ 60	Physical functioning	SF-36, physical	0.34 [CI NR], p=0.19
				General psychological functioning	SF-36, mental	0.01 [CI NR], p= 0.70
				Symptom mgmt	EPIC, urinary	0.14 [CI NR], p=0.49
					EPIC, bowel	0.31 [CI NR], p=0.24
					EPIC, sexual	0.34 [CI NR], p=0.18
					EPIC, hormonal	0.30 [CI NR], p=0.12
Kayser 2010[32] *1) Partners in Coping Program* *2) Standard social work*	63	breast	early	QoL - Global	FACT-B	0.38 [-0.20, 0.96]
Manne 2005[8] *1) Couple-focused group* *2) Usual care*	238	breast	early	General psychological functioning	Impact of Events Scale	-0.11 [-0.37, 0.14]
					MHI, well being	0.08 [-0.17, 0.33]
					MHI, loss of behavioral and emotional control	0.04 [-0.22, 0.29]
				Depression/Anxiety	MHI, depression	-0.11 [-0.36, 0.14]
					MHI, anxiety	0.03 [-0.23, 0.28]
Manne 2011[27] *1) Intimacy-enhancing therapy* *2) Usual care*	71	prostate	localized	General psychological functioning	MHI, psychol. distress	NR*, NS between groups
					Impact of Events Scale	NR*, NS between groups
					MHI, well-being	Data NR*, p=0.08
				Relationship adj	DAS	NR*, NS between groups

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; QoL=quality of life; NR=not reported; NS=not statistically significant; See Abbreviations Table for assessment tools

Overview of Trials of Interventions that Include Family Assisted Approaches to Patient Care

Four studies, one of fair[34] and three of poor quality,[28, 35, 36] tested family approaches for improving patient care.

The focus of these interventions was not on the needs of the family member, but on strategies that family members could use to "coach" or assist patients. They typically included problem-solving (with the family member providing coaching),[36] or problem-solving as part of a multi-component intervention (patient and family education, emotional support, and symptom control).

In Keefe,[34] the intervention included a partner-guided pain management training that included education about pain and pain management, coping strategies, and coaching skills for partners to help patients cope with pain from advanced cancer. In Kozachik,[35] the intervention included five in-person and four telephone nurse contacts with patients and family to instruct them on the disease and treatment, symptom management and surveillance, and, for family members, how to mobilize and coordinate support. In McCorkle,[28] a standardized nursing intervention that included education on symptom control and problem solving training was tested to determine its effect on patient depression, sexual function, and relationship adjustment. In Nezu,[36] the intervention tested problem-solving training for patients and problem-solving "coach" training for family members to determine the effect on patients' psychological functioning, quality of life, depression, and symptom management.

Overall, trials ranged in size from 78 to 150 participants. All of the interventions were reported to be either manualized or standardized. Three compared the study intervention to usual care[28, 34, 35] and one to a wait list control.[36] Three studies included patients with any type of cancer[34-36] and one included prostate cancer patients.[28] Patients at all stages of cancer were included in all but one trial which included only patients with advanced stage cancer in hospice.[34] Patients were, on average, 55.7 years old and 68% were married. Family members were, on average, 55 years old. Of the three trials reporting, an average of 19% of the patients was not white. None of the studies reported whether they enrolled Veterans.

Findings from Trials of Interventions that Include Family Assisted Approaches to Patient Care

A summary of results is shown in Table 4, and calculated effect sizes for each trial and outcome are shown in Table 7. Two trials, both of poor quality, showed significant improvements in symptom control/management.[28, 36] One of these trials also showed significant effects across other outcomes (general psychological functioning, and depression/anxiety).[36] Two studies[34, 35] did not report any significant intervention effects.

For symptom control, as previously noted, the McCorkle trial[28] found significant intervention effects for sexual functioning, and in Nezu,[36] patients whose families received training in problem solving reported significant improvements in day-to-day problems and rehabilitation needs compared to the wait list group.[36] The Nezu trial also reported improvements in psychiatric symptomatology (BSI, ES=-4.39 [-5.18, -3.60]), improvements in mood and distress (Omega, ES=-1.97 [-2.48, -1.45]), and in depression at post-treatment (HAM-D, ES=-4.30 [-5.08, -3.53]). However, two other studies, using the CES-D instead of the HAM-D, did not find any significant differences in depression.[28, 35] Pooling the results from these two studies produced similar

findings; post-intervention depression was not significantly different between the intervention and control groups. The pooled standard mean difference was 0.17 (95% CI -0.10, 0.44).

Summary from Trials of Interventions that Include Family Assisted Approaches to Patient Care

- Few studies assessed outcomes of interest. Two interventions improved symptom management. One improved sexual functioning[28] and the other, day to day problems and rehabilitation needs.[36]
- One study found significant differences in several measures of patient general psychological functioning and depression.[36] 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.

Table 7. KQ1 – Cancer: Outcomes at Post-Treatment – Trials Comparing Family Assisted Approaches to Patient Care to Usual Care or Wait List Control

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Keefe 2005[34] *1) Partner-guided pain mgmt.* *2) Usual care*	78	any	late	Physical functioning	FACT-G, physical	-0.08 [-0.60, 0.45]
				Social functioning	FACT-G, social	0.42 [-0.11, 0.95]
				Symptom mgmt	BPI, usual pain	-0.30 [-0.82, 0.23]
					BPI, worst pain	-0.22 [-0.74, 0.31]
Kozachik 2001[35] *1) Cancer Care Intervention* *2) Usual care*	120	any	1 (48%) to 4 (52%)	Depression/Anxiety	CES-D	0.11 [-0.31, 0.53]
McCorkle 2007[28] *1) Standard-ized Nursing Intervention Protocol* *2) Usual care*	126	prostate	N/A*	Depression/Anxiety	CES-D	0.21 [-0.14, 0.56]
				Symptom mgmt	CARES, sexual functioning	**1 month post-surgery -0.45 [-0.83, -0.07]**
						1 month post-intervention 0.33 [-0.05, 0.72]
				Relationship Adj	CARES, marital interaction	Group effect p=NS
Nezu 2003[36] *1) Problem solving-individual* *2) Problem solving with significant other* *3) Wait list*	150	any	1 to 3 (mostly local)	General psychological functioning	Omega	**-1.97 [-2.48, -1.45]**
					POMS	**-2.01 [-2.53, -1.49]**
					BSI	**-4.39 [-5.18, -3.60]**
				QoL - Global	QL Index	0.20 [-0.22, 0.63]
				Depression/Anxiety	Hamilton	**-4.30 [-5.08, -3.53]**
				Symptom mgmt	CARES, day-to-day problems and rehab needs	**-4.77 [-5.61, -3.93]**

*All patients elected to have a radical prostatectomy as their primary treatment
CI=confidence interval; QoL or QL=quality of life; NR=not reported; NS=not statistically significant; See Abbreviations Table for assessment tools

Overview of Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving to Address Patient Behaviors and Family Issues

Four trials, all of fair quality and enrolling a total of 1,128 dyads, tested interventions that targeted family coping and problem solving strategies to improve patient outcomes.[37-40] Unlike the interventions using family-assisted approaches for improving patient care, these interventions, using cognitive behavioral therapy strategies, directly targeted family members' psychosocial needs and coping skills in order to address patient outcomes. Blanchard[37] tested the effectiveness of a problem-solving intervention for a family member in reducing patient depression and improving functioning and quality of life. In Kurtz,[39] a similar problem-solving strategy, tailored to the practical and support needs of the family member, was tested to determine its effect on patient depression, functioning, and symptom severity. McMillan[40] tested the effect of a coping intervention (COPE or Creativity, Optimism, Planning, and Expert information) for family members of hospice patients with cancer on patient symptoms and quality of life. The same intervention (COPE) was tested by Meyers et al.[38] in a group of patients with recurrent, advanced cancer.

Study sample sizes ranged from 86 to 476. All trials enrolled patients with any type of cancer. Unlike the other interventions, these trials included either a majority of patients with late stage cancer,[39] advanced cancer,[38] or exclusively hospice patients.[40] Demographic variables were sporadically reported. Mean age was 64 years (range: 52-71 years).[37, 38, 40] Three trials reported gender[38-40] and two trials reported ethnicity[37, 38] of the patients. Less than half of the patients were male (45%, range: 27-60%) and most were white (89%, range: 88-98%). Of the three trials reporting marital status, 71% were married or cohabitating with their family member (range: 66-100%).[37-39] Sixty-four percent of patients in two trials reporting had an education level beyond high school,[37, 38] and one trial reported a mean education level of 12.2 years.[40] Veteran status of the patients was not reported in any of the trials.

As with the patients, demographic variables of the family members were inconsistently reported. Approximately 70% were married or cohabitating with the patient (range: 66-100%).[37, 38, 42] The family members were slightly younger, with a mean age of 58 (range: 53-61 years).[37-39] Women comprised 40% (range: 31-54%) of the family members in trials reporting[37-39] and most were white (86%, range: 85-97%).[37, 38] None of the trials reported on Veteran status of the family members.

Findings from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving to Address Patient Behaviors and Family Issues

A summary of results is shown in Table 4, and calculated effect sizes for each trial and outcome are shown in Table 8. Of the four trials, two reported significant outcomes.[39, 40] McMillan et al.[40] reported significant improvements in symptom control, showing that the COPE intervention significantly reduced overall symptoms associated with cancer but not three specific symptoms (intensity of pain, dyspnea, and constipation) compared to the controls. The COPE intervention was not effective in improving quality of life in either the McMillan[40] or Meyers[38] trial. Kurtz et al.[39] reported multiple significant outcomes. The intervention showed a medium effect on improving physical (ES=0.38 [0.12, 0.64]) and social functioning (ES=0.35 [0.10, 0.61]) and on depressive symptoms (ES=-0.39 [-0.64,-0.13]).

Summary from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving to Address Patient Behaviors and Family Issues

- Family focused interventions did not consistently improve patient symptoms. One adaptation of cognitive behavior therapy for family members aimed to help caregivers manage patients' symptoms and reduce emotional distress improved physical and social functioning, and depression,[39] but another similar study showed no effect.[37]
- 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.[40] Another study that did not include hospice patients showed no effect on these same outcomes.[37]

Table 8. KQ1 – Cancer: Outcomes at Post-Treatment – Trials Comparing Family Focused CBT Interventions that Include Family Coping and Problem Solving to Usual Care

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Blanchard 1996[37] *1) Spouse-directed problem solving* *2) Usual care*	86	any	not reported but not eligible for hospice	Physical functioning	SF 20	-0.14 [-0.66, 0.39]
				General psychological functioning	SF 20	-0.25 [-0.78, 0.28]
				Social functioning	SF 20	-0.14 [-0.66, 0.39]
				QoL-global	FLIC	-0.33 [-0.86, 0.19]
				Depression/Anxiety	CES-D	0.06 [-0.46, 0.58]
				Symptom mgmt	SF 20, pain	0.02 [-0.51, 0.54]
				Relationship adj	DAS	0.13 [-0.40, 0.65]
Kurtz 2005[39] *1) Clinical nursing intervention* *2) Usual care*	237	any	all stages	Physical functioning	SF 36	**0.38 [0.12, 0.64]**
				Social functioning	SF 36	**0.35 [0.10, 0.61]**
				Depression/Anxiety	CES-D	**-0.39 [-0.64, -0.13]**
McMillan 2007[40] *1) Usual care + friendly visits* *2) COPE* *3) Usual care*	329	any	late stage	QoL-global	HQLI	Data NR*, p=NS between groups
				Symptom mgmt	MSAS, Symptom Assessment	**Data NR*, group by time interaction p=0.009**
					Pain, dyspnea, & constipation scales	Data NR*, p=NS between groups
Meyers 2011[38] *1) Simultaneous Care Educational Intervention* *2) Usual care*	476	any	late stage (advanced)	QoL-global	City of Hope QoL	Data NR*, p=NS between groups**

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
**Six months post-randomization
CI=confidence interval; QoL=quality of life; NR=not reported; NS=not statistically significant; See Abbreviations Table for assessment tools

Overview of Unique Interventions Examined in Single Trials

Only one family-involved trial was considered a unique intervention that was not consistent with our other intervention categories.[22] In this trial, male cancer patients and intimate partners/spouses were enrolled in either usual care or a nurse-facilitated program with personalized treatment to improve patient quality of life and symptom management. The intervention included a menu-driven, interactive computer program which nurses used to help tailor the intervention to the dyad. The patient participants were primarily white (90%) and had a mean age of 64 years with 96% married and 68% with education beyond high school. One of the recruitment sites for this study was a VA hospital, but the number of Veterans enrolled was not reported. A summary of results is shown in Table 4 and calculated effect sizes for each outcome are shown in Table 9.

Findings from Unique Interventions Examined in Single Trials

Compared to usual care, Giesler and colleagues[22] found no intervention effect on outcomes of interest, including quality of life (physical, general psychological, or social functioning); depression; pain; urinary, bowel, or sexual function and bother; and relationship adjustment. There was a reduction in sexual limitations, or the extent to which sexual dysfunction interfered with social roles, but this difference did not reach the significance level of $p<0.05$ (ES=0.45, $p=0.05$). Patients with greater baseline depression had greater improvements in physical functioning when assigned to the intervention than to usual care (ES=0.81, $p=0.01$) and those with lower rates of baseline depression experienced greater improvements in urinary bother than control participants (ES=0.96, $p<0.01$), suggesting that patient depression may modify the effect of the intervention on outcomes.

Summary of Unique Interventions Examined in Single Trials

- 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.[22]

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Table 9. KQ1 – Cancer: Outcomes at Post-Treatment – Trials Comparing Unique Interventions to Usual Care

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI]
Giesler 2005[22] *1) Cancer care intervention 2) Usual care*	99	prostate	localized	Physical functioning	SF-36 physical functioning	0.00 [CI NR], p=0.99
				General psychological functioning	SF-36 mental health index	0.17 [CI NR], p=0.46
				Social functioning	SF-36 social functioning	0.00 [CI NR], p=0.99
				Depression/Anxiety	CES-D	0.36 [CI NR], p=0.12
				Symptom mgmt	SF-36 pain	0.25 [CI NR], p=0.27
					Urinary, bowel, and sexual function, bother, and limitation	Range -0.27 to 0.45 [CIs NR] For sexual limitation, ES was 0.45, p=0.05 All others p>0.05
				Relationship adj	DAS, dyadic cohesion	0.19 [CI NR], p=0.43
					DAS, dyadic satisfaction	0.24 [CI NR], p=0.31

CI=confidence interval; NR=not reported; See Abbreviations Table for assessment tools

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?**

Description of Study Design and Quality

Thirteen cancer trials met inclusion criteria for KQ2. Details of study characteristics for each included study are found in Appendix D, Table 1. Four trials included men with prostate cancer[21, 24, 41, 43] and two included women with breast cancer.[9, 30] Two studies included men and women with lung cancer[44, 45] and one with gastrointestinal cancers.[46] Four studies included men and women with any cancer source.[36, 40, 47, 48] Nine studies were of fair quality,[9, 21, 24, 30, 40, 41, 44, 47, 48] two were rated poor quality,[36, 43] and two were good quality.[45, 46] Studies ranged in size from 12 to 329, with a median 130 dyads per trial. Four studies included long-term follow up, with outcomes assessed at six months,[43] 12 months post-intervention,[36, 41] and survival at 24 months after the start of the intervention.[44]

Description of Interventions and Comparators

Of the thirteen trials that addressed KQ2, four 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. Comparisons of interventions to the usual care or wait list control group are reviewed above in KQ1.[24, 30, 36, 40]

Three trials compared a family intervention to an individual intervention.[24, 36, 43] In Canada,[43] the trial directly compared individual counseling to couples counseling. In Mishel,[24] the trial compared individual telephone counseling to individual telephone counseling plus separate, but concurrent, counseling for the patient's partner. In Nezu,[36] as noted in KQ1, three arms were compared: a wait list control, a patient-only problem-solving training, and the same patient problem solving training in addition to training for a "coach."

All other trials included comparisons of at least two family-involved interventions. The comparison conditions in these trials were either: 1) an attention control condition that included a low intensity family-involved intervention where families were minimally engaged, such as a providing families with health education only;[9, 21, 30, 45, 46, 48] 2) a less-intense or structured version of the family-involved intervention being tested;[40, 44, 47] or 3) the same intervention, but using two different modes of delivery.[41]

The same intervention categories used in KQ1 were also used in KQ2: telephone or web-based counseling interventions; adaptations of couples cognitive behavior therapy (CBT); family assisted approaches to patient care; family focused CBT interventions that include family coping and problem solving; and unique interventions.

Five trials included telephone or web-based interventions that provided counseling separately to the patient and family member either over the telephone or over the internet.[9, 21, 24, 30, 41] As described in KQ1, two of the trials compared usual care to either additional interventions, including combinations of different family-involved interventions[30] or individual patient counseling and family member counseling.[24] The other three compared telephone counseling to an attention control condition;[21] an attention control condition and a self-managed exercise program;[9] and, instead of telephone, a web-based counseling program to face to face counseling.[41]

Two trials[43, 46] included an adaptation of couples CBT. In Canada,[43] a multi-component couples' intervention was compared to an intervention where patients received the same information, but without their partner. In Porter,[46] CBT was compared to a cancer and health education control condition.

Two trials compared the effectiveness of family assisted approaches to patient care to either an individual intervention or to a health education attention control condition. In Nezu,[36] the problem solving training program for patients and families was compared to the same program targeted only to patients. In Porter,[46] an education program for patient and family members, delivered over the phone, was compared to a similar program that included coping skills training, where family members were trained to "coach" patients in coping skills.

One trial[40] compared friendly visits to hospice patients from staff and family to multi-component intervention that integrates problem solving, support, and coping skills for family members.

Finally, three trials[44, 47, 48] compared unique family involved interventions to either another, less intense family intervention[44, 47, 48] or to a patient-directed intervention. Gustafson[44] compared the effect of internet-based educational and support materials to CHESS, an online support system. Mokuau[47] tested the effectiveness of a culturally specific intervention compared to a culturally non-specific

intervention. Stephenson[48] tested the effectiveness of a one-time reflexology treatment for patients (delivered by their partner) to attention control (the partner reading a selection of the patient's choice).

Treatment Adherence

All but one study reported some indicator of treatment adherence.[47] As with KQ1, the level of detail on adherence varied greatly and differences across treatment conditions were not always reported. Six studies reported the proportion of participants attending sessions or completing the intervention.[21, 36, 40, 43, 44, 46] Reported session attendance averaged around 80%. Four studies reported dropout rates.[9, 41, 43, 45] Dropout rates varied widely across studies-as low as 8.1%[9] and as high as 39%.[43] The majority of studies, however, reported the proportion of post-treatment data collected.[21, 24, 30, 36, 40, 45, 46, 48] Overall, post-intervention data were available for 71-100% of participants.

Outcomes Assessed

The most frequently assessed outcomes were symptom control/management (10/13 trials);[21, 24, 30, 36, 40, 41, 43-45, 48] general psychological functioning (7/13 trials);[21, 30, 36, 41, 43, 46, 47] depression/anxiety (5/13 trials);[9, 21, 36, 45, 48] physical functioning (4/13 trials);[21, 30, 44, 45] relationship functioning (3/13 trials);[41, 43, 46] global quality of life (2/13 trials);[36, 40] and social functioning (2/13 trials).[30, 45] Specific information about cancer trials, including instruments used to assess each outcome and abstracted outcome data, can be found in Appendix D, Tables 2-8.

Findings

Overall Benefits

Overall, as shown in Table 10, we found either low or insufficient evidence on the effectiveness of family-involved interventions compared to 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. There was insufficient evidence on the comparative effectiveness of family-involved interventions for physical functioning, social functioning, or global quality of life due to few trials reporting these outcomes and inadequate reporting of outcomes between conditions post-intervention. What evidence we did find indicated that interventions with a family component generally were not more effective compared to an active control or an alternative family or individual intervention for global quality of life; physical, general psychological, or social functioning; or relationship adjustment. Some evidence exists to suggest that interventions that actively involved families did improve general psychological functioning, depression/anxiety, and symptom control or management. There were no data on health care utilization, including hospitalizations or institutionalization. Few studies reported statistically significant effects on any outcome.[9, 36, 46-48] A number of studies provided inadequate outcome data to assess an effect between interventions.[24, 30, 40] The variability in study populations and interventions made pooling of data problematic and generalizing findings from any single study difficult. We emphasize caution about the broader applicability of any one intervention, because of the potential that the benefits may be due to chance.

A summary of all study outcomes is presented in Table 11. In total, eight of thirteen trials reported at least one significant intervention effect on an outcome of interest.[9, 21, 30, 36, 44, 46-48] Of these, three

showed more than one outcome with significant intervention effects.[21, 36, 48] As we found in KQ1, these interventions had little in common with each other, limiting our ability to make generalizations. 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.

Four interventions reported significantly better symptom control/management[21, 36, 44, 48] compared to alternative interventions. Likewise, three trials reported better reductions in depression/anxiety[9, 21, 48] and four reported general psychological functioning[21, 30, 36, 47] than alternative interventions. One trial reported an intervention with significant improvements in relationship adjustment,[46] but none reported any significant differences for physical and social functioning or global quality of life.

Of the three trials comparing a family-involved intervention to an individual intervention,[24, 36, 43] only one trial showed that including a family member significantly improved outcomes of interest. In that trial, couples counseling significantly improved general psychological functioning and symptom control, compared to individual counseling, but not until six months after the intervention.[36]

In comparing a family-involved intervention to one in which families were minimally engaged, such as providing only cancer or health education, findings were mixed. In the six trials that compared family-involved interventions to interventions that required minimum engagement from the family, including health or psychoeducation only,[9, 21, 30, 45, 46, 48] four interventions were better at improving outcomes. In one, relationship adjustment improved for those receiving partner-assisted emotional disclosure therapy.[46] In the second, a three-arm intervention with two alternative family interventions and a health education attention control condition, counseling patients and family members over the phone was significantly more effective than exercise at reducing patient anxiety. Depression also decreased among those receiving telephone counseling when compared to those who just received phone calls and information about cancer.[9] In the third, training families in specific skills (e.g., foot reflexology) reduced patient anxiety and improved pain relief compared to an attention control condition.[48] In the fourth study, general psychological functioning was improved in the telephone counseling group compared to those receiving psychoeducation or a combined intervention.[30]

Another trial, however, unexpectedly showed that those receiving health education only significantly improved their general psychological functioning, depression, and symptom control compared to those receiving the more intensive family-involved intervention.[21]

Of the three studies that compared more structured and intensive interventions to less intensive family interventions,[40, 44, 47] two showed significant improvements in outcomes of interest. One showed significant improvements in general psychological functioning[47] and one showed significant improvements in symptom distress.[44]

No significant differences were found in general psychological functioning, symptom control, or relationship functioning when a web-based counseling program for families was compared to face-to-face counseling with families.[41]

Overall Harms

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

Table 10. 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

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Table 11. KQ2 – Cancer: Outcomes Reported in Trials Comparing Therapy with Family Component to Alternative Interventions

Author, year	Type?	N#	Study quality+	Quality of Life				Depression/ anxiety	Symptom control/ management	Relationship adjustment
				Physical functioning	Psychological functioning*	Social functioning	Global QoL			
CANCER: Telephone or web-based counseling for family and patients (n=5)										
Badger 2007[9]	breast	97	fair					↔/↑		
Badger 2011[21]	prostate	71	fair	↔	↔/↓[a]			↓[a]	↓[a]	
Budin 2008[30]	breast	249	fair	↔[c]	↑[c]	↔[c]			↔[c]	
Mishel 2002[24]	prostate	239	fair						±	
Schover 2012[41]	prostate	115	fair		↔[b]				↔[b]	↔[b]
CANCER: Adaptations of couples CBT (n=2)										
Porter 2009[46]	GI	130	good		↔					↑
Canada 2005[43]	prostate	84	poor		↔[c]				↔[c]	↔[c]
CANCER: Family assisted approaches to patient care (n=2)										
Nezu 2003[36]	any	150	poor		post ↔ 6 mo post ↔/↑		post ↔ 6 mo post ↔	post ↔ 6 mo post ↔	post ↔ 6 mo post ↑	
Porter 2011[45]	lung	233	good	↔		↔		↔	↔	
CANCER: Family focused CBT interventions that include family coping and problem solving (n=1)										
McMillan 2007[40]	any	329	fair				±		±	
CANCER: Unique interventions (n=3)										
Gustafson, 2013[44]	lung	285	fair	6 mo post↔					↑	
Mokuau 2008[47]	any	12	fair		↑					
Stephenson 2007[48]	any	90	fair					↑	↑	

RATINGS: ↑ Tx significantly better than comparator; ↔ No significant difference between intervention and comparator; ↓ Treatment significantly worse than comparator; ± Significance not reported or could not be determined

#Number randomized

*Includes broad measures of general psychological functioning or psychological or emotional distress that do not directly correspond with conditions or diagnoses in the Diagnostic and Statistical Manual (DSM)

+Good (low risk of bias): 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. Fair (moderate risk of bias): The trial met or was unclear for allocation concealment and blinding with no more than one of the remaining domains (ITT, withdrawals) unmet. A trial with adequate allocation concealment that did not meet other domains was rated fair. Poor (high risk of bias): The trial had inadequate allocation concealment or blinding and/or clearly met only one of the established risks of bias domains.

[a]Health education attention control showed significantly more improvement than interpersonal telephone counseling

[b]Compared face-to-face intervention to similar content delivered via Internet

[c]Authors report significance of group by time interactions but no data were reported and, therefore, no effect sizes were calculated. Arrows reflect authors report of the significance of group x time interaction

Intervention Categories

Below we summarize findings by intervention category.

Overview of Trials of Telephone or Web-Based Counseling for Family and Patients

Five studies, all of fair quality, examined interventions that compared a telephone or web-based counseling component with patients and partners to another intervention.[9, 21, 24, 30, 41] Two studies[24, 30] compared multiple conditions, including usual care, and are described in detail under Key Question #1. Three others[9, 21, 41] directly compared different interventions. On average 156 participants were enrolled in the studies (ranging from 71-249). Patients were, on average, 61 years old and white (76%). Two studies recruited women with breast cancer[9, 30] and the others recruited men with prostate cancer.[21, 24, 41] Participants across different stages of cancer were recruited, although most were either early stage or an unknown stage. One study reported recruiting patients at VA Medical Centers but did not report the number of Veterans enrolled or separate findings for Veterans.[21]

All five studies included family members or friends who were involved with the patient's cancer experience. None of the interventions were limited to spouses. Three studies did not report the relationship between the family member and the patient, but in the two that did report, the majority was spouses (83% and 98%).[21, 41] The average age of family members was 54 years (range: 55-67 years). Three studies reported the gender of the family members, with 93% female family members in one study enrolling prostate cancer patients[21] and 26%[9] and 42%[30] female family members in two studies enrolling breast cancer patients. Like the patients, the majority of family members had education beyond high school and nearly 80% were white. None of the studies reported whether family members were Veterans.

Four studies excluded patients with any ongoing chronic disease or psychiatric diagnosis, including drug abuse.[9, 21, 24, 30] Two studies excluded those who were being treated for another malignancy[24] or with a prior cancer diagnosis.[30] Two studies included only patients with life expectancies of either greater than 6 months[29] or greater than 12 months.[23]

Findings from Trials of Telephone or Web-Based Counseling for Family and Patients

A summary of results is shown in Table 11 and calculated effect sizes or other findings for each trial and outcome are shown in Table 12. Three of five studies reported significant differences between interventions.[9, 21, 30] In one of these,[21] there was no difference in physical functioning between those receiving telephone counseling and those receiving health education, however, those in the health education group (the less intensive intervention) did show significant improvements ($p<0.05$) in reported fatigue, depression, and some measures (specifically negative affect and perceived stress) of general psychological functioning. The authors noted that quality of life was relatively high in the study sample at baseline and that, given the mean time since diagnosis of 187 weeks, was also likely relatively stable. Therefore, the health education content might have been more suited to their needs. In another study,[9] both telephone counseling and a self-managed exercise intervention were intended to reduce depression and anxiety symptoms in women with breast cancer. As previously noted, telephone counseling was significantly more effective than exercise at reducing patient anxiety and, compared to supportive and informative telephone calls from a nurse, telephone counseling also reduced depression.[9] In the third study,[30]

the telephone counseling group experienced a significant improvement in psychological well-being between post-surgery and adjuvant therapy compared to psychoeducation alone or a combined intervention of telephone counseling and psychoeducation. All patients received disease management.

A fourth study, which did not show significant differences, is also important to note.[41] Researchers hypothesized that face-to face or web-based counseling interventions for men treated for prostate cancer would be equivalent in their effect on erectile dysfunction. They found that, while erectile functioning significantly improved from baseline to 1 year post-treatment for both conditions (both $p<0.01$), it did not significantly differ by condition. For both intervention conditions, the effect size was 0.35, suggesting that web-based counseling may be as effective as face-to-face counseling for improving erectile dysfunction.

Summary from Trials of Telephone or Web-Based Counseling for Family and Patients

- Telephone counseling for cancer patients and family members compared to alternative interventions had mixed results, showing both improvements and worsening of depression and general psychological functioning. Counseling had little effect on physical, social or global functioning, symptom control, or relationship adjustment relative to other interventions.
- Both face-to-face counseling and internet-based counseling for patients with localized prostate cancer and their family member had similar improvements in physical and global functioning, suggesting that the web-based counseling was equally as effective as face-to-face counseling in improving physical and global functioning for patients.[41]

Overview of Trials of Couple Therapy Interventions

Summarized in Table 11 with detailed findings on Table 13, two trials, one of good quality and one of poor quality, were categorized as adaptations of couples CBT.[43, 46] In Porter,[46] men (71%) and women (130 randomized) with gastrointestinal cancer (Stages II through IV) and their spouses or intimate partners were enrolled. The mean age of both patients and partners was 59 years. Most were white (85% of patients, 82% of partners) and over half had post-high school education (55% of patients, 60% of partners). Veteran status was not reported. The authors compared a four session, face-to-face intervention (partner-assisted emotional disclosure) to four face-to-face education/support sessions. In Canada,[43] couples sex therapy that included multiple components, such as education, coping and communication skills about sex was compared to the same multi-component intervention, but with only patients receiving the counseling. Most of the participants in this trial were white (93%) and family members were required to be intimate partners.

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Table 12. KQ2 – Cancer: Outcomes at Post-Treatment – Trials Comparing Telephone or Web-based Counseling to Alternative Interventions

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Badger 2007[9] *1) Telephone Interpersonal Counseling (TC)* *2) Exercise* *3) Attention control*	97	breast	I-3	Depression/ Anxiety	CES-D	**TC vs. attention 0.51 [0.03, 0.98]** TC vs. exercise 0.30 [-0.24, 0.83]
					Anxiety, composite index	**TC vs. attention 0.99 [0.49, 1.48]** **TC vs. exercise 1.75 [1.12, 2.37]**
Badger 2011[21] *1) Telephone Interpersonal Counseling* *2) Health Education Attention Condition (HEAC)*	71	prostate	all stages	Physical functioning	UCLA PCI	0.13 [-0.35, 0.62]
				General psychological functioning	PANAS-negative	0.30 [-0.19, 0.78]
					PANAS-positive	-0.17 [-0.65, 0.31]
					PSS-perceived stress	0.19 [-0.30, 0.67], **change over time between groups p<0.001 favoring group 2 (HEAC)**
				Depression/Anxiety	CES-D	0.23 [-0.25, 0.71]
				Symptom mgmt	MFI-fatigue	0.14 [-0.34, 0.62], **change over time between groups p<0.001 favoring group 2 (HEAC)**
Budin 2008[30] *1) Psycho-education (SE)* *2) Telephone counseling (TC)* *3) SE+TC+DM* *4) Disease management (DM)*	249	breast	NR	Physical functioning	SRHS subscale	Data NR*, Group x time interaction, NS
				General psychological functioning	Psych. well being PAL-C subscale	**Data NR*, Group x time interaction p=0.01**
				Social functioning	PAIS (Domestic)	Data NR*, Group x time interaction, NS
					PAIS (Social)	Data NR*, Group x time interaction, NS
					PAIS (Vocational)	Data NR*, Group x time interaction, NS
				Symptom mgmt	Side Effects Severity	Data NR*, Group x time interaction, NS
Mishel 2002[24] *1) Uncertainty management direct* *2) Uncertainly management supplemented* *3) Usual care*	252	prostate	localized	Symptom mgmt	# of symptoms	Data NR*
					Symptom intensity	Data NR*
					Urine flow	Data NR*
					Ability for erection	Data NR*
					Sexual function	Data NR*
Schover 2012[41] *1) Face-to-face counseling* *2) Internet-based counseling*	115	prostate	localized	General psychological functioning	BSI-18	NR* at post-treatment, NS between groups at follow-up
				Symptom mgmt	IIEF	0.14 [-0.38, 0.66]
				Relationship adj	DAS	NR* at post-treatment, NS between groups at follow-up

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; NR=not reported; NS=not statistically significant; See Abbreviations Table for assessment tools

Findings from Trials of Couple Therapy Interventions

In Porter,[46] the general psychological functioning among those in couple therapy did not show any greater improvements compared to the alternative, less intensive intervention, but couple therapy did significantly improve relationship quality over time compared to the alternative intervention (group by time interaction *B*=-0.07, p=0.02). In Canada,[43] no significant differences were reported. Although no test statistics or means for the treatment conditions were provided, the authors reported no significant differences on men's bowel and bladder symptoms, sexual functioning, or relationship adjustment between those who received sex therapy delivered solely to individual patients versus sex therapy delivered conjointly to patients and their intimate partners.

Summary from Trials of Couple Therapy Interventions

- 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.[43]
- 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.[46]

Overview of Trials of Interventions that Include Family Assisted Approaches to Patient Care

Two studies, one of poor quality[36] and one of good quality,[45] compared a family assisted approach for improving patient care to alternative interventions. In Nezu,[36] also described under Key Question #1, the intervention tested a problem solving training program for patients and families. The program was compared to the same program targeted only to patients. In Porter[45] an education program about lung cancer and treatment for patient and family members, delivered over the phone, was compared to a similar program that included coping skills training, where family members were trained to "coach" patients in coping skills. This trial enrolled 233 patients with early stage or limited stage lung cancer. Mean age of the participants was 65 years, 54% were male, 85% were white, and 55% had some post-high school education. Family members in this study were predominantly spouses (76%), sons or daughters (14%), or siblings/friends (8%) and 73% resided with the patient. Their mean age was 59 years, 69% were women, 82% were white, and 60% had some post high-school education. Veteran status was not reported for either study.

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Table 13. KQ2 – Cancer: Outcomes at Post-Treatment – Trials Comparing Couple Therapy Interventions to Alternative Interventions

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Porter 2009[46] *1) Partner-assisted Emotional Disclosure 2) Education and support*	130	GI	II-IV	General psychological functioning	POMS-SF	No significant main effects or interaction; ITT or completers (n=112)
				Relationship adj	QMI	**ITT: Group x time interaction (*B*=-0.07, p=0.02);** increase quality for Group 1, decrease for Group 2 **Completers (n=112): Group x time interaction (*B*=-0.08, p=0.02)**
Canada 2005[43] *1) Couples counseling 2) Patient counseling*	84	prostate	A-C	General psychological functioning	BSI/GSI	NR*
				Symptom mgmt	IIEF	NR*
				Relationship adj	A-DAS	NR*

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; NR=not reported; See Abbreviations Table for assessment tools

Findings from Trials of Interventions that Include Family Assisted Approaches to Patient Care

A summary of results for Family Assisted Approaches to Patient Care is shown in Table 11. Calculated effect sizes for each trial are shown in Table 14. Only one of the two studies[36] reported significant improvements in outcomes of interest. However, in a post-hoc exploratory analyses in the Porter trial,[45] authors report a significant time by treatment by cancer stage interactions for depression (β=-2.38, SE=0.86, p=0.006) and anxiety (β=-8.28, SE=2.85, p=0.005), indicating that patients with stage I cancer benefited more from education and support and patients with Stage II cancer benefited more from the coping skills training (with their family member). In the Nezu trial,[36] problem solving training that included both the patient and family member instead of just the patient did not improve symptom control, depression/anxiety, global quality of life, or general psychological functioning at post-intervention. However, at long-term follow up (6 months), patients in the family-involved intervention showed significant improvements in two of these four outcomes, symptom control and general psychological functioning.

Summary from Trials of Interventions that Include Family Assisted Approaches to Patient Care

- 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.

Table 14. KQ2 – Cancer: Outcomes at Post-Treatment – Trials Comparing Family Assisted Approaches to Patient Care to Alternative Interventions

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI]
Nezu 2003[36] *1) Problem solving-individual* *2) Problem solving with significant other* *3) Wait list*	150	any	1 to 3 (mostly local)	General psychological functioning	Omega-vulnerability	0.26 [-0.16, 0.68]
					POMS	0.17 [-0.25, 0.59]
					BSI	-0.39 [-0.81, 0.03]
				QoL-global	QL Index	0.21 [-0.21, 0.63]
				Depression/Anxiety	Hamilton	-0.12 [-0.54, 0.30]
				Symptom mgmt	CARES	-0.28 [-0.70, 0.14]
				6 month follow-up		
				General psychological functioning	Omega-vulnerability	-0.38 [-0.80, 0.04]
					POMS	-0.37 [-0.79, 0.05]
					BSI	**-0.77 [-1.21, -0.34]**
				QoL-global	QL Index	0.17 [-0.25, 0.59]
				Depression/Anxiety	Hamilton	-0.03 [-0.44, 0.39]
				Symptom mgmt	CARES	**-0.74 [-1.18, -0.31]**
Porter 2011[45] *1) Coping Skills Training* *2) Education*	233	lung	1 to 3	Physical functioning	FACT-L	NR*
				Social functioning	FACT-L	NR*
				Depression/Anxiety	BDI	NR*
					STAI	NR*
				Symptom mgmt	BPI	NR*
					FACT-L-symptoms	NR*

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; QoL or QL=quality of life; NR=not reported; See Abbreviations Table for assessment tools

Overview and Findings from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

One fair quality trial compared the multi-component COPE intervention (described above under Key Question #1) to friendly visits from hospice staff to patients and family members. Comparisons of these two interventions to the trial's usual care control are discussed in KQ1. Of the 329 cancer patients with non-specific late-stage cancers enrolled, 220 patients were enrolled in these two active treatment arms.[40] Unfortunately, data were not reported on study outcomes post-intervention. The authors did report a significant group by time interaction (Table 8, p=0.009) but did not compare outcomes from the COPE intervention group and the supportive visits group. There was no significant group by time interaction for quality of life or three targeted symptoms (intensity of pain, dyspnea, and constipation) and no individual comparisons between groups were reported for those outcomes.

Summary from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

- 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).

Overview of Unique Interventions Examined in Single Trials

Three trials, all of fair quality,[44, 47, 48] were considered unique interventions. Sample sizes ranged from 12 to 285 and patient age ranged from 55 to 62. The percentage of patients with post-high school education ranged from 34-68%, with one study not reporting. In one study 59%[48] were white; one study only included individuals identifying as Native Hawaiian;[47] the third did not report race.[44] All three studies included any family member and were not limited to spouses. No trial reported on the Veteran status of patients or family members. No studies reported excluding participants for relationship distress or co-occurring mental health conditions, including substance use.

Findings from Unique Interventions Examined in Single Trials

A summary of results for the unique interventions is shown in Table 11 and specific findings are shown in Table 15. All three studies showed significant differences in outcomes. Compared to providing internet access and online resources for supporting cancer patients, those who received internet access with the CHESS Website reported improvement in symptom control (i.e., symptom distress). They did not, however, report significant differences in patient mortality over time, which was operationalized as physical functioning.[44] A culturally specific intervention showed significant improvements in general psychological functioning compared to those in a more culturally neutral intervention[47] and family administered reflexology was associated with less pain and less anxiety than the attention control intervention, with differences more pronounced among patients with severe to moderate baseline pain and severe to moderate baseline anxiety.[48]

Summary of Unique Interventions Examined in Single 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 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.

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Table 15. KQ2 – Cancer: Outcomes at Post-Treatment – Trials Comparing Unique Interventions to Usual Care or Wait List Control

Study	N	Cancer	Stage	Outcome	Assessment	Effect size [95%CI] or other findings
Gustafson 2013[44] *1) Standard care + CHESS* *2) Standard care + internet*	285	lung	III or IV	Physical functioning	Mortality	RR 0.85 [0.71, 1.01]; 62 (77/124) vs. 73% (89/122)
				Symptom mgmt	ESAS	**Adj mean difference=5.3 [1.60, 8.97]** **ES=0.46, p=0.005**
Mokuau 2008[47] *1) Cultural intervention* *2) Educational intervention*	12	any	NR	General psychological functioning	BSI	Mean scores: Group 1: 17.0 **Group 2: 36.3; p<0.01 favoring Group 1 over time**
Stephenson 2007[48] *1) Reflexology* *2) Special attention*	90	any	Meta-static	Depression/ anxiety	Visual Analog Scale for Anxiety	**Moderate effect, adjusted for baseline anxiety (F=12.27, p<0.01, eta squared=0.13)**
				Symptom mgmt	BPI or SF-MPQ	**Moderate effect, adjusted for baseline pain (F=11.74, p<0.01, eta squared=0.12)**

CI=confidence interval; NR=not reported; RR=risk ratio; See Abbreviations Table for assessment tools

MEMORY-RELATED DISORDERS

Population Studied

As summarized in Table 16, over 4,600 (n=4,631) patients/family dyads were randomized into the 29 memory-related disorder trials, with 4,108 analyzed. Studies ranged in size from 36 to 642 dyads, with a median of 117 per trial. Patients in these trials were older than those in the cancer studies, averaging 78 years (range: 73-86 years). Perhaps related to the older age of these patients, in these trials more women than men were patients (55% vs. 45%). Although few trials reported marital status (31%, 9/29) and race (55%, 16/29), of those that did, 80% of patients were married and approximately 19% were not white. Family members were also slightly older, averaging 65 years (range: 48-74 years) and most were women (73%, range: 54-100%). One study reported the Veteran status of the patients,[49] and two studies[50, 51] reported recruiting from VA clinics.

Table 16. Memory-Related Disorders – Summary of Baseline Characteristics

Characteristics	Number/mean (range)	Number of trials reporting
Total number of patient/family dyads randomized	4631	29
Total number of patients from dyads analyzed	4108	29
Age of patients, years	78 (73-86)	26
Age of family members, years	65 (48-74)	26
Patient gender, % male	45 (11-65)	22
Family member gender, % female	73 (54-100)	26
Participant marital status, % married	80 (51-100)	9
Race, % non-white patients	19 (4-65)	16
Veterans, %	100%	1

The study methods for the memory studies varied as well, as summarized in Table 17. Interventions ranged in duration from one session to multiple sessions over two years, but on average, were 16 weeks long. However, one study, aimed at reducing institutionalization, is a long, ongoing trial, initiated 18 years prior to the paper's publication.[52] Authors reported using a manual or a standardized protocol in about 55% of the trials. Four trials required the family member to be a spouse (14%), while all the others included any family member or unpaid caregiver involved in care. All interventions included both men and women.

Participants in the memory-related disorders trials were heterogeneous, but in different ways than the cancer trials. Patients and family members in memory trials, for example, were older and fewer interventions required the family member to be a spouse. Participants also varied in the severity of their memory loss and cognitive function. Although seven trials[11, 52-58] 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. Six trials included patients with mild to moderate cognitive impairment,[59-64] six included patients with moderate to severe cognitive impairment,[49, 65-69] and ten trials included patients with mild to severe impairment.[10, 12, 50, 51, 64, 70-75]

Ten studies included interventions that focused on training family members on skills to change patient behavior or improve outcomes; eleven targeted multi-component interventions that, in addition to training for symptom management, included components targeted at family member and family coping and problem solving; and eight were unique interventions targeting different aspects of providing effective care to reduce depression and institutionalization, control or manage symptoms and improve functional status.

Table 17. Memory-Related Disorders – Summary of Heterogeneity

Trial Characteristic		Number of trials reporting
Manualized intervention	Yes	16
	Not reported	13
Family intervention exclusively with:	Wife/female intimate partner	0
	Husband/male intimate partner	0
	Husband/wife or male/female intimate partner	5
	Any identified family member	24
Family intervention compared to*:	Wait list	6
	Usual care	13
	Individual treatment	1
	Other family treatment(s)	11
Patient gender:	Men	0
	Women	0
	Both men and women	29

*Four trials included multiple conditions; thus, total number of comparison conditions exceeds the number of trials

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?**

Description of Study Design and Quality

We identified 19 trials on memory-related conditions that met criteria for KQ1. Details of study characteristics for each included study are found in Appendix D, Table 9. 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[49, 52, 54, 59, 62] while the others included any family member involved in care. Interventions ranged from one to twelve sessions, typically lasting 12-16 weeks long. Manual or standardized protocols were used in about 60% of trials. Six trials included long-term (at least 6 months) follow up assessments.[12, 49, 52, 54, 59, 65, 66]

We categorized studies by intervention type. These included: 1) family assisted approaches to patient care, where family members were taught new skills to assist with patient care and improve outcomes;[57, 60, 62, 65-67, 74] 2) family focused CBT interventions that targeted family member and family well-being in order to address patient behaviors and family issues;[49, 50, 52, 54, 59, 70, 75] and 3) unique interventions.[11, 12, 53, 56, 63, 68]

We summarize findings between the intervention group and the control group and address comparative effectiveness between family or family and patient interventions in KQ2.

Description of Interventions and Comparators

Twelve studies compared a family involved intervention to usual care[12, 49, 52-54, 56, 57, 59, 65-68, 75] and six to a wait list control condition.[50, 60, 62, 63, 70, 74] One included a cross-over design in which each site was randomly assigned one of three treatment conditions to be delivered over one of three periods of time. Each study site received each intervention condition with a wash-out period between conditions.[11] Fifteen trials compared a single family-involved intervention to a control condition,[12, 49, 50, 52-54, 56, 57, 59, 60, 63, 66-68, 74, 75] and four included multiple family-involved interventions and a control condition.[11, 62, 65, 70]

Seven trials compared family assisted approaches to usual care[57, 65-67] or wait list.[60, 62, 74] These interventions typically included developing family members' problem solving skills, teaching them strategies to reduce problem behaviors, and training them to reduce risks or hazards in a patient's environment. They did not focus on supporting family member psychosocial needs or support.

Six trials compared a CBT-based intervention, a multi-component intervention targeted to family members, which included skill building and problem solving for patient safety and behavior as well as coping skills for caregivers and families, to either usual care[49, 52, 54, 59, 75] or wait list control.[50, 70]

Six trials were unique, single interventions.[11, 12, 53, 56, 63, 68] They compared usual care to the efficacy of providing case consultation services from the local Alzheimer's Association,[56] the impact of support groups for patients with Early Stage Memory Loss,[63] the efficacy of a family visit education program,[68] the effect of nursing facilities teaching communication techniques and problem solving to families,[53] or the effect of an in-home exercise program for patients.[12] One intervention compared a wait list control to the effect on patients of listening to personalized audiotapes made by a family member or surrogate.[11]

Treatment Adherence

Six studies did not report any data on treatment adherence[11, 49, 52, 54, 59, 62, 65] and adherence data were not clear in another.[67] Of the thirteen studies that did report some indicator of treatment adherence, the level of detail varied greatly and differences across treatment conditions were not always reported. Five reported session adherence,[50, 57, 60, 66, 70] but only one of these reported differences by condition.[50] The proportion of study or treatment dropouts was reported in six studies[12, 57, 60, 63, 66, 74] and two of these reported differences by condition.[12, 63] Instead of drop outs, Robison[53] reported retention rates, but again, not by condition. A number of studies reported the proportion of participants completing outcome assessments. These varied widely, from 58% completing the final follow up[12] to 85-90% completing the intervention or post-intervention assessments,[56, 68, 75] but only Gitlin[75] reported by condition.

Outcomes Assessed

The most frequently assessed outcomes were symptom control/management (58%, 11/19 trials);[11, 50, 53, 54, 57, 62, 65, 67, 68, 73, 75] physical functioning (42%, 8/19 trials);[12, 54, 57, 59, 60, 63, 65, 67] and cognitive functioning (26%, 5/19 trials).[50, 60, 62, 66, 70] Four trials assessed global quality of life (21%, 4/19 trials);[63, 67, 70, 74] four trials assessed depression/anxiety (21%, 4/19 trials);[12, 63, 68, 70, 74] and five trials assessed health care utilization (26%, 5/19 trials).[49, 52, 56, 59, 67] No trials assessed relationship adjustment. Specific information about memory disorder trials, including instruments used to assess each outcome and abstracted outcome data, can be found in Appendix D, Tables 10-15.

Findings

Overall Benefits

Compared to usual care or wait list, family involved interventions did not consistently improve outcomes for physical or cognitive functioning and health care utilization, including hospitalizations or institutionalization. Some interventions did improve symptom control, depression/anxiety, and quality of life, however, most of the significant effect sizes were small to moderate in magnitude.

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 Table 18. 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 outcomes within each intervention category. This precluded us from calculating more reliable

estimates with confidence intervals to determine the strength of evidence for each intervention on particular outcomes.

Table 19 presents an overview of outcomes reported. We found evidence that suggests that targeted interventions to groups of patients with specific symptoms (e.g., incontinence, depression, etc.) may be more effective than usual care or wait list. General interventions for managing and controlling symptoms and reducing depression were less likely to be more effective than usual care. Of the eleven studies assessing symptom management or control, five[53, 57, 68, 74, 75] showed significant improvements compared to usual care or wait list control conditions. Two of these studies were unique interventions that included targeted strategies to help families control or manage specific symptoms (e.g., agitation, affect).[53, 68] The other three specifically targeted family members who reported either significant distress about patient problem behaviors[75] or patients who needed a great deal of assistance with daily tasks.[57, 74] Therefore, these interventions were designed to target these symptoms instead of a broader array of symptoms and outcomes.

For interventions targeting depression, we found the same trend. Of the five studies that assessed depression or anxiety, four showed significant improvements over usual care or wait list control conditions. Three of these were unique interventions: an exercise promotion intervention,[12] training for effective family visits with institutionalized patients,[68] and an early-stage memory loss support group.[63] The other intervention, reported by Teri et al.,[70] sought to improve depressive symptoms through behavioral therapy. One arm included behavioral therapy and problem solving for family members and the other, behavioral therapy and training for family members to provide pleasant activities for the patient. Compared to those in a usual care condition and in a wait list control, those in both intervention arms reported significant improvements in depressive symptoms using both the Hamilton Depression Rating Scale and the Cornell Scale for Depression in Dementia.

Interventions also showed some promise in improving quality of life. Two of four trials assessing patient quality of life[63, 66] showed significant improvements over control conditions. One compared a CBT-based intervention that included home visits with family members to usual care[66] and the other compared an early-stage memory loss support group for families to a support group wait list control.[63]

Evidence does not show, however, that interventions targeting either general functioning and well-being or specific patient symptoms consistently improve other important outcomes, such as physical and cognitive functioning and health care utilization. Two of eight trials assessing physical functioning showed significant improvements compared to control conditions. Two of the five trials assessing cognitive functioning showed significant improvement over comparators and only one of six trials assessing health care utilization showed significant reductions in the use of care when compared to controls.[52]

Overall Harms

Most studies did not explicitly report on whether patients were harmed by the intervention. 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.

Table 18. KQ1 – Memory-Related Disorders: Strength of Evidence for Trials of Therapy with Family Component versus 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; one 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.	Unknown	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; one 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)	Inconsistent	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).	Unknown	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

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Table 19. KQ1 – Memory-Related Disorders: Outcomes Reported in Trials of Therapy with Family Component versus Usual Care or Wait List Control

Author, year	N[#]	Study quality[+]	Physical functioning	Cognitive function	Quality of life/overall functioning	Symptom management/ control	Depression/ anxiety	Utilization	Relationship adjustment
MEMORY: Family assisted approaches, including skill training, to improve patient outcomes (n=7)									
Burgener 1998[65++]	54	poor	±			±			
Gitlin 2001[57]	202	poor	↔/↑			↔/↑			
Gitlin 2008[74]	60	good			↔	↔/↑	↔		
Martin Cook 2005[60]	47	poor	↔	↔					
Quayhagen 2000[62++]	103	poor		↔		↔			
Teri 2005[66]	95	fair		↔/↑	↔/↑				
Wright 2001[67]	93	poor	↔		±	↔		↔	
MEMORY: Family focused CBT interventions: skill building, family coping and problem solving to address patient behaviors and family issues (n=6)									
Brodaty 2009[59]	52	poor	↔					↔	
Gitlin 2010[75]	272	fair				±/↑			
Mittelman 2004,[54] 2006[52]	406	good	±			↔		↔/↑	
Ostwald 1999[50]	117	good		↔		↔			
Teri 1997[70++]	72	fair		↔/↑			↑/↔		
Wray 2010[49]	158	fair						↔	
MEMORY: Unique intervention (n=6)									
Bass 2003[56]	182	fair						↔	
Camberg 1999[11++]	54	fair				↔			
Logsdon 2010[63]	142	poor	↔		↑		↑		
McCallion 1999[68]	66	fair				↔/↑	↑/↔		
Robison 2007[53]	388	poor				↑			
Teri 2003[12]	153	fair	↔/↑				↑	↔	

RATINGS: ↑ Tx significantly better than comparator; ↔ No significant difference between intervention and comparator; ↓ Treatment significantly worse than comparator; ± Significance not reported or could not be determined

[#]Number randomized

[+]Good (low risk of bias): 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. Fair (moderate risk of bias): The trial met or was unclear for allocation concealment and blinding with no more than one of the remaining domains (ITT, withdrawals) unmet. A trial with adequate allocation concealment that did not meet other domains was rated fair. Poor (high risk of bias): The trial had inadequate allocation concealment or blinding and/or clearly met only one of the established risks of bias domains.

[++]Multi-arm trials that are also evaluated in KQ2.

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Intervention Categories

Below we summarize findings for each outcome by intervention category. We use semi-quantitative descriptions of individual study results and review the patterns of findings to highlight interventions and populations that may yield potential benefit. In Table 19 we summarize findings by intervention category.

Overview of Trials of Interventions that Include Family Assisted Approaches to Patient Care

Seven studies, five of poor,[57, 60, 62, 65, 67] one of fair,[66] and one of good quality,[74] compared family assisted interventions to usual care or wait list. Interventions ranged from a one-time session to 8 sessions. Studies ranged in size from 47 to 202, with a median of 93 dyads per study. Patients ranged in age from 73 to 80. On average, 49% of patients were men. Family members' average age was 65 years. Nearly three-fourths were women. Few studies reported patient race or marital status.

One of the studies included patients with mild to severe dementia or Alzheimer's disease,[74] two enrolled patients with mild to moderate dementia or Alzheimer's disease,[60, 62] and three enrolled patients with moderate to severe dementia or Alzheimer's disease.[65-67] One trial did not require patients meet a specific level of dementia or Alzheimer's disease.[57] Two studies required that the family member live with the patient[57, 74] and one required that the family member provide at least 4 hours of care per day.[74]

Findings from Trials of Interventions that Include Family Assisted Approaches to Patient Care

Interventions generally did not improve outcomes over usual care or wait list control conditions. Most studies reported physical and cognitive functioning and symptom control (e.g., disruptive behavior). Only three studies, however, reported patient quality of life, one reported depression, and one reported utilization of healthcare resources. No studies reported relationship adjustment. Reporting of outcomes of interest was often inconsistent, with some studies assessing outcomes, but not providing post-intervention data, or reporting overall improvements in outcomes, but not by intervention condition.

A summary of results for this group of interventions is shown in Table 19 and calculated effect sizes and other findings for each trial are shown in Table 20. Of the five studies assessing symptom control, two reported significant intervention effects.[57, 74] One trial,[74] which aimed to help family members manage patient neurobehavioral symptoms by creating tailored activities for the patient, reduced the frequency of problem behaviors in the intervention group while in the wait list control group, problem behaviors increased (ES=0.72, $p<0.05$). The intervention was particularly effective on reducing shadowing behavior, where patients follow and imitate their family member (ES=3.1, p=0.003) and repetitive questioning by patients (ES=1.22, p=0.023). In the second trial,[57] which helped caregivers modify their living space to facilitate caregiving, the unadjusted effect size for number of problem behaviors was significant although the adjusted mean difference was not.

Of the five studies reporting physical functioning outcomes, only one reported significant improvements. Physical functioning is assumed to decline in patients with dementia, so one goal is to slow the rate of decline. In the trial by Gitlin,[57] patients in both groups experienced increased instrumental activities of daily living dependence, but the intervention group had

significantly less decline than the control group (adjusted mean difference -0.13 [-0.24, -0.01], p=0.03; ES=-0.58 [-0.88, -0.27]).

Three trials assessed global quality of life. In one of these, a trial that included a 6 month intervention focused on problem solving and increasing communication, family members in the intervention groups reported that patients reported a small effect at post-intervention (ES=0.04 [-0.44, 0.52]), but after adjusting for baseline and subsequent assessments, the intervention group showed significant improvements in quality of life compared to the control group.[66]

Overall, we lack sufficient evidence to make valid conclusions about whether interventions to train family members to develop skills to improve patient outcomes are more effective than usual care. Additional studies that address potential validity threats and utilize consistent intervention protocols and outcome measures are needed to clarify the relationship between targeting family skills and improving patient outcomes.

Summary from Trials of Interventions that Include Family Assisted Approaches to Patient Care

- Interventions generally did not improve outcomes over usual care or wait list control. No study reported an improvement in depression/anxiety or utilization.
    - 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.[66]
        - 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.[57]
        - 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.[74]

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Table 20. KQ1 - Memory-Related Disorders: Outcomes at Post-Treatment – Trials Comparing Family Assisted Approaches to Patient Care to Usual Care or Wait List Control

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Burgener 1998[65] *1) Education and behavioral* *2) Education* *3) Behavioral* *4) Comparison*	47	Physical functioning	Composite of OARS, IADL, & SCS	Data NR*
		Symptom control	DBDS	Data NR*
Gitlin 2001[57] *1) Home environment program* *2) Usual care*	202	Physical functioning	ADL	ES -0.26 [-0.57, 0.04]
			IADL	**ES -0.58 [-0.88, -0.27]** **MD (adjusted) -0.13 [-0.24, -0.01]**
		Symptom control	Number of problem behaviors	**ES 0.32 [0.02, 0.62];** MD (adjusted) 1.85 [-0.42, 4.13]
Gitlin 2008[74] *1) Tailored Activity Program* *2) Wait list*	60	Global quality of life	QoL-Alzheimer's	ES NR; reported p=0.095
		Symptom control	Problem behavior frequency	**ES 0.72 [CI NR], p<0.05**
			Number of problem behaviors	ES -0.13 [-0.65, 0.40]
		Depression/anxiety	CSDD	ES NR; reported p>0.05
Martin-Cook 2005[60] *1) Caregiver skills training* *2) Wait list*	47	Physical functioning	ADCS-MCI	ES 0.50 [-0.08, 1.08]
		Cognitive functioning	MMSE	ES 0.30 [-0.28, 0.87]
			NPI	ES 0.05 [-0.52, 0.62]
Quayhagen 2000[62] *1) Cognitive stimulation* *2) Dyadic counseling* *3) Dual seminar* *4) Early day care* *5) Wait list*	103	Cognitive functioning	Problem solving	1. Cog. stimulation ES 0.35 [-0.32, 1.02] 2. Dyad counseling ES 0.01 [-0.61, 0.64] 3. Dual seminar ES 0.10 [-0.56, 0.75] 4. Early day care ES 0.05 [-0.66, 0.75]
			Immediate memory	1. Cog. stimulation ES 0.25 [-0.41, 0.92] 2. Dyad counseling ES 0.05 [-0.57, 0.68] 3. Dual seminar ES -0.04 [-0.70, 0.62] 4. Early day care ES 0.16 [-0.54, 0.87]
			Delayed memory	1. Cog. stimulation ES 0.31 [-0.36, 0.97] 2. Dyad counseling ES 0.13 [-0.49, 0.76] 3. Dual seminar ES 0.11 [-0.55, 0.77] 4. Early day care ES 0.22 [-0.49, 0.93]
			Verbal fluency	1. Cog. stimulation ES 0.34 [-0.33, 1.01] 2. Dyad counseling ES -0.05 [-0.67, 0.57] 3. Dual seminar ES 0.03 [-0.63, 0.68] 4. Early day care ES 0.13 [-0.57, 0.84]
		Symptom control	MBPC, Part A	1. Cog. stimulation ES -0.19 [-0.85, 0.48] 2. Dyad counseling ES -0.23 [-0.85, 0.40] 3. Dual seminar ES -0.04 [-0.69, 0.62] 4. Early day care ES 0.23 [-0.48, 0.94]
Teri 2005[66] *1) STAR caregivers* *2) Usual care*	95	Cognitive functioning	RMBPC, memory subscale	ES -0.33 [-0.83, 0.17]; **longitudinal p=0.031 (adjusted for baseline values; includes 2 and 6 month assessments)**
		Global quality of life	QoL-Alzheimer's	ES 0.04 [-0.44, 0.52]; **longitudinal p=0.031 (adjusted for baseline values; includes 2 and 6 month assessments)**

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Wright 2001[67] *1) Education and counseling* *2) Usual care*	93	Physical functioning	% deceased	11% (Tx) vs. 22% (Usual Care), p=NS
		Symptom control	CMAI	NR*; No significant difference for group x time, p=0.52)
		Utilization	% Institutionalized	28% (Tx) vs. 22% (Usual Care), p=NS
			# Days before institutionalization	121 (107.6) days (Tx) vs. 126 (110.5) days (Usual Care), p=0.89

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; ES=effect size; MD=mean difference; NR=not reported; NS=not statistically significant; RR=risk ratio; See Abbreviations Table for assessment tools

Overview of Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

Six studies, two of good,[50, 52, 54] three of fair,[49, 70, 75] and one of poor quality[59] compared family CBT with coping and problem solving interventions to usual care or wait list. A total of 1,077 patients with memory-related disorders were enrolled across the six trials (range: 52-406 patients); the median number of participants per trial was 180. Interventions ranged from five to ten sessions. Patients ranged in age from 73 to 82. Slightly over half were men (52%, range: 47-65%). Across all studies, 88% of the patients were married and three trials included married couples only.[49, 52, 54, 59] Few studies reported patient race or marital status. Veterans were recruited in two trials.[49, 50] In one, the number of Veterans in the trial was not reported;[50] in the other, all patient participants were Veterans.[49]

Family members' average age was 69 years (range: 62-74 years) and 68% were women. Based on reporting from two studies, family members were mainly white. Nearly two-thirds (62%, range: 54-75%) had an education level beyond high school. No trial reported on Veteran status of the family members.

Findings from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

A summary of results for family focused CBT interventions is shown in Table 19 and calculated effect sizes and other findings for each trial are shown in Table 21. Half of the trials that included this type of intervention reported symptom control (e.g., disruptive behavior),[50, 54, 75] however, only one showed significant improvements in outcomes. In a trial that compared usual care to advanced training for family members in order to help them manage the behavioral problems of patients with dementia, significantly greater rates of improvements in the targeted problem behaviors were found for those in the intervention group (67.5%) than control group patients (45.8%).[75]

Two trials reported physical[54, 59] and two reported cognitive functioning outcomes,[50, 70] but only the trial by Teri et al.[70] showed any significant intervention effects. This multi-arm trial compared a usual care and a wait list control to 1) behavioral therapy for family members with training on creating pleasant events or 2) behavioral therapy for family members that included training on problem solving. Compared to the wait list condition, those receiving behavioral therapy plus pleasant event training reported greater improvements in cognitive functioning (ES -0.86 [-1.62,

-0.11]). Both groups showed significant improvements in depression compared to the wait list and usual care control conditions.

Three trials reported utilization outcomes.[49, 52, 59] Brodaty et al.[59] found no significant differences between the family-involved intervention and control condition in time to nursing home placement. Wray et al.[49] found no differences in hospital, intensive care unit or nursing home admissions or outpatient visits. Mittelman et al.,[52] however, found that patients under the care of a family member who received CBT-based counseling and support had a longer period before nursing home placement compared to those in the control condition (1,766 vs. 1,181 days; HR=0.71 [0.54, 0.94]).

Overall, there was insufficient evidence on the effect multi-component family member interventions that included coping skills, skill building, and problem solving had on physical and cognitive functioning, global quality of life, depression, and utilization. There are no data to evaluate the effect of these interventions on relationship adjustment or quality of life.

Summary of Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

- 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.[75]
- 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 effects on increasing time to nursing home placement.[52, 54]
- One fair quality trial found that compared to usual care, 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.[70]

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Table 21. KQ1 – Memory-Related Disorders: Outcomes at Post-Treatment – Trials Comparing Family Focused CBT Interventions to Usual Care or Wait List Control

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Brodaty 2009[59] *1) #2 + psycho-logical caregiver intervention* *2) Donepezil + usual care*	52	Physical functioning	Death	RR 0.86 [0.50, 1.48]; 46 (12/26) vs. 54% (14/26)
		Utilization (Hospitalization)	Nursing home placement	RR 1.17 [0.45, 3.00]; 27 (7/26) vs. 23% (6/26)
Gitlin 2010[75] *1) Advanced caregiver training* *2) Usual care*	272	Symptom control	Improvement in occurrence of primary targeted problem behavior	**67.5% vs. 45.8% (p=0.002)**
Mittelman 2004,[54] 2006[52] *1) Multi-component intervention* *2) Usual care*	406	Physical Functioning	OARS Physical Health	NR*
			GDS	NR*
		Symptom control	MBPC	NR*; no difference at follow-up between groups, group x time p=0.97
		Utilization (Hospitalization)	Nursing home placement	RR 0.89 [0.74, 1.08]; 49% (99/203) vs. 55% (111/203) at follow-up
			Median time to placement	**HR (unadj)=0.71 [0.54, 0.94]; p=0.01**
Ostwald 1999[50] *1) Minnesota Family Workshop* *2) Wait list*	117	Cognitive functioning	MMSE	NR*; no difference at follow-up between groups, p=0.28
		Symptom control	RMBPC	ES 0.27 [-0.17, 0.72]; Intervention x time p=0.08
Teri 1997[70] *1) Behavior Therapy – Pleasant Events (BT-PE)* *2) Behavior Therapy – Problem Solving (BT-PS)* *3) Usual care* *4) Wait list*	72	Cognitive functioning	MMSE	1a. BT-PE vs. UC ES -0.29 [-1.03, 0.46] 1b. BT-PE vs. WL ES -0.06 [-0.66, 0.54] 2a. BT-PS vs. UC ES -0.32 [-1.09, 0.45] 2b. BT-PS vs. WL ES -0.09 [-0.72, 0.54]
			DRS	1a. BT-PE vs. UC ES -0.56 [-1.43, 0.31] **1b. BT-PE vs. WL ES -0.86 [-1.62, -0.11]** 2a. BT-PS vs. UC ES -0.31 [-1.27, 0.65] 2b. BT-PS vs. WL ES -0.67 [-1.53, 0.20]
		Depression/anxiety	HDRS	**1a. BT-PE vs. UC ES -1.16 [-1.96, -0.36]** **1b. BT-PE vs. WL ES -1.46 [-2.14, -0.77]** **2a. BT-PS vs. UC ES -1.03 [-1.85, -0.21]** **2b. BT-PS vs. WL ES -1.35 [-2.05, -0.65]**
			CSDD	**1a. BT-PE vs. UC ES -1.04 [-1.83, -0.25]** **1b. BT-PE vs. WL ES -1.04 [-1.68, -0.40]** **2a. BT-PS vs. UC ES -1.09 [-1.91, -0.26]** **2b. BT-PS vs. WL ES -1.02 [-1.69, -0.35]**
			Clinically significant improvement	1a. BT-PE vs. UC RR 2.61 [0.71, 9.57] 1b. BT-PE vs. WL RR 2.61 [1.00, 6.80] 2a. BT-PS vs. UC RR 3.42 [0.95, 12.30] **2b. BT-PS vs. WL RR 3.42 [1.40, 8.70]**

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Wray 2010[49] *1) Education and counseling* *2) Usual care*	158	Utilization	Total admissions	ES -0.11 [-0.42, 0.20]
			Acute admissions	ES 0.00 [-0.31, 0.31]
			ICU admissions	ES 0.00 [-0.31, 0.31]
			Nursing home admissions	ES -0.20 [-0.51, 0.12]
			Outpatient visits	ES -0.20 [-0.51, 0.12]

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; ES=effect size; HR=hazard ratio; MD=mean difference; NR=not reported; NS=not statistically significant; RR=risk ratio; UC=usual care; WL=wait list; See Abbreviations Table for assessment tools

Overview of Unique Interventions Examined in Individual Trials

Six studies, four of fair[11, 12, 56, 68] and two of poor quality,[53, 63] were considered unique and could not be categorized into any of the defined intervention groups. Enrollment ranged from 54 to 388 patient/family dyads. The mean age of the patients was 80 years and ranged from 75 to 86 years. Males made up 11% to 59% of the patients in the trials. Patients included those with memory impairment,[56] early stage memory loss,[63] and ADRD[12] living in the community and patients with moderate dementia or ADRD living in nursing facilities.[11, 53, 68] Race/ethnicity was reported in four studies, and of these, between 4% and 11% were non-white. None reported Veteran status of patients.

Five of the six studies reported the relationship of the family member to the patient. Of those, the proportion of spouses ranged from 11% to 80%. Of the non-spouse family members, the proportion of children caring for a parent ranged from 12% to 80% and siblings or other relatives ranged from 6% to 20%. Family members ranged in age from 59 to 70 years (4 studies reporting) and 65% to 80% were female (5 studies reporting).

Findings from Unique Interventions Examined in Individual Trials

A summary of results for unique interventions is shown in Table 19 and calculated effect sizes and other findings for each trial are shown in Table 22. Two of six unique interventions reported significant improvement in symptom control; both were targeted to family members of patients living in institutional settings. One study[68] targeted the patient's primary visitor and provided eight weeks of manualized training and feedback to improve patient/family interaction during visits. The second study[53] targeted the both institution and the family, providing training and teaching conflict resolution to both the patient's family member and nursing staff with subsequent discussion of issues of concern with administrators. For McCallion,[68] a significant difference in agitation emerged four months post-treatment, suggesting that people learned from the intervention, but it took time for that knowledge to translate into changes in patient behaviors.

Three of the six unique trials also reported significant improvements in patient depression/anxiety. Teri[12] targeted patients still living at home, but with at least moderate cognitive impairment and, using a combination of behavioral management techniques for the family member and an exercise regimen for the patient, showed significantly improvements in patient depression (mean difference=-1.03 [-0.17, -1.19]). This intervention also had a large effect on improving patient physical functioning (ES=0.59 [0.25, 0.93]) and led to fewer days with

restricted activities (OR=3.10 [1.08-8.95]) at post-treatment compared to controls. It did not, however, have any effect on institutionalization at up to 21 months post-intervention. In Logsdon,[63] structured support groups for both patients with early stage dementia and their family member resulted in a reduction of depressive symptoms while symptoms increased in the wait list control (ES 0.36, $p<0.01$). The intervention also improved global quality of life compared to those in the wait list control group (ES=0.44, $p<0.01$), although this benefit was most pronounced among those who started the study distressed. The McCallion trial[68] also showed small to moderate effects on patient depression, with patients of family members in the family visit education program reporting fewer symptoms than those in usual care. However, because of significant differences in the characteristics of patients in the two groups (more females in the intervention group and longer lengths of stay), some caution is needed when considering the size of the effect.

Overall, the unique interventions for family members were more effective than usual care or wait list control in controlling behavior symptoms and reducing depressive symptoms. Few trials assessed an effect on physical functioning, global quality of life, and health care utilization and those that did found few significant differences compared to usual care or wait list. There are no data to evaluate the effect of these interventions on cognitive functioning or relationship adjustment.

Summary of Unique Interventions Examined in Individual Trials

- Two interventions assessing symptom management showed significant effects on the targeted behaviors, though the magnitude of effect was small to moderate.[53, 68]
- All three interventions assessing depression showed significant reductions in depressive symptoms; the magnitude of effect was small to moderate.[12, 63, 68]
- An intervention using support groups for both patients with early stage dementia and their family member also significantly improved quality of life.[63]

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Table 22. KQ1 – Memory-Related Disorders: Outcomes at Post-Treatment – Trials Comparing Unique Interventions to Usual Care or Wait List Control

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Bass 2003[56] *1) Care consultation* *2) Usual care*	157	Utilization (hospitalization)		NR*; number of ER visits, hospital admissions, and physician visits showed no significant intervention effects at follow-up
Camberg 1999[11] *1) SimPres audio* *2) Placebo* *3) Usual care*	54	Symptom control	SCMAI agitated behaviors scale	SimPres vs. Usual care, p=0.71
Logsdon 2010[63] *1) Early Stage Memory Loss program* *2) Wait list*	142	Physical functioning	SF-36 physical functioning subscale	ES -0.05 [-0.41, 0.31]
		Global quality of life	QOL-AD	**ES 0.44 [CI NR]; p<0.01**
				"Improvers"(*post hoc*) RR 1.57 [0.97, 2.55] 48% vs. 30%; p<0.05
		Depression	GDS	**ES 0.36 [CI NR]; p<0.01**
McCallion 1999[68] *1) Family Visit Education Program (FVEP)* *2) Usual care*	66	Depression	MOSES, depression	**ES 0.91 [0.40, 1.42]**; group x time interaction p=NS
			CSDD, mood signs	ES -0.05 [-0.54, 0.43]; **group x time interaction p=0.003; mean change FVEP -0.3, Control 0.5**
			CSDD, behavioral disturbance	ES 0.00 [-0.48, 0.48]
			CSDD, physical signs	ES -0.39 [-0.88, 0.09]; **group x time interaction p=0.024; mean change FVEP -0.4, Control 0.2**
			CSDD, cyclic functions	ES -0.07 [-0.56, 0.41]; **group x time interaction p=0.02; mean change FVEP -0.3, Control -0.9**
			CSDD, ideational disturbance	ES 0.00 [-0.48, 0.48]; **group x time interaction p=0.02; mean change FVEP -0.1, Control 0.2**
		Symptom control	MOSES, self-care	ES 0.03 [-0.45, 0.52]; group x time interaction p=NS
			MOSES, disorientation	**ES 0.58 [0.09, 1.08]; group x time interaction p=0.046**
			MOSES, irritability	**ES 0.52 [0.03, 1.01]**; group x time interaction p=NS
			MOSES, withdrawal	ES 0.27 [-0.21, 0.76]; group x time interaction p=NS
			CMAI-N, CMAI-O, physically aggressive	ES can't be estimated; group x time interaction p=NS
			CMAI-N, CMAI-O, physically non-aggressive	ES can't be estimated; group x time interaction p=NS
			CMAI-N, CMAI-O, verbally agitated	ES can't be estimated; group x time interaction p=NS

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Robison 2007[53] *1) Partners in Caregiving in Special Care Unit* *2) Control unit*	388	Symptom control	CMAI	**Significant difference between groups for cursing/verbal expression, other aggression, self-abuse or sexual advances, inappropriate dress/disrobing, constant requests for attention/help, pacing/wandering** Non-significant difference for grabbing people/ destroying property, restlessness
Teri 2003[12] *1) Reducing Disability in Alzheimer's Disease* *2) Usual care*	153	Physical functioning	SF-36, physical component	**ES 0.59 [0.25, 0.93]; MD 19.29 [8.75, 29.83]; p<0.001 for pretrial and post-trial analysis regressed on treatment group, controlling for baseline value**
			Sickness Illness Profile Mobility	ES 0.05 [-0.28, 0.38]
			# restricted activities and days spent in bed	**OR 3.10 [1.08, 8.95]; p<0.001 for pretrial and post-trial analysis regressed on treatment group, controlling for baseline value**
		Depression	CSDD	**MD -1.03 [-0.17, -1.19]; p=0.02 for pretrial and post-trial analysis regressed on treatment group, controlling for baseline value**

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; ES=effect size; HR=hazard ratio; MD=mean difference; NR=not reported; NS=not statistically significant; OR=odds ratio; RR=risk ratio; UC=usual care; WL=wait list; See Abbreviations Table for assessment tools

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?**

Description of Study Design and Quality

We identified 14 trials on memory-related conditions that met criteria for KQ2. Details of study characteristics for each included study are found in Appendix D, Table 9. Six were rated as poor, five as fair, and three as good quality trials. A total of 2,198 dyads were included in these studies and 1,817 were included in analyses. The trials ranged in size from 36 to 518 dyads with a median of 97 per trial. Interventions with standard protocols or manuals included 1 to 38 sessions, averaging 10. Two trials included only spouses;[62, 72] the others included any family member or primary family member involved in care. Only one trial[70] included long-term (at least 6 months post-intervention) follow up assessments.

Description of Interventions and Comparators

Only one trial compared an individual intervention (i.e., targeting self-change for the family member) to a family involved intervention (i.e., targeting patient behavior).[72] The remaining trials compared different family interventions.[10, 11, 51, 55, 58, 61, 62, 64, 65, 69-71, 73]

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),[10, 51, 55, 61, 64, 71, 73] another unique family intervention,[69] or an individual intervention.[72] Five trials had multiple conditions and compared at least two family interventions.[11, 62, 65, 70, 72]

Studies were grouped into similar categories of interventions. Five trials tested family assisted approaches to usual patient care.[62, 65, 69, 71, 72] All five can generally be characterized as testing a skill-building program for family members to manage and improve patient outcomes.

Six trials tested comprehensive psychosocial interventions that focused on family issues, including coping skills and patient behaviors.[10, 51, 55, 64, 70, 73] These interventions used cognitive behavioral therapy strategies to support family members' personal psychosocial needs and coping skills and to assist them in developing skills and strategies to address patient outcomes. Three of these studies used the Resources for Enhancing Alzheimer's Caregiver Health (REACH) intervention, a multi-component program that includes education, skills training (including coping, stress management and problem solving skills). and social support. The REACH initiative was a multi-site cooperative study aimed to test innovations to reduce family member burden and depression. Two trials in our review[51, 73] reported findings from REACH I, the initial development phase of the REACH initiative; one other[55] reported findings from REACH II, a second trial that used findings from REACH I to modify and revise the intervention. Different sites and different intervention components are tested in these papers; therefore, we review them as separate trials.

Three studies that fit our criteria for KQ2 were categorized as unique interventions. One compared the two active interventions, a placebo audio tape and simulated presence (a recording of a family member recalling pleasant events).[11] The second tested the effect of two interventions on nighttime insomnia, depression, and problem behaviors.[61] The third study tested an intervention that included scheduled toileting reminders to reduce functional urinary incontinence.[58]

Treatment Adherence

Three studies did not report any data on treatment adherence.[11, 62, 65] Of the ten studies that did report some indicator of treatment adherence, the level of detail varied greatly. Three trials reported high rates of session attendance (98%,[72] 78%,[10]and 90%[61]) and two of these reported no difference by condition.[10, 61] Four trials reported varying rates of drop outs or lost to follow up (15%;[71]37%;[58] 18% and 11% for intervention and control group, respectively;[61] and 13.2%[69]). Three studies reported the proportion of participants completing the study (74%,[73] 82%,[70] and 80% completed[64]). Gitlin et al.[73] reported a significantly higher rate of attrition in the intervention condition.

Outcomes Assessed

The most frequently assessed outcomes were symptom control/management (86%, 12/14 trials);[10, 11, 51, 55, 58, 61, 62, 65, 69, 71-73] physical functioning (36%, 5/14 trials);[10, 65, 69, 71, 73] and cognitive functioning (43%, 6/14 trials).[58, 62, 64, 70, 73] Three trials assessed global quality of life (21%, 3/14 trials)[10, 55, 70]and two assessed depression/anxiety (14%, 2/14 trials).[61, 70] One trial assessed

utilization,[55] but no trial assessed relationship adjustment. Specific information about memory trials, including instruments used to assess each outcome and abstracted outcome data, can be found in Appendix D, Tables 10-15.

Findings

Overall Benefits

We rated the evidence for the effectiveness of family-involved interventions for memory-related disorders as low, as shown in Table 23. Overall, few trials showed significant differences in improving outcomes between interventions. Evidence is not strong enough to suggest that interventions beyond providing education and minimal support to family members are beneficial to patients. Studies comparing a family-involved intervention to an attention control condition showed few improvements on outcomes. Likewise, data were insufficient to suggest that one type of intervention is superior to another at improving patient outcomes.

In Table 24, we summarize findings by intervention category. Three of the twelve studies that assessed symptom control showed improvements. All were narrowly focused interventions intended to change specific symptoms. One was a sleep hygiene intervention that showed that educating and training family members about patient sleep behavior reduced the number of night time awakenings and total time awake at night compared to an attention control condition that included only supportive contact.[61] The second reported that families trained to use a toileting protocol for patients reduced incontinence compared to those receiving a monthly phone call.[58] The third trial showed that two intervention conditions, one training family to manage patient behavior and the other to change their own behavior to improve their coping, improved patient problem behavior compared to simply receiving information about problem behaviors. Additional analyses found that training family to manage patient behavior improved those behaviors more than providing strategies for self-care.[72] Only two other trials had a significant effect on an outcome of interest. One was a cognitive behavioral intervention to reduce environmental stressors and improve problem solving.[10] In this trial, the intervention significantly improved physical functioning of patients compared to those in the attention control group. The second was an intervention designed to enhance caregiver skills.[55] In this trial, caregivers in the skills training group were more likely to report that the intervention improved the care recipients' quality of life than caregivers in the attention control group. Beyond the findings for these five of the twelve trials, no other trials reported significant differences between a family involved intervention and an alternative intervention on symptom control, physical functioning, or quality of life, and, although assessed, no trials reported significant group differences in cognitive functioning, depression, or utilization. The success of narrowly focused and tailored interventions that fit the very specific symptoms and needs of the patients suggests that targeted interventions may be more advantageous than general psychosocial interventions that aim to improve quality of life or overall functional status.

Overall Harms

Few studies explicitly reported if the family intervention investigated may have led to harms for patients, and among those trials that did report this information, no harms were reported to patients or family members who participated in the interventions investigated.

Table 23. 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

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Table 24. KQ2 – Memory-Related Disorders: Outcomes Reported in Trials Comparing Therapy with Family Component to Alternative Interventions

Author, year	N#	Study quality+	Physical functioning	Cognitive function	Quality of life/ overall functioning	Symptom management/ control	Depression/ anxiety	Utilization	Relationship adjustment
MEMORY: Family assisted approaches, including skill training, to improve patient outcomes (n=5)									
Bourgeois 2002[72]	63	good				↔\↑			
Burgener 1998[65]	54	poor	±			±			
Chang 1999[71]	65	poor	↔			↔			
Gerdner 2002[69]	241	fair	±			±			
Quayhagen 2000[62]	103	poor		↔		↔			
MEMORY: Family focused CBT interventions that include skill building, family coping and problem solving to address patient behaviors and family issues (n=6)									
Belle 2006[55]	518	fair			↑	↔		↔	
Burns 2003[51]	76	poor				↔			
Gitlin 2003[73]	255	fair	↔	↔		↔			
Gitlin 2010[10]	237	good	↔\↑		↔	↔			
Gonyea 2006[64]	91	poor		↔					
Teri 1997[70]	72	fair		↔			↔		
MEMORY: Unique interventions (n=3)									
Camberg 1999[11]	54	fair				↔			
Jirovec 2001[58]	118	poor		↔		↔/↑			
McCurry 2005[61]	36	good		↔		↔/↑**	↔/↑***		

RATINGS: ↑ Tx significantly better than comparator; ↔ No significant difference between intervention and comparator; ↓ Treatment significantly worse than comparator; ± Significance not reported or could not be determined

#Number randomized

+Good (low risk of bias): 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. Fair (moderate risk of bias): The trial met or was unclear for allocation concealment and blinding with no more than one of the remaining domains (ITT, withdrawals) unmet. A trial with adequate allocation concealment that did not meet other domains was rated fair. Poor (high risk of bias): The trial had inadequate allocation concealment or blinding and/or clearly met only one of the established risks of bias domains.

*Both KQ2 trials compared two similar interventions of varying intensity, with null hypotheses that interventions would differ. Non-significant findings support the alternate hypothesis.

**Authors report symptom control did not improve post-treatment, but did improve significantly longitudinally (assessed at 2 and 6 months and controlling for baseline values).

***Authors report significant improvement in depression both post-treatment and longitudinally (assessed at 2 and 6 months and controlling for baseline values). Calculated effect sizes were not significant.

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Intervention Categories

Below we summarize findings by intervention category.

Overview of Trials of Interventions that Include Family Assisted Approaches to Patient Care

Five studies, three of poor,[62, 65, 71] one of fair,[69] and one of good quality,[72] compared family assisted interventions to either a patient-centered intervention,[72] to modified versions or components of the experimental condition,[65, 71] or to alternative family interventions.[62, 69] Interventions varied widely in length, ranging from 2 contacts over 2 weeks[69] to an undisclosed number of contacts over 8 weeks.[71] Studies ranged in size from 54 to 241, with a median of 54 per study. Patients ranged in age from 75 to 79 years. On average, 55% of patients were men. Family members' average age was 69 years. Nearly three-fourths of participating family members were women. Few studies reported patient race or marital status of patients or family members.

Of the five studies in this intervention group one included patients with mild to moderate dementia,[62] one included patients with mild to severe dementia,[71] and two reported including patients with moderate to severe dementia or Alzheimer's disease.[65, 69] Bourgeois et al.[65] included patients with a diagnosis of probable Alzheimer's disease.

Burgener[65] tested a one session intervention to help family members of home-dwelling patients with Alzheimer's disease manage difficult patient behaviors. Participants were randomized to receive either: 1) education only, 2) behavior change only, 3) both education and behavior change, or 4) a control condition (which was not described). In Quayhagen[62] four interventions to improve coping for family members caring for someone with dementia were compared. Participants were randomized to receive 8 sessions over 8 weeks of either: 1) a learning cognitive stimulation for the patient, 2) dyadic counseling, 3) dual supportive group therapy, or 4) an early memory loss day care (with a family member support group). Like Quayhagen, in Bourgeois,[72] the trial's aim was to test strategies for improving coping for spouses of patients with Alzheimer's disease. With 10 contacts over 12 weeks, families were either: 1) trained to change patient behavior, 2) trained in self-care and coping strategies, or 3) supported in their efforts during nurse visits to family member homes. In Chang,[71] homebound families caring for a patient with Alzheimer's disease were randomized to receive either: 1) videotapes that modeled caregiving tasks, such as eating and dressing and take part in an 8 week nurse-led program to reinforce coping strategies and information in the videos or 2) weekly nurse phone calls. In the trial by Gerdner et al.,[69] the aim was to reduce the frequency of patient problem behaviors. Family members were randomized to receive either: 1) two home visits over two weeks in which a nurse would help develop an individualized plan of care to modify environmental stressors and provide guidance on how to execute the plan or 2) two home visits that included general information about ADRD, caregiving and referrals for community resources, case management and support groups.

Findings from Trials of Interventions that Include Family Assisted Approaches to Patient Care

A summary of results for interventions using family assisted approaches is shown in Table 24 and calculated effect sizes and other findings for each trial are shown in Table 25. Only one of the six trials testing family focused interventions to improve patient care showed a significant

improvement in our outcomes of interest over another intervention. In Bourgeois,[72] families in the patient-change condition reported significantly fewer problem behaviors than those in the attention control group (1.3 vs. 2.0, $p<0.05$). This effect continued with significant differences between groups at long-term follow up (-0.2 vs. 1.9, $p<0.01$). Post-intervention, patients across conditions did not differ in aggressivity/activity disturbance but at long term follow up, both the patient-change and self-change groups reported significantly less of these behaviors than the control group (5.6 vs. 8.4, $p<0.05$; 5.2 vs. 8.4, $p<0.01$, respectively).

None of the trials were superior to alternative interventions for improving physical or cognitive functioning. No studies assessed any of our other outcomes of interest.

Summary from Trials of Interventions that Include Family Assisted Approaches to Patient Care

- One study showed a significant effect on improving patient symptoms (i.e., problem behaviors).[72]
- Two trials reported assessing patient physical functioning and symptom control but did not report post-intervention data.[65, 69]

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Table 25. KQ2 – Memory-Related Disorders: Outcomes at Post-treatment – Trials Comparing Family Assisted Approaches to Patient Care to Alternative Interventions

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Bourgeois 2002[72] *1) Patient-change* *2) Self-change* *3) Visitation control*	42	Symptom control	Behave-AD, Total score	1) vs. 3) ES -0.30 [-0.99, 0.39] 2) vs. 3) ES -0.55 [-1.25, 0.15]; **p<0.05 after adjustment for baseline scores**
			Problem behavior frequency (weekly average)	1) vs. 3) ES NR*; **p<0.05 after adjustment for baseline scores** 2) vs. 3) ES NR*; p=NS
Burgener 1998[65] *1) Education & behavioral* *2) Education* *3) Behavioral* *4) Comparison*	47	Physical functioning	Composite of OARS, IADL, and SCS	1) 9.3 (Δ=-2.5)‡ 2) 10.6 (Δ=-1.9) 3) 10.1 (Δ=1.4) 4) 12.6 (Δ=-2.0) ‡Change from baseline to 6 months p=NR
		Symptom control	DBDS	1) 27.9 (Δ=-0.56)‡ 2) 36.6 (Δ=-0.21) 3) 28.1 (Δ=2.22) 4) 28.3 (Δ=2.71) ‡Change from baseline to 6 months p=NR
Chang 1999[71] *1) Nurse line CBT* *2) Placebo calls*	65	Physical functioning	Functional Rating Scale for the Symptoms of Dementia, ADL subscale	NR*; reported no significant difference for group x time interaction
		Symptom control	Functional Rating Scale for the Symptoms of Dementia, Overall Function	ES -0.06 [-0.54, 0.43]
			Functional Rating Scale for the Symptoms of Dementia, Behavior Subscore	ES -0.03 [-0.52, 0.46]
Gerdner 2002[69] *1) Progressively Lowered Stress Threshold* *2) Referrals, case mgmt*	241	Physical functioning	RMBPC, subscale	NR*
		Symptom control	MBPC	NR*
Quayhagen 2000[62] *Cognitive stimulation vs. 3 active controls (dual seminar, dyadic counseling, and early day care)*	88	Cognitive functioning	Problem solving	vs. Dual ES 0.33 [-0.27, 0.94] vs. Dyad ES 0.40 [-0.16, 0.97] vs. Early ES 0.41 [-0.25, 1.07]
			Immediate memory	vs. Dual ES 0.33 [-0.27, 0.93] vs. Dyad ES 0.25 [-0.31, 0.81] vs. Early ES 0.12 [-0.53, 0.77]
			Delayed memory	vs. Dual ES 0.22 [-0.38, 0.82] vs. Dyad ES 0.21 [-0.35, 0.77] vs. Early ES 0.04 [-0.61, 0.69]
			Verbal fluency	vs. Dual ES 0.37 [-0.23, 0.97] vs. Dyad ES 0.48 [-0.09, 1.05] vs. Early ES 0.27 [-0.38, 0.93]
		Symptom control	MPBC, Part A	vs. Dual ES -0.17 [-0.77, 0.43] vs. Dyad ES 0.02 [-0.54, 0.58] vs. Early ES -0.46 [-1.12, 0.20]

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Quayagen 2000, cont. *Dual seminar vs. 3 active controls (cognitive stimulation, dyadic counseling, and early day care)*		Cognitive functioning	Problem solving	vs. CS ES -0.33 [-0.94, 0.27] vs. Dyad ES 0.10 [-0.46, 0.65] vs. Early ES 0.07 [-0.57, 0.71]
			Immediate memory	vs. CS ES -0.33 [-0.93, 0.27] vs. Dyad ES -0.11 [-0.67, 0.44] vs. Early ES -0.24 [-0.89, 0.40]
			Delayed memory	vs. CS ES -0.22 [-0.82, 0.38] vs. Dyad ES -0.02 [-0.57, 0.54] vs. Early ES -0.15 [-0.79, 0.50]
			Verbal fluency	vs. CS ES -0.37 [-0.97, 0.23] vs. Dyad ES 0.09 [-0.46, 0.65] vs. Early ES -0.13 [-0.77, 0.52]
		Symptom control	MPBC, Part A	vs. CS ES 0.17 [-0.43, 0.77] vs. Dyad ES 0.20 [-0.35, 0.76] vs. Early ES -0.30 [-0.95, 0.35]
Dyad counseling vs. 3 active controls (cognitive stimulation, dual seminar, and early day care)		Cognitive functioning	Problem solving	vs. CS ES 0.40 [-0.97, 0.16] vs. Dual ES -0.10 [-0.65, 0.46] vs. Early ES -0.04 [-0.65, 0.57]
			Immediate memory	vs. CS ES -0.25 [-0.81, 0.31] vs. Dual ES 0.11 [-0.44, 0.67] vs. Early ES -0.14 [-0.75, 0.47]
			Delayed memory	vs. CS ES -0.21 [-0.77, 0.35] vs. Dual ES 0.02 [-0.54, 0.57] vs. Early ES -0.14 [-0.75, 0.47]
			Verbal fluency	vs. CS ES -0.48 [-1.05, 0.09] vs. Dual ES -0.09 [-0.65, 0.46] vs. Early ES -0.24 [-0.85, 0.37]
		Symptom control	MPBC, Part A	vs. CS ES -0.02 [-0.58, 0.54] vs. Dual ES -0.20 [-0.76, 0.35] vs. Early ES -0.53 [-1.15, 0.09]
Early daycare vs. 3 active controls (cognitive stimulation, dual seminar, and dyadic counseling,)		Cognitive functioning	Problem solving	vs. CS ES 0.41 [-1.07, 0.25] vs. Dual ES -0.07 [-0.71, 0.57] vs. Dyad ES 0.04 [-0.57, 0.65]
			Immediate memory	vs. CS ES -0.12 [-0.77, 0.53] vs. Dual ES 0.24 [-0.40, 0.89] vs. Dyad ES 0.14 [-0.47, 0.75]
			Delayed memory	vs. CS ES -0.04 [-0.69, 0.61] vs. Dual ES 0.15 [-0.50, 0.79] vs. Dyad ES 0.14 [-0.47, 0.75]
			Verbal fluency	vs. CS ES -0.27 [-0.93, 0.38] vs. Dual ES 0.13 [-0.52, 0.77] vs. Dyad ES 0.24 [-0.37, 0.85]
		Symptom control	MPBC, Part A	vs. CS ES 0.46 [-0.20, 1.12] vs. Dual ES 0.30 [-0.35, 0.95] vs. Dyad ES 0.53 [-0.09, 1.15]

*Data were either not reported or presented in a fashion that did not permit an effect size calculation
CI=confidence interval; ES=effect size; NR=not reported; NS=not statistically significant; See Abbreviations Table for assessment tools

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Overview of Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

Six trials, one of good,[10] three of fair,[55, 70, 73] and two of poor quality,[51, 64] compared family assisted interventions to family-focused CBT-based interventions. These interventions were typically multi-component. Trials ranged in size from 72 to 518, a total of 1,249 memory patients were enrolled across the six trials. The median number of participants per trial was 164. Interventions ranged from 5 to 38 sessions. Patients ranged in age from 76 to 82 years. Over 40% were men (41.5%, range: 35-55%). Only one trial reported marital status of patients. In that trial, 59% of patients were married.[55] Three of the six trials reported race and, of those, 54% were white. One study reported recruiting from VA clinics.[51]

Family members average age was 63 years (range: 61-67 years) and 78% were women. Based on data from five studies, family members were mainly white (60%). Nearly 60% (range: 43-69%) had an education level beyond high school. No trial reported on Veteran status of the family members.

In Teri,[70] two active, non-pharmacologic interventions for depression in Alzheimer's dementia patients were compared: the Behavior Therapy-Pleasant Events (BT-PE) intervention and the Behavior Therapy-Problem Solving (BT-PS) intervention. In Gitlin,[10] a biobehavioral home-based intervention on functional dependence, quality of life, and problem behaviors (the COPE intervention) was compared to an attention control group that received up to 3 telephone calls from research staff, asking about concerns and following up by sending educational materials specific to those concerns. In Gonyea,[64] a multi-component behavioral intervention designed to teach family members techniques in managing Alzheimer's patients' neuropsychiatric symptoms was compared to an attention control condition that included general information on Alzheimer's disease, aging, home safety, and communication support. Three trials were based on the REACH initiative as previously described.[51, 55, 73]

Findings from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

A summary of results for interventions using family focused CBT interventions is shown in Table 24 and calculated effect sizes and other findings for each trial are shown in Table 26. Two trials reported a significant difference in outcomes of interest. One trial, the cognitive behavioral intervention to reduce environmental stressors and improve problem solving, reported a difference in outcomes between interventions.[10] In this trial, the intervention significantly improved physical functioning of patients compared to those in the attention control group. The second trial, which involved skill building for caregivers, found significantly improved patient quality of life in the intervention group.[55] No other trial was superior to alternative interventions for improving physical or cognitive functioning, symptom control, depression/anxiety, or utilization. None of the trials assessed relationship adjustment.

Summary from Trials of Family Focused CBT Interventions that Include Family Coping and Problem Solving

- 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 statistically significant effects on overall functional independence, Instrumental Activities of Daily Living (IADL) dependence, and activity engagement post-intervention compared to the attention control group.[10]

- The REACH II intervention, targeting five elements of caregiving, had a significant effect on patient quality of life compared to an attention control group.[55]

Table 26. KQ2 – Memory-Related Disorders: Outcomes at Post-treatment – Trials Comparing Family Focused CBT Interventions to Alternative Interventions

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Belle 2006[55] *1) Multi-component* *2) Attention control (calls)*	518	Quality of life	Single question, improved recipient's life "a great deal"	**RR 2.47 [1.86, 3.27]; 40.4% (130/323) vs. 16.3% (52/319)**
		Symptom control	RMBPC	Hispanic or Latino 1) 45% improved; 13% worsened 2) 23% improved; 28% worsened White or Caucasian 1) 32% improved; 20% worsened 2) 26% improved, 27% worsened Black or African American 1) 27% improved, 33% worsened 2) 25% improved, 27% worsened (significance NR)
		Utilization	Institutionalization	4.3 vs. 7.2%, p=0.12
Burns 2003[51] *1) Behavior care* *2) Enhanced care*	76	Symptom control	MBC	ES 0.63 [0.17, 1.10]
Gitlin 2003[73] *1) Environ-mental Skill Building* *2) Resource information*	190	Physical functioning	ADL	ES -0.06 [-0.34, 0.23]
			IADL	ES 0.12 [-0.17, 0.40]
		Cognitive functioning	RMBPC – memory subscale	ES 0.00 [-0.28, 0.28]
		Symptom control	RMBPC	ES -0.06 [-0.34, 0.23]
Gitlin 2010[10] *1) COPE* *2) Calls + educational material*	237	Physical functioning	Overall functional dependence	**Cohen's d 0.21 [CI NR]; p=0.02**
			Overall functional dependence, % improved	**49 vs. 29%; MD 19.2% [2.7, 36.0]; p=0.02**
			IADL dependence	**Cohen's d 0.43 [CI NR]; p=0.007**
			IADL dependence, % improved	**62 vs. 44%; MD 17.9% [1.9, 34.0]; p=0.03**
			ADL dependence	Cohen's d NR; p=0.21
			Activity engagement	**Cohen's d 0.26 [CI NR]; p=0.03**
			Activity engagement, % improved	13 vs. -2%; MD 14.6 [−8.8, 38.0]; p=0.22
		Quality of life	Quality of life-Alzheimer's disease	Cohen's d 0.14 [CI NR], p=0.06
		Symptom control	ABID (based on # and frequency of behaviors)	ES 0.13 [-0.14, 0.40]

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Gonyea 2006[64] *1) Behavioral* *2) Psycho-education attention control*	91	Cognitive functioning	NPI	ES -0.26 [-0.70, 0.18]
Teri 1997[70] *1) Behavior Therapy (BT) – Pleasant Events* *2) BT – Prob Solving* *3) Usual Care* *4) Wait list*	42	Cognitive functioning	MMSE	ES 0.03 [-0.58, 0.64]
			DRS	ES -0.33 [-1.16, 0.49]
		Depression/ anxiety	HDRS	ES -0.44 [-1.06, 0.18]
			CSDD	ES -0.12 [-0.73, 0.49]
			Clinically significant improvement	RR 0.76 [0.46, 1.25]

CI=confidence interval; d or ES=effect size; MD=mean difference; NR=not reported; NS=not statistically significant; RR=risk ratio; See Abbreviations Table for assessment tools

Overview of Unique Interventions Examined in Individual Trials

Three studies, one of good,[61] one of fair,[11] and one of poor quality,[58] compared unique interventions. Trials ranged in size from 36 to 118; a total of 208 family member and patient dyads were enrolled across the three trials. The median number of participants per trial was 54. Interventions ranged from three to ten sessions. Patients ranged in age from 78 to 83 years and nearly all were white. Half of the patients were men (52%, range: 11-56%). None of the trials reported marital status or Veteran status.

One of these studies, by Camberg et al.,[11] was a small three-arm study that compared two active interventions: a placebo audio tape (neutral events) and a simulated presence (a recording of a family member recalling pleasant events). The third arm was usual care as described under KQ1. The second study, by McCurry,[61] tested the effect of two interventions on nighttime insomnia, depression, and problem behaviors in a small sample (n=36). The third study[58] tested an intervention that included scheduled toileting reminders to reduce functional urinary incontinence for the patient, taking into account both the patient and family member's schedule and routine.

All three of these trials included patients with documentation of possible or probably ADRD, although in the Camberg trial[11] patients were institutionalized and the McCurry[61] and Jirovec[58] studies included community dwelling patients. Patients in the Camberg trial were required to show signs of agitation or withdrawn behavior. In McCurry, patients were required to have sleep problems and in Jirovec, patients were required to have functional urinary incontinence.

Findings from Unique Interventions Examined in Individual Trials

Two trials reported significant improvements in symptom control. A summary of results for unique interventions is shown in Table 24 and findings for each trial are shown in Table 27. In McCurry,[61] the sleep hygiene intervention showed a significant decrease in night wake time compared to the contact control group. At 6-month follow up, controlling for baseline scores, patients in the NITE-AD intervention showed significantly less night wake time, fewer night awakenings, fewer wakes per hour, and less time awake at each awakening than the contact control.

In Jirovec's trial to reduce incontinence,[58] incontinent episodes decreased for the intervention group, but increased for the control group by post-treatment (moderate effect size, -0.38, p=not reported). The number of patients whose incontinence decreased by post-treatment was significantly higher in the intervention group (64% vs. 50%, $p<0.05$). Although patient cognitive ability over the treatment period declined at a similar rate for both groups, cognitive ability was the best predictor of the intervention's success; thus the authors concluded the intervention would most benefit moderately cognitively impaired incontinent elders.

None of the trials reported physical functioning, global quality of life, utilization, or relationship adjustment.

Summary of Unique Interventions Examined in Individual Trials

- Nursing home patients with Alzheimer's disease who received a personalized audiotape made by a family member recalling positive memories of the patient showed no difference in agitated behaviors compared to those receiving an audio tape of someone reading an emotionally neutral article.[11]
- Among patients with Alzheimer's disease, a sleep education intervention for family members decreased patient night wake time compared to the attention control group.[61]
- The toileting training program for family members significantly decreased patient incontinence compared to 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.[58]

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Table 27. KQ2 – Memory-Related Disorders: Outcomes at Post-treatment – Trials Comparing Unique Interventions to Alternative Interventions

Study	N	Outcome	Instrument	Effect size [95%CI] or other findings
Camberg 1999[11] *1) SimPres audio* *2) Placebo* *3) Usual care*	54 *crossover*	Symptom control	SCMAI agitated behaviors scale	SimPres vs. Placebo, p=0.13
Jirovec 2001[58] *1) Scheduled toileting* *2) Monthly call*	118	Cognitive functioning	SPMSQ	ES -0.05 [-0.51, 0.42]
		Symptom control	Incontinence (UI episodes/# voiding episodes)	ES -0.38 [-0.85, 0.09]
			Patients showing decrease in UI	**64% (28/44) vs. 50% "small decrease" (15/30) p<0.05**
McCurry 2005[61] *1) Nighttime Insomnia Treatment and Education for Alzheimer's Disease* *2) Supportive contact*	36	Cognitive functioning	RMBPC, memory	ES 0.62 [-0.13, 1.37]
		Symptom control	RMBPC, disruption	ES 0.00 [-0.73, 0.73]
			Night wake time (hours)	ES -0.51 [-1.25, 0.24] **Authors reported p<0.05**
			Number of night awakenings	ES -0.58 [-1.32, 0.17]
			Percentage of time asleep (sleep hrs/time in bed)	ES 0.39 [-0.35, 1.13]
			Wake index (wakes/ hour)	ES -0.60 [-1.35, 0.15]
			Duration of night awakenings (minutes)	ES 0.06 [-0.67, 0.79]
		Depression/anxiety	RMBPC-depression	ES 0.15 [-0.59, 0.88]; **Comparison of mean change from baseline to post-tx between groups p=0.04**
			CSDD	ES 0.26 [-0.48, 0.99]

CI=confidence interval; ES=effect size; UI=urinary incontinence; See Abbreviations Table for assessment tools

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SUMMARY AND DISCUSSION

In this review we assessed the evidence published in the United States since 1995 of family-involved interventions for improving outcomes in adult patients with cancer and memory-related conditions. We posed two key questions, first asking if these interventions are more effective at improving outcomes than usual care/wait list and second, if they are more effective at improving outcomes than other types of interventions, including health education, patient-only interventions and alternative family interventions.

Our search yielded 59 articles, representing 56 trials. Among these, 27 trials included family interventions aimed at improving outcomes for cancer patients and 29 for patients with memory-related disorders. Trials were heterogeneous and varied in the populations targeted, study size, methods of delivering interventions, and outcomes assessed. In most cases, the family intervention followed a protocol, withdrawals from the trials were adequately described (although often not by intervention condition), and exclusion/inclusion criteria for participation were clearly described. However, few studies included a description of allocation concealment or blinding procedures and measures used to assess the same construct were highly variable across trials. Treatment integrity was frequently not described, and for many studies, multiple comparisons were made, samples were small, and analyses underpowered. Veteran status of patients or family members was not explicit in most studies. While post-treatment outcomes were frequently reported, some trials did not report post-intervention data.

The purposes of family involvement also varied. In most cancer studies, the intention of the trial was to integrate families to improve patient outcomes, including relationship adjustment. However, for memory-related trials, the intention of some interventions was to reduce the burden of care for family members by helping them manage patient functioning and care. Therefore, the primary target of the intervention was family member outcomes and the secondary target was patient outcomes.

SUMMARY OF EVIDENCE FOR CANCER TRIALS

The disease course 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 uncertainty about how the disease and their lives will progress. With the majority of trials including patients with early or mid-staged cancers, the family-involved interventions focused on improving quality of life and functional status, reducing depression and anxiety, managing symptoms, and adjusting to one's intimate relationship.

We found some evidence that favors family-involved interventions over usual cancer care for improving patient symptoms and depression/anxiety. We also found some evidence, albeit weak, that family-involved interventions are superior to ones that are patient-focused or provide only health education or psychoeducation in improving symptoms. The evidence suggests that family involved interventions designed for specific sub-groups (e.g., cancer patients with late stage cancer, couples in newer relationships, hospice patients) may be more effective at improving

a broad range of cancer-related symptoms and depression/anxiety than usual care. Likewise, family interventions teaching a specific skill (e.g., reflexology) to address a symptom or problem (e.g., pain) may be more effective for improving symptoms than providing general support or education. However, we recommend that these findings be viewed with caution. All but two of the 27 trials were of poor or fair quality, and although a broad range of symptoms improved within a single trial (e.g., sexual functioning, side effect severity, symptom-related distress), we found little evidence across trials that specific symptoms commonly associated with cancer and cancer treatment, such as pain, fatigue, or nausea improved. Across all trials we also did not find a strong evidence base supporting family interventions to improve overall quality of life or components of quality of life (including physical, general psychological, and social functioning) or relationship adjustment.

SUMMARY OF EVIDENCE FOR MEMORY TRIALS

Family roles can be significantly disrupted when a family member with a memory disorder begins to show signs of disease progression. Unlike cancer, however, there is little ambiguity about the unalterable course of these diseases. Families are typically aware that patient functioning will decline over time and not improve. Compared to the cancer trials, family interventions tended to target more traditional forms of caregiving, concentrating more on maintaining or improving patient quality of life and managing problem behaviors as they evolve than on adjusting to changes in roles, relationships, and overall functional status.

Like the cancer trials, for memory-related conditions we also found weak evidence to suggest that family-involved interventions improve patient outcomes more than usual care. The strength of evidence for family-involved interventions improving outcomes over patient-focused or other health education or psychoeducation interventions for patients with memory-related disorders is also low. Our findings are unfortunate in that they do not provide clear answers to how families can improve cognitive functioning or symptom management or reduce health care utilization. However, we did find some evidence that suggests that targeted interventions to groups of patients with specific symptoms (e.g., depression) may be more effective in managing and controlling symptoms and reducing depression than usual care and that unique interventions that included targeted strategies to help families control or manage specific symptoms (e.g., agitation, affect) were more effective than usual care. Data were insufficient to suggest that one type of intervention is superior to another at improving most patient outcomes, although for symptom control, a number of trials, all narrowly focused to change specific symptoms (e.g., insomnia, incontinence), did show some significant improvement over alternative interventions.

CONCLUSIONS

Our findings echo a previous review that used similar criteria to ours.[5] In that review, Martire reported that studies were very heterogeneous and that the evidence suggested 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 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 experienced greater improvement or less decline than those in the control group.[10-12]

LIMITATIONS

Our review has a number of limitations. First, although we had a large number of RCTs to review, it is possible that by including evidence from rigorous observational evidence we would have different conclusions, although these studies 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 family member burden), not patient outcomes. This may have affected how the data were reported and the strength of the evidence for single trials. The REACH trials, for example, have shown significant improvements in caregiver[55, 76, 77] outcomes, but patient outcomes reviewed for this report were not consistently different than control conditions. It is possible that effective interventions targeting caregiver outcomes may subsequently benefit patients, but that the effect on caregivers must be large enough that any diluting of the benefit that is transmitted from caregivers to patients is perceptible. 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 the consistency of findings with 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 family member programs that VHA has recently implemented (e.g., Caregiver Hotline; OEF/OIF Caregiver Support Program, etc.). None of the interventions we reviewed tested the impact on patients of supporting caregivers financially or in providing access to health care and health services. Therefore, we have insufficient evidence to determine if current programs targeting family members will, in fact, affect short- or long-term patient outcomes. This is an area that needs further study.

RECOMMENDATIONS FOR FUTURE RESEARCH

Based on our findings, we have a number of recommendations to consider. First, our review suggests that general interventions for families may not improve patient outcomes, but family interventions targeting specific conditions, behaviors, or symptoms will likely be more effective, particularly when resources are limited. Second, other studies have shown that family interventions can reduce burden.[3] However, it remains unclear if by reducing family burden,

families can provide better care which then, in turn, improves 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. Identifying sub-groups (e.g., by disease stage or severity of condition, relationship between patient and family member, education level, etc.) should be considered for each condition in order to verify if tailoring interventions is more advantageous than a one-size-fits-all intervention. These types of trials would provide important data for making both policy and clinically meaningful decisions about which interventions to implement to whom and at what stage in the disease course. Fourth, although the evidence is inconclusive about whether telephone or web-based counseling or other supportive programs that rely on technology are as effective as other forms of counseling, they have potential benefit to rural or home-bound family and patients, families who are poor and have few means, and families who have little access to other forms of support. Methodologically rigorous research will be important to pursue in future research in order to assess whether the benefit of these types of programs are equivalent to usual care and in-person programs. In future research, researchers should attend to issues of study quality, including blinding, allocation concealment, descriptions of dropouts, and intent to treat analyses. Outcome data should be reported post-treatment for each condition for direct group comparison and, when feasible, longer term outcomes should be included to assess intervention sustainability. Additionally, 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 study sample size as much as it is feasible.

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 within the US since 1995 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 patient 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.

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