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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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Prepared by:
Evidence-based Synthesis Program (ESP) Center
Minneapolis VA Medical Center
Minneapolis, MN
Timothy J. Wilt, M.D., M.P.H., Director

Investigators:
Principal Investigator:
Joan M. Griffin, Ph.D.

Co-Investigator:
Laura Meis, Ph.D.

Research Associates:
Maureen Carlyle, M.P.H.
Nancy Greer, Ph.D.
Agnes Jensen, B.S.
Roderick MacDonald, M.S.
Indulis Rutks, B.S.

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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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BACKGROUND

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

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

We addressed the following key questions:

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

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

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

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

METHODS

DATA SOURCES

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

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

DEFINITIONS OF KEY CONCEPTS OF FAMILY AND OUTCOMES

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

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

CATEGORIZATION OF INTERVENTIONS

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

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

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

DATA EXTRACTION AND QUALITY ASSESSMENT

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

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

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

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

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

DATA SYNTHESIS

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

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

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

PEER REVIEW

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

RESULTS

OVERVIEW OF ALL STUDIES

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

STUDY DESIGN AND QUALITY

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

CANCER

Description of Cancer Studies

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

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

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

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

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

Benefits

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

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

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

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

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

Harms

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

Intervention Categories

Below we summarize findings by intervention category.

<u>Telephone or Web-Based Counseling for Family and Patients (4 Trials)</u>

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

<u>Adaptations of Couples CBT (5 Trials)</u>

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

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

Family Assisted Approaches to Patient Care (4 Trials)

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

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

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

Unique Interventions (1 Trial)

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

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

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

*Number of subjects randomized

**Some studies had multiple outcome measures

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

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

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

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

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

Benefits

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

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

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

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

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

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

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

Harms

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

Intervention Categories

Below we summarize findings by intervention category.

Telephone or Web-Based Counseling for Family and Patients (5 Trials)

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

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

Adaptations of Couples CBT (2 Trials)

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

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

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

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

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

Unique Interventions (3 Trials)

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

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

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

*Number of subjects randomized

**Some studies had multiple outcomes measures

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

MEMORY-RELATED DISORDERS

Description of Memory Studies

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

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

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

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

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

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

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

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

Benefits

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

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

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

Harms

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

Intervention Categories

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

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

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

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

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

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

Unique Interventions (6 Trials)

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

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

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

*Number of subjects randomized

**Some studies had multiple outcome measures

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

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

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

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

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

Benefits

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

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

Harms

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

Intervention Categories

Below we summarize findings by intervention category.

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

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

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

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

Unique Interventions (3 Trials)

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

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

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

*Number of subjects randomized
**Some studies had multiple outcomes measures
Intervention Category: Phone=Telephone or Web-based; CBT=Couples cognitive behavior therapy; FAA=Family assisted approaches to patient care; FFSM=Family focused CBT with coping and problem solving; Misc=Unique intervention

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SUMMARY AND DISCUSSION

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

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

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

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

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

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

CONCLUSIONS

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

ABBREVIATIONS TABLE

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

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

EVIDENCE REPORT

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?

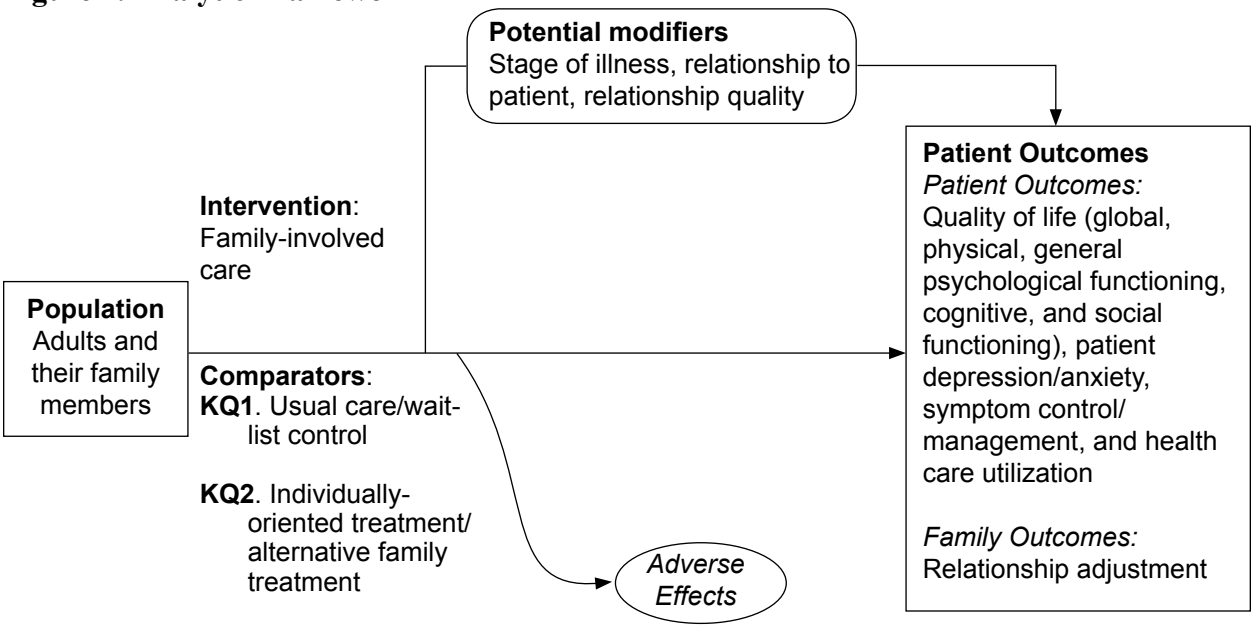
a. What are the harms of these interventions?
b. Do these benefits/harms vary by type of intervention, health condition, or patient functional status, or across outcomes?

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.

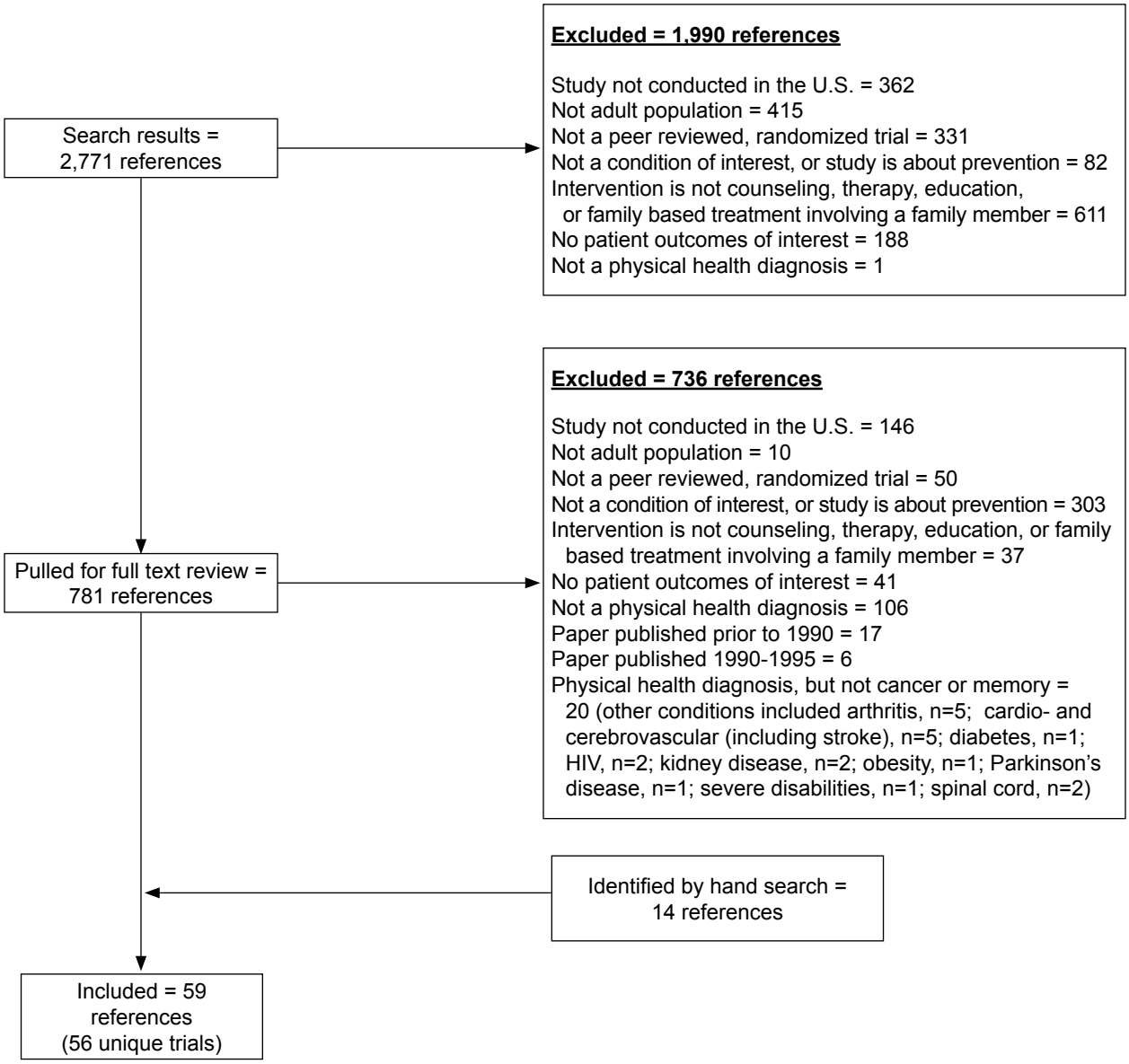
LITERATURE FLOW

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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APPENDIX A. SEARCH STRATEGIES

Database: **Ovid MEDLINE**(R)
Search Strategy:

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1 exp family/
2 couples.mp.
3 exp home nursing/
4 (grandparent: or grandmother: or grandfather:).mp.
5 exp legal guardians/
6 or/1-5
7 couples therapy/ or family therapy/ or marital therapy/ (8466)
8 6 or 7
9 exp Infertility/ or exp Infertility, Male/ or exp Infertility, Female/ or exp Fertilization in Vitro/ or exp Reproductive Techniques, Assisted/ or exp Insemination, Artificial/
10 8 not 9
11 limit 10 to (English language and yr="1980 -Current")
12 limit 11 to ("newborn infant (birth to 1 month)" or "infant (1 to 23 months)" or "preschool child (2 to 5 years)" or "child (6 to 12 years)")
13 11 not 12
14 limit 13 to meta analysis
15 (systematic adj review:).mp.
16 13 and 15
17 14 or 16
18 limit 13 to randomized controlled trial

Database: **PsycINFO**
Search Strategy:

---

1 exp family/ or exp family members/ or exp spouses/ or exp couples/
2 exp caregivers/ or exp stepparents/ or exp siblings/ or caretaker:.mp.
3 exp grandparents/ or legal guardian:.mp.
4 or/1-3
5 couples therapy/ or family therapy/ or marital therapy/
6 4 or 5
7 exp Infertility/ or exp Reproductive Technology/
8 6 not 7
9 limit 8 to (English language and yr="1980 -Current")
10 limit 9 to 100 childhood <birth to age 12 yrs>
11 9 not 10
12 meta analysis/ or (systematic adj review:).mp.
13 11 and 12
14 (randomized or rct).mp.
15 11 and 14

APPENDIX B. CRITERIA USED IN QUALITY ASSESSMENT[20]

Criterion	Description
Risk of bias	Internal validity: study design and the quality of individual studies included in the review. Study design limitations may bias the estimates of treatment effect (such as lack of allocation concealment, or lack of blinding). Other areas for potential bias include stopping early for benefit and selective outcome reporting.
Consistency	The effect sizes from the included studies are similar and have the same direction of effect (positive or negative).
Directness	Interventions are directly related to health outcomes. For comparative effectiveness reviews, head-to-head comparisons are made. Indirectness is suspected if surrogate or intermediate outcomes are used instead of health outcomes. For CERs, indirectness is also suspected if more than one body of evidence is needed to link interventions, ad in the das with placebo controlled trials. Directness also includes applicability and relevance of the included studies to the VA population or to specific subpopulations within the VA. Applicability may also include settings (e.g., primary care vs. specialty care) and physician experience.
Precision	The degree of certainty surrounding an estimate of effect for each outcome of interest. Uncertainty of effect does not allow for a clinically useful conclusion, and is unable to rule out an important benefit or harm.
Risk of publication bias	Publication bias can result in an overestimate of effect. Publication bias is suspected if evidence is derived from a small number of commercially funded trials with small sample sizes and a small number of event.

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APPENDIX C. PEER REVIEW COMMENTS/AUTHOR RESPONSES

REVIEWER COMMENT	RESPONSE
1. Are the objectives, scope, and methods for this review clearly described?	
Yes. This is a well-done systematic review.	Thank you.
In general, yes. Although I was confused by the term alternative family oriented intervention in KQ2 and remained so during my reading.	Our intention in Key Question #2 was to evaluate the comparative effectiveness of interventions. Typically one family–involved intervention was the primary intervention and it was compared to an alternative intervention. For example, one trial compared a skill building and problem solving intervention to an intervention where families received supportive telephone calls. The alternative family condition was the group receiving the phone calls. We have revised the wording throughout the report to better reflect this description.
Yes	No response needed
Yes	No response needed
Yes. The objectives, scope, and methods are clearly described in significant detail ensuring that the reader is aware of the implications as well as the limitations of the review.	Thank you.
Yes. I'm not quite sure why it was appropriate to exclude non-U.S. studies. A supporting citation would be useful for the strength of evidence ratings.	We have added a reference to the strength of evidence tables in Executive Summary and report.
No. 1. It is unclear how the 'quality' of studies was determined; no reference was included. I am particularly concerned about the lack of consideration given to power (studies that were adequately powered to detect differences in the primary outcome should be rated highly) and the over consideration given to blinding (most behavioral interventions cannot be blinded to the subject or the interventionalist – it's just not feasible- the only place where blinding is possible is at the level of analysis). 2. I believe that it is not appropriate to extract data on any outcomes that the study was not originally designed to affect or powered to detect. I would prefer an approach where no primary outcomes of interest were chosen by the authors of the synthesis; the synthesis team would simply judge the quality of each study and list each study's primary outcomes as they were originally published. An alternative approach would be to examine results by outcome including only RCTs that were powered to detect that outcome (e.g. Table 2 Cancer Studies – Quality of Life – Physical Functioning would only include those studies that had physical function as an outcome of interest, rather than including those who had physical function as a possible modifier or confounder). 3. Your search strategy did not include the words "caregiver" or "carer". Not sure this would make a difference, but those terms have been used successfully in other reviews.	1. We have revised the description of the method we use for assessing risk of bias and quality. We base these assessments on approaches used by the Cochrane Collaboration and AHRQ-EPC (Higgins, et al, 2001; Owens, et al 2010). Risk of bias assessments do not include power/sample size as quality measures (though this would be incorporated into the strength of evidence we have included). Power is more likely to affect the precision of the estimate rather than bias results and alter study quality (we could have a high quality small study and a poor quality large study). We agree that blinding is difficult, though the subjects and assessors could be blinded to the study objective, and outcome assessors, when used, could be blinded to the randomized condition. Risk of bias is most concerning in these situations where outcomes are subjective. Our findings did not change materially when focusing on studies of low risk of bias (good to fair quality studies). 2. We respectively disagree. While the reviewer's approach certainly would be sound for choosing an intervention for a specific patient, our approach is consistent with standard systematic review methodology and guidance statements used by AHRQ-EPC and Cochrane. 3. We used two databases for our search: PsycInfo and MEDLINE. Our search strategy for PsycInfo did include the word caregiver. For MEDLINE, however, you are correct, we did not include "caregiver" as a MeSH term in our final search. The definition (in MEDLINE) includes trained medical, nursing, and other health professionals as well as family, teachers, clergy, social workers, and fellow patients. In our work to refine the search terms, we found that many of the articles captured when searching with the term caregiver included formal, paid caregivers. Therefore, we first used the terms family and couples. We then also used the term "home nursing." Home nursing focused more on non-professional care.

REVIEWER COMMENT	RESPONSE
4. A large number of studies were excluded because "intervention is not counseling, therapy, education, or family based treatment involving a family member." How many were excluded because of the modality of the intervention and how many were excluded because they did not involve a family member? 5. I do not believe it is fair to say that "evidence does not favor family-involved interventions over …" but rather "there is insufficient evidence to say that family involved interventions improve x,y,z outcomes". If you judge that most of the studies you examined were methodologically weak, then you need to temper the strength of the conclusions you can make.	4. We did not identify how many studies were uniquely excluded for each specific reason. The exclusion typically was for the full phraseology not separated items. Therefore, studies may have met multiple exclusion criteria (e.g., conducted outside the US and included teachers, instead of family members). Each specific reason was not recorded; instead, if any of the exclusion criteria were met, the study was excluded. 5. We have reviewed and revised this statement to include that there is insufficient evidence for outcomes. However, we revised this statement because the heterogeneity of the studies makes it difficult to be unequivocal. We retain our statement that positive effects were infrequent, not consistently seen, typically small in magnitude, often based on multiple outcome reporting or subscale findings. Thus any positive effects and the clinical importance of these findings should be viewed with caution.
2. Is there any indication of bias in our synthesis of the evidence?	
No. Although there were few studies that were of "good" quality, at times I felt there was not enough attention to weighting these studies more than those of poorer quality. This concern was somewhat lessened given that only RCTs were included	Because we did not conduct a meta-analyses we could not formally weight studies. We do note, however, that only 2 of 26 cancer trials were rated good quality. For memory trials, six trials were rated good quality. Five of the 6 reported one significant intervention effect each. However, these effects were across 3 different outcomes. Limiting our evaluation to just good quality studies did not change the strength of evidence.
No	No response needed
No	No response needed
No	No response needed
No. There is no evidence of bias in the review.	No response needed
No. I do wonder about the precision of the comparisons, in the sense that it's pretty hard to know the quality of the family-oriented interventions reflected in these studies. They also are likely to vary quite a bit in the degree to which they *include* family members vs. *involve* family members, etc. In other words, systemic interventions vary a lot and that makes this review challenging. The general vs. specific focus the authors identify is helpful and should be pursued. Perhaps the authors could give some specific examples when they make this point so readers have even greater clarity	Thank you. We have incorporated this suggestion into the discussion.
Yes. 1) By extracting data on outcomes that the studies were not powered to detect, the synthesis is systematically biasing towards finding no effect. I believe your conclusions would be very different if you examined only the outcomes originally chosen as the primary outcomes for each study. 2) Also, if the authors of the synthesis examined only data that was unadjusted, this would also bias the results of the synthesis towards finding no effect. One major challenge in caregiver interventions is sample size – recruitment of dyads is difficult and, thus, studies typically have small samples. With a smaller sample size, the chances are higher that the intervention and control groups have differences at baseline that need adjusting in the final analysis. Thus, unadjusted data is often not reported in caregiving studies (as you saw) – and, when it is reported, should NOT be used to base conclusions upon.	We agree that recruitment to these studies is difficult and that future, large and methodologically rigorous randomized trials are needed. We do, however, respectfully disagree about our decisions on data extraction and study inclusion. We conducted the systematic review based on standard and validated methodology established by the AHRQ Evidence-based practice centers. We commented on the size, quality, applicability of studies and consistency of findings. Not including smaller studies or studies not powered for certain outcomes would systematically eliminate findings from many studies and result in a small study publication bias that would artificially increase effect size. We have commented on findings where adjusted results were provided throughout the report. Small studies, while potentially resulting in "imbalance," are unlikely to result in systematic bias-the purpose that randomization is intended to avoid.

REVIEWER COMMENT	RESPONSE
3. Are there any published or unpublished studies that we may have overlooked?	
Yes. The effect of telephone support groups on costs of care for veterans with dementia. Wray LO, Shulan MD, Toseland RW, Freeman KE, Vásquez BE, Gao J. Gerontologist. 2010 Oct;50(5):623-31. Epub 2010 May 27.	Thank you for the reference information. We have added this study to the review
Maybe. I wondered why you didn't include the REACH II study, which used RMBPC as one of its outcome measures – it is included as part of the multicomponent outcome. 1. Coon, David, W., et al. (2004). Ethnicity and time to institutionalization of dementia patients: A comparison of latina and caucasian female family caregivers. Journal of American Geriatrics Society, 52, 1077-1084. 2. REACH II Investigators (alphabetical order: Belle, S.H., Burgio, L., Burns, R., Coon, D., Czaja, S., Gallagher-Thompson, D., Gitlin, L., Klinger, J., Koepke, K. M., Lee, C. C., Martindale-Adams, J., Nichols, L., Schulz, R., Stahl, S., Stevens, A., Winter, L. & Zhang, S.) (2006). Enhancing the quality of life of dementia caregivers from different ethnic or racial groups: A randomized, controlled trial. Annals of Internal Medicine, 145, 727-738.	Thank you for the suggested references. We have reviewed the two papers. Coon (Mausbach 2004) reported results by ethnicity but not by intervention group so the study did not address our key questions. Belle et al. 2006 has been added to the review.
No	No response needed
Yes Good selection of articles. Other potential articles: 1. Belle, SH et al. (2006). Ann Intern Med 2006, Nov 21;145(10): 727-38 (includes institutionalization of dementia patients as an outcome of a caregiver RCT 2. Linda Nichols' research with the REACH program (although I could not easily find articles in PubMed related to her intervention with dementia caregivers – I think she has unpublished results) 3. 2012 articles: a. Failho, PP et al. (2012) Arq Neuropsiquiatr. October 70(10) 786-790 b. Liddle, J et al Int Psychogeriatr Dec 24 (12) 1927-42	Thank you for the suggested references. We have reviewed the three suggested papers: We have added Belle 2006 to the review. We identified another reference from the REACH study (Burns 2003) and have added that paper to the review. Failho did not meet our criteria; it was conducted in Brazil. Liddle did not meet our criteria; it was conducted in Australia.
No. I am not aware of any published or unpublished studies that were overlooked.	No response needed
I'm not aware of any.	No response needed
No	No response needed
4. Please write any additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.	
1. Executive Summary – Terms are not defined before they are mentioned in the ES – is that function assumed to be managed by the glossary of terms at the end of the ES? 2. I remained confused about the definition of alternative family oriented interventions. 3. The criteria for good, fair and poor quality of studies are not explicitly defined until (the first place I could find) page 72 (but I did not read the Cancer section). 4. page 4, - paragraph 1 under KQ1, last sentence is confusing	1. We have corrected this-terms are now defined. 2. Please see explanation in first comment. 3. We have clarified the definitions of good, fair, and poor quality studies in the Methods and Results sections of the Executive Summary and full report. 4. Thank you. We have revised this sentence.

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REVIEWER COMMENT	RESPONSE
5. page 7, paragraph 3, bullet 2, are weekly nurse telephone calls counseling? 6. Tables. Several comments about tables. I could not find definitions for risk of bias, directness, precision, consistency or evidence rating in the text. Some of them are later, after the tables have been presented for example strength of evidence rating is on page 32; others I could not find it all. Also table information is not consistent, for example, sometimes there is in and between entries under risk of bias sometimes a semicolon, sometimes commas are used sometimes not. This type of sentence is often under precision: Three trials reported (one good, one far, one poor)… I believe that the parenthetical expression should modify trials and not reported as in: Three trials (one good, one far, one poor) reported 7. the word veteran is not always capitalized. 8. Figure 1 is presented before it is referenced in the text/ 9. Page 30, paragraph 1. Text says articles were conducted in the US. this sentence needs to be clarified. 10. Page 30/31, last paragraph area in general psychological function does not correspond with mental health conditions in the DSM; where does this leave depression and anxiety which are secondary outcomes. 11. I know you will fix all this later on-multiple references within parentheses are not organized. some references are not found or are mislabeled-Gitlin has a 2010 a and a2010 ACT; Mittleman is sometimes done as 2004/2006. 12. Page 66, paragraphs 3 and 5. I am not exactly sure how these two paragraphs are different. Also, paragraph 2 talks about family focused CBT interventions while talks about multicomponent intervention targeted at family members. In the first instance the CBT appears to be the most important, in the second instance the multicomponent. This is also the case on page 76 where the heading is family focused CBT interventions, not multicomponent. 13. page 67, paragraph 2. Support groups for patients with early-stage memory loss does not indicate that there is a family component 14. The formatting changes somewhere in the text and the headings are smaller. 15. Page 82. Paragraph 4, first sentence is confusing. 16. Page 88 – paragraph 3. None were superior to alternative interventions (such as? – ones that they have listed in their studies?) Also, last sentence is unclear – where were there no data? 17. Page 93, paragraph 1 (and in conclusion of Executive Summary). Needs to read: In this review we assess the evidence of family-involved interventions for improving *outcomes of* adult patients with cancer and memory-related conditions. Next sentence is a bit unclear. Does individually-focused mean patient focused? And interventions that provide only health or psychoeducation? Not sure what the health means in this – health education?	5. We have clarified this statement by clarifying that nurse phone calls were to manage uncertainty and patient concerns. 6. We have added these definitions to the text and corrected the inconsistency in reporting; we agree with your comment about placement of the parenthetical expressions. 7. We have corrected this throughout. 8. We have corrected the reference to Figure 1. 9. We have clarified this sentence. 10. General psychological functioning is grouped under quality of life and corresponds to psychological functioning. This is in contrast to more specific mental health conditions, such as depression and anxiety, which are in the DSM. In order to avoid any confusion about this, we have removed the classification of primary and secondary outcomes. 11. We have changed the references to superscripts and clarified the multiple reference citations. 12. We agree this was not clear and have made changes to clarify the differences across the types of interventions. 13. We have clarified this statement. 14. We have reviewed the formatting and font size and made changes as needed. 15. We have revised this sentence. 16. We have revised these sentences. 17. We have revised these sentences to indicate patient-focused instead of individually-focused and health education and psychoeducation, instead of health and psychoeducation.

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REVIEWER COMMENT	RESPONSE
While we understand the rationale for limiting results to patient outcomes, we question the wisdom of this with regard to dementia and memory impairment. We think that preventing caregiver burnout is a critical issue that has major implications for the well-being of the person with the disease. The data on caregiver interventions thus far do not indicate they reduce out-of-home placements, but these are likely overdetermined by many other factors—number of available caregivers, finances, health of the caregiver, kinds of care facilities available, etc. However, it is certainly plausible that caregivers who feel more supported and educated can adhere better to patient treatment plans, provide better care, etc. With regard to aging related memory disorders, having a psychosocial intervention goal of improving patient behavior seems unlikely at this point.	The topic nominated for this review was to examine the effect of caregiver interventions on patient outcomes. We agree that caregiver burnout is a critical issue and that by limiting the review to only patient outcomes, we are not able to present evidence on the potential pathways by which caregiver experiences affect patient outcomes. We do acknowledge this as a limitation in the discussion and recommend this as a potential area for further research. We should note that there have been recent VA reviews on caregiver interventions to improve caregiver outcomes, such as managing problem behavior (Goy, et al, 2010; Kansagara, 2012), but, as we describe in the background section for the report, few reviews have extended beyond the caregivers to examine the effects of these interventions on the patient.
Well written and comprehensive	Thank you.
The review is very thorough and certainly thought provoking in light of VA's focus on supporting family members and Caregivers. Most studies focus on family/caregiver outcomes and not patient outcomes. It will be essential to establish a balance of these two outcomes in order to provide the best programming.	Thank you. We agree with the need to consider family/caregiver and patient outcomes in making program decisions.
I don't know what style guide is being used – text citations don't appear to be listed by author or year. p. 83 – Font size shifts p. 94 – I find the second sentence in the paragraph beginning 'based on our findings' hard to follow. p. 96 – is an author name missing for the first citation in the reference list?	Thank you. We have addressed these concerns.
Personally, I prefer using the term "informal caregiver" rather than "family" (especially if you are including friends as possible subjects).	We agree that in many cases, caregiver is the appropriate term. However, in others, where more emphasis is on psychosocial adjustment to the disease or treatment, it may be less appropriate.
5. Are there any clinical performance measures, programs, quality improvement measures, patient care services, or conferences that will be directly affected by this report? If so, please provide detail.	
Caregiver Support Services and GEC would be interested. There is a caregiver conference call led by John Piette, PhD that would be interested. There have been a couple of VHA Caregiver conferences largely organized by Caregiver support Services.	Thank you for this suggestion.
Not that I know	No response needed
Conferences for geriatric clinicians, such as AGS and GSA would be appropriate	Thank you for this suggestion.
The Caregiver Support Program Office as well as the Office of Mental Health will be impacted by this review as they continue to roll out legislatively mandated programs to support families and Caregivers. In addition, there is much interest in Congress, Veteran Service Organizations, Non Governmental Organizations, Veterans and their families and Caregivers as well as other stakeholders to provide support and assistance to families, especially of those ill and injured. VA will need to evaluate the impact that such programs have, both on family members or Caregivers, as well as the impact on Veterans in order to proceed with such programming.	Thank you for this suggestion.
I'm sorry, but I'm not sufficiently familiar with the VA to be able to say	No response needed

REVIEWER COMMENT	RESPONSE
The VA's national caregiver program may be affected by this report; funding for expanding programs to help caregivers provide better care for cancer and dementia patients may be affected if there is a sense that research shows no benefit to such interventions. Similarly, VA HSRD may choose to reduce the funding it provides to caregiving research if the impression is given that studies show no benefit.	We thank the reviewer for these comments and appreciate that our report has implications for health care practice, policy and research. Our goal is to objectively identify and synthesize the existing evidence and provide an assessment of the effectiveness and harms of interventions. We do not set policy, make practice implementation or research funding decisions. These may be made by factors beyond the available evidence, though we hope our report provides evidence based guidance in these decisions. We have reviewed our discussion and summary recommendations to make these issues clear. We believe that this report provides strong support that future research is needed particularly assessing the effect of currently rolled out VA programs and any future design and implementation of caregiver programs. We also believe that this report may help reduce implementation of ineffective and costly programs and target interventions of established effectiveness.
6. Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.	
It would be useful to draft 1-2 RFPs for VA R&D to address gaps in literature that are nicely outlined in review.	Thank you for this suggestion.
Do you have any recommendations on what we should be doing clinically?	We have added to the discussion how clinicians might use this report. Because the evidence does not strongly favor one intervention over another, it is difficult to make recommendations on how our findings can directly affect practice.
We think these negative results, especially regarding aging related memory disorders, may have implications for the VA Social Work and Care Management Program Office as they consider their program goals	No response needed
The authors conclude that the previous interventions have had no or modest effects on patient outcomes, thus implementation most of the interventions would not be helpful. However, it is commendable that the authors provide recommendations for improving research in this area and emphasize that interventions, which target specific areas (sleep, etc.) are most effective.	Thank you.
No additional comments	No response needed
My main uncertainty is whether sufficient attention was paid to the quality of the family interventions in the studies examined. I notice fairly frequently that the sophistication of measurement about families is low – could the same be true of the quality of the family-focused intervention strategy?	Throughout this revised report, we call attention to the quality of the family interventions, and we agree that not all studies are methodologically rigorous. We have also added our criteria for assessing quality to the executive summary. One recommendation in the discussion is for more methodologically sound research to be developed, using measures that are validated, comparable, and reporting findings at consistent intervals.
For the reasons stated in #5, I would strongly recommend that the summary and discussion state that the science is limited and, while there is insufficient evidence to say that caregiver interventions improve patient outcomes, there have been some promising findings in the areas of x, y, z…	As noted above, our goal was to identify, synthesize and communicate the evidence on the key questions. We have, however, reviewed and revised our discussion section. While we conclude that there is low to moderate strength of evidence that family directed caregiver interventions are not more effective than usual care or other patient- or family- directed interventions for improving patient outcomes, we have revised the conclusions to point to areas that have insufficient evidence and where additional, methodologically rigorous research is needed.

APPENDIX D. EVIDENCE TABLES

Table 1. Cancer Studies – Study Characteristics

Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Badger 2007[9] Funding Source: Government Condition: Breast cancer, Stage I-III, receiving adjuvant treatment **KQ1 ☐ KQ2 ☒** **Intervention Type:** 1) Multicomponent (education, support, management of depression and anxiety symptoms) 2) Exercise	N=96 (of 97 randomized) Age (years): 54.1 Gender (% male): 0 Race/ethnicity (%): *White* 85; *African-American* 0; *other* 15 Marital Status (%): *Married* 73 Education (%): *HS or less 21; Post HS 79* Veterans (%): NR Recruitment Method: local cancer center, oncologists' offices, support groups, and self-referral Family Characteristics: Relationship to patient: *Any person patient viewed as significant in coping and recovery* Age (years): 51.7 Gender (% female): 26 Race/ethnicity (%): *White* 87; *African-American* 2; *other* 12 Education (%): *HS or less 16; Post HS 84* Veterans (%): NR	Inclusion: diagnosis of Stage I-III breast cancer; currently receiving adjuvant treatment for breast cancer; ability to speak English and talk on the telephone; no physical or psychological disabilities that would prevent participating in the interventions; availability of a partner who was willing to participate in the investigation Exclusion: NR	1st Intervention: Telephone interpersonal counseling (TIP-C) (n=38): 6 weekly calls from psychiatric nurse counselor; average call duration = 34 min; call to partners every other week to discuss emotional well-being and relationship with patient 2nd Intervention: Self-managed exercise (n= 23): 6 weekly calls; focus on regular, low-impact exercise; calls to partner every other week; encouraged exercise and tracked progress; average call duration = 11 min Comparator: Attention control (n=37): Information about breast cancer; 6 weekly calls; biweekly calls to partner; average call duration = 7 min; no counseling or exercise encouragement; questions or problems referred to primary physician Length of Follow-up: 4 weeks (post tx)	***Depression/ anxiety:*** a. Depression (CES-D) b. Anxiety (composite of PANAS, SF-12, and Index of Clinical Stress) Self-reported outcomes assessed at baseline, post-treatment (6 weeks after baseline), and 1 month post-treatment ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: *treatment dropouts* – TIP-C = 0 Exercise = 2/23 (8.7%) Control = 3/37 (8.1%) Treatment integrity: interventions delivered by counselors trained in the intervention for which they were responsible; interventions taped and reviewed for quality control **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Badger, 2011[21] Funding Source: Government Condition: Prostate cancer, undergoing or completed tx (Stage I = 16%, II=9%, III = 11%, IV=11%, unknown = 53%) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Multicomponent (education, support, management of depression and anxiety symptoms)	N=70 (of 71 randomized) Age (years): 67 Gender (% male): 100 Race/ethnicity (%): *White* 84; *African-American* 9; *other* 7 Marital Status (%): *Married* 79 Education (%): *HS or less* 14; *Post HS* 86 Veterans (%): NR Recruitment Method: regional cancer centers; VA centers; cancer support groups; oncologists' offices; research study websites Family Characteristics: Relationship to patient: *Spouse 83%; Sibling 4%; Adult Child 2%; other 11%* Age (years): 61 Gender (% female): 93 Race/ethnicity (%): *White* 81; *African-American* 9; *other* 10 Marital Status (%): *Married* 81 Education (%): *HS or less* 18; *Post HS* 82 Veterans (%): NR	Inclusion: diagnosis of prostate cancer, currently undergoing or had completed treatment within the past 6 months, ability to speak English, no physical or psychological disabilities that would prevent participation; availability of a "social network member" (i.e., anyone patient felt was significant to his recovery – most were spouses) willing to participate Exclusion: NR	Intervention: Telephone interpersonal counseling (TIP-C) (n=36): targets social support behaviors of cancer pts & partners; 8 weekly calls to pts (first call average 56 min, then 31 min) from master's prepared nurse or social worker; calls to partners every other week (discussed emotional well-being; 4 calls, average 31 min), individualized, but followed structured protocol Comparator: Health education attention condition (HEAC) (n=35): written materials (cancer and other health topics) from National Cancer Institute for 8 weeks; weekly calls to review materials; delivered by research assistants (RA) – most from non-health disciplines; no counseling; calls to partners every other week (4 sessions); average of 28 min for all calls Length of Follow-up: 8 weeks post-tx	***Physical functioning:*** a. UCLA Prostate Cancer Index (prostate specific health related QOL) ***General psychological functioning:*** a. Spiritual well-being (QoL Breast Cancer subscale) b. Positive & negative affect schedule (PANAS) c. Perceived stress scale (PSS) ***Depression/ anxiety:*** a. Depression (CES-D) ***Symptom control/ management:*** a. Multidimensional Fatigue Inventory (MFI) Outcomes assessed at baseline, post-tx, 8 weeks post-tx ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes T2 (end of treatment) – 5 total dyad withdrawals T3 (end of follow-up) – 2 additional dyads lost to follow-up *Treatment adherence*: # of sessions completed: TIP-C survivor = 85% HEAC survivor = 89% TIP-C partner = 85% HEAC partner = 93% *Outcomes assessed*: Baseline 100% Post-tx: 93% 8 weeks post-tx: 90% Treatment integrity: both interventions manualized; Interventions recorded and investigators reviewed recordings, giving feedback to maintain fidelity and prevent drift; had to maintain >90% on protocol implementation at all times **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Baucom, 2009[31] Funding source: Government, Foundation Condition: Stage I or II breast cancer **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (educational, skill-based, emotional, conflict resolution)	N=14 couples (demographic data for patients and partners combined) Age (years): 50 (median) Gender (% male): 0 Race/ethnicity (%): *White 86; African-American NR; other NR* Marital Status (%): *Married/cohabitating* 100 Education (years): 16 (median) Veterans (%): NR Recruitment Method: medical records of one hospital Family Characteristics: Relationship to patient: *Male romantic partner* Age (years): See above Gender (% female): 0 Race/ethnicity (%): See above Education (%): See above Veterans (%): See above	Inclusion: recently diagnosed with Stage I or II breast cancer; no history of other breast cancer; no history of cancer within the last 5 years; currently married or living together with a male romantic partner for at least 12 months; both partners willing to participate and able to speak English Exclusion: NR	Intervention: Relationship enhancement (RE) (n=8): 6 bi-weekly, face-to-face, 75 min. sessions; each couple seen individually by therapist in outpatient setting, teaching how to communicate effectively and reach important decisions jointly; manualized Comparator: Usual care (n=6): Couples received list of community resources for additional support; no cancer education or psychosocial intervention from the project therapists or as part of their routine hospital-based treatment for cancer Length of Follow-up: Assessments were conducted before treatment, post treatment, and 12 months later	***Physical functioning:*** a. Functional Assessment of Cancer Therapy (FACT-B) ***General psychological functioning:*** a. Brief Symptom Inventory (BSI-18) ***Symptom control/ management:*** a. Brief Fatigue Inventory (BFI) b. Brief Pain Inventory (BPI) c. Rotterdam Symptom Checklist (RSC) ***Relationship adjustment:*** a. Quality of Marriage Index *All assessed by self-report at pretreatment, post treatment, and 12 months after treatment (e.g., Depression, BDI, SR, post tx, 6 moss, 12 mos)* **☐ Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: unclear (at initial assessment, couples and assessor blinded to subsequent treatment assignment; unclear if all assessments were blinded) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: no Treatment adherence: outcomes given for 8 patients only, and the N for each arm is not reported; text reports on only 2 dropouts (1 per group) Treatment integrity: supervisor reviewed videotapes of treatment sessions; group discussion of completed sessions **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Blanchard, 1996[37] Funding Source: Foundation Condition: Cancer (any, 51% breast) diagnosed more than 3 months before recruitment but patient not eligible for hospice **KQ1 ☒ KQ2 ☐** **Intervention Type:** Problem solving	N=57 (of 86 randomized) Age (years): 52 Gender (% male): NR Race/ethnicity (%): *White 98; African-American 2; other 0* Marital Status (%): *Married/cohabiting 100* Education (%): *HS or less 28; Post HS 72* Veterans (%): NR Recruitment Method: convenience sample - regional medical oncology clinic Family Characteristics: Relationship to patient: *Spouse* Age (years): 52.5 Gender (% female): 48 Race/ethnicity (%): *White 97; African-American1.5; other 1.5* Education (%): *HS or less 65; Post HS 35* Veterans (%): NR	Inclusion: cancer diagnosed >3 months before recruitment; not eligible for hospice; married Exclusion: NR	Intervention (n=25): Standardized intervention protocol to teach spouses how to reduce or manage specific problems; 6 1-hr one-on-one training sessions with social worker (how to identify a problem, generate alternate solution; examine benefits; discuss, rehearse action plan; carry out and evaluate the plan) Comparator (n=32): Usual care; did not receive any part of the intervention but were allowed to receive usual services offered by clinical practice Length of Follow-up: 6 months	***Physical functioning:*** a. Medical Outcomes Study (MOS) SF20 ***General psychological functioning:*** ***a.*** Medical Outcomes Study (MOS) SF20 ***Social functioning:*** a. Medical Outcomes Study (MOS) SF20 ***Global quality of life:*** a. Functional Living Index-Cancer (FLIC) ***Depression/anxiety*** a. Depression (CES-D) ***Symptom control/ management:*** a. Medical Outcomes Study (MOS) SF20 (pain subscale) ***Relationship adjustment:*** a. Dyadic Adjustment Scale (DAS) Outcomes assessed at baseline, post-treatment (within 2 wks), and at 6 months post-baseline **☐ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: yes - single (interviewer blinded to condition) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: partial, dropouts mentioned, but not explained Treatment adherence: NR Treatment integrity: sessions were audiotaped; authors reviewed 20% of tapes **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Budin, 2008[30] Funding Source: Government Condition: Breast lesion – confirmed or strongly suspected diagnosis of cancer **KQ1 ☒ KQ2 ☒** **Intervention Type:** Multicomponent (psychoeducation, support, coping, communication)	N=249 Age (years): 53.8 Gender (% male): 0 Race/ethnicity (%): *White* 69; *African-American* 16;*other* 15 Marital Status (%): *Married/cohabiting* 56 Education (%): *HS or less* 23; *Post HS* 74 Veterans (%): NR Recruitment Method: participating surgeons from four medical centers Family Characteristics: Relationship to patient: *Person most intimately involved in cancer experience* Age (years): 51.6 Gender (% female): 42 Race/ethnicity (%): *White* 70; *African-American* 13; *other* 17 Education (%): *HS or less* 15; *Post HS* 74 Veterans (%): NR	Inclusion: breast lesion with confirmed or strongly suspected diagnosis of cancer; enrolled in 1 of 4 oncology services that were part of study; no previous history of cancer; identified person intimately involved in breast cancer experience; willing to participate in 1 of 4 groups; able to read and understand English; no concurrent, uncontrolled, chronic medical illness; neither patient nor partner had history of psychiatric hospitalization or drug abuse Exclusion: no additional exclusion criteria	1st Intervention: Psychoeducation (SE) (n=66): 4 videos, viewed separately by patients and partners 2nd Intervention: Telephone Counseling (TC) (n=66): 4 sessions, separate scripts for patient and partner, conducted by nurse interventionist; manualized 3rd Intervention SE + TC (n=58) Comparator (n=59): Disease Management (DM), evidence-based national treatment protocols **NOTE: Groups 1, 2, & 3 also received DM** Length of Follow-up: Interventions were administered at 4 phases: 1) T0/T1 – baseline/diagnostic (diagnosis determined) 3) T2 – post surgical (within 2 days) 4) T3 – adjuvant therapy (making decisions about therapy) 5) T5 – ongoing recovery (2 wks after chemotherapy or radiation or 6 months after surgery)	***Physical functioning:*** a. Overall Health Status (subscale of SRHS) (SR) ***General psychological functioning:*** a. Psychological Well-being (subscale of PAL-C) (SR) ***Social functioning:*** a. Psychosocial Adjustment to Illness Scale (social adjustment) – Domestic, Vocational and Social Environments (SR) ***Symptom control/ management:*** a. Side Effects Severity (subscale of BCTRI) (SR) b. Side Effect Distress (subscale of BCTRI) (SR) All outcomes at baseline/ diagnostic phase, post-surgery phase, adjuvant therapy phase, ongoing recovery phase ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): modified Withdrawals/dropouts adequately described: partial (specific numbers of withdrawals/dropouts for each reason not provided) Treatment adherence: data received from 79% at T0/T1, 80% at T2, 78% at T3, and 71% at T4 Treatment integrity: nurse interventionist for TC was trained and supervised in individualized TC approaches **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Campbell, 2004,[25] 2007[26] Funding Source: Government Condition: Prostate cancer with Karnofsky Performance Status scores >= 60 **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (education, problem solving, coping skills)	N=40 Age (years): 61 Gender (% female): 0 Race/ethnicity (%): *African-American 100* Marital Status (%): *Married/cohabiting 85* Education (%): *HS or less 53; Post HS 48* Veterans (%): NR Recruitment Method: urology clinic, regional tumor registry, community Family Characteristics: Relationship to patient: *Intimate partner* Age (years): 58 Gender (% female): NR Race/ethnicity (%): NR Education (%): *HS or less 60; Post HS 38* Veterans (%): NR	Inclusion: African-American men; beyond the acute diagnosis and treatment phase for prostate cancer; Karnofsky Performance Status scores 60 or higher (only occasional assistance needed in caring for self) Exclusion: NR	Intervention (n=12): Coping Skills Training (CST); 6 weekly 1-hour telephone sessions; followed detailed written outline Comparator (n=18): Usual care though patient's outpatient program Length of Follow-up: None after 6 week treatment phase	***Physical functioning:*** a. Short Form-36 Health Survey (SF-36) ***General psychological functioning:*** a. Short Form-36 Health Survey (SF-36) ***Symptom control/ management:*** a. Expanded Prostate Cancer Index Composite (EPIC) (urinary, bowel, sexual functioning symptoms) Self-reported outcomes assessed pre-treatment and post-treatment (6 weeks) **☐ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 77.5% (31/40) completed intervention; one additional couple not included in data analysis Treatment integrity: sessions audiotaped and reviewed for adherence to protocol **Study quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Canada, 2005[43] Funding Source: Government/ foundation Condition: Localized prostate cancer; Stages A-C **KQ1 ☐ KQ2 ☒** **Intervention Type:** Multi-component; Education; skill-based training; emotional support	N=84 Age (years): 64.3 Gender (male): 100 Race/ethnicity (%): *White* 83; *African-American* 11; *Hispanic* 6 Marital Status (%): *Married/cohabiting* 100 Education (%): *HS or less* 12; *Post HS* 88 Veterans (%): NR Recruitment Method: letters to clinic registry members; flyers posted in clinics; physicians encouraged during visits to ED clinics; outreach to cancer ministries at African-American churches Family Characteristics: *Spouses or cohabiting female partners* Age (years): 59.6 Gender (% female): 100 Race/ethnicity: NR Education (%): NR Veterans (%): NR	Inclusion: undergone treatment for localized prostate cancer; Stage A-C, with either surgery or radiation 3-60 months previously; married or living with female partner ≥1 year who was willing to participate; speak English; reside with reasonable distance of clinic. Exclusion: currently receiving hormonal therapy for prostate cancer; currently using a successful or satisfactory medical treatment for ED; or able to achieve erection without medical or mechanical assistance on ≥ 50% attempts during last 3 months	Couples Counseling (n=25); manualized and standardized; 4 sessions of 1 hour each; education provided concerning sexual impact of surgery/therapy, coping strategies, communication skill training; cognitive-behavioral techniques, homework assignments. Patient Counseling alone (n=26); Same intervention as Couples Counseling (described above) but information presented to patient alone over 4 sessions. Length of Follow-up: 6 months	***General psychological functioning:*** a. Brief Symptom Inventory, Global Symptom Inventory (BSI/ GSI) [SR] ***Symptom control/ management:*** a. IIEF International Index of Erectile Functioning [SR] ***Relationship adjustment:*** a. Abbreviated Dyadic Adjustment Scale (A-DAS) [SR] Outcomes assessed at baseline, post-tx, 3 and 6 months post-tx. Scores by group not provided. **☒ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: Session adherence: Session 1: 100% (84/84) Session 2: 90% (76/84) Session 3: 67% (56/84) Session 4: 61% (51/84) Dropouts (no outcomes assessed): 39% (33/84) Treatment integrity: manualized treatment, weekly supervision of counselors **Study quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Giesler, 2005[22] Funding Source: NR Condition: Prostate cancer (localized); Stage T1a-T2c **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (psychoeducational, symptom management	N=99 Age (years): 64 Gender (% male): 100 Race/ethnicity (%) *White 90; African-American 8; other 2* Marital Status (%) *Married/cohabiting 96* Education (%): *HS or less 32; Post HS 68* Veterans (%): some recruited from a VA hospital Recruitment Method: NR Family Characteristics: Relationship to patient: *Spouse or relationship partner* Age (years): NR Gender (% female): NR Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: Diagnosis of Stage T1a-T2c prostate carcinoma; scheduled to undergo or to have undergone surgery, external beam radiation, or brachytherapy; spouse or relationship partner willing to participate and who enrolled within 2 weeks after conclusion of therapy; age ≥ 18 years, fluent English Exclusion: NR	Intervention (n=48): Cancer Care Intervention; 6 monthly sessions (2 in-person, 4 telephone); facilitated by computer program (standardized questions and strategies for solving problems); goal was to eliminate or reduce the impact of identified problems related to sexual, urinary, & bowel dysfunction, cancer worry, dyadic adjustment, depression, and other sequelae of cancer (e.g., fatigue and pain) Comparator (n=51): Standard care (no description) Length of Follow-up: 12 months post treatment	***Physical functioning:*** a. SF-36 Short Form Health Survey (physical health subscale) ***General psychological functioning:*** a. SF-36 Short Form Health Survey (mental functioning subscale) ***Social functioning:*** a. SF-36 Short Form Health Survey (social functioning subscale) ***Depression/anxiety:*** a. Center for Epidemiologic Studies-Depression (CES-D) ***Symptom control/ management:*** a. SF=36 Short Form Health Survey (pain subscale) b. Prostate Cancer Quality of Life Instrument, urinary function, limitation, and bother scales ***Relationship adjustment:*** a. Dyadic Adjustment Scale (DAS) [SR] Outcomes assessed at baseline and 4, 7, and 12 months post-tx **☐ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: yes (outcome assessment) Intention-to-treat analysis (ITT): unclear Withdrawals/dropouts adequately described: partial (primary reason for dropping out was inconvenience; no other reasons provided) Treatment adherence: 85.9% (85/99) completed all assessments Treatment integrity: NR (computer program documented intervention process) **Study quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gustafson, 2013[44] Funding Source: Government Condition: Lung cancer (nonsmall cell) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Psychosocial (information, communication, coaching)	N=varies by parameter (of 285 dyads randomized) Age (years): 62 (n=224) Gender (% male): 51 (n=121) Race/ethnicity (%): NR Marital Status (%): *Cohabiting 78 (n=190)* Education (%): *HS or less 34 (n=82)* Veterans (%): NR Recruitment Method: 4 cancer center hospitals in east, midwest, and southwest US; identified by oncologists Family Characteristics: Relationship to patient: NR Age (years): 56 (n=234) Gender (% female): 68 (n=168) Race/ethnicity (%): NR Education (%): *HS or less 21 (n=51)* Veterans (%): NR	Inclusion: English speaking; adults *Care recipient* - nonsmall cell lung cancer stage IIIA, IIIB, or IV; caregiver (identified by patient) willing to participate in study; clinician-perceived life expectancy of at least 4 months; brain metastasis stable (if present) *Caregiver* – providing instrumental, emotional, and/or financial support Exclusion: NR	Intervention (n=144): Standard care plus CHESS (Comprehensive Health Enhancement Support System); CHESS Website provided information, channel for communication with and support from peers, experts, clinicians, & social networks, coaching, and tools to improve caregiving experience; could receive intervention for 25 months or 13 months after patient death (whichever was less) Comparator (n=141): Standard care plus the Internet (training and list of sites about lung cancer) Both groups received computers and Internet service if needed plus reimbursement for cost of Internet service Length of Follow-up: None (study period of 25 months or up to 13 months after patient death)	***Physical functioning:*** a. Mortality ***Symptom control/ management:*** a. Patient symptom distress using modified Edmonton Symptom Assessment Scale (ESAS) [PR] Assessed at pretest and 2, 4, 6, and 8 months after start of intervention ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: no Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: CHESS used at least once: 73% of caregivers, 50% of patients CHESS used 5 or more times: 52% of caregivers, 35% of patients Median minutes of CHESS use: 103 for caregivers, 146 for patients Median logins: 8 for caregivers, 12 for patients Treatment integrity: not applicable **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Kayser, 2010[32] Funding Source: Government Condition: Breast cancer (early-stage) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (mainly emotional, with some skill-based training and education)	N=47 (of 63 randomized) Age (years): 46 Gender (% male): 0 Race/ethnicity (%): NR Marital Status (%) *Married/cohabiting 100* Education (%): NR Veterans (%): NR Recruitment Method: 2 breast oncology centers; protocol to identify and refer potential patients; met with or sent invitation letter Family Characteristics: Relationship to patient: *Spouse or intimate partner* Age (years): 49 Gender (% female): Unclear if all male (87% married to female patient) Race/ethnicity (%): NR Education (%): *Post HS 89* Veterans (%): NR	Inclusion: diagnosis of primary, non-metastatic breast cancer within the last three months; currently receiving treatment such as chemotherapy, radiation, or a combination of treatments; married or in an intimate relationship Exclusion: NR	Intervention (n=36): Partners in Coping Program (PICP) - couples with clinical social worker; protocol of specific psycho-social interventions (cognitive–behavioral framework); 9 biweekly, 1-hour sessions; average 5-month intervention Comparator (n=27): Standard social work services (SSWS) available at the hospital (individual & family counseling, crisis intervention, community referrals, tangible assistance, discharge planning) Length of Follow-up: 6 months and 1 year after enrollment	***Global quality of life:*** a. Functional Assessment of Cancer Therapy–Breast (FACT-B) Self-report, at 6 months and 1 year after enrollment (1 and 7 months post-treatment) ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: no Intention-to-treat analysis (ITT): no, 25% excluded from analyses Withdrawals/dropouts adequately described: yes Treatment adherence: *Study dropouts* *PICP*=2/36 (33%); 9 did not receive intervention, 1 withdrew, 2 did not return questionnaires *Usual care*=4/27 (15%); 1 withdrew, 3 did not return questionnaires Treatment integrity: manualized, 8 item adherence checklist for each session; competencies rated; biweekly meetings to provide feedback to therapists **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Keefe, 2005[34] Funding Source: Government Condition: Advanced cancer with disease-related pain, life-expectancy < 6 months **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (pain management, education, coping)	N=78 Age (years): 60 Gender (% male): 56 Race/ethnicity (%) *White* 78; *African-American* 21 Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: collaborating hospices, cancer center, and medical center Family Characteristics: Relationship to patient: *Spouses 49%; daughters 9%; NR 42%* Age (years): 58 Gender (% female): 62 Race/ethnicity (%) *White* 79; *African-American* 20 Education (%): NR Veterans (%): NR	Inclusion: advanced cancer diagnosis (metastatic or disseminated disease) with disease related pain; worst pain rating > 3 on the Brief Pain Inventory (BPI); life expectancy <6 mo; no change in disease treatment planned; >18 years of age (Note: all patients met Medicare hospice benefit definition for hospice eligibility) Exclusion: NR	Intervention (n=41): Partner-guided pain management training; 3 in person sessions of 45-60 minutes in patient's home; conducted over 1-2 weeks by RN-level nurse educator; manualized, (detailed written outline for each session); educate patient and partner about cancer pain and management; teach coping strategies; teach partner to help patient acquire coping skills Comparator (n=37): Usual care; routine care provided through patient's medical outpatient or hospice program Length of Follow-up: post-tx only	***Physical functioning:*** a. Functional Assessment of Cancer Therapy-General (FACT-G) ***Social functioning:*** a. Functional Assessment of Cancer Therapy-General (FACT-G) ***Symptom control/ management:*** a. Brief Pain Inventory (BPI) Self-report; assessments made pre- and post-treatment, mean follow-up = 7.6 days (range 0-31 days) **☐ Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: yes (outcome assessment); no (patients & caregivers) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: *Intervention* – 13/41 (32%) no post-treatment evaluation (8 died, 3 could not be reached, 2 too ill to complete evaluation) *Usual care* - 9/37(24%) no post-treatment evaluation (4 died, 1 could not be reached, 2 too ill to complete evaluation, 1 dropped out) Treatment integrity: manualized treatment; sessions audiotaped; 58% reviewed & rated for therapist competence (scale 0-5) & treatment fidelity; mean therapist competence rating 4.7; treatment fidelity 81.7% **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Kozachik, 2001[35] Funding Source: Unclear Condition: recent cancer diagnosis (48% Stage I or II; 52% Stage III or IV) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multi-component; educational and skill based	N=120 Age (years): 56 Gender (% male): 24 Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: convenience sampling; 2 cancer treatment sites Family Characteristics: Relationship to patient: *"Primary person assisting the patient with care needs at home"* Age (years): 52 Gender (% female): 51 Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: newly diagnosed lung, breast, colorectal, pancreatic or other solid tumor cancer or non-Hodgkin's lymphoma; undergoing or eligible to receive chemotherapy; within 56 days of initiating chemo for active treatment; could identify a caregiver Exclusion: NR	Cancer Care Intervention (CCI) (n=61): instructions to patients & caregivers on symptom management and surveillance; training on disease and treatment; how to coordinate and mobilize support; 9 standardized sessions with each dyad over 16 weeks; 5 in-person sessions (60 min each) and 4 telephone sessions (20 min each); in person meetings took place together; phone encounters patient and family member separate Comparator (n=59): Usual care (UC) Length of Follow-up: post-tx only (8 weeks)	***Depression/anxiety:*** a. Depression CES-D [SR] Outcomes assessed at baseline, mid-tx (week 9 of 16 week tx) and post-tx (24 weeks post baseline), **☒ Negative caregiver outcomes reported** *NOTE: post-tx control group CG's slightly less depressed than intervention CG's. Noted in discussion though that high attrition in intervention group, and among CG's who were more depressed at baseline may have made it difficult to accurately test the intervention.*	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): unclear Withdrawals/dropouts adequately described: yes Treatment adherence: *Study dropouts* 31/120=26% did not complete post-tx assessment CCI: 5 died, 15 withdrew UC: 6 died, 5 withdrew p=0.04 attrition between groups Treatment integrity: nurse interventionists trained to standard using both paper and mock patient cases. **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Kurtz, 2005[39] Funding Source: Government Condition: Recent diagnosis of a solid tumor (breast, lung and other); early stage, 33.0%; late stage, 67.0% **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multi-component; Skill building; educational; emotional	N=237 Age (years): 60 Gender (% male): 27 Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: nurse recruiters from 2 comprehensive cancer centers and 4 community oncology settings approached patients undergoing a first course of chemotherapy Family Characteristics: Relationship to patient: *Spouse 66%* Age (years): 55 Gender (% female): 54 Race/ethnicity (%) *White 92%; African-American 5; other 3* Education (%): NR Veterans (%): NR	Inclusion: ≥21 years of age, recently diagnosed with a solid tumor, undergoing a first course of chemotherapy, and have completed no more than the first two cycles prior to their baseline interview; identify a family caregiver; both patient and caregiver able to speak and read English; both patient and caregiver cognitively intact (as screened by recruiters) Exclusion: patients with previous chemotherapy treatment not eligible, nor were patients receiving radiation therapy at time of entry into study	Intervention (n=118): Clinical nursing intervention; alternating in person and telephone sessions – 10 sessions up to 20 weeks; intervention used cognitive behavioral model for both patient and caregiver in managing patient symptoms and reducing emotional distress Comparator (n=119): Usual care for each setting (not described further) Length of Follow-up: post -tx only	***Physical functioning:*** a. SF-36 Short Form Health Survey (physical health subscale) [SR] ***Social functioning:*** a. SF-36 Short Form Health Survey (social functioning subscale) [SR] ***Depression/anxiety:*** a. Depression CES-D All scales were self-report and assessed at baseline, mid-tx (10 weeks) and post-tx (20 weeks) **☐ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): unclear Withdrawals/dropouts adequately described: yes Treatment adherence: *Study dropouts* 59/237=25% lost to attrition before 10 weeks 39/237=16% lost to attrition between 10-20 weeks 139/237=59% of dyads remained for assessment for all 3 time points (ns dropouts between groups) Treatment integrity: monthly quality assurance for all nurse interventionists, audiotaped sessions, review of encounters, feedback sessions. **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Manne, 2005,[8] 2007[33] Funding Source: Government Condition: Breast cancer (early-stage) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Emotional and skill-based	N=238 Age (years): NR Gender (% male): 0 Race/ethnicity (%): NR Marital Status (%): *Married/cohabiting 100* Education (%): NR Veterans (%): NR Recruitment Method: 3 comprehensive cancer centers; approached by research assistant either after outpatient visit or by telephone Family Characteristics: Relationship to patient: *Married or living with* Age (years): 50 Gender (% female): NR Race/ethnicity (%): *White 89; African-American 5; other 6* Marital Status (%): *Married/cohabiting 100* Education (%): *HS or less: 34; Post HS: 66* Veterans (%): NR	Inclusion: primary diagnosis of ductal carcinoma in situ or Stage 1, 2, or 3a breast cancer; Eastern Cooperative Oncology Group performance status of 0 (*fully active, able to carry on all pre-disease performance without restriction*) or 1 (*restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature*); had undergone breast cancer surgery; married or living with significant other of either gender; both partners 18 years of age or older; competent to give informed consent; English speakers Exclusion: NR	Intervention (n=120): Couple focused group; 6 weekly 90-min sessions; Session 1 - group rapport & connections; Session 2 - couple-level stress management; Session 3 - couple-focused coping; Session 4 - basic communication concepts and skills; Session 5 - constructive ways to communicate support needs; Session 6 - anticipating post-treatment transition phase (esp. changes relationship before, during, & after cancer); 20 therapists provided intervention; 6 hrs training in manual based protocol Comparator (n=118): Usual care Length of Follow-up: post-treatment, 6 months post-treatment	***General psychological functioning:*** a. Impact of Event Scale (IES); 15-item self-report measure focusing on intrusive and avoidant ideation associated with a stressor (breast cancer and its treatment) b. Mental Health Inventory - (MHI–18); 3 distress subscales, and Loss of Behavioral and Emotional Control (BEC) (4 items) Well-Being subscale (6 items). ***Depression/anxiety:*** a. Mental Health Inventory - (MHI–18); Anxiety (4 items), Depression (4 items) subscales Both self-report and assessed at 1 week and 6 months post treatment ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: yes Treatment adherence: 42 (35%) in intervention group attended no sessions; 93 (78%) and 84 (70%) completed Time 2 and 3 surveys 94 (80%) and 79 (66%) controls completed Time 2 and 3 surveys Treatment integrity: yes manual with suggested text for leaders and co-leaders; in-session handouts; ongoing supervision provided; sessions audiotaped and treatment fidelity rated **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Manne, 2011[27] Funding Source: Government, Foundation Condition: Prostate cancer (localized, diagnosed within last year; 15% stage 1, 85% stage 2) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multi-component; skill-based and emotional; therapy for couples based on cognitive and marital behavioral therapy.	N=71 Age (years): 60 Gender (% male): 100 Race/ethnicity (%): *White* 88; *other* 11 Marital Status (%): *Married/cohabiting: 100* Education (%): *HS or less 11; Post HS 89* Veterans (%): NR Recruitment Method: 2 cancer centers; approached after outpatient visit or by telephone Family Characteristics: Relationship to patient: *Married or living with* Age (years): 56 Gender (% female): 97 Race/ethnicity (%): *White 83; other 11; Missing 6* Marital Status (%): *Married/cohabiting* 99; *Missing* 1 Education (%): *HS or less* 21; *Post HS* 78; *Missing* 1 Veterans (%): NR	Inclusion: localized prostate cancer diagnosed within last year; Eastern Cooperative Oncology Group (ECOG) 0 or 1; married or living with significant other of either gender; age ≥18 years;, living within 2 hours of cancer center; English speaking; no hearing impairment Exclusion: NR	Intervention (n=37): Intimacy-enhancing therapy (IET) – 5 90-min couples sessions; based on cognitive-behavioral and behavioral marital therapy; in session skills & practice + homework; manualized treatment Comparator (n=34): Usual care – standard psychosocial care provided by social workers with referral to psychiatrist or psychologist if indicated (provided to both groups) Length of Follow-up: 8 weeks (end of intervention)	***General psychological functioning:*** a. Mental Health Inventory (MHI) - Psychological Well-Being scale b. MHI Psychological Distress scale c. Impact of Events Scale – Cancer Specific Distress ***Relationship adjustment:*** a. DAS (Relationship Functioning) All outcomes self-report and assessed at baseline and at 8 wks post-baseline (end of 5 session intervention) **☒ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear (outcomes assessed by survey) Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: yes Treatment Adherence: 8/37 = 22% in IET group did not attend any sessions 27/37 = 73% attended 4 or 5 sessions Treatment integrity: therapists trained in manualized IET, sessions audiotaped for fidelity, monthly group supervision **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
McCorkle, 2007[28] Funding Source: Foundation Condition: Prostate cancer **KQ1 ☒ KQ2 ☐** **Intervention Type:** Emotional; problem solving; educational	N=107 (of 126 randomized) Age (years): 60 Gender (% male):100 Race/ethnicity (%): *White 87; Non-White 12; missing 1* Marital Status (%): *Married/cohabiting: 94* Education (%): *HS or less 21.5; Post HS 78.5* Veterans (%): NR Recruitment Method: men or spouses from 1-hour pre-op preparation class provided by nurses in urology department Family Characteristics: Relationship to patient: *Spouse/partner* Age (years): 56.0 Gender (% female): 100 Race/ethnicity (%): *White 85; Non-White 12; Missing 3* Education (%): *HS or less 36.4; Post HS 63.6* Veterans (%): NR	Inclusion: newly diagnosed men with prostate cancer; married or in committed relationship; elected radical prostatectomy as primary tx; lived within 50 miles of study center where recruited Exclusion: NR	Intervention (n=62): Standardized intervention: SNIP (Standardized Nursing Intervention Protocol) (symptom control; education; and exploiting resources) Comparator (n=64): Usual Care Length of Follow-up: 6 months	***Depression/anxiety:*** a. CES-D (Center for Epidemiologic Studies-Depression) ***Symptom control/ management:*** a. Cancer Rehabilitation Evaluation System (CARES)-Sexual function subscale ***Relationship adjustment:*** a. CARES-Marital interaction All self-reported at 6 months **☒ Negative caregiver outcomes reported** NOTE: Spouses in intervention group reported greater distress, worse sexual functioning and reduced marital interaction after the intervention	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: N=19 study dropout (8 intervention/11 control) No report of treatment dropout Treatment adherence: NR Treatment integrity: NR **Study quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
McMillan, 2007[40] Funding Source: Government Condition: Late stage cancer (patients in hospice) **KQ1 ☒ KQ2 ☒** **Intervention Type:** Problem-solving (COPE – creativity, optimism, planning, expert information)	N=329 Age (years): 70.6 Gender (% male): 60 Race/ethnicity (%): NR Marital Status (%): NR Education (mean): 12.2 years Veterans (%): NR Recruitment Method: identified by study staff at large nonprofit hospice Family Characteristics: Relationship to patient: *Family member (not specified)* Age (years): NR Gender (% female): NR Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: Adults with diagnosis of cancer; identified family caregiver; patient and caregiver with a) at least 6th grade education, b) able to read and understand English, and c) score of 7 or higher on Short Portable Mental Status Questionnaire (SPMSQ); patient with score of 40 or higher on Palliative Performance Scale Exclusion: excluded if patient did not have at least 2 of the following symptoms: pain, dyspnea, or constipation	1st Intervention (n=109): Standard care from hospice staff plus friendly visits on same schedule as 2nd intervention; focus on support, feelings, fears, relationships 2nd Intervention (n=111): **manualized** COPE intervention – caregiver problem solving; 3 visits during 9 day intervention plus telephone call between visits; caregiver given *Home Care Guide for Advanced Cancer* Comparator (n=109): Standard care from hospice staff; included some caregiver education and support Length of Follow-up: 9 day intervention with follow-up to 30 days after hospice admission	***Global quality of life:*** a. Hospice Quality of Life Index (HQLI) [SR] ***Symptom control/ management:*** a. Memorial Symptom Assessment Scale (MSAS) [SR] b. Numeric rating scale (NRS) for PAIN [SR] c. Dyspnea intensity scale [SR] d. Constipation assessment scale (CAS) [SR] Data collected at baseline (within 24-48 hours of hospice admission), 2 weeks after entry (day 16), and 2 weeks later (day 30) ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: no Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: no (numbers provided but no details) Reported post-intervention data: Control: 37% Intervention 1: 29% Intervention 2: 28% Treatment adherence: both interventions received by 100% of caregivers in those groups Treatment integrity: caregivers given guide on home care; study staff trained on COPE intervention and home care guide; all intervention visits audio recorded; investigators reviewed 10% of tapes **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Meyers, 2011[38] Funding Source: Government Condition: relapsed, refractory or recurrent solid tumors or lymphoma (gastrointestinal, genito-urinary, thoracic, breast, gynecologic, sarcoma, melanoma or other cancer) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Standardized, cognitive behavioral educational, emphasizing problem solving	N=441 (of 476 randomized) Age (years): 62 Gender (% male): 44 Race/ethnicity (%): *White 88; African-American 5; other 7* Marital Status (%): NR Education (%): *HS or less 35; Post HS 63; NR 2* Veterans (%): NR Recruitment Method: patients in qualifying phase 1, 2 or 3 clinical treatment trials at 4 participating cancer centers Family Characteristics: "Adult regularly involved with patient and their care" Relationship to patient: *Spouse 70; Adult child 16; other 12; NR 2* Age (years): 61 Gender (% female): 31 Race/ethnicity (%): *White 85; African-American 6; other 9* Education (%): *HS or less 32; Post HS 66; NR 2* Veterans (%): NR	Inclusion: Adults with "relapsed, refractory, or recurrent solid tumors or lymphoma enrolled onto phase 1 or 2, or phase 3 trials that compared therapy for advanced cancer." (Patients among the sickest and most distressed, as clinical trial participation usually follows depleting conventional therapies, or because few therapies available for that diagnosis.) Exclusion: Patients receiving concomitant chemotherapy and radiation; on adjuvant phase III studies; those with hematopoietic malignancies; with primary brain tumors; not fluent in English; < 18 years of age or lacking a willing caregiver.	Intervention (n=348): COPE: (Creativity, Optimism, Planning and Expert Information) Dyads received a copy of "The Home Care Guide for Cancer," then had three conjoint educational sessions (pt, caregiver, educator). Standardized, cognitive behavioral intervention. First session conducted up to 7 days prior to day the pt started their investigational clinical trial and focused on familiarity with the guide and COPE problem-solving model, to solve a pt and caregiver identified problem. Two other sessions conducted within 30 days, reinforcing learning using COPE model on two additional pt/caregiver identified problems. Comparator (n=128): Usual care Length of Follow-up: 6 months	***Global quality of life:*** a. City of Hope Quality of Life instrument (COH QOL) Self-reported outcome assessed at baseline and 30, 60, 90, 120, 180 days after randomization ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: no Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: yes Treatment adherence: *SCEI* -Withdrew a) before intervention = 5% (27/348); b) before end of study = 65% (227/348) (Of this 53 deaths = 15%) *Usual care* -Withdrew a) before intervention = 8% (10/128); b) before end of study = 67% (86/128) (Of this 27 deaths = 21%) *Outcomes assessed:* 444/476=94% completed at least one assessment; 156/376=33% completed through six month follow up Treatment integrity: educators trained in "COPE" model; sessions reviewed to increase consistency; educators documented sessions **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Mishel, 2002[24] Funding Source: Government Condition: localized prostate cancer **KQ1 ☒ KQ2 ☒** **Intervention Type:** Psychoeducational	N=239 (of 252 enrolled) Age (years): 64 Gender (% male): 100 Race/ethnicity (%): *White 56; African-American 44* Marital Status (%): *Married/cohabiting 84* Education (%): *HS or less* 43; *Post HS* 57* Veterans (%): NR *Noted that may not be accurate - time lost while harvesting Recruitment Method: approached at clinic visits (9 facilities); potential African-American participants personally visited by "two African-American men well known in the community" Family Characteristics: Patient selected family member helping with cancer care ("mostly spouses" but exact numbers not reported) Demographics: NR	Inclusion: African-American and Caucasian men; localized prostate carcinoma within 2 wks post catheter removal after surgical treatment and/or within 3 wks into current radiation therapy; access to telephone; identifiable family member willing to participate; and planned to reside in current community for 12 months Exclusion: major cognitive impairment or concurrent treatment for another form of malignancy.	1st Intervention: Uncertainty Management Direct (UMD) (n=NR): 8 weekly calls from male nurse matched to ethnicity; semi-structured interview format; assess patients' concerns and uncertainty; standardized lists of problems to discuss + discussion of specific concerns 2nd Intervention: Uncertainty Management Supplemented (UMS) (n=NR): same as UMD group; family support person received a matching concurrent intervention from a female nurse (matched to ethnicity) Comparator: Usual care (n=NR): printed general health info. (not related to prostate cancer or side effects of treatment) Length of Follow-up: 8 weeks post-treatment (considered post-treatment) and 5 months post-treatment	***Symptom control/ management:*** a. Symptom Distress Scale (# of symptoms) b. Symptom Distress Scale (average intensity of symptoms) c. Urine flow d. Ability to have an erection e. Satisfaction with sexual function All outcomes self-reported and assessed at baseline, baseline + 8 weeks post-treatment and 5 months post-treatment ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): unclear Withdrawals/dropouts adequately described: yes Treatment adherence: study dropouts = 95% of 252 enrolled completed measurements at all 3 time points Treatment integrity: none reported **Study quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Mokuau, 2008[47] Funding Source: Government Condition: Cancer **KQ1 ☐ KQ2 ☒** **Intervention Type:** Educational, skill-based, problem solving or conflict resolution	N=10 (of 12 randomized) Age (years): 55 Gender (% male): 0 Race/ethnicity (%): *other 100 (Hawaiian)* Recruitment Method: through physicians, providers, print and electronic media Family Characteristics: Age (years): 54 Gender (% female): 50	Inclusion: Native Hawaiian; female; diagnosis of cancer in last 12 months Exclusion: none reported	Intervention (n=6): Two health educators provided a culturally-specific (Hawaiian) intervention to increase knowledge, behavioral capabilities and support for women cancer survivor and one or 2 family members. Six visits/sessions over 3 months conducted in various places (homes, offices and libraries). Comparator (n=4): Two health educators introduced a culturally non-specific intervention, mostly consisting of educational brochures. Two sessions (Baseline and one additional session at the end of intervention) over 3 months. Length of Follow-up*:* none (3 month intervention only)	***General psychological functioning:*** a. Global severity index of the Brief Symptom Inventory (BSI) for distress ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: no Intention-to-treat analysis (ITT): unclear Withdrawals/dropouts adequately described: unclear Treatment adherence: treatment dropouts and study dropouts not assessed Treatment integrity: unclear **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Nezu, 2003[36] Funding Source: Government Condition: Cancer, diagnosed in the past 6 months, 28% Stage I, 56% Stage II, 16% Stage III **KQ1 ☒ KQ2 ☒** **Intervention Type:** Problem solving	N=132 (of 150 randomized) Age (years): 47 Gender (% male): 33 Race/ethnicity (%): *White 77; African-American 17; other 6* Marital Status (%): *Married/cohabiting 61* Education (years): 14.6 Veterans (%): NR Recruitment Method: receiving oncology-related services at 2 sites; neighboring hospitals; cancer centers; local cancer referral agencies Family Characteristics: Relationship to patient: *Spouses 95%, Adult son/ daughter 5% (except 1 friend)* Age (years): NR Gender (% female): NR Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: ages 18-65; meet screening criteria for psychological distress; able to read English (6th gr. level+); person to participate in study; prognosis of 5-yr survival rate of ≥50%; Karnofsky Performance Status Scale score of 70+ Exclusion: known psychiatric disturbance prior to diagnosis of cancer; diagnosis of mental retardation; acute suicidal behavior; current treatment for emotional or psychological problem	Intervention 1 - PST (n=45): Problem-solving training, manualized; provided on individual basis during 10 1.5 hr/wk session Intervention 2 – PST-SO (n=43): Problem-solving training (as above) with significant other included as problem-solving coach (social support, encouragement, feedback) Comparator (n=44): wait list controls; contacted twice to assess need for crisis mgmt or referral; no direct counseling Length of Follow-up: Mean of 13 weeks treatment	***General psychological functioning:*** a. Emotional distress, Omega (clinician report) b. Mood, POMS (SR) c. Psychological distress, BSI (SR) ***Global quality of life:*** a. QL Index (clinician report) ***Depression/anxiety:*** a. Depression, HRSD (clinician report) ***Symptom control/ management:*** a. Day-to-day problems and rehab needs, CARES (SR) All assessments at post tx, 6 months, 12 month ☐ **Negative caregiver outcomes reported**	Allocation concealment: inadequate Blinding: yes (outcome assessment) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: PST group completed mean of 9.7 sessions in 12.8 weeks; PST-SO group completed mean of 9.6 sessions in 13.1 weeks Treatment integrity: weekly supervision of therapists to foster adherence to therapy manuals; sessions audiotaped and reviewed for adherence **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Northouse, 2005[29] Funding Source: Foundation Condition: Recurrent or progressing breast cancer; analysis included only patients with Stage 3 or 4 cancer **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (FOCUS - Family involvement, Optimistic attitude, Coping effectiveness, Uncertainty reduction, Symptom management)	N=134 (of 200 randomized) Age (years): 54 Gender (% male): 0 Race/ethnicity (%): *White 77; African-American 19; other 4* Marital Status (%): NR Education (mean): 14 years Veterans (%): NR Recruitment Method: staff in medical oncology clinics Family Characteristics: Relationship to patient: *Primary source of support - husband 62%, sibling 9%, adult daughter 13%, adult son 3%, other relatives or friends 13%* Age (years): 52 Gender (% female): NR Race/ethnicity (%): *White 77; African-American 19; other 4* Education (mean): 14 years Veterans (%): NR	Inclusion: *Patient* - Confirmed diagnosis of recurrent breast cancer within previous month (reappearance after any disease-free interval) OR confirmation that breast cancer had progressed in past month (laboratory test, radiologic test, or clinical exam that required a change in treatment); life expectancy ≥ 6 months; able to identify family caregiver willing to participate *Patient and caregiver* – age 21 or older; mentally and physically able to participate; able to speak and understand English *Caregiver* – confirmed as primary support for patient Exclusion: NR	Intervention (n=69): FOCUS Program + usual care; manualized; initial phase of 3 home visits with patient and caregiver (one month apart, 90 min/visit); booster phase of 2 phone calls to patient and caregiver (30 min/call) Comparator (n=65): Usual care Length of Follow-up: 6 months post-baseline (initial treatment + booster phase)	***Physical functioning:*** a. Combined measure using FACT-B (SR) and SF-36 (SR) to create overall QOL (physical functioning) ***Mental functioning:*** a. Combined measure using FACT-B (SR) and SF-36 (SR) to create overall QOL (mental health functioning) ***Depression/anxiety:*** a. Beck Hopelessness (depression) Outcomes assessed at baseline, 3 mo (after initial phase of FOCUS) and 6 mo (after booster phase of FOCUS) ☐ ***Negative caregiver out comes reported***	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: attendance not reported; 74% (134/182) completed 3 and 6 month assessments Treatment integrity: intervention staff met regularly to review caseload of dyads **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Northouse, 2007[23] Funding Source: Government Condition: Prostate cancer; newly diagnosed (65%); biochemical recurrence (14%); or advanced (21%) **KQ1 ☒ KQ2 ☐** **Intervention Type:** educational, skill-based, emotional problem solving or conflict resolution, decision support	N=263 dyads Age (years): 63 Gender (% male): 0 Race/ethnicity (%): *White 84; African-American 14; Multiracial 2* Marital Status (%): *Married/cohabiting 100* Education (mean): 16 years Veterans (%): NR Recruitment Method: three large cancer centers in Midwest; patients identified by clinical staff, recruited by research staff Family Characteristics: Relationship to patient: *Spouse/partner* Age (years): 59 Gender (% female): 100 Race/ethnicity (%): *White 84; African-American 15; Multiracial 1.5* Education (mean): 15 years Veterans (%): NR	Inclusion: Either newly diagnosed, biochemical recurrence, or advanced metastases; ≥30 yrs old; ≥12 months of life expectancy; lived within 75 miles of cancer center; married or with a partner Exclusion: *patients* - a second, primary cancer; *dyads* - spouse ≤21 yrs or diagnosed with cancer within the prior year or was receiving cancer treatment	Intervention (n=129): Manualized; family Intervention; 3 90-min home visits and 2 30-min telephone sessions; spaced 2 weeks apart for 4 months Comparator (n=134): Usual care Length of Follow-up: 8 months post-treatment	***Physical functioning:*** a. SF-12 ***General psychological functioning:*** a. SF-12 b. OSQ (Omega Screening Questionnaire) (77-item) ***Global quality of life:*** a. FACT-G (Functional Assessment of Cancer Therapy; 27 items, ***Depression/anxiety:*** a. Beck Hopelessness (depression) ***Symptom management/ control:*** a. EPIC (Expanded Prostate Cancer Index Composite) (50-item) All outcomes self-report and assessed at 4, 8, 12 months post-baseline); or post, 4, and 8 months post-treatment. **☒ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: yes, data collectors blinded to dyad condition Intention-to-treat analysis (ITT): unclear Withdrawals/dropouts adequately described: yes Study dropouts: Refused assignment (inter=9; control=1) Incomplete 4-mo assessment (inter=17; control=11) Incomplete 8-mo assessment (inter=5; control=2) Incomplete 12-mo assessment (inter=3; control=7) Treatment adherence: 82.9% (218/263) Treatment integrity: yes **Study quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Porter, 2009[46] Funding Source: Government Condition: Gastrointestinal (GI) cancer; stage II through IV **KQ1 ☐ KQ2 ☒** **Intervention Type:** a. Partner-Assisted Emotional Disclosure: Multicomponent (skill-based, emotional, problem solving or conflict resolution) b. Cancer Education/ Support: Multicomponent (educational, skill-based)	N=130 Age (years): 59.4 Gender (% male): 71 Race/ethnicity (%): *White 85; African-American 12; other 4* Marital Status (%): NR Education (%): *HS or less 45; Post HS 55* Veterans (%): NR Recruitment Method: GI oncology clinics at 2 university affiliated hospitals Family Characteristics: Relationship to patient: *Spouse or intimate partner* Age (years): 59 Gender (% female): 71 Race/ethnicity (%): *White 82; African-American 11; other 6* Education (%): *HS or less 41; Post HS 60* Veterans (%): NR	Inclusion: stage II through IV GI cancer; life expectancy of 6 months or longer; spouse or intimate partner Exclusion: NR	Intervention (n=65): Partner-Assisted Emotional Disclosure; 4 face-to-face sessions (45-75 min each) completed in up to 8 weeks; focus on patient disclosure of feelings and concerns about cancer experience Comparator (n=65): Couple Cancer Education/ Support; 4 face-to-face sessions for presenting information about cancer, available resources, communicating with health care providers, and maintaining quality of life Length of Follow-up: 8 week intervention only	***General psychological functioning:*** a. Profile of Moods States-Short Form (POMS-SF) ***Relationship adjustment:*** a. Quality of Marriage Index (QMI) Outcomes self-report and assessed at baseline and post-treatment ☐ ***Negative caregiver outcomes reported***	Allocation concealment: unclear Blinding: yes (outcome assessment) Intention-to-treat analysis (ITT): yes (and analysis with completers only) Withdrawals/dropouts adequately described: yes Treatment adherence: 112/130 (86%) attended at least 1 treatment session; 108/130 (83%) completed post-treatment assessments Treatment integrity: Therapists were trained, detailed treatment outlines were used, sessions were audiotaped; assessments of adherence and competence **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Porter, 2011[45] Funding Source: Government Condition: Lung cancer, stages 1-3 **KQ1 ☐ KQ2 ☒** **Intervention Type:** a. Caregiver Assisted Coping Skills Training: Education; skill-based; emotional; problem solving or conflict resolution b. Education and Support (including caregiver): Educational	N=233 Age (years): 65 Gender (% male): 53 Race/ethnicity (%): *White 85; African-American 12; other 4* Marital Status (%): NR Education (%): *HS or less 45; Post HS 55* Veterans (%): NR Recruitment Method: oncology programs and clinics Family Characteristics: Relationship to patient: *Spouses 76%, sons/ daughters 14%, sibling/ friend 8%; 73% resided together* Age (years): 59 Gender (% female): 69 Race/ethnicity (%): *White 82; African-American11; other 6* Education (%): *HS or less 41%* *Post HS 60%* Veterans (%): NR	Inclusion: diagnosis of early stage lung cancer (stages I-III) or limited stage small-cell lung cancer; no other cancers in the past 5 years; ability to read and write English; caregiver willing to participate Exclusion: NR	Intervention (n=117): Caregiver assisted coping skills training (CST); Patients & caregivers received training in conjoint sessions by speaker phone; delivered by registered nurses; Caregivers trained to be "coaches" (help patients learn coping skills and apply them); 8 month intervention; 14 standardized sessions, 45-min each; Sessions 1-3 weekly; sessions 4-10 biweekly; sessions 11-14 monthly Comparator (n=116): *Education/Support*,; Patients & caregivers received training in conjoint sessions by speaker phone; information about lung cancer and treatment; discussions guided by specific topics; same schedule as above Length of Follow-up: Post-treatment and four month follow up	***Physical functioning:*** a. Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L) (Physical functioning subscale) ***Social functioning:*** a. Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L)(social functioning subscale) ***Depression/ anxiety:*** a. Beck Depression Inventory (BDI) b. State trait anxiety inventory (STAI) ***Symptom control/ management:*** a. Brief Pain Inventory (BPI) b. Functional Assessment of Cancer Therapy-Lung Cancer (FACT-L) (cancer symptoms subscale) All self-report, post-treatment and follow-up ☐ **Negative caregiver outcomes reported**	Allocation concealment: yes Blinding: yes (assessors) Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: yes Treatment adherence: **CST**: 24.3% (26 of 107 surviving at post-treatment) dropped out and were not assessed at post-treatment; at follow-up, 36.3% dropped out of those who survived to follow-up (37 of 102) **Education/Support**: 14.4% (15 of 104 surviving at post-treatment) dropped out and were not assessed at post-treatment; At follow-up, 23.5% dropped out of those who survived to follow-up (23 of 98) Treatment integrity: yes **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Schover, 2012[41] Funding Source: Foundation Condition: Localized prostate cancer ($T_{1-3}N_0M_0$) **KQ1 ☐ KQ2 ☒** NOTE: Study included a wait list control group but provided no results; findings are reported for KQ2 only **Intervention Type:** Educational, emotional	N=81 (of 115 randomized) Age (years): 64 Gender (% male): 100 Race/ethnicity (%): *White 85; African-American 8; other 7* Marital Status (%): *Married/cohabiting* 98 Education (%): *HS or less* 6; *Post HS* 94 Veterans (%): NR Recruitment Method: invitations to men in center tumor registry; physician referral; fliers in outpatient clinics; public service announcements (local media, web sites); active effort to recruit African Americans Family Characteristics: Relationship to patient: *Spouse: 98; other: 2%* Age (years): NR Gender (% female): NR Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: heterosexual males; age ≥18 yrs; treated for localized prostate cancer ($T_{1-3}N_0M_0$) with definitive surgery or radiotherapy in previous 3 mos to 7 yrs; couples married or living together for ≥1 yr; both partners agreed to participate; reasonable English fluency; men either unable to achieve and maintain erection sufficient for sexual intercourse on ≥50% of attempts or had not attempted intercourse for past 3 months; no noted firm erections on waking from sleep; willing to come to cancer center 3 times during 12-wk tx Exclusion: using hormone therapy for prostate cancer; using a satisfactory medical treatment for erectile dysfunction	Intervention: Face-to-face counseling [FF] (n=60): 3 face-to-face sessions; 50-90 min; 12 weeks; printed handouts & homework exercises (expression of affection, sexual communication, comfort in initiating sexual activity, & resuming sex without performance anxiety); decision aid for choosing ED treatment; relapse prevention exercise; booster phone calls to discuss progress Comparator: Internet-based counseling (WEB1) (n=55): internet-based format of face-to-face counseling (e-mail contact with therapist, web-based instructions); same relapse prevention & booster calls; participants could e-mail therapists any time; loaner laptops provided, if needed Length of Follow-up: 12 months	***General psychological functioning:*** a. Brief Symptom Inventory-18 (BSI-18) ***Symptom management/ control*** a. International Index of Erectile Function (IIEF) b. % men achieving near normal erectile function over time (IIEF Erectile Function subscale ≥22) ***Relationship adjustment:*** a. Abbreviated Dyadic Adjustment Scale (DAS) All self-reported outcomes assessed at baseline, post-tx, 3, 6, and 12 months post tx. ☐ **Negative caregiver outcomes reported** NOTE: study also included 1) wait list control group – no changes over 3 months; patients then randomized into the intervention groups and 2) WEB2 group – too far away geographically to participate in randomized trial	Allocation concealment: adequate Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: partial – only report number of drop-outs during intervention and number lost to follow-up, no reasons reported Treatment adherence: treatment dropouts: FF [n=60] *During intervention = 28% (17/60)* *Lost to f/u = 5% (3/60)* WEB1 [n=55] *During intervention = 13% (7/55)* *Lost to f/u = 13% (7/55)* Treatment integrity: manual used to train therapists; biweekly group supervision **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Stephenson, 2007[48] Funding Source: *Government* Condition: Metastatic cancer **KQ1 ☐ KQ2 ☒** **Intervention Type:** Skill-based	N=86 (of 90 randomized) Age (years): 58 Gender (% male): 51 Race/ethnicity (%): *White 59; African-American 40; other 1* Education (%): *HS or less 66.3 Post HS NR* Veterans (%): NR Recruitment Method: selected from patients from four hospitals Family Characteristics: None reported	Inclusion: any kind of metastatic cancer; pain score ≥2 (0-10); dyad had to be 21 yrs old; living together as spouse/partners, family, or friends; English speaking; live within100 miles of hospital; partner available from 2-10pm Exclusion: any surgery in previous 6 weeks; any open skin wounds to feet, foot tumors or foot metastases; radiation to feet or site of pain; >50% loss of feeling due to peripheral neuropathy	Intervention (n=42): a. *One 30-minute session of reflexology using Ingham method* b. *Partners were trained in basic techniques of reflexology and received materials about conducting reflexology and signs and symptoms of deep vein thrombosis* Comparator (n=44): *Usual care plus "special attention." Special attention included partners reading a selection of patient's choice to the patient.* Length of Follow-up: Baseline and post-intervention	***Depression/anxiety:*** a. Visual Analog Scale for Anxiety (SR) ***Symptom control/ management:*** a. Brief Pain Inventory (BPI; SR) b. Short-Form McGill Pain Questionnaire (SF-MPQ; SR) *All measures assessed at pre and post-intervention. Data collected for 21 months.* ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: treatment adherence not reported; One control group patient did not complete post treatment assessments (2.3% did not complete); Post-treatment data available on all who received the intervention Treatment integrity: unclear **Study Quality: Fair**

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Table 2. Cancer Studies – Quality of Life – Physical Functioning

Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Badger, 2011[21] 1) TIP-C (n=36) 2) HEAC (n=35)	Prostate cancer	Currently undergoing or completed treatment w/in 6 months (Stage I=16%, II=9%, III=11%, IV=11%, unknown=53%)	UCLA Prostate Cancer Index – Prostate specific health-related QOL	1) 63.2 (25.8) (n=36) 2) 62.0 (21.3) (n=35) p=ns (NR)	1) 63.2 (19.4) (n=34) 2) 60.5 (20.6) (n=32) Change over time: 1) ns 2) ns Group 1) vs 2): p=ns (NR)	
Baucom, 2009[31] 1) Couple-based relationship enhancement (n=8 couples) 2) Treatment-as-usual (n=6 couples)	Breast cancer	Stage I or II (recently diagnosed); no history of other breast cancer; no history of cancer within last 5 years	Functional Assessment of Cancer Therapy (FACT-B) (higher score = greater daily functioning)	1) 2.48 (0.58) 2) 2.86 (0.56)	1) 3.08 (0.27) 2) 2.76 (1.15) (n=NR) d=0.97 (pre tx to post tx)	1) 3.22 (0.34) 2) 2.89 (0.91) (12 months) (n=NR) d=1.14 (pre tx to follow up)
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Physical Functioning subscale of Medical Outcomes Scale (SF-20)	1) 38.7 (21.7) 2) 38.1 (21.2) p=ns (NR)	1) 38.3 (22.0) 2) 37.1 (22.2) p=ns (NR)	NR
Budin, 2008[30] 1) Psychoeducation (SE) +DM, n=66 2) Telephone counseling (TC) + DM, n=66 3) SE+TC+DM, n=58 4) Disease Management (DM), n=59	Breast cancer	Lesion with confirmed or strongly suspected diagnosis of cancer	Overall Health Status (subscale of SRHS); scores from 4 to 13 with higher score = better overall perceived health status	1) 8.9 (1.9) 2) 9.2 (1.6) 3) 9.6 (1.6) 4) 9.3 (1.8)	Values not reported **Main effect for time (p<0.0001)** Main effect for group (ns) Group x time interaction (ns)	

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Campbell, 2007[26] 1) Coping Skills Training (CST) (n=20) 2) Usual Care (UC) (n=20)	Prostate cancer	Karnofsky Performance Status score >= 60	SF-36 (Short Form Health Survey) (higher score = better functioning)	NR	Physical Function 1) 27.5 (SE=0.8) (n=12) 2) 26.1 (SE=0.7) (n=18) d=0.34, p=0.19	6 weeks
Giesler, 2005[22] 1) Cancer care intervention (n=48) 2) Standard care (n=51)	Prostate cancer (post-treatment)	T1a-T2c	SF-36 Short Form Health Survey (higher score = better functioning)	NR	Physical Functioning d=0.00, p=0.99 1 month post-intervention (n=NR)	Physical Functioning d=0.05, p=0.83 6 months post-intervention (n=85)
Gustafson, 2013[44] 1) Standard care plus CHESS (n=144) 2) Standard care plus Internet (n=141)	Nonsmall Cell Lung Cancer	16% Stage IIIA, 18% Stage IIIB, 66% Stage IV 71% ECOG 0 or 1 30% ECOG 2, 3, or 4	Mortality/Survival	NA	NR	**Deaths at 24 months** 1) 77/124 (62%) 2) 89/122 (73%) **Median Survival** 1) 14.8 months (SE=1.2) 2) 10.1 months (SE=1.5) Adjusted p=0.08
Keefe, 2005[34] 1) Partner guided (n=41) 2) Usual care (n=37)	Cancer (any)	Eligible for hospice care; life expectancy ≤ 6 months	Functional Assessment of Cancer Therapy-General (FACT-G, v4) physical functioning sub scale (scale 0-4; higher score = problem with function)	Physical well-being NR; but reported p=ns between groups (n=78)	Physical well-being 1) 2.0 (0.8) (n=28) 2) 2.1 (0.8) (n=28) p=NR	NR
Kurtz, 2005[39] 1) Clinical nursing intervention (n=118) 2) Usual care (n=119)	Cancer (any)	Recent diagnosis of a solid tumor (breast, lung, other); early stage, 3%; late stage, 67.0%	MOS SF-36 physical functioning subscale (scale 0-100, higher score = fewer limitations on activity)	Physical Functioning 1) 65.8 (28.6) 2) 63.2 (30.0) n=NR	Physical Functioning 1) 77.2 (22.9) 2) 67.0 (30.2) n=NR p=NR	NR
Northouse, 2005[29] 1) FOCUS (n=69) 2) Usual care (n=65)	Breast cancer	Recurrent or progressing, Stage 3 or 4	Composite of FACT-B and SF-36-physical health (converted to T scores with mean of 50 and SD of 10)	1) 51.7 (9.6) (n=NR) 2) 49.6 (9.3) (n=NR)	1) 49.7 (9.2) (n=NR) 2) 49.8 (9.7) (n=NR) 6 months (after booster phase of FOCUS) Group x time (p=0.19)	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Northouse, 2007[23] 1) Couples intervention (FOCUS) (n=129) 2) Usual care (UC) (n=134)	Prostate cancer	Newly diagnosed (65%); biochemical recurrence (14%); advanced (21%)	SF12-Physical (post-tx and follow up control for baseline scores)	1) NR 2) NR	1) 48.6 (6.7) (n=113) 2) 48.7 (6.5) (n=133) ES=-0.02 (F=0.01, p=0.96)	8 months post-tx 1) 42.7 (6.5) (n=104) 2) 42.5 (6.4) (n=114) ES=0.03 (F=0.02, p=0.88)
Porter, 2011[45] 1) Coping skills training (CST) (n=117) 2) Education (EDU) (n=116)	Lung cancer	Stage I-III	FACT-L: Physical Well-Being	1) NR 2) NR	1) NR 2) NR Time x Treatment interaction: p=ns Time x Treatment x Cancer Stage interaction: p=ns	NR

*Last follow-up reported only if > 6 months post-treatment
[1]Scale of -3 to +3; higher score indicates better well-being
d or ES=effect size, NR=not reported, ns=not statistically significant

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Table 3. Cancer Studies – Quality of Life – General Psychological Functioning

Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Badger, 2011[21] 1) TIP-C (n=36) 2) HEAC (n=35)	Prostate cancer	Currently undergoing or completed treatment w/in 6 months (Stage I=16%, II=9%, III=11%, IV=11%, unknown=53%)	Spiritual well-being (QoL Breast Cancer subscale) (higher score = greater influence of cancer on pt's spirituality)	1) 43.6 (14.8) (n=36) 2) 44.2 (11.6) (n=35) p=ns (NR)	1) 42.8(14.0) (n=34) 2) 46.5 (11.9) (n=32) Change over time: 1) ns **2) p<0.05** **Group 1) vs 2): p<0.01 (favoring group 2)**	
			Positive affect (PANAS) (score range 20-50; higher score = more positive affect)	1) 35.1 (6.6) (n=36) 2) 36.7 (7.4) (n=35) p=ns (NR)	1) 36.7 (7.7) (n=34) 2) 37.9 (6.1) (n=32) Change over time: 1) ns 2) ns Group 1) vs 2): p=ns (NR)	
			Negative affect (PANAS) (score range 20-50; higher score = more negative affect)	1) 16.0 (6.3) (n=36) 2) 17.0 (7.4) (n=35) p=ns (NR)	1) 16.8 (7.1) (n=34) 2) 14.8 (6.2) (n=32) Change over time: 1) ns **2) p<0.05** **Group 1) vs 2): p<0.001 (favoring group 2 – less negative affect)**	
			Perceived stress (PSS) (score 0-40; higher score = more perceived stress)	1) 12.7 (6.5) (n=36) 2) 13.2 (7.1) (n=35) p=ns (NR)	1) 12.5 (6.5) (n=34) 2) 11.2 (7.3) (n=32) Change over time: 1) ns **2) p<0.05** **Group 1) vs 2): p<0.001 (favoring group 2)**	
Baucom, 2009[31] 1) Couple-based relationship enhancement (n=8 couples) 2) Treatment-as-usual (n=6 couples)	Breast cancer	Stage I or II (recently diagnosed); no history of other breast cancer; no history of cancer within last 5 years	Brief Symptom Inventory (BSI-18)	1) 11.9 (10.8) 2) 16.3 (9.5)	1) 8.0 (5.9) 2) 12.5 (14.7) n=NR d=0.07 (pre tx to post tx)	1) 6.7 (5.8) 2) 15.8 (20.9) (12 months) n=NR d=0.45 pre tx to follow-up)
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Mental Health Functioning subscale of Medical Outcomes Scale (SF-20)	1) 66.3 (22.1) 2) 70.4 (15.1) p=ns (NR)	1) 70.0 (17.6) 2) 74.1 (15.0) p=ns (NR)	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Budin, 2008[30] 1) Psychoeducation (SE) +DM, n=66 2) Telephone counseling (TC) + DM, n=66 3) SE+TC+DM, n=58 4) Disease Management (DM), n=59	Breast cancer	Lesion with confirmed or strongly suspected diagnosis of cancer	Psychological Well-Being (subscale of PAL-C) (scores of 5 to 20; higher score = higher level of well-being)	1) 14.9 (3.2) 2) 14.5 (2.6) 3) 15.7 (2.9) 4) 15.5 (2.6)	Values NR Main effect for patients (ns) Main effect for time (p=0.03) **Group x time interaction (p=0.01)**	NR
Campbell, 2007[26] 1) Coping Skills Training (CST) (n=20) 2) Usual Care (UC) (n=20)	Prostate cancer	Karnofsky Performance Status score >= 60	SF-36 (Short Form Health Survey) (higher score = better functioning)	NR	Mental Health 1) 24.9 (SE=0.7) (n=12) 2) 25.2 (SE=0.5) (n=18) d=0.01, p=0.70	
Canada, 2005[43] 1) Couples Counseling (n=25) 2) Patient Counseling (n=26)			Brief Symptom Inventory/Global Symptom Inventory (BSI/GSI) (lower score = better functioning)	1) NR 2) NR Groups 1 and 2 combined: 0.38 (0.29) (n=51)	1) NR 2) NR Groups 1 and 2 combined: 0.29 (0.26) (n=44)	6 months post-tx: 1) NR 2) NR Groups 1 and 2 combined: 0.29 (0.22) (n=39) Group 1 vs 2: p=NR, ns
Giesler, 2005[22] 1) Cancer care intervention (n=48) 2) Standard care (n=51)	Prostate cancer (post-treatment)	T1a-T2c	SF-36 Short Form Health Survey (higher score = better functioning)	NR	Mental Health d=0.17, p=0.46 1 month post-intervention, n=NR	Mental Health d=-0.06, p=0.78 6 months post-intervention (n=85)
Manne, 2005[8] 1) Couple focused group (n=120) 2) Usual care (n=118)	Breast cancer	Early-stage, Eastern Cooperative Oncology Group performance status of 0 (*fully active*) or 1 (*restricted but ambulatory; able to carry out light or sedentary work*)	Mental Health Inventory (MHI) – Loss of Behavioral and Emotional Control scale (4 items)	1) 8.8 (3.0) (n=120) *1a) Attenders only 8.9 (2.8) (n=78)* 2) 8.9 (2.8) (n=118) p=NR	1) 8.1 (2.8) (n=120) *1a) Attenders only 7.6 (2.4) (n=78)* 2) 8.0 (2.8) (n=118) p=NR	6 months 1) 7.7 (2.9) (n=120) *1a) Attenders only 7.2 (2.4) (n=78)* 2) 8.5 (4.3) (n=118) p=NR
			Impact of Events Scale (15-items)	1) 24.2 (14.8) (n=120) *1a) Attenders only 23.3 (15.0) (n=78)* 2) 23.3 (15.0) (n=118) p=NR	1) 19.3 (13.7) (n=120) *1a) Attenders only 19.4 (13.9) (n=78)* 2) 20.9 (14.7) (n=118) p=NR	6 months 1) 16.8 (13.9) (n=120) *1a) Attenders only 15.7 (13.9) (n=78)* 2) 17.6 (15.5) (n=118) p=NR
			Mental Health Inventory (MHI) - Well-Being subscale (6 items)	1) 24.1 (5.1) (n=120) *1a) Attenders only 24.5 (5.0) (n=78)* 2) 24.5 (5.0) (n=118) p=NR	1) 26.0 (5.0) (n=120) *1a) Attenders only 26.7(4.7) (n=78)* 2) 25.6 (4.90) (n=118) p=NR	6 months 1) 26.5 (5.2) (n=120) *1a) Attenders only 27.3 (4.5) (n=78)* 2) 25.6 (6.2) (n=118) p=NR

Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Manne, 2011[27] 1) IET (n=37) 2) Usual Care (n=34)	Prostate cancer	Diagnosed within past year; 15% stage 1, 85% stage 2	Mental Health Inventory (MHI) Psychological Distress scale	NR	NR p=ns treatment effects	NR
			Impact of Events Scale – Cancer Specific Distress	NR	NR p=ns treatment effects.	NR
			Mental Health Inventory (MHI) - Psychological Well-Being scale; 15 items (higher score = greater well-being)	NR	Controlling for co-variates: 1) 67.5 (n=37) 2) 65.0 (n=34) p=0.08	NR
Mokuau, 2008[47] 1) Cultural Intervention with SO (n=6) 2) Education with SO (n=4)	Cancer (any)	Cancer diagnosed in the last 12 months, any stage	Brief Symptom Inventory (BSI) Global Severity Index (53 items)	1) 26.67 2) 36.75 p<0.01	1) 17.00 2) 36.25 p<0.01 (group 1 over time)	NR
Nezu, 2003[36] 1) Problem solving (individual) (n=45) 2) Problem solving with SO (n=43) 3) Wait list (n=44)	Cancer (any)	Diagnosed in past 6 months, currently receiving treatment, experiencing significant psychological distress	Omega Vulnerability Rating Scale (Omega) (higher score = more distress)	1) 25.2 (4.2) 2) 25.6 (4.3) 3) 25.4 (4.5)	**1) 14.9 (3.8)** **2) 15.8 (2.9)** 3) 24.3 (5.3) Groups 1 & 2 decreased over time and different than group 3 post tx	1) 17.0 (6.0) (n=41) 2) 15.0 (4.3) (n=38) 3) not assessed (12 months)
			Profile of Mood States (POMS); 65 adjectives; rated 0 (not at all) to 4 (extremely)	1) 73.0 (21.3) 2) 70.4 (23.7) 3) 75.7 (25.7)	**1) 33.3 (21.6)** **2) 37.0 (21.0)** 3) 83.3 (24.5) Groups 1 & 2 decreased over time and different than group 3 post tx	1) 37.0 (25.6) (n=41) 2) 25.0 (28.2) (n=38) 3) not assessed (12 months)
			Brief Symptom Inventory/Global Severity Index (BSI/GSI) (higher score = greater distress)	1) 1.3 (0.4) 2) 1.3 (0.4) 3) 1.4 (0.3)	**1) 0.4 (0.3)** **2) 0.3 (0.2)** 3) 1.5 (0.3) Groups 1 & 2 decreased over time and different than group 3 post tx	1) 0.4 (0.3) (n=41) 2) 0.2 (0.2) (n=38) 3) not assessed (12 months)
Northouse, 2005[29] 1) FOCUS (n=69) 2) Usual care (n=65)	Breast cancer	Recurrent or progressing, Stage 3 or 4	Composite of FACT-B and SF-36-mental health (converted to T scores with mean of 50 and SD of 10)	1) 51.9 (10.4) (n=NR) 2) 49.2 (9.4) (n=NR)	1) 51.1 (10.8) (n=NR) 2) 48.8 (10.7) (n=NR) 6 months (after booster phase of FOCUS) Group x time (p=0.79)	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Northouse, 2007[23] 1) Couples intervention (FOCUS) (n=129) 2) Usual care (UC) (n=134)	Prostate cancer	Newly diagnosed (65%); biochemical recurrence (14%); advanced (21%)	SF12-Mental (post-tx and follow up control for baseline scores)	1) NR 2) NR	1) 52.4 (6.5) (n=113) 2) 51.9 (6.6) (n=133) Effect size=0.08 (F=0.41, p=0.53)	8 months post-tx 1) 53.1 (7.1) (n=104) 2) 53.6 (7.1) (n=114) ES=-0.07 (F=0.01, p=0.96)
Porter, 2009[46] 1) Partner-assisted Emotional Disclosure, n=65 2) Education/ Support, n=65	Gastro-intestinal cancer	Stage II through IV	Profile of Moods States-Short Form (POMS-SF); score 0 to 90 with higher scores = "very much like this"	1) NR 2) NR	1) NR 2) NR No significant main effects or interaction ITT or completers (n=112)	
Schover, 2012[41] 1) Face-to-face counseling (FF) (n=60) 2) Internet-based counseling (WEB1) (n=55)	Prostate cancer	Localized prostate cancer ($T_{1-3}N_0M_0$)	Brief Symptom Inventory/General Severity Index (BSI/ GSI-18)	1) NR 2) NR Groups 1 and 2 combined: 4.6 (6.2)	NR	1) NR 2) NR Groups 1 and 2 combined: 4.6 (5.6) (12 months) p=NR, ns

*Last follow-up reported only if > 6 months post-treatment.
[1]Scale of -3 to +3; higher score indicates better well-being
d or ES=effect size, NR=not reported, ns=not statistically significant, SO=significant other

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Table 4. Cancer Studies – Quality of Life – Social Functioning

Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Social functioning subscale of the Medical Outcomes Scales SF-20	1) 75.2 (31.6) 2) 81.1 (22.1) p=ns (NR)	1) 74.8 (32.6) 2) 78.9 (27.4) p=ns (NR)	NR
Budin, 2008[30] 1) Psychoeducation (SE) +DM, n=66 2) Telephone counseling (TC) + DM, n=66 3) SE+TC+DM, n=58 4) Disease Management (DM), n=59	Breast cancer	Lesion with confirmed or strongly suspected diagnosis of cancer	Psychosocial Adjustment to Illness Scale (PAIS) – Domestic, Social, Vocational Environments (social adjustment) – higher score = poorer adjustment	Domestic Environment 1) 3.1 (3.3) 2) 3.6 (3.1) 3) 2.6 (3.0) 4) 3.1 (2.5)	Values NR Main group effect for patients (p=NR, ns) Main effect for time (p=NR, ns) Group x time interaction (p=NR, ns)	NR
				Social Environment 1) 4.0 (3.5) 2) 3.7 (3.6) 3) 2.7 (3.9) 4) 3.6 (4.0)	Values NR Main group effect for patients (p=0.92) **Main effect for time (p<0.0001)** Group x time interaction (p=0.63)	NR
				Vocational Environment 1) 3.4 (2.3) 2) 3.8 (3.5) 3) 3.3 (2.9) 4) 3.5 (3.6)	Values NR Main group effect for patients (p=0.52) Main effect for time (p=0.08) Group x time interaction (p=0.37)	NR
Giesler, 2005[22] 1) Cancer care intervention (n=48) 2) Standard care (n=51)	Prostate cancer (post-treatment)	T1a-T2c	SF-36 Short Form Health Survey (higher score = better functioning)	NR	Social Functioning d=0.00, p=0.99 1 month post-intervention, n=NR	Social Functioning d=0.21, p=0.35 6 months post-intervention (n=85)
Keefe, 2005[34] 1) Partner guided (n=41) 2) Usual care (n=37)	Cancer (any)	Eligible for hospice care; life expectancy ≤ 6 months	Functional Assessment of Cancer Therapy-General (FACT-G, v4) (scale 0-4, higher score = problem with function)	Social/family well-being NR; but reported p=ns between groups (n=78)	Social/family well- being 1) 3.6 (0.5) (n=28) 2) 3.3 (0.5) (n=28) p=0.13	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Kurtz, 2005[39] 1) Clinical nursing intervention (n=118) 2) Usual care (UC) (n=119)	Cancer (any)	Recent diagnosis of a solid tumor (breast, lung, other); early stage, 3%; late stage, 67.0%	MOS SF-36 (scale 0-100, higher score = fewer limitations on social activity)	Social Functioning 1) 57.0 (28.3) 2) 57.2 (30.0) n=NR	Social Functioning 1) 80.0 (26.8) 2) 69.8 (30.4) n=NR p=NR	
Porter, 2011[45] 1) Coping skills training (CST) (n=117) 2) Education (EDU) (n=116)	Lung cancer	Stage I-III	FACT-L: Social Well-Being	1) NR 2) NR	1) NR 2) NR Time x Treatment interaction: p=ns Time x Treatment x Cancer Stage interaction: p=ns	NR

*Last follow-up reported only if > 6 months post-treatment
[1]Scale of -3 to +3; higher score indicates better well-being
d or ES=effect size, NR=not reported, ns=not statistically significant

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Table 5. Cancer Studies – Quality of Life – Global Quality of Life

Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Functional Living Index-Cancer (FLIC)	1) 112.8 (17.8) 2) 118.0 (15.6) p=ns	1) 114.6 (20.6) 2) 120.8 (16.5) p=ns	NR
Kayser, 2010[32] 1) Partners in Coping Program (PICP) (n=24) 2) Standard social work services (SWSS) (n=23)	Cancer, breast	Early-stage, non-metastatic (diagnosed within past three months)	Functional Assessment of Cancer Therapy–Breast (FACT-B) (27 generic items (4 well-being subscales) + 9 items specific to breast cancer; scale 0-4; higher score = better quality of life)	Total well-being 1) 105.6 (13.4) (n=24) 2) 101.2 (20.7) (n=23)	Total well-being 1) 112.0 (12.2) (n=24) 2) 105.7 (19.7) (n=23) p=NR, ns ES=0.38	At 12 months (7 months post-tx) Total well-being 1) 119.0 (14.0) (n=24) 2) 111.3 (20.3) (n=23) p=NR, ns ES= 0.44
McMillan, 2007[40] 1) Standard care + friendly visits, n=109 2) COPE, n=111 3) Standard care, n=109	Cancer	Hospice care	Hospice Quality of Life Index (HQLI); scores from 0 to 280	NR	Values not reported Time, group, and group x time interaction (all ns) (30 day)	NR
Meyers, 2011[38] 1) SCEI (Simultaneous Care Educational Intervention) (n=348) 2) Usual care (n=128)	Cancer (any)	Relapsed, refractory or recurrent solid tumors or lymphoma enrolled onto phase 1 or 2, or phase 3 trials that compared therapy for advanced cancer	City of Hope QOL (higher score indicates better outcome; rescaled by authors 0-100 for comparison between pts and caregivers)	1) 61.7 (15.2) (n=331) 2) 64.4 (15.6) (n=118) p=0.11	NR	NR
Nezu, 2003[36] 1) Problem solving (individual) (n=45) 2) Problem solving with SO (n=43) 3) Wait list (n=44)	Cancer (any)	Diagnosed in past 6 months, currently receiving treatment, experiencing significant psychological distress	QL Index (higher score=better QOL)	1) 8.1 (2.3) 2) 8.7 (1.1) 3) 7.9 (1.8)	1) 8.3 (1.7) 2) 8.6 (1.0) 4) 8.3 (1.8) No changes over time and no difference between groups	1) 8.7 (2.0) (n=41) 2) 8.4 (1.8) (n=38) 3) not assessed (12 months)
Northouse, 2007[23] 1) Couples intervention (FOCUS) (n=129) 2) Usual care (UC) (n=134)	Prostate cancer	Newly diagnosed (65%); biochemical recurrence (14%); advanced (21%)	FACT-G (post-tx and follow up control for baseline scores)	1) NR 2) NR	1) 87.2 (10.6) (n=113) 2) 85.5 (10.3) (n=133) ES=0.16 (F=2.67, p=0.10)	8 months post-tx 1) 86.1 (10.9) (n=104) 2) 85.8 (10.7) (n=114) ES=0.03 (F=0.09, p=0.77)

*Last follow-up reported only if > 6 months post-treatment
[1]Scale of -3 to +3; higher score indicates better well-being
d or ES=effect size, NR=not reported, ns=not statistically significant, SO=significant other

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Table 6. Cancer Studies – Depression and Anxiety

Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Badger, 2007[9] 1) Telephone interpersonal counseling (TIP-C) (n=38) 2) Exercise (n=23) 3) Attention Control (n=36)	Breast cancer	Stage I-III currently receiving adjuvant treatment	Depression: CES-D (score ≥16 positive for depression)	1) 16.4 (1.7) 2) 13.3 (2.4) 3) 9.9 (1.8)	1) 14.1 (1.5) (n=38) 2) 11.3 (2.1) (n=21) 3) 9.4 (1.6) (n=33)	
			Anxiety: 8-item composite index using PANAS (4 items), SF-12 (1 item), and Index of Clinical Stress (3 items) (scale 1-10, higher score = more anxiety)	1) 4.4 (0.3) 2) 4.1 (0.5) 3) 3.1 (0.3)	1) 3.2 (0.3) (n=38) 2) 2.6 (0.4) (n=21) 3) 2.9 (0.3) (n=33)	
Badger, 2011[21] 1) Telephone Interpersonal Counseling (TIP-C) (n=36) 2) Health Education Attention Condition (HEAC) (n=35)	Prostate cancer	Currently undergoing or completed treatment w/in 6 months (Stage I=16%, II=9%, III=11%, IV=11%, unknown=53%)	Depression: CES-D	1) 11.4 (9.0) (n=36) 2) 12.4 (9.7) (n=35) p=ns (NR)	1) 11.3 (9.2) (n=34) 2) 9.1 (9.7) (n=32) Group change over time: 1) ns **2) p<0.05** **Group 1) vs 2): p<0.001 (favoring group 2)**	
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Depression: CES-D	1) 18.9 (8.3) 2) 15.7 (6.9)	1) 16.3 (6.9) 2) 18.9 (8.3)	
Giesler, 2005[22] 1) Cancer care intervention (n=48) 2) Standard care (n=51)	Prostate cancer (post-treatment)	T1a-T2c	Depression: CES-D NOTE: CES-D score was also a moderator	1) 6.9 2) 8.8	d=0.36, p=0.12 (7 months or post intervention; n=NR)	d=0.24, p=0.29 (n=85) (12 months)
Kozachik, 2001[35] 1) Cancer Care intervention (CCI) (n=61) 2) Usual care (UC) (n=59)	Cancer (46% breast, 24% lung, 21% colon, 9% other)	Newly diagnosed solid tumor (48% Stage I or II; 52% Stage III or IV)	Depression: CES-D (higher score = greater depression)	1) 12.6 (7.8) (n=61) 2) 10.8 (7.6) (n=59) p=NR	1) 8.8 (6.7) (n=40) 2) 8.0 (7.4) (n=49) p=NR	
Kurtz, 2005[39] 1) Clinical nursing intervention (n=118) 2) Usual care (n=119)	Cancer (any)	Recent diagnosis of a solid tumor (breast, lung, other); early stage, 33%; late stage, 67.0%	Depression: CES-D (20 items scored on a scale of 0-60; higher score = greater depressive symptoms)	1) 12.2 (9.0) 2) 13.6 (9.0) n=NR	1) 6.6 (7.7) 2) 9.9 (9.2) n=NR p=NR	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Manne, 2005[8], 2007[33] 1) Couple focused group (n=120) 2) Usual care (n=118)	Breast cancer	Early-stage, Eastern Cooperative Oncology Group performance status of 0 (*fully active*) or 1 (*restricted but ambulatory; able to carry out light or sedentary work*)	Depression: Mental Health Inventory (MHI–18) subscale (4 items)	1) 9.4 (2.9) (n=120) *1a) Attenders only* 9.1 (2.5) (n=78) 2) 9.1 (2.5) (n=118) p=NR	1) 8.6 (2.7) (n=120) *1a) Attenders only* 8.1 (2.3) (n=78) 2) 8.9 (2.8) (n=118) p=NR	6 months 1) 8.1 (3.0) (n=120) *1a) Attenders only* 7.7 (2.3) (n=78) 2) 9.0 (3.9) (n=118) p=NR
			Anxiety: Mental Health Inventory (MHI–18); subscale (4 items)	1) 10.3 (3.5) (n=120) *1a) Attenders only* 10.1 (3.6) (n=78) 2) 10.1 (3.6) (n=118) p=NR	1) 9.9 (3.4) (n=120) *1a) Attenders only* 9.5 (3.2) (n=78) 2) 9.8 (3.6) (n=118) p=NR	6 months 1) 9.2 (3.2) (n=120) *1a) Attenders only* 8.8 (3.0) (n=78) 2) 10.3 (4.97) (n=118) p=NR
McCorkle, 2007[28] 1) Standardized Nursing Intervention Protocol (SNIP) (n=62) 2) Usual care (UC) (n=64)	Prostate cancer	Newly diagnosed, undergoing radical prostatectomy	Depression: CES-D (higher score = greater depression)	1) 11.30 (6.84) (n=54) 2) 11.40 (7.40) (n=53) p=ns	3 months post-surgery 1) 7.74 (6.81) (n=54) 2) 6.35 (5.34) (n=53) p=ns	NR
Nezu, 2003[36] 1) Problem solving (individual) (n=45) 2) Problem solving with SO (n=43) 3) Wait list (n=44)	Cancer (any)	Diagnosed in past 6 months, currently receiving treatment, experiencing significant psychological distress	HRSD	1) 20.4 (4.2) 2) 21.3 (3.7) 3) 21.2 (3.3)	**1) 6.4 (3.8)** **2) 6.0 (2.7)** 3) 22.1 (4.5) Groups 1 & 2 decreased over time and different than group 3 post tx	1) 7.1 (4.2) (n=41) 2) 6.2 (3.0) (n=38) 3) not assessed (12 months)
Northouse, 2005[29] 1) FOCUS, n=69 2) Usual care, n=65	Breast cancer	Recurrent or progressing, Stage 3 or 4	Depression: Beck Hopelessness Scale (higher score indicates more hopelessness)	1) 4.5 (4.8) (n=NR) 2) 3.0 (4.0) (n=NR) p<0.05 (controlled for in subsequent analyses)	1) 4.2(4.9) (n=NR) 2) 3.5 (4.0) (n=NR) 6 months (after booster phase of FOCUS) Group x time F=1.72, p=0.19	
Northouse, 2007[23] 1) Couples intervention (FOCUS) (n=129) 2) Usual care (UC) (n=134)	Prostate cancer	Newly diagnosed (65%); biochemical recurrence (14%); advanced (21%)	Depression: Beck Hopelessness Scale (higher score indicates more hopelessness) (post-tx and follow up controlled for baseline scores)	1) NR 2) NR	1) 2.2 (2.4) (n=113) 2) 2.7 (3.1) (n=133) ES=0.17 (F=3.22, p=0.07)	8 months post-tx 1) 2.7 (2.7) (n=104) 2) 2.6 (3.1) (n=114) ES=0.01 (F=0.19, p=0.67)

Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Porter, 2011[45] 1) Coping skills training (CST) (n=117) 2) Education (EDU) (n=116)	Lung cancer	Stage I-III	Depression: Beck Depression Inventory (scores from 0-63)	1) NR 2) NR	1) NR 2) NR Time x Treatment Interaction: p=ns Time x Treatment x Cancer Stage interaction: *B*=-2.38; SE=0.86; p=0.006	NR
			Anxiety: State-Trait Anxiety Scale (STAI) (scores from 20-80)	1) NR 2) NR	1) NR 2) NR Time x Treatment Interaction: p= ns Time x Treatment x Cancer stage Interaction: *B*=-8.28; SE=2.85; p=0.006	
Stephenson, 2007[48] 1) Reflexology that included education for partner 2) Usual care plus special attention (reading a chosen selection to patient)	Cancer	Metastatic cancer	Anxiety: Visual Analog Scale for Anxiety	Anxiety 1) 5.0 2) 5.6	Anxiety 1) 1.9 2) 4.3 *F*=12.27, *p*<0.01, eta squared=0.13, moderate effect, adjusted for baseline anxiety	Subgroup: *patients with severe to moderate anxiety* (Pain ≥5) *Baseline:* 1) 7.9 (n=12) 2) 8.0 (n=20) *Post-treatment:* 1) 2.9 (n=12) 2) 5.5 (n=20) *F*=8.16, *p*=0.01, eta squared=0.15, moderate effect, adjusted for baseline anxiety

*Last follow-up reported only if > 6 months post-treatment
[1]higher score indicates higher level of emotion
[2]higher score indicates poorer adjustment
SO=significant other, d or ES=effect size, NR=not reported, ns=not statistically significant

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Table 7. Cancer Studies – Symptom Control/Management

Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Badger, 2011[21] 1) TIP-C (n=36) 2) HEAC (n=35)	Prostate cancer	Currently undergoing or completed treatment w/in 6 months (Stage I=16%, II=9%, III=11%, IV=11%, unknown=53%)	Multidimensional Fatigue Inventory (MFI) (Higher scores indicate more fatigue)	1) 26.8 (15.8) (n=36) 2) 28.2 (18.1) (n=35) p=ns (NR)	1) 27.1 (17.5) (n=34) 2) 24.5 (19.2) (n=32) Group change over time: 1) ns **2) p<0.05** **Group 1) vs 2): p<0.01 (favoring group 2)**	
Baucom, 2009[31] 1) Couple-based relationship enhancement (RE) (n=8 couples) 2) Treatment-as-usual (TAU) (n=6 couples)	Breast cancer	Stage I or II (recently diagnosed); no history of other breast cancer; no history of cancer within last 5 years	Brief Fatigue Inventory (BFI) (higher score = greater fatigue)	1) 4.9 (1.4) 2) 3.6 (2.1)	1) 2.9 (1.4) 2) 4.4 (1.9) n=NR d=1.67 (pre tx to post tx)	1) 3.0 (1.0) 2) 3.2 (2.3) (12 months) n=NR d=0.90 (pre tx to follow-up)
			Brief Pain Inventory (BPI) (higher score = greater pain)	1) 2.8 (2.0) 2) 2.0 (1.3)	1) 2.3 (1.4) 2) 2.7 (2.7) n=NR d=0.59 (pre tx to post tx)	1) 2.3 (1.5) 2) 2.4 (1.7) (12 months) n=NR d=0.53 (pre tx to follow-up)
			Rotterdam Symptom Checklist (RSC) (higher score = more symptoms)	1) 23.1 (4.5) 2) 24.5 (5.6)	1) 20.7 (3.8) 2) 27.2 (8.7) n=NR d=0.86 (pre tx to post tx)	1) 18.7 (2.4) 2) 23.8 (9.8) d=0.61 (pre tx to follow-up)
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Pain subscale of Medical Outcomes Scale (SF-20)	1) 57.0 (19.6) 2) 59.0 (18.2) p=ns (NR)	1) 56.5 (21.0) 2) 56.2 (18.1) p=ns (NR)	1) 54.0 (19.4) 2) 57.3 (16.4) p=ns (NR)
Budin, 2008[30] 1) Psychoeducation (SE) +DM, n=66 2) Telephone counseling (TC) + DM, n=66 3) SE+TC+DM, n=58 4) Disease Management (DM), n=59	Breast cancer	Lesion with confirmed or strongly suspected diagnosis of cancer	Side Effects Severity (subscale of BCTRI); scores from 1 to 60 with higher score = greater severity	1) NR 2) NR 3) 28.0 (1.4) 4) 27.7 (1.3) Post-surgery values	1) NR 2) NR 3) 25.7 (1.5) 4) 31.8 (1.4) **Main effect for time (p=0.002) but only SE+TC group had decrease** Differences ns (group or group x time)	
			Side Effect Distress (subscale of BCTRI) (scores of 0 to 60; higher score = more side effect distress)	1) NR 2) NR 3) 20.4 (2.0) 4) 19.5 (1.8) Post-surgery values	1) NR 2) NR 3) 18.7 (2.1) 4) 26.9 (2.0) Differences ns (group, time, or group x time)	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Campbell, 2007[26] 1) Coping Skills Training (CST) (n=20) 2) Usual Care (UC) (n=20)	Prostate cancer	Karnofsky Performance Status score >= 60	EPIC (0 to 100 scale; higher score = better QOL)	NR	Urinary total 1) 78.0 (SE=3.5) 2) 74.8 (SE=2.8) d=0.14, p=0.49 Bowel total 1) 86.3 (SE=2.5) 2) 82.4 (SE=2.0) d=0.31, p=0.24 Sexual total 1) 34.4 (SE=5.2) 2) 25.0 (SE=4.3) d=0.34, p=0.18 Hormonal total 1) 88.8 (SE=2.3) 2) 84.2 (SE=1.8) d=0.30, p=0.12	
Canada, 2005[43] 1) Couples Counseling (n=25) 2) Patient Counseling alone (n=26)	Prostate cancer	Localized prostate cancer; Stage A-C	International Index of Erectile Functioning (IIEF) Total score (higher score indicates better functioning)	1) NR 2) NR Groups 1 and 2 combined: 24.8 (18.7) (n=51)	1) NR 2) NR Groups 1 and 2 combined: 36.3 (17.3) (n=44)	6 months post-tx: 1) NR 2) NR Groups 1 and 2 combined: 31.1 (20.1) (n=39) Group 1 vs 2: p=NR, ns
Giesler, 2005[22] 1) Cancer care intervention (n=48) 2) Standard care (n=51)	Prostate cancer (post-treatment	T1a-T2c	SF-36 Short Form Health Survey-pain subscale (higher score = better functioning)	NR	Pain Index d=0.25, p=0.27 At 7 months (post-intervention, n=NR)	Pain Index d=0.23, p=0.30 At 12 months (n=85)
			Urinary function; Prostate Cancer Quality of Life Instrument (range 0-100, higher score = better outcome)	NR	Difference scores from baseline (1 month post-intervention) 1) 18.86 (19.71) 2) 22.35 (19.32) d=-0.18, p=0.44	Difference scores from baseline (6 mos post-intervention) 1) 19.55 (23.57) 2) 23.09 (22.34) d=-0.15, p=0.49
			Urinary bother; Prostate Cancer Quality of Life Instrument (range 0-100, higher score – better outcome)	NR	Difference scores from baseline (1 month post-intervention) 1) 27.55 (21.91) 2) 20.51 (21.72) d=0.32, p=0.19	Difference scores from baseline (6 mos post-intervention 1) 21.76 (30.93) 2) 25.84 (24.48) d=0.15, p=0.53

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Giesler, 2005[22] (continued)			Urinary limitation; Prostate Cancer Quality of Life Instrument (range 0-100^)	NR	Difference scores from baseline (1 month post-intervention) 1) 23.05 (23.26) 2) 17.58 (24.17) d=0.23, p=0.34	Difference scores from baseline (6 mos post-intervention) 1) 23.40 (24.14) 2) 17.19 (26.72) d=0.24, p=0.28
			Bowel bother; Prostate Cancer Quality of Life Instrument (range 0-100)^	NR	Difference scores from baseline^ (1 month post-intervention 1) 15.56 (24.51) 2) 12.18 (23.96) d=0.14, p=0.58	Difference scores from baseline (6 mos post-intervention) 1) 14.00 (23.67) 2) 10.22 (25.49) d=0.15, p=0.53
			Bowel function; Prostate Cancer Quality of Life Instrument (range 0-100)^	NR	Difference scores from baseline^ (1 month post-intervention 1) 6.79 (13.97) 2) 11.42 (19.26) d=-0.27, p=0.25	Difference scores from baseline (6 mos post-intervention) 1) 4.80 (16.91) 2) 8.35 (15.71) d=10.22, p=0.34
			Bowel limitation; Prostate Cancer Quality of Life Instrument (range 0-100)^	NR	Difference scores from baseline^ (1 month post-intervention 1) 6.01 (11.62) 2) 5.04 (13.88) d=0.08, p=0.76	Difference scores from baseline (6 mos post-intervention) 1) 2.80 (10.99) 2) 3.27 (10.60) d=0.04, p=0.86
			Sexual function; Prostate Cancer Quality of Life Instrument (range 0-100)^	NR	Difference scores from baseline^ (1 month post-intervention) 1) 21.90 (22.72) 2) 12.60 (26.33) d=0.38, p=0.10	Difference scores from baseline (6 mos post-intervention) 1) 25.26 (26.60) 2) 15.32 (27.77) d=0.37, p=0.10
			Sexual bother; Prostate Cancer Quality of Life Instrument (range 0-100)^	NR	Difference scores from baseline^ (1 month post-intervention) 1) 5.54 (23.74) 2) -0.20 (19.67) d=0.26, p=0.25	Difference scores from baseline (6 mos post-intervention) 1) 9.21 (29.63) 2) 3.3 (25.35) d=0.21, p=0.34
			Sexual limitation; Prostate Cancer Quality of Life Instrument (range 0-100^)	NR	Difference scores from baseline^ (1 month post-intervention) 1) 10.68 (15.93) 2) 3.80 (15.05) d=0.45, p=0.05	Difference scores from baseline (6 mos post-intervention) 1) 12.35 (17.28) 2) 3.11 (19.61) d=0.50, p=0.02

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Gustafson, 2013[44] 1) Standard care plus CHESS (n=144) 2) Standard care plus Internet (n=141)	Nonsmall Cell Lung Cancer	16% Stage IIIA, 18% Stage IIIB, 66% Stage IV 71% ECOG 0 or 1 30% ECOG 2, 3, or 4	Caregiver-reported patient symptom distress (7 physical symptoms, rated 0 (absence) to 10 (worst possible); range=0-70)	NR	**1) 17.0 (SE=1.8) (n=NR)** **2) 22.3 (SE=1.9) (n=NR)** **d=0.46, p=0.005** scores adjusted for pretest ESAS score, study site, caregiver-patient relationship, and caregiver race	NR
Keefe, 2005[34] 1) Partner guided (n=41) 2) Usual care (n=37)	Cancer (any)	Eligible for hospice care; life expectancy ≤ 6 months	Pain intensity – Brief Pain Inventory (BPI); scale 0-10 with higher score indicating greater pain intensity	Week's usual pain (BPI): values NR; reported p=ns between groups (n=78) Week's worst pain (BPI): values NR; reported p=ns between groups (n=78)	Week's usual pain (BPI): 1) 4.6 (2.0) (n=28) 2) 5.2 (2.0) (n=28) p=0.28 Week's worst pain (BPI): 1) 6.5 (2.2) (n=28) 2) 6.9 (2.2) (n=28) p=0.37 BOTH adj for pre-tx scores	NR
McCorkle, 2007[28] 1) Standardized Nursing Intervention Protocol (SNIP) (n=62) 2) Usual Care (UC) (n=64)	Prostate cancer	NR	CARES (Sexual Function); 8 items (scale 0 – 4; higher score = poorer function)	1) 9.82 (5.48) (n=54) 2) 12.67 (7.03) (n=53) p=ns This outcome first assessed at 1 month post-surgery (or 1 month into the intervention period)	1) 12.96 (6.20) (n=54) 2) 10.86 (6.30) (n=53) p=ns 1 month post intervention	NR
McMillan, 2007[40] 1) Standard care + friendly visits, n=109 2) COPE, n=111 3) Standard care, n=109	Cancer	Hospice care	Memorial Symptom Assessment Scale (MSAS); scores from 0 (no distress) to 90 (very much distress)	NR	Values NR (30 day) Time and group main effects (ns) **Group x time interaction (p=0.009); Group 2 vs. 3; p=0.013**	
			Numeric rating scale (NRS) for pain	NR	Values NR (30 day) Time, group, and group x time interaction (all ns)	NR
			Dyspnea intensity scale	NR	Values NR (30 day) Time, group, and group x time interaction (all ns)	NR
			Constipation assessment scale (CAS)	NR	Values not reported Time, group, and group x time interaction (all ns) (30 day)	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Mishel, 2002 [24] 1) Uncertainty management direct (n=NR) 2) Uncertainty management supplemented (n=NR) 3) Usual care (n=NR)	Prostate cancer	TNM staging classification 8% T1 61% T2 27% T3 4% unknown	# of symptoms reported	1) 7.7 (2.8) (n=NR) 2) 7.4 (3.0) (n=NR) 3) 7.6 (2.7) (n=NR)	1) 6.2 (2.8) (n=NR) 2) 5.7 (2.9) (n=NR) 3) 6.5 (2.7) (n=NR) (assessed at baseline + post-intervention - 8 weeks after intervention) p=NR Sub group analyses: White men in intervention grps had sign decrease in symptoms compared to white men in control group from baseline to post-intervention. AA men in tx direct group compared to AAs in control grp from post-inter. to follow up had sign decrease in symptoms	NR
			Control over urine flow (scale 1-5; higher score = more improvement in the symptom)	1) 3.6 (1.2) (n=NR) 2) 3.6 (1.2) (n=NR) 3) 3.9 (1.2) (n=NR)	1) 4.5 (0.7) (n=NR) 2) 4.6 (0.8) (n=NR) 3) 4.4 (0.7) (n=NR) (8 weeks post- intervention) p=NR NOTE: Interv. grps vs. control showed more control over urine flow ($F_{2, 212}$=3.7, p=.03)	NR
			Ability to have an erection (scale 1-5; higher score = more improvement)	1) 1.9 (1.2) (n=NR) 2) 1.7 (1.3) (n=NR) 3) 1.9 (1.2) (n=NR)	1) 2.4 (1.0) (n=NR) 2) 2.4 (1.2) (n=NR) 3) 2.4 (1.1) (n=NR) (8 weeks post- intervention) p=NR	NR
			Overall Symptom intensity (scale 1-5; higher score = more improvement in the symptom)	1) 1.9 (0.4) (n=NR) 2) 1.8 (0.4) (n=NR) 3) 1.8 (0.4) (n=NR)	1) 1.7 (0.3) (n=NR) 2) 1.5 (0.3) (n=NR) 3) 1.7 (0.3) (n=NR) (8 weeks post- intervention) p=NR	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Mishel, 2002[24] (continued)			Satisfaction with sexual function (scale 1-5; higher score = more improvement)	1) 2.2 (1.4) (n=NR) 2) 1.6 (1.5) (n=NR) 3) 2.2 (1.4) (n=NR)	1) 2.2 (1.3) (n=NR) 2) 2.4 (1.4) (n=NR) 3) 2.2 (1.3) (n=NR) (8 weeks post- intervention) p=NR AA men in tx supplemented group compared to AAs in control grp from baseline to post-inter. had higher satisfaction with sexual functioning ($F_{1,186}$=6.57, p=0.01)	NR
Nezu, 2003[36] 1) Problem solving (individual) (n=45) 2) Problem solving with SO (n=43) 3) Wait list (n=44)	Cancer (any)	Diagnosed in past 6 months, currently receiving treatment, experiencing significant psychological distress	CARES (Total Score, higher=more severe)	1) 2.4 (0.4) 2) 2.4 (0.4) 3) 2.4 (0.4)	**1) 0.8 (0.3)** **2) 0.7 (0.4)** 3) 2.4 (0.3) Groups 1 & 2 decreased over time and different than group 3 post tx	1) 0.8 (0.4) (n=41) 2) 0.6 (0.4) (n=38) 3) not assessed (12 months)
Northouse, 2007[23] 1) Couples intervention (FOCUS) (n=129) 2) Usual care (UC) (n=134)	Prostate cancer	Newly diagnosed (65%); biochemical recurrence (14%); advanced (21%)	Expanded Prostate Cancer Index Composite (EPIC) Urinary Symptoms (higher score = better prostate-specific symptom outcome) *Post-tx and follow up controlling for baseline scores*	1) NR 2) NR	1) 86.9 (12.7) (n=113) 2) 81.6 (13.8) (n=133) d=0.19 (F=2.86, p=0.09)	8 months post-tx 1) 84.5 (12.5) (n=104) 2) 83.9 (13.6) (n=114) d=0.05 (F=0.19, p=0.67)
			EPIC Bowel Symptoms	1) NR 2) NR	1) 89.5 (7.0) (n=113) 2) 90.3 (8.4) (n=133) d=-0.10 (F=0.33, p=0.57)	8 months post-tx 1) 89.6 (7.4) (n=104) 2) 90.5 (8.0) (n=114) d=0.12 (F=0.59, p=0.44)
			EPIC Sexual Symptoms	1) NR 2) NR	1) 28.5 (21.4) (n=113) 2) 29.3 (20.9) (n=133) d=-0.04 (F=0.13, p=0.72)	8 months post-tx 1) 30.4 (21.7) (n=104) 2) 31.3 (21.1) (n=114) d=-0.04 (F=0.14, p=0.71)
			EPIC Hormonal Symptoms	1) NR 2) NR	1) 83.7 (9.9) (n=113) 2) 83.8 (10.4) (n=133) d=0.01 (F=0.01, p=0.95)	8 months post-tx 1) 83.9 (10.0) (n=104) 2) 85.2 (10.3) (n=114) d=-0.13 (F=0.85, p=0.36)

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Porter, 2011[45] 1) Coping skills training (CST) (n=117) 2) Education (EDU) (n=116)	Lung cancer	Stage I-III	BPI (higher score=greater pain intensity)	1) NR 2) NR	1) NR 2) NR Time x Treatment Interaction: p=ns Time x Treatment x Cancer Stage interaction: p=ns	NR
			FACT-L: Lung Cancer Symptoms (shortness of breath, coughing, weight loss, loss of appetite)	1) NR 2) NR	1) NR 2) NR Time x Treatment Interaction: p=ns Time x Treatment x Cancer Stage interaction: p=ns	NR
Schover, 2012[41] 1) Face-to-face counseling (FF) (n=60) 2) Internet-based counseling (WEB1) (n=55)	Prostate cancer	Localized prostate cancer ($T_{1-3}N_0M_0$)	International Index of Erectile Function (IIEF) (higher score indicates better function)	1) 26.4 (18.2) (n=39) 2) 27.4 (17.3) (n=33)	1) 34.4 (22.2) (n=30) 2) 31.3 (20.4) (n=27)	1) 33.6 (23.1) (n=26) 2) 34.5 (22.5) (n=25) (12 months) **Group 1) improvement over time: p<0.0001, d=0.35** **Group 2) improvement over time: p=0.04, d=0.35** Group 1) vs 2) p=NR
			% men achieving near normal erectile function over time (IIEF Erectile Function subscale ≥22)	1) 12% 2) 15%	NR	1) 32% 2) 31% **Group 1 and 2 over time: p<0.005** Group 1) vs 2) p=NR, ns

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Symptom Assessment	Baseline	Post-Treatment	Follow-up* (time assessed)
Stephenson, 2007[48] 1) Reflexology that included education for partner (n=42) 2) Usual care plus special attention (reading a chosen selection to patient) (n=44)	Cancer	Metastatic cancer	Pain (reported using BPI or SF-MPQ)	1) 3.2 (n=42) 2) 4.5 (n=44)	1) 2.1 (n=42) 2) 4.4 (n=44) *Decrease in pain from pre to post* 1) 1.1 2) 0.1 F=11.74, p<0.01, eta squared=0.12, moderate effect, adjusted for baseline pain Subgroup: *patients with severe to moderate pain* (Pain ≥5) *Baseline:* 1) 7.3 (n=12) 2) 7.7 (n=20) *Post treatment:* 1) 4.6 (n=12) 2) 7.2 (n=20) *Decrease in pain from pre to post* 1) 2.7 (n=12) 2) 0.5 (n=20) *F*=8.41, *p*<0.01, eta squared=0.23, large effect, adjusted for baseline pain	

*Last follow-up reported only if > 6 months post-treatment

[1]Univariate analyses of covariance, with baseline measures of HbA1c, FBP and diabetes knowledge as covariates (no significant differences between groups at baseline)

^Larger difference = better outcome

d or ES=effect size; NR=not reported; ns=not statistically significant, SO=significant other

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Table 8. Cancer Studies – Relationship Adjustment

Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Baucom, 2009[31] 1) Couple-based relationship enhancement (RE) (n=8 couples) 2) Treatment-as-usual (TAU) (n=6 couples)	Breast cancer	Stage I or II (recently diagnosed); no history of other breast cancer; no history of cancer within last 5 years.	Quality of Marriage Index (QMI) (higher score = greater quality)	1) 34.0 (13.6) 2) 40.8 (6.0)	1) 39.3 (4.7) 2) 42.2 (4.1) (n=NR) d=0.48 (pre tx to post tx)	1) 39.7 (3.5) 2) 40.2 (5.1) (12 months) (n=NR) d=0.77 (pre tx to follow-up)
Blanchard, 1996[37] 1) Spouse directed problem-solving intervention (n=25 couples) 2) Treatment-as-usual (TAU) (n=32 couples)	Any cancer	Diagnosed more than 3 months before recruitment but patient not eligible for hospice	Dyadic Adjustment Scale (DAS)	1) 35.2 (3.5) 2) 34.6 (3.6) p=ns (NR)	1) 34.8 (3.8) 2) 34.3 (3.9) p=ns (NR)	
Canada, 2005[43] 1) Couples Counseling (n=25) 2) Patient Counseling alone (n=26)	Prostate cancer	Localized prostate cancer; Stage A-C	Abbreviated Dyadic Adjustment Scale (A-DAS)	1) NR 2) NR Groups 1 and 2 combined: 25.3 (4.8) (n=51)	1) NR 2) NR Groups 1 and 2 combined: 25.3 (4.7) (n=44)	6 months post-tx: 1) NR 2) NR Groups 1 and 2 combined: 24.8 (4.9) (n=39) Group 1 vs 2: p=NR, ns
Giesler, 2005[22] 1) Cancer care intervention (n=48) 2) Standard care (n=51)	Prostate cancer (post-treatment)	T1a-T2c	DAS - Dyadic Cohesion	NR	d=0.19, p=0.43 (7 months or post intervention; n=NR)	d=0.07, p=0.75 (12 months; n=85)
			DAS - Dyadic Satisfaction	NR	d=0.24, p=0.31 (7 months or post intervention; n=NR)	d=0.37, p=0.10 (12 months; n=85)
Manne, 2011[27] 1) IET (n=37) 2) Usual Care (n=34)	Prostate Cancer	Diagnosed within past year; 15% stage 1, 85% stage 2	DAS (Relationship Functioning)	NR	NR; ns treatment effects	NR
McCorkle, 2007[28] 1) Standardized Nursing Intervention Protocol (SNIP) (n=62) 2) Usual care (UC) (n=64)	Prostate cancer	Newly diagnosed, undergoing radical prostatectomy	CARES (Marital Interaction) (higher score=poorer function)	1 month post-surgery 1) 2.69 (4.21) (n=54) 2) 3.58 (4.56) (n=53) p=ns (between groups)	3 months post-surgery 1) 5.92 (7.55) (n=54) (p=0.002 from initial value) 2) 5.23 (6.69) (n=53) Group effect: p=ns	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Porter, 2009[46] 1) Partner-assisted Emotional Disclosure, n=65 2) Education/ Support, n=65	Gastro-intestinal Cancer	Stage II through IV	Quality of Marriage Index (QMI)	1) NR 2) NR	1) NR 2) NR ITT: Group x time interaction (*B* = -.07, p=0.02); increase in relationship quality for Group 1, decrease for Group 2 Completers (n=112): Group x time interaction (*B* = -.08, p=0.02)	
Schover, 2012[41] 1) Face-to-face counseling (FF) (n=60) 2) Internet-based counseling (WEB1) (n=55)	Prostate cancer	Localized prostate cancer ($T_{1-3}N_0M_0$)	Dyadic Adjustment Scale (A-DAS)	1) NR 2) NR Groups 1 and 2 combined: 24.4 (4.7)	NR	1) NR 2) NR Groups 1 and 2 combined: 24.6 (4.5) (12 months) p=NR, ns

*Last follow-up reported only if > 6 months post-treatment; d or ES=effect size; NR=not reported; ns=not statistically significant

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Table 9. Memory-Related Disorders – Study Characteristics

Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Bass, 2003[56] Funding Source: Foundation, Government Condition: Dementia, Alzheimer's disease, memory loss **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent (education, and coaching/care consultation to enhance competence and self-efficacy)	N=157 (of 182 randomized) Age (years): NR Gender (% male): NR Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: medical records of health plan members Family Characteristics: Relationship to patient: *"Primary family caregiver"* Age (years): NR Gender (% female): NR Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: diagnosis of dementia or symptom code indicating memory loss; age 55 or older; non-nursing home resident; living in area served by Cleveland Area Alzheimer's Association Exclusion: NR	Intervention (n=109): Integration of services from managed care system & Alzheimer's Association care consultation service; standardized protocol; worked with families to create individualized plan of care; plan then completed by patients, family members, Association staff/volunteers; care consultants followed-up biweekly then at 1- and 3-month intervals or as needed (i.e., in difficult periods may have daily contact); average, care consultants have 12 direct contacts with patients and caregivers per year Comparator (n=73): Usual care within managed care medical system; families able to contact Alzheimer's Association and use any individual services offered other than care consultation Length of Follow-up: 1 year intervention only	***Utilization:*** a. # hospital admissions past 12 months (MR) b. # ER visits past 12 months (MR) c. # physician visits past 12 months (MR) MR=Medical Record report Outcomes assessed at baseline and post-treatment ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: providers not told of treatment group Intention-to-treat analysis (ITT): no (only analyzed data from those who allowed medical record access – see below) Withdrawals/dropouts adequately described: yes Treatment adherence: treatment dropouts (from sessions) - NR 157/182 (86%) completed follow-up assessment 120/182 (66%) allowed medical record access Treatment integrity: NR **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Belle, 2006[55] REACH II Funding Source: Government Condition: Alzheimer's disease or related disorders **KQ1 ☐ KQ2 ☒** **Intervention Type:** Education, role-playing, skills training, stress management, support	N=518 (of 642 randomized) Age (years): 79 Gender (% male): 35 Race/ethnicity (%): *Hispanic/Latino 32; white 35; black/African American 32 (used stratified randomization)* Marital Status (%): *married 59* Education (%): *<HS 16; HS 20; >HS 50* Veterans (%): NR Recruitment Method: memory disorder and primary care clinics, social service agencies, churches, community centers, brochures, media, targeted newsletters, presentations Family Characteristics: Relationship to patient (%): *Spouse 38; child 41; sibling 2* Age (years): 61 Gender (% female): 85 Race/ethnicity (%): see above Education (%): <HS 16; HS 20; >HS 50 Veterans (%): NR	Inclusion: *Care Recipient* – diagnosed Alzheimer's disease or related disorder *Caregiver* - Hispanic or Latino, white/ Caucasian, or black or African-American race or ethnicity; 21 years or older; living with or sharing cooking facilities with care recipient; providing care for relative with diagnosed Alzheimer's disease or related disorders at least 4 hrs/day for past 6 months; reported distress associated with caregiving (at least 2 of 6 items); have telephone; will remain in area for at least 6 months; competent in English or Spanish Exclusion: *Care Recipient* – bedbound, MMSE score of 0 *Caregiver* – involved in another caregiver intervention study; participated in REACH I; illness preventing 6 months participation	Intervention (n=261): education, skills training, problem solving, support directed at 5 target areas – depression, burden, self-care and healthy behaviors, social support, problem behaviors; 12 session (9 1.5-hr in-home + 3 0.5-hr telephone) plus 5 telephone support group sessions over 6 months; study provided resource notebooks and telephones with display screens; delivered by certified interventionists; unclear if manualized; tailored to meet individual needs Control (n=257): mailed educational materials; 2 <15-min telephone "check-in" calls at 3 and 5 months after randomization; invited to workshop on dementia & caregiving after 6 month assessment Length of Follow-up: 6 month intervention only	***Quality of life:*** a. Single question about whether participation in study helped improve the care recipient's life ("not at all," "some," or "a great deal") ***Symptom control/ management:*** a. Change in problem behaviors (3 items from Revised Memory and Behavior Problem Checklist – memory, depression, & disruption; scored from1 [substantial improvement] to 5 [substantial decline] (PR) ***Utilization:*** a. Institutional placement (permanent institutionalization) (PR) Outcomes assessed at baseline and 6 months (post tx) ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 60% of intervention group completed all 12 sessions; 5% did not complete any session; 90% of control group received both telephone contacts; 3% did not receive any Treatment integrity: Certified interventionists; intensive training (reading materials, role-playing, practice); first session audiotaped and feedback provided (plus additional audiotaping during study); delivery assessment form for each contact **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Bourgeois, 2002[72] Funding Source: Government Condition: Alzheimer's disease **KQ1 ☐ KQ2 ☒** **Intervention Type:** a. Patient change group: skill-based; educational, problem solving (to change patient behavior) b. Self-change group: skill-based, educational, problem solving (to change caregiver coping behavior)	N=63 (of 93 caregivers randomized) Age (years): 75 Gender (% male): 54 Race/ethnicity (%): *white 87; African-America 13; other 0* Marital Status (%): *Married/cohabiting: 100* Education (%): NR Veterans (%): NR Recruitment Method: professional referral from geriatric and Alzheimer's centers and self-referral (via media notices) Family Characteristics: Relationship to patient: *Spouse (primary caregiver)* Age (years): 73 (primary), 48 (secondary) Gender (% female): 54 (primary), 63 (secondary) Race/ethnicity (%): *white 87 (primary and secondary); African-American 13 (primary and secondary); other 0* Education (%): NR Veterans (%): NR	Inclusion: 45 years or older; met ADRDA-NINCDS criteria for probable Alzheimer's disease; score of 20 or less on MMSE within 4 weeks of enrollment; average score of at least 1.0 (mild behavioral disturbance) on Global Rating Item of Behave-AD; stable medical condition; reside with spousal caregiver who had no major debilitating health problems, who agreed to random assignment, and who spent at least 8 daytime hours/day in home with patient; had secondary caregiver (adult relative, neighbor, or friend) who spent at least 4 hours/ week in direct contact and who would complete subsample of assessment battery Exclusion: Documented history of alcoholism, schizophrenia, Parkinson's disease, or head trauma with cognitive sequelae; MRI or CAT scan evidence of focal stroke	Intervention #1 (n=22): Patient-change – behavior management plan for frequent and stressful problem behaviors Intervention #2 (n=21): Self-change – strategies for caregiver coping Comparator (n=20) Visitation control – general information about caregiver's concerns; no skills training content All caregivers had 2 1-hour home visits in 1st week, attended a 3-hour workshop (different workshops for each group) in 2nd week, and had a 1-hour home visit each week during weeks 3-12; procedures manual for all groups Length of Follow-up: 12 week intervention	***Symptom control/ management:*** a. Behave-AD Scale (PR) -Total Score -Aggressivity/Activity Disturbance Subscale -Psychosis/Delusion Subscale b. Frequency of patient problem behaviors (PR) Outcomes assessed post tx, and at 3 months and 6 month follow-up ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: yes (outcomes assessment) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 100% attended workshop 96-99% of intervention visits were conducted 68% (63/93) completed study Treatment integrity: notes written at end of each visit reviewed by investigator and at staff meetings **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Brodaty, 2009[59] Funding Source: Industry Condition: Alzheimer's disease **KQ1 ☒ KQ2 ☐** **Intervention Type:** Emotional	N=52 (US study group only) Age (years): 73 Gender (% male): 65 Race/ethnicity (%): NR Marital Status (%): *married/cohabiting* 100 Education (%): *HS or less NR; Post HS NR* Veterans (%): NR Recruitment Method: recruited from the Silberstein Aging & Dementia Research Center at the New York University School of Medicine Family Characteristics: Relationship to patient: *Spouse* Age (years): 70 Gender (% female): 64 Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: stable physical health for previous year; meet National Institute of Neurological and Communicative Diseases and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) and the Diagnostic and Statistical Manual of Mental Disorders 4th Edition criteria for probable Alzheimer's disease (AD); Global Deterioration Scale score of 4-5 at time of enrollment; no contraindication to taking donepezil; stable with other medications; able to give informed consent (or not object to participating); be community dwelling with spouse; be the spouse & primary caregiver of the patient [caregiver] Exclusion: previously received formal caregiver counseling [caregiver]	Intervention (n=26): donepezil + standard services + psychological caregiver intervention; caregivers received 5 counseling sessions w/ in 3 months of enrollment (1 individual session with spouse, 3 counseling sessions with family members invited by caregiver, & 1 more individual session with spouse); content of sessions individualized & could include education about AD, information about community resources, family issues (helping caregiver & patient), and management of difficult behavior; manualized; based on NYU intervention Comparator (n=26): donepezil + standard services (resource information, emergency help, & routine service); no formal structured counseling sessions Length of Follow-up: 5.4 yr (range: 5 mo – 8.5 yr)	***Physical functioning:*** a. Death (PR); follow-up = 8.5 years ***Utilization:*** a .Nursing home placement (PR); follow-up = 8.5 years ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear – "dyads were randomly assigned by lottery", no other details Blinding: yes – "caregivers and patients were assessed by independent raters… Strenuous efforts were made to keep rates blind to group assignment" Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: no – only withdrawals from the UK group are reported Treatment adherence: NR Treatment integrity: unclear – "Principal investigators at each site were involved in regular meetings with counselors as well" **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Burgener, 1998[65] Funding Source: NR Condition: Alzheimer's or multi-infarct dementia; moderate to severe **KQ1 ☒ KQ2 ☒** **Intervention Type**: Educational, behavioral	N=47 (of 54 randomized) Age (years): 78 Gender (% male): 47 Race/ethnicity (%): NR Marital Status (%): NR Education (mean): 12 years Veterans (%): NR Recruitment Method: NR Family Characteristics: Relationship to patient: *"Primary caregiver"* Age (years): 67 Gender (% female): 74 Race/ethnicity (%): NR Education (mean): 13 years Veterans (%): NR	Inclusion: Alzheimer's/ multi-infarct dementia Exclusion: NR	Intervention (n=11): Caregiver Education/ Behavioral Intervention; script and videotape for education information and booklet for behavioral information; one 90 min session Comparator (n =12): Education component only; one session Comparator (n=12): Behavioral component only; one session Comparator (n =12): Comparison group (not described) Length of Follow-up: 6 months after study entry	***Physical functioning:*** a. Instrumental Activities of Daily Living b. Social Competence scale (SCS) c. Older Americans Resources and Services (OARS) ***Symptom control/ management:*** a. Dementia Behavior Disturbance Scale (DBDS) All outcomes assessed at baseline and 6 months ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: no Treatment adherence: NR Treatment integrity: NR **Study quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Burns, 2003[51] REACH Funding Source: Government Condition: Alzheimer's and related dementias **KQ1 ☐ KQ2 ☒** **Intervention Type:** a. Behavior Care (management of care recipient's behavioral problems) b. Enhanced Care (Behavior Care plus skills training for caregiver's well-being)	N=76 (of 167 randomized) Age (years): 80 Gender (% male): 55 Race/ethnicity (%): black 42 Marital Status (%): NR Education (mean): 11 years Veterans (%): NR (included VA patients) Recruitment Method: recruited from physicians' offices (14 sites, 19 physicians) in Memphis Family Characteristics: Relationship to patient: *Spouse 50%, child 38%, other 12%* Age (years): 65 Gender (% female): 82 Race/ethnicity (%): black 42 Education (mean): 13 years Veterans (%): NR	Inclusion: *Care recipients* – medical diagnosis of probable Alzheimer's disease or related disorders or score <24 on MMSE; at least 1 limitation in basic ADLs or 2 dependencies in IADLs as reported by caregiver *Caregivers* - over age 21; live with relative with Alzheimer's disease or related dementia; provided minimum of 4 hrs supervision or direct care per day for at least past 6 months Exclusion: *Caregivers* – involved in another caregiver study; care recipient had terminal or severe illness or disability that would prohibit them from participating in study	Behavior Care (n=85): Improving caregiver's management of care recipient's behavior problems; 25 pamphlets addressing particular behaviors; possible triggers and coping strategies for specific behaviors; sessions no more than 30 min Enhanced Care (n=82): Behavior Care plus improving caregiver's well-being in response to problem behaviors (stress-behavior management – cognitive behavioral skills training); no more than 60 min Both interventions: interventionists met with caregiver during scheduled primary care visits (every 3 months); telephone contacts (10 min or less) with caregivers 2X/month for 1st 6 months; then 1X/ month Length of Follow-up: 2 year active intervention	***Symptom control/ management:*** a. Behavioral functioning: Memory and Behavior Problem Checklist (PR) All outcomes assessed at baseline and every 6 months for 2 years ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: outcome assessors masked to intervention assignment Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: contact time shorter than planned for both groups (3 hrs for Behavior Care, 4 hrs for Enhanced Care) Treatment integrity: NR **Study quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Camberg, 1999[11] Funding Source: Government and University Condition: Alzheimer's disease and dementia **KQ1 ☒ KQ2 ☒** **Intervention Type:** Emotional	N=54 randomized Age (years): 83 Gender (% male): 11 Race/ethnicity (%): *white 95* Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: nine nursing homes in Massachusetts and New Hampshire (including one VA) Family Characteristics: Relationship to patient: *"family member"* Note: 75% of 54 family members contacted were able to be "callers"; for 14 patients with family members unavailable or unwilling to make SimPres recording, an experienced SimPres staff person conducted recorded conversation Age (years): NR Gender (%female): NR Race/ethnicity (%): NR Education (%): NR Veterans (%): NR	Inclusion: documented diagnosis of ADRD; age ≥50 years; presence of ≥1 agitated behavior/ day (Cohen-Mansfield Agitation Inventory Scale (SCMAI) short form) or 1 indication of withdrawn behavior ("sounding sad" or "crying" that occurred at least "often"); or "seldom" interested in activities, social interaction (from Multidimensional Observation Scale for Elderly Subjects); medically stable; resident in current nursing home for ≥3 months; no planned discharge; verbal interactive capacity Exclusion: subjects who did not tolerate listening through headphones for 5 minutes to a non-personalized interactive conversation tape, or known to have a severe hearing impairment or premorbid history of psychiatric illness	*Crossover design –all patients received each treatment for 17 days over a 4-week course, followed by a 10-day washout period* Intervention (n=54): Simulated Presence (SimPres) – Information packet plus coaching; personalized, interactive audio tape; nursing staff used audio tape ≥2x/day (M-F) in place of usual intervention when patient exhibited agitated behavior; tape played using headset and auto-reverse tape recorder Comparator A (n=54): "placebo" audio tape; same study procedures but recording contained non-family voice reading emotionally neutral articles from newspaper Comparator B (n=54): Usual care Length of Follow-up: NR	***Symptom control/ management:*** a. SCMAI agitated behaviors scale **Proxy report method 3 (weekly staff surveys)** Measurements occurred during the 17 days of treatments ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear – Latin Squares crossover design Blinding: double blinded staff were blinded to which tape was used for treatment, observers were blinded to study intervention Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: no Treatment adherence: dropouts/ withdrawals not reported Treatment integrity: yes; study monitors were assigned to spend 20 hours/week at each facility to ensure adherence to the protocol and to provide feedback to the staff **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Chang, 1999[71] Funding Source: Foundation Condition: Dementia (MMSE<21); significant dressing and eating problems **KQ1 ☒ KQ2 ☐** **Intervention Type:** Cognitive-behavioral	N=65 (of 87 recruited) Age (years): 79 Gender (% male): NR Race/ethnicity (%): NR Marital Status (%): NR Education (years): 13 Veterans (%): NR Recruitment Method: Alzheimer's association; local support groups; Alzheimer's clinics Family Characteristics: Relationship to patient: *Spouse 85%; daughter 15%* Age (years): 67 Gender (% female): 100 Race/ethnicity (%): w*hite 79; African-American 16* Education (years): 14 Veterans (%): NR	Inclusion: dementia; significant dressing and eating problems (Zarit's memory/ behavioral scale 3 or 4 on tasks of dressing and eating); MMSE <21; both members of dyad English speaking; access to videotape player and telephone Exclusion: none stated	Intervention (n=34): Nurseline video-assisted modeling program (NVAMP); videotape showing assisted modeling behavior (eating and dressing) & Nurseline support (8 weekly guideline-based structured calls for reinforcement, problem solving) Comparator (n=31): 8 weekly calls to assess caregiver general well-being; no specific strategies for eating or dressing; referred caregiver to other resources if needed Length of Follow-up: 4 weeks post-tx	***Physical functioning:*** a. Subscale of Functional Rating Scale (data not provided) (PR, 8 weeks [post tx]) ***Symptom control/ management:*** a. Functional Rating Scale for the Symptoms of Dementia – Overall and Behavioral subscore(PR, 8 weeks [post tx]) ☒ **Negative caregiver outcomes reported** (decreased caregiver satisfaction over time)	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 25% dropped out of study; dropouts had lower baseline MMSE (p=0.04) Treatment integrity: NR **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gerdner, 2002[69] Funding Source: Government Condition: Alzheimer's disease (67%) or a related disorder (moderate to severe cognitive impairment with Global Deterioration Scale (GDS) scores from 4-6) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Educational, skill-based	N=237 (of 241 randomized) Age (years): NR Gender (% male): NR Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: geriatric assessment clinics & Alzheimer's disease centers affiliated with 1 of 8 universities (brochures, church bulletins, radio, newspaper ads, service clubs, caregiver support groups, and word of mouth) Family Characteristics: Relationship to patient: *Spouse 65%; non-spouse 35%; caregiver residing with care recipient 97%* Age (years): 64.8 Gender (% female): 73.8 Race/ethnicity (%): w*hite* 94; *non-white* 6 Education (%): *HS or less* 44; *Post HS* 56 Veterans (%): NR	Inclusion: unpaid informal caregivers who provided 4 or more hours of care per week to someone with Alzheimer's disease or related disorder; Lived within 125 miles of a study site Exclusion: no to mild cognitive impairment in caregivers as indicated by a GDS of 2 or lower	Intervention (n=132): Progressively Lowered Stress Threshold (PLST) training program – Home visits where a plan of care was developed to increase the structure of the patient's routine, make necessary environmental modifications, and develop activities for the patient, additional referrals provided as needed; 4 hours of in-home intervention; Comparator (n=105): Routine information, community referrals, case management, and support groups; 2 one hour visit 2 weeks apart for providing general information, referrals, and self-help material Length of Follow-up: 3, 6, and 12 months	***Physical functioning:*** a. Subscale from The Memory and Behavior Problems Checklist 1989R (PR) ***Symptom control/ management:*** a. Memory and Behavior Problems Checklist (PR) ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: partial – exact numbers that dropped out per condition not reported Treatment adherence: 54% dropped out of the study over the 12 month follow up. Authors report attrition rates were similar across treatment conditions and sites. Treatment integrity: unclear **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gitlin, 2010[10] COPE Funding Source: Government (partial) Condition: Dementia (MMSE score <24) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Multicomponent – increase caregiver skills, provide caregiver education in problem solving ; and caregiver training to address caregiver identified concerns and help reduce stress.	N=209 (of 237 randomized) Age (years): 82 Gender (% male): 32 Race/ethnicity (%): w*hite 70; African-American 27; other 2* Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: media announcements and mailings by social agencies targeting caregivers Family Characteristics: Relationship to patient: *Spouse 38%; non-spouse 62* Age (years): 62 Gender (% female): 89 Race/ethnicity (%): w*hite 70; African-American 28; other 2* Education (%): *HS or less 31; Post HS 69%* Veterans (%): NR	Inclusion: *patients* had a physician; diagnosis of probable dementia or MMSE score <24; ≥21 years; English speaking; needed help with daily activities or had behavioral symptoms; lived with or within 5 miles of family caregivers *caregivers* provided oversight or care for ≥8 hours weekly; planned to live in area for 9 months; not seeking nursing home placement; reported difficulty managing patient functional decline or behaviors Exclusion: *patients* schizophrenia or bipolar disorder; dementia secondary to probable head trauma; MMSE score of 0; bed –bound *dyads* terminal illnesses with life expectancy < 9 months; active treatment for cancer; > 3 acute hospitalizations in the past year; involvement in another caregiver trial	Intervention (n=117): Care of Persons with Dementia in their Environments (COPE); reduce environmental stressors & enhance caregiver skills (problem solving, communication, engaging patients & simplifying tasks); focus on caregiver identified concerns & patient capabilities; 10 sessions in 4 months with occupational therapists; 1 face-to-face and 1 telephone session with advance practice nurse; patients provided blood, urine samples; lab evaluations and medications reviewed with caregivers Comparator (n=120): 3 20-minute telephone calls from trained staff (not occupational therapists or nurses); educational materials discussed and mailed to caregiver Length of Follow-up: post-treatment and 5 months post-treatment (4 and 9 months post baseline respectively)	***Physical functioning:*** a. Overall function - 15-item FIM-based measure; means and net % improvers b. 7 item ADL FIM-based measure; means only c. 8 item IADL FIM-based measure; means and net % improvers d. Activity engagement (Albert, 1996); means and net % improvers ***Quality of life:*** a. Quality of Life–Alzheimer's Disease scale ***Symptom control/ management:*** a. 16-item Agitated Behavior in Dementia scale All outcomes were by proxy report (caregiver). Outcomes assessed post- treatment and 5 months post-treatment (4 and 9 months post baseline respectively) ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: assessors Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: *outcomes assessed post-tx*: COPE: 102/117 = 87% Comparator: 107/120=89% *sessions completed*: COPE: 78% completed 8-12 sessions; 3% <3 sessions Comparator: received mean 2.8 phone contacts Treatment integrity: Interventionists for both groups trained; COPE treatment fidelity monitored via twice monthly supervision and review of audiotapes; for control group, random phone calls were monitored for adherence; both groups documented interactions for delivery content (reviewed for adherence) **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gitlin, 2010[75] ACT Funding Source: Government (partial) Condition: Dementia (MMSE score <24) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent – provided education, skill building, problem solving techniques, looked for co-morbid medical problems	N=272 Age (years): 82 Gender (%male): 47 Race/ethnicity (%): w*hite 70* Marital Status (%) NR Education (%): NR Veterans (%): NR Recruitment Method: media announcements and mailings by social agencies targeting caregivers Family Characteristics: Relationship to patient: *Spouse 51%; other NR* Age (years): 62 Gender (% female): 82 Race/ethnicity (%): w*hite 70* Education (%): *HS or less 33; Post HS 67* Veterans (%): NR	Inclusion: caregiver of a patient with a physician diagnosis of dementia or MMSE score <24; caregiver 21 years or older, English speaking, planned to live in area for >6 months; not actively seeking nursing home placement, manages problem behaviors, and reports upset with those behaviors (>5 on 10 point scale) Exclusion: *patients* schizophrenia or bipolar disorder, had dementia secondary to probable head trauma, or had an MMSE score of 0 and was bed bound. *For dyads* –either having a terminal illnesses with life expectancy of < 9 months, active treatments for cancer, > 3 acute hospitalizations in the past year, or involvement in another caregiver trial concerning problem behaviors	Intervention (n=137): Advanced Caregiver Training (ACT) 16 weeks; up to 9 occupational therapy (OT) sessions, 2 nursing sessions, and a 16-24 week maintenance phase of 3 brief OT contacts; OTs introduced goals, observed home environment for hazards; caregivers instructed in stress reduction, self-care, problem solving; nurse provided education on medical conditions that can exacerbate problem behaviors; blood samples collected from patients & medications reviewed Comparator (n=135): "Control" – no intervention contact (no further description provided) Length of Follow-up: post 16 week treatment only	***Symptom control/ management:*** a. # problem behaviors at baseline b. frequency of problem behaviors at baseline c. Using validated scales (i.e. RMBPC), selected one problem behavior to target for improvement and measured % whose targeted behavior improved, stayed same, or worsened All outcomes were by proxy report; outcome c assessed post-16 week treatment only ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: none (patients, investigators) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: Outcomes assessed: ACT: 117/137 = 85% Control: 122/135=90% Treatment integrity: Therapists and nurse received 35 hours training; fidelity monitored via twice monthly meetings and case presentations, home sessions audiotaped and 10% randomly selected for review and feedback from investigator **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gitlin, 2008[74] TAP Funding Source: Government (partial) Condition: Dementia (MMSE score <24) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Activity-based	N=60 Age (years): 79 Gender (% male): 57 Race/ethnicity (%): w*hite 77; African-American 22; other 2* Marital Status (%): m*arried/cohabiting: (see below)* Education (%): < *HS* 54; < *college* 32; g*raduate degree* 14 Veterans (%): NR Recruitment Method: media notices and social service mailing Family Characteristics: Relationship to patient: *Spouse 62%* Age (years): 65 Gender (% female): 88 Race/ethnicity (%): w*hite* 77; *African-American* 22; *other* 2 Education (%): < *HS* 27; < *college 56; graduate degree 17* Veterans (%): NR	Inclusion: *Patients* - dementia (physician diagnosis or MMSE score <24), English-speaking, able to feed self and participate in ≥2 self-care activities (e.g., bathing, dressing) C*aregivers* - English-speaking, ≥21 years of age, lived with patient, provided ≥4 hours of daily care, and reported dementia patient's boredom, sadness, anxiety, agitation, restlessness, or trouble focusing on a task Exclusion: *Patients* - schizophrenia, bipolar disorder, or dementia secondary to head trauma, MMSE score=0, bed-bound or non-responsive *Caregivers* - involved in another study, seeking nursing home placement, terminally ill, in active cancer treatment, or ≥3 hospitalizations in past year	Intervention (n=30): Tailored Activity Program (TAP); 6 90-minute home visits and 2 15-minute telephone contacts by occupational therapists over 4 months; written plan developed for each activity Comparator (n=30): Wait list Length of Intervention: 4 months; wait list controls then received the TAP intervention and were re-tested 4 months later (8 months from baseline)	***Quality of life:*** a. 12-item Quality of Life-AD scale (PR) ***Symptom control/ management:*** a. Frequency of occurrence of 24 behaviors (PR): 16 from Agitated Behaviors in Dementia Scale, 2 from RMBPC, 4 from previous research, and 2 "others" identified by families - not coded elsewhere ***Depression/anxiety:*** a. 19-item CSDD (SR + PR) All outcomes assessed at 4 months ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: yes (outcome assessment) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 4/60 study dropouts (6.7%) Treatment integrity: interventionists documented time spent, who participated (caregiver, patient), and number of activities introduced **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gitlin, 2003[73] REACH Funding Source: Government Condition: Alzheimer's disease or related disorder (Mini-Mental State Examination score of less than 24 or diagnosis of dementia) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Multicomponent **–** education, problem solving, skill building; home environment focus	N=190 (of 255 enrolled) Age (years): 81 Gender (% male): 33 Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: primarily from area agency on aging for 1 county; secondarily via media announcements Family Characteristics: Relationship to patient: *Spouse 35%, non-spouse 65%* Age (years): 60.5 Gender (% female): 76 Race/ethnicity (%): w*hite 45; African-American 53; other 3* Education (%) :*HS or less 57; Post HS 43* Veterans (%): NR	Inclusion: *Patients* - MMSE <24 or diagnosis of dementia *Caregivers* - primary caregiver; reported patient had at least 1 limitation in basic ADL or 2 dependencies in IADLs; ≥21 years old; caregiving for ≥6 months; provide ≥4 hr of care each day Exclusion: *Patients* -bedridden and nonresponsive to touch or environment *Caregivers* - did not live with care recipient; undergoing chemo-therapy or radiation therapy; > 3 hospitalizations in past year; planning to place patient in nursing home within next 6 months	Intervention (n=89): Environmental Skill-Building Program (ESP); protocol; education about dementia & impact of home environment on behaviors & ADL deficits; *instruction in problem solving and developing effective approaches* to manage caregiving concerns involving environment; *implementation of environmental strategies* tailored to caregiver's context; generalization of strategies to emerging problems; 5 90-min home visits & 1 30-min telephone contact over 6 months by occupational therapists. Comparator (n=101): Usual care +resource information at each testing period Length of Follow-up: None reported (6 mo active phase only)	***Physical functioning:*** a. ADL assistance needed (Mobility subdomain of Functional Independence Measure [FIM] - 8 items, bathing, eating, etc.); rated from complete independence (7) to complete dependence (1); total score=average scores across all items (PR) b. IADL assistance needed (7-point FIM scale as described above) (PR) ***Symptom control/ management:*** a. Revised Memory and Behavior Problem Checklist, modified by the REACH initiative; high scores indicate occurrence of greater number of behaviors (PR) All by proxy (caregiver) *Outcomes assessed at baseline and 6, 12, and 18 months post-baseline (only 6 month data reported)* ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 67/255 (26%) did not complete 6 month interview; significantly higher rate of attrition in experimental group Treatment integrity: interventionists received 25 hours training; formal case reviews (biweekly to monthly); direct observation of randomly selected visits with caregivers; treatment documentation reviewed; brief interviews with caregivers **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gitlin, 2001[57] Funding Source: Government Condition: Dementia *(*dependence in at least two ADLs*)* **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent – education and physical and social environmental modifications	N= 171 (of 202 randomized) Age (years): 78 Gender (% male): 34 Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: local social service and medical centers; media notices in Philadelphia region Family Characteristics: Relationship to patient: *Spouse 25%; daughter (includes in-laws) 59%; sons/in-laws/grandsons 13%; other 3%* Age (years): 61 Gender (% female): 73 Race/ethnicity (%): *white 74; African-American 25; other 1* Education (years): 14 (mean) Veterans (%): NR	Inclusion: Caregivers of patients with medical diagnosis of Alzheimer's or related disorder; living with patient; perceive themselves as the primary caregiver; report patient dependence ≥ 2 ADLs, and report ≥1 difficulty managing either IADL or ADL assistance or a dementia-related behavior (e.g., wandering, agitation) Exclusion: Caregivers of patients who were bedridden, nonresponsive to touch or physical environment; patients for which environmental adaption would have relatively no benefit (due to severity of their dementia)	Intervention (n=100): Multi-component intervention; protocol; 5 90-min home visits, bi-weekly over 3 months; occupational therapists provided education & suggested physical and social environmental modifications; developed targeted plan with caregiver to address problematic care, educated about disease process, & engaged caregivers in problem solving strategies; provided caregivers coaching, validated and reinforced their strategies Comparator (n=102): Usual care Length of Follow-up: post-treatment only (3 months post-baseline)	***Physical functioning:*** a. ADL dependence, using modified FIM b. IADL dependence using modified FIM ***Symptom control/ management:*** a. Memory and Behavior Problems Checklist – total number of problems Outcomes assessed: All proxy report (by caregivers); baseline and post-tx (3 months post baseline) ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: Outcomes assessed for: ACT: 93/100 = 93% Control: 78/102=76% (p=0.001) Treatment adherence: 69% participated in ≥4 home sessions 9% in only 1 session Treatment integrity: therapists provided 20 hours training; fidelity monitored through formal case reviews, on-site observation of randomly selected visits, and follow-up interviews with caregivers to evaluate satisfaction **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Gonyea, 2006[64] Project CARE Funding Source: Foundation Condition: Alzheimer's (mild to moderate [MMSE 10 or higher], at least one neuropsychiatric symptom) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Multicomponent (behavior management, pleasant events training, relaxation training)	N= 80 (of 91 randomized) Age (years): 77 Gender (% male): NR Race/ethnicity (%) NR Marital Status (%): NR Education (%) NR Veterans (%): NR Recruitment Method: media ads, community-based lectures, elder day program referrals Family Characteristics: Relationship to patient: *Spouses 59%, adult children 32%* Age (years): 64 Gender (% female): 67 Race/ethnicity (%): *white 94* Education (%): NR Veterans (%): NR	Inclusion: Caregiver who provides at least 4 hours/week and is willing to accept random assignment; care recipient with a) physician-confirmed diagnosis of Alzheimer's disease, b) mild to moderate dementia severity (MMSE 10+), c) at least 1 neuropsychiatric symptom Exclusion: NR	Intervention (n=40): Behavioral therapy and behavioral activation – to manage care recipient neuropsychiatric symptoms in home environment and caregiver distress Comparator (n=40): General information on aging and Alzheimer's disease, home safety, communication, support Both groups: highly structured weekly meetings of 90 minutes; 5 to 10 caregivers attended (no care recipients) Length of Follow-up: 5 week intervention	***Cognitive function:*** a. Neuropsychiatric Inventory Outcomes assessed at baseline and post-treatment ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): no (only included in analysis if completed at least 2 sessions) Withdrawals/dropouts adequately described: no Treatment adherence: 80% completed intervention; 88% of those attended at least 4 of 5 weekly sessions Treatment integrity: investigator met with therapists to review group sessions **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Jirovec, 2001[58] Funding Source: Government Condition: Memory impairment **KQ1 ☐ KQ2 ☒** **Intervention Type:** Educational (symptom management)	N=118 Age (years): 80 Gender (% male): 31 Race/ethnicity *(%): African-American 30* Marital Status (%): NR Education (years): 10 Veterans (%): NR Recruitment Method: announcements in newsletters, flyers, newspaper advertisements Family Characteristics: Relationship to patient: *Spouse 41%; child 39%; sibling, other family, friend 20%* Age (years): 63 Gender (% female): 67 Race/ethnicity (%): *African-American 30* Education (years): 14 Veterans (%): NR	Inclusion: "Elders" with memory impairment and functional urinary incontinence (UI) Exclusion: NR	Intervention #1 (n=38) Visits every 2 months; individualized scheduled toileting procedure with reminders for patient; monthly telephone calls for progress and difficulties Intervention #2 (n=39): Visits every 6 months; content same as above Comparator (n=41): Control; monthly call for "friendly" visit NOTE: 2 intervention groups were combined for data analysis when no differences were noted in UI at 6 month follow-up Length of Follow-up: post 6 month treatment only	***Symptom control/ management:*** a. % Incontinent episodes (UI) (Caregiver report) b. # patients whose incontinence decreased c. Short Portable Mental Status Questionnaire (SPMSQ) Outcomes measured at baseline post-tx only ☐ **Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 37% lost but no difference between groups Treatment integrity: consistency with implementing the protocol was assessed at 6-month visit; caregiver records and self-ratings compared **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Logsdon, 2010[63] Funding Source: Foundation, Government Condition: Early stage Alzheimer's and dementia; MMSE ≥ 18 **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multi-component - weekly groups providing both education and emotional support of peers	N=142 Age (years): 75 Gender (% male): 51 Race/ethnicity (%): *white 96; African-American 1; other 3* Marital Status (%) Married 72 Education (%): *Post HS (college degree)* 47 Veterans (%): NR Recruitment Method: recruited via referrals from the Alzheimer's Association Western and Central Washington State chapter Family Characteristics: Relationship to patient: *Spouse 68%; adult child 12%; sibling/friend 6%; NR: 15* Age (years): 68 Gender (% female): 58 Race/ethnicity (%): w*hite 96; African-American 1 other 3* Education (%): *Post HS (college degree),*40 Veterans (%): NR	Inclusion: Dementia diagnosis confirmed by the individual's primary care physician; MMSE ≥18; aware of their memory loss and able to communicate verbally; able to participate independently in a group setting (without their family members present); had no significant history of severe mental illness that would impede their ability to take part in support group activities; both the person with dementia and a family care partner agreed to participate. Exclusion: NR	Intervention (n=96): Early Stage Memory Loss (ESML) - Structured Support Group, manualized; weekly 90 minute meetings for 9 weeks. Patient and partner met together for part of session, then separately. Comparator (n=46): Wait List - subjects received written educational materials routinely provided by Alzheimer's Association chapter. Length of Follow-up: post-tx only.	***Physical functioning:*** a. SF-36 physical health component (SR) ***Quality of life:*** a. QOL-AD (Quality of Life-Alzheimer's) (PR) b. SF-36 social functioning scale (PR) ***Depression/anxiety:*** a. Depression - Geriatric Depression Scale (GDS) (SR) b. SF-36 Mental Health component (SR) All outcomes were assessed at post-tx ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: no Treatment adherence: *Study dropouts* 6/142=4% no post-tx assessment 4/96=4% ESML 2/46=4% Wait list Treatment integrity: Standardized treatment manual, all facilitators participated in an annual day long training workshop. **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Martin-Cook, 2005[60] Funding Source: Foundation Condition: Primarily Alzheimer's Dementia; mean MMSE = 19.4 (moderate impairment) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Education, skills-based	N= 47 (of 49 randomized) Age (years): 73 Gender (% male): 63 Race/ethnicity (%): *white 92; African-American 6; other 2* Marital Status(%): NR Education (years): 15 (mean) Veterans (%): NR Recruitment Method: retirement & assisted living facilities Family Characteristics: Relationship to patient: *Spouse 92%; daughter 6%; other 2%* Age (years): NR Gender (% female): 70 Race/ethnicity (%): NR Education (years): 16 Veterans (%): NR	Inclusion: Diagnosed with "various dementing illnesses (primarily AD)" by established clinical criteria; community dwelling; mildly to moderately cognitively impaired; consistent caregiver; if maintained on psychotropic medications and/or cognitive enhancers had been on stable doses ≥1 month before enrollment. Exclusion: NR	Intervention (n=24): 4 weekly skills training sessions, individualized based on functional level of patient and coping level of caregiver; skills based training, safety, education designed to decrease gap between patient's actual abilities and caregiver's expectations; unclear if manualized Comparator (n=23): Wait list; provided information about community services and resources Length of Follow-up: to 17 weeks (12 weeks post-tx)	***Physical functioning:*** a. Mini-Mental Status Examination (MMSE) b. Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory - MCI version (ADCS-MCI) (PR) ***Cognitive functioning:*** a. Neuropsychiatric Inventory (NPI) (PR) **☒ Negative caregiver outcomes reported** Outcomes assessed at 7 weeks (2 weeks post-tx) and 17 weeks (12 weeks post-tx)	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: 100% of intervention group completed all 4 sessions. Study dropouts: 96% (47/49) at week 7 96% (45/47) at week 17 Treatment integrity: NR **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
McCallion, 1999[68] Funding Source: Government Condition: Moderate to severe dementia; weighted mean MMSE = 6.9 **KQ1 ☒ KQ2 ☐** **Intervention Type:** Educational, skill-based, emotional	N=66 Age (years): 86 Gender (% male): 21 Race/ethnicity (%): *White 95; African-American 5* Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: nursing staff at 5 skilled care nursing homes identified all residents with at least moderate level of dementia and problem behaviors; primary visitor of patient approached regarding patient participation Family Characteristics: Relationship to patient: *Individuals who visited patient regularly, family or "close personal friends for >2 years"; Spouse11%; Adult child 29%; other 60%* Age (years): 59 Gender (% female): 80 Race/ethnicity (%): *White 94; African-American 3; other 3* Education (%): *HS or less 24; Post HS 45; Not reported 29* Veterans (%): NR	Inclusion: Patients with moderate level of dementia and who displayed problem behaviors such as physical aggression, verbally abusive behaviors, disruptive vocalizations, or motor restlessness (as identified by staff judgment and medical records); moderate level of dementia as screened by study staff using Mini-Mental State Exam (MMSE) and Global Deterioration Scale (GDS); patient had to have a primary visitor Exclusion: NR	Intervention (n=32): FVEP (Family Visit Education Program) manualized program addressing: verbal and non-verbal, communication, and effective structuring of family visits; delivered over 8 weeks, four, 1½-hour group sessions and three 1-hour individual family conferences; family sessions had two parts, a therapeutic observation of interaction with in vivo feedback and a face-to-face feedback session with individual family members not in the presence of the resident Comparator (n=34): Usual Care - usual social and recreational programming offered by each facility; UC families offered program after study was complete Length of Follow-up: 1 month and 4 months post-tx follow ups were completed	***Symptom control/ management*** a. MOSES Subscales (PR): -Self care -Disorientation -Irritability -Withdrawal b. CMAI-N (Cohen-Mansfield Agitation Inventory) Nurse completed c. CMAI-O - study assessor ("observer") completed (PR) ***Depression/Anxiety:*** a. MOSES (Multi-dimensional Observation Scale for Elderly Subjects) Depression subscale (PR) b. CSDD (Cornell Scale for Depression in Dementia) Subscales: (SR and PR combined) -Mood related signs -Behavioral disturbance -Physical signs -Cyclic functions -Ideational disturbance Outcomes assessed at baseline and 1 and 4 months post-tx. **☐ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: outside observers and nursing staff were blinded to study hypotheses (but limitations section noted observers became aware of arm for 30% of study subjects during data collection, due to comments made by family members) Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: outcomes assessed: 86.4% (57/66) (not provided by group) Treatment integrity: videotapes of group and family sessions were reviewed and leaders provided with weekly supervision sessions; written intervention manual, participant workbooks, and a training videotape were prepared and made available to the leaders **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
McCurry, 2005[61] Funding Source: Government and Foundation Condition: Alzheimer's disease (probable or possible; community dwelling; dementia for mean of 5.8 years; mean Mini-Mental State Exam of 11.8) **KQ1 ☐ KQ2 ☒** **Intervention Type:** Multi-component: (educational, skill-based)	N=36 Age (years): 78 Gender (% male): 56 Race/ethnicity (%): *White 92; African-American 0; other 8* Marital Status (%): *Spouse caregiver 58* Education (years): 14 (mean) Veterans (%): NR Recruitment Method: articles, ads, and presentations (all in senior and caregiver media or to senior groups) Family Characteristics: Relationship to patient: *Spouse 58%, Child 33%, other 8%* Age (years): 63 Gender (% female): 72 Race/ethnicity (%): *White 89; African-American 0; other 11* Education (years): 15 (mean) Veterans (%): NR	**Inclusions:** Probable or possible Alzheimer's disease, confirmed in writing by primary care physician; two or more sleep problems on the Neuropsychiatric Inventory Nighttime Behavior Scale occurring 3 or more times per week; community-dwelling, ambulatory, and without an existing primary sleep disorder **Exclusions:** None reported	Intervention (n=17): *Nighttime Insomnia Treatment and Education for Alzheimer's Disease (NITE-AD):* Manualized sleep-education program; 6 1-hour in-home sessions over 2 months; sleep hygiene education; goal setting; individualized sleep hygiene programs; instruction for daily 30 minute walks & daily light exposure; caregivers attended all sessions, typically attended patient's walks, & supervised light exposure Comparator (n=19): *Supportive contact control*: Manualized attention control group; 6 1-hour in-home sessions over 2 months; sleep hygiene education; goal setting; nondirective, supportive approaches Length of Follow-up: 2 (post-tx) and 6 months post randomization	***Cognitive function:*** a. Revised Memory and Behavior Problems Checklist – Memory (PR) ***Symptom control/ management:*** a. Revised Memory and Behavior Problems Checklist – Disruption (PR) b. Sleep outcomes (all measured by wrist movement recorder) 1. Night wake time (hrs) 2. Number of night awakenings 3. % of time asleep 4. Wake index (wakes/hr) 5. Duration of night awakenings (min) ***Depression/anxiety:*** a. Cornell Depression Scale (SR) b. Revised Memory and Behavior Problems Checklist – Depression (SR) ☐ **Negative caregiver outcomes reported** All measures assessed at baseline, post-treatment, 6 month	Allocation concealment: adequate Blinding: yes – assessors blind to condition Intention-to-treat analysis (ITT): partially (ITT for pre-post change scores only) Withdrawals/dropouts adequately described: yes Tx adherence: overall attendance: 90%; no difference between groups *Intervention*: 3/17 dropped out by post-tx (17.6%); 3 more were not assessed at 6 month follow-up due to patient death (35.3% of original sample not assessed) *Control*: 2/19 dropped out by post-tx (10.5%; 1 due to death); 5 more were not assessed at 6 month follow-up (36.8% of original sample not assessed; 2 due to patient death) Tx integrity: yes (sessions recorded and randomly selected for review) **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Mittelman, 2004.[54] 2006[52] Funding Source: Government Condition: Alzheimer's disease **KQ1 ☒ KQ2 ☐** **Intervention Type:** Skill-based, emotional, problem solving or conflict resolution, decision support	N=406 Age (years): 74.3 Gender (% male): NR Race/ethnicity (%): NR Marital Status (%): *Married/cohabiting 100* Education (%): NR Veterans (%): NR Recruitment Method: patient population at New York University Aging and Dementia Research Center (NYU-ADRC), referrals from local Alzheimer's Association; media announcements; adult day care, social worker, physician referral Family Characteristics: Relationship to patient: *Spouse 100%* Age (years): 71.3 Gender (% female): 60.1 Race/ethnicity (%): *white 91; African-American 6; other 3* Education (%): *HS or less 46; Post HS 54* Veterans (%): NR	Inclusion: Spouses of community dwelling patients with a clinical diagnosis of Alzheimer's disease; living with patient (at baseline) and has primary responsibility for AD patient's care; patient or caregiver has at least 1 relative living in metropolitan New York City Exclusion: caregivers could not be participating in another caregiving counseling program at baseline; caregivers could not have a "serious medical condition"	Intervention (n=203): Multi-component and 'indefinite'; 1) 4 months of counseling sessions (2 caregiver only, 4 family but not patient); content determined by caregiver needs; 2) caregiver weekly support groups (ongoing); 3) "ad hoc" counseling (on-going; via telephone when needed) Usual Care (n=203): Usual counseling services for all families & patients at NYU-ADRC (advice & information on requested, no formal counseling sessions); participants could seek additional assistance & support elsewhere Length of Follow-up: For assessments-- 4 years; interview every 4 months during first year; every 6 months thereafter (in person or by phone) For nursing home placement – up to 18 years for first recruited participants	***Physical functioning:*** a. Global Deterioration Scale (GDS) (Patient functioning***)*** (PR) b. Older Americans Resources and Services (OARS) Physical Health portion (PR) ***Symptom control/ management:*** a. Frequency of patient problem behaviors -- Memory and Behavior Problem Checklist - original (MBPC) (PR) ***Utilization*** a. Nursing home placement (PR) ☐ **Negative caregiver outcomes reported**	

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Ostwald, 1999[50] Funding Source: Government Condition: Dementia(mild to severe) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Psychoeducational	N=117 Age (years): 77 Gender (% male): 56 Race/ethnicity (%): NR Marital Status (%): NR Education (%): *HS or less NR; Post HS 57* Veterans (%): Veterans included, % NR Recruitment Method: recruited through memory loss clinics, the Minneapolis VA, senior clinics and health centers and Mpls/ St. Paul Alzheimer's Association, local hospitals and social service agencies. Family Characteristics: Relationship to patient: NR Age (years): 66 Gender (% female): 65 Race/ethnicity (%): NR Education (%): *HS or less NR; Post HS 75* Veterans (%): NR	Inclusion: Caregivers caring for a community dwelling patient with diagnosis of nonreversible dementia (mild to severe); who displays problem behaviors (per caregiver report), and patient is able to accompany caregiver to at least the first 2 weekly intervention sessions; at least one family member, in addition to primary caregiver, needed to be willing to accompany the primary caregiver and patient to all sessions Exclusion: Caregivers of patients who were either on-ambulatory or required total care (score 7b on Functional Assessment Staging Test)	Intervention (n=72): Minnesota Family Workshop (MFW) – Manualized; 7 weekly 2-hr sessions with at least 4 families; provide caregivers with info about dementia; skills; self-efficacy; family communication and cooperation; patients attended testing sessions (2 sessions) then an optional "day care like" group with activities (last 5 sessions); all families given packet of resources available in the community for Alzheimer's care Comparator (n=45): wait list for intervention; all families given packet of resources available in the community for Alzheimer's care Length of Follow-up: Baseline, post-intervention, 2 months post	***Cognitive function:*** a. MMSE [PR] ***Symptom control/ management:*** a. Disruptive behavior subscale of Revised Memory and behavior problem checklist [PR] All measures assessed at baseline, post-treatment, 2 months post-treatment **☒ Negative caregiver outcomes reported**	Allocation concealment: adequate Blinding: yes (those who assessed patients for MMSE were blinded to group allocation) Intention-to-treat analysis: yes Withdrawals/dropouts adequately described: yes; dropouts significantly older-no other significant demographic differences between dropouts and completers Tx adherence: completed assessments Intervention: 60/72 = 83% Wait list: 34/45 = 76% Tx integrity: one investigator monitored each session to ensure adherence to curricular plan **Study Quality: Good**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Quayhagen, 2000[62] Funding Source: Government Condition: Dementia (mild to moderate; score > 100 on Mattis Dementia Rating Scale, Mattis, 1988) **KQ1 ☒ KQ2 ☒** **Intervention Type:** 1) Cognitive Simulation: Skill based 2) Dyadic Counseling: Emotional, problem solving, conflict resolution 3) Dual Supportive Seminar Groups: Educational, skill based, emotional, problem solving 4) Early Stage Day Care: Education, skill based, emotional	N=103 Age (years): 75 Gender (% male): 63 Race/ethnicity (%): *white 93; African-American 2; other 5* Marital Status (%): *Married/cohabiting: 100* Education (years): 15 (mean) Veterans (%): NR Recruitment Method: Alzheimer's Association; Alzheimer's Disease Research Center; and media Family Characteristics: Relationship to patient: *Spouse 100%* Age (years): 72 Gender (% female): 63 Race/ethnicity (%): NR Education (years): 14 (mean) Veterans (%): NR	Inclusion: diagnosed with possible or probable Alzheimer's dementia, cardiovascular dementia, or Parkinson's dementia; mild to moderate stages of dementia; score above 100 on Mattis Dementia Rating Scale (Mattis, 1988); physically capable of participating in intervention activities and willing to drive to intervention sites Exclusion: NR	1) Cognitive Stimulation (n=21): in-home; cognitively oriented; caregiver helped cognitively stimulate patient; 1.5 hour sessions 2) Dyadic Counseling (n=29): in-home; affectively oriented; systems & cognitive behavioral couple therapy approach; 1.5 hour sessions 3) Dual Supportive Seminar Groups (n=22): in community; affectively oriented; group format; information exchange, support, discussion,; 1.5 hour sessions 4) Early-Stage Day Care (n=16): in community, cognitively oriented; group format; education/training for caregivers; supportive environment for patients; 4 hours/wk (patients), 2 sessions (caregivers) 5) Wait List Control (n=15) All interventions: 8 weeks; unclear if manualized Length of Follow-up: none	***Physical functioning:*** a. Problem Solving: Composite of Geriatric Coping Schedule and conceptualization factor from Dementia Rating Scale (DRS) b. Immediate Memory: Composite of Logical Memory I and Visual Reproduction I from Wechsler Memory Scale – Revised (WMS-R) and memory factor of DRS c. Delayed Memory: Composite of WMS-R Logical Memory II and Visual Reproduction II d. Verbal Fluency: Composite of 2 recalled word scales (Benton & Hamsher, 1976; Goodglass & Kaplan, 1953), and initiation factor score on the DRS ***Symptom control/ management:*** a. Behavioral functioning: Memory and Behavior Problem Checklist, Part A All measures assessed at pre and post-tx (3 months) and obtained through self-report **☒ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: yes (assessors blinded to treatment assignment) Intention-to-treat analysis (ITT): unclear (only 15 dyads randomized to control group agreed to second randomization to a treatment group and therefore were included in analysis) Withdrawals/dropouts adequately described: not reported Treatment adherence: not reported Treatment integrity: ongoing monitoring of performance of individuals involved in interventions and assessment **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Robison, 2007[53] Funding Source: Government Condition: Dementia (participants were all institutionalized at specialized skilled nursing facilities) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Educational, skill-based	N=388 (of 412 invited for participation) Age (years): NR Gender (% male): NR Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: 20 randomly selected skilled nursing facilities with special care units or dementia programs in 3 CT counties; all nursing staff recruited + one family member for each resident; facilities randomly assigned to intervention or control Family Characteristics: Relationship to patient: *Spouse 19.3%; child 80.7%* Age (years): 59.5 Gender (% female): 65 Race/ethnicity (%): w*hite* 86; *African-American*10; *other* 3.4 Education (%): *HS or less* 30; *Post HS* 70 Veterans (%): NR	Inclusion: Nursing staff and one family member of each resident of the 20 selected skilled nursing facilities with special care units or dementia programs in three Connecticut counties	Intervention (n=209): Partners in Caregiving in the Special Care Unit Environment (PIC-SCU) *(Note: Unit of intervention is facility; N=209 family members of residents on intervention unit who participated)* parallel training sessions for family & staff; enhance communication, conflict-resolution skills, & empathy for other group (staff or family); mini-lectures, case discussions, brainstorming sessions, & role plays; unit goals, facility family procedures, & policies; manualized; one 4-5 hour initial training + 2 hour family/staff meeting. Comparator (n=179): (*Note: N=179 reflects family members of residents on unit who participated) U*sual care with usual staff/family interaction Length of Follow-up: 6 month post-treatment	***Symptom control/ management:*** a. Cohen-Mansfield Agitation Inventory (CMAI) (PR) ***Utilization:*** a. # resident transfers off the unit b. # resident transfers out of the facility *Assessments conducted 2 and 6 months post treatment* ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: unclear Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Treatment adherence: rates of intervention drop out not provided; retention rate overall: 92% baseline to 2 month post-tx; 87% 2 month to 6 month post-tx; 84% baseline to 6 month post-tx Treatment integrity: unclear **Study Quality: Poor**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Teri, 1997[70] Funding Source: Government Condition: Alzheimer's disease (and comorbid depression; average baseline dementia duration =35.6 months; MMSE =16.5; Dementia Rating Scale =108.6) **KQ1 ☒ KQ2 ☒** **Intervention Type:** Behavior Therapy – Pleasant Events: multicomponent –educational, skill-based, emotional, problem solving Behavior Therapy – Problem Solving: multicomponent –educational, skill-based, emotional, problem solving	N=72 Age(years): 76.4 Gender (% male): 53 Race/ethnicity (%): NR Marital Status (%): NR Education (years): 14.1 Veterans (%): NR Recruitment Method: referrals from Alzheimer's clinic and research center Family Characteristics: Relationship to patient: *Spouse 79%; adult child 14%; close friend 7%* Age (years): 66.9 Gender (% female): 69% Race/ethnicity (%): NR Marital Status (%): NR Education (years): 14.2 (mean) Veterans (%): NR	Inclusion: Patients meet NINCDS-ADRDA criteria for probable Alzheimer's disease; co-morbid DSM-III-R criteria for major or minor depressive disorder; ≥6 month history of cognitive problems; live with their caregiver in the community. Exclusion: NR	Behavior Therapy – Pleasant Events (BT-PE) (n=23): 9 weekly 60 min sessions; patients & caregivers; identifying, planning, & increasing pleasant activity, caregiver support system, & problem solving strategies for problem behaviors Behavior Therapy – Problem Solving (BT-PS) (n=19): 9 weekly 60 min sessions for patients & caregivers; problem solving; education, support, advice to caregiver; pleasant activity only as appropriate Typical care control (TCC) (n=10): 9 weekly 60 min sessions for patients & caregivers; advice & suggestions of unstructured nature; no homework/ recordkeeping Wait list control (TCC) (n=20): No contact with therapists over 9 wk period Length of Follow-up: Pre and post tx for all; 6 month for active txs	***Cognitive Function:*** a. Mini Mental Status Exam, SR post tx, 6 months b. DRS (Dementia Rating Scale) SR post tx, 6 months ***Depression/anxiety:*** a. HDRS (Hamilton Depression Rating Scale) SR and PR, post tx, 6 months b. CSDD (Cornell Scale for Depression in Dementia), SR and PR, post tx, 6 months c. BDI (Beck Depression Inventory) PR, post tx, 6 months ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: yes – outcome assessors Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: yes Tx adherence: report treatment dropouts (from sessions): Intervention: 33.5% by post tx Control: 28.6% by post tx (difference = NS) Study dropouts 16/88 = 18% (serious medical illness n=4; change in living situation n=4; exclusionary medication prescribed during intervention n=2; caregiver stopped participating n = 6). NS Tx integrity: manualized; interrater reliability assessed by independent ratings of videotapes **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Teri, 2003[12] Funding Source: Government Condition: Alzheimer's disease (moderate to severe cognitive impairment) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent –educational, skill-based	N=153 Age (years): 78 Gender (% male): 59 Race/ethnicity (%): w*hite 89; African-American 9; other 3* Marital Status (%): *Married/ cohabiting 82* Education (%): *HS or less NR; Post HS NR* *Mean years: 13* Veterans (%): NR Recruitment Method: from ongoing, community based Alzheimer's disease patient registry and referrals from physician practices and community advertisements Family Characteristics: Relationship to patient: *Spouse 80%; adult child 6%; other 14%* Age (years): 70 Gender (% female): 70 Race/ethnicity (%): w*hite 87; African-American 8; other 5* Education (%): *HS or less NR; Post HS NR* *Mean years: 13.5* Veterans (%): NR	Inclusion: met National Institute of Neurological and Communicative Diseases and Stroke/ Alzheimer's Disease and Related Disorders Association criteria for probable or possible Alzheimer's disease, were required to be community dwelling, ambulatory, and to have a caregiver who was willing to participate in training sessions Exclusion: none stated	Intervention (n=76): Reducing Disability in Alzheimer's Disease (RDAD). Patient-caregiver dyads seen in own homes for 12 1-hr sessions (2 sessions/ wk for first 3 wks, then weekly for 4 wks, and biweekly for next 4 weeks); exercise component goal was for patients to engage in at least 30 min/ day of moderate-intensity exercise; behavioral management component - caregivers given specific instructions about dementia, how to reduce occurrence of behavioral problems, how to identify and modify precipitants of patient distress, how to modulate their own response to problems; positive interactions were encouraged. Comparator (n=77): Routine medical care Length of Follow-up: Post-treatment (3 months post-baseline); and 6, 12, 18, and 24-months post randomization (3, 9, 15 and 21 months post-tx)	***Physical functioning:*** a. SF-36 physical health component [SR] b. Sickness Impact profile – mobility, subscales [SR] c. # of restricted activity days and days spend in bed in past 2 weeks ***Depression/anxiety:*** a. CSDD (Cornell Scale for Depression in Dementia) b. HDRS (Hamilton Depression Rating Scale) *(assessed, but values only reported for most distressed pts)* (both measures assessed by proxy, independent assessor observing caregiver and patient) ***Utilization:*** a. # patients institutionalized ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: outcome assessments, interviewers blind to treatment assignment Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: yes Tx adherence: 13 study dropouts to post-treatment (all included in the analyses); 8 of the intervention group dropped out before post treatment (10.5%) and 5 of the routine care group (6.5%); 58% completed the final follow-up Tx integrity: yes **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Teri, 2005[66] Funding Source: Foundation Condition: Alzheimer's disease (moderate impairment; MMSE =14) **KQ1 ☒ KQ2 ☐** **Intervention Type:** Multicomponent –problem-solving, education, and support for the caregiver	N=95 Age (years): 80 Gender (% male): 34 Race/ethnicity (%): *white 86.1; African-American 5.4; other 8.6* Marital Status (%): *Married: 56.7* Education (%): *HS or less 8.4; Post HS 51.6* Veterans (%): NR Recruitment Method: NR Family Characteristics: Relationship to patient: *Spouse 55 %; son/daughter 31%; other 14%* Age (years): 65.1 Gender (% female): 69 Race/ethnicity *(%): white 87.2; African-American 4.3; other 8.6* Education (%): *HS or less 28.5; Post H: 71.5* Veterans (%): NR	Inclusion: Alzheimer's disease and three or more agitated or depressed behavior problems reported by caregivers; occurring at least three or more times in the past week; caregivers were spouse or adult relative caring for person with dementia in the home Exclusion: none stated	Intervention (n=47): STAR Caregivers: Consultants met with caregivers in-home for 8 weekly sessions, followed by 4 monthly phone calls; first 3 sessions focused on teaching caregivers rationale and use of A-B-C problem-solving approach to behavior change; subsequent sessions focused on improving caregiver communication, increasing pleasant events as means to improve care recipients' mood, & developing strategies to enhance caregiver support; manualized program Comparator (n=48): Routine medical care Length of Follow-up: none (6 month treatment)	***Cognitive functioning:*** a. Revised Memory and Behavior Problems Checklist – Memory subscale (PR) ***Quality of life:*** a. Quality of Life-Alzheimer's Disease (QOL-AD) (PR) All outcomes assessed at baseline, 2 months, and 6 months (post-tx) ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: outcome assessments, interviewers blind to treatment assignment Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: yes Treatment adherence: 83% of caregivers attended 8 or more treatment sessions (mean=7.6 sessions; range=1-10) 12 (13%) dropped out by end of 8 weekly session; 29 (31%) dropped out by end of 6 months Treatment integrity: audiotapes and paperwork reviewed by supervisors **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Wray, 2010[49] Funding Source: Government (Dept. of Veterans Affairs) Condition: Dementia **KQ1 ☒ KQ2 ☐** **Intervention Type:** Education, support	N=158 dyads Age (years): 78 Gender (% male): NR Race/ethnicity (%): *white 92* Marital Status (%): NR Education (years): 12.5 (mean) Veterans (%): 100 Recruitment Method: potential participants identified by encounter coded for dementia diagnosis, clinician referral, or self/family referral in response to information and publicity about study Family Characteristics: Relationship to patient: *spouse or spousal equivalent* Age (years): 74 Gender (% female): NR Race/ethnicity (%): *white 91* Education (years): 12.5 (mean) Veterans (%): NR	Inclusion: *Caregiver* – primary family caregiver (spouse or spousal equivalent); lived with care recipient at least 1 year; at least moderate level of caregiving strain (score of 7 or more on Caregiver Strain Index) *Care Recipient* - Living in own home/apartment; definitive diagnosis of dementia in medical record; spouse or partner living with them for at least 1 year; at least moderate level of dementia (3 or higher on Global Deterioration Scale) or dependent on at least 1 ADL and at least 3 IADLs Exclusion: Caregiver participating in any other caregiver support group at enrollment	Intervention (n=83): Telephone Education Program (TEP); telephone conference with up to 8 caregivers; education about dementia and caregiving skills, coping strategies, & support; 10 weekly 1-hour sessions; workbook for participants; manualized Comparator (n=75): Usual care (all usual VA services) Length of Follow-up: up to 12 months following start of intervention	***Utilization:*** a Total admissions b. Acute admissions c. ICU admissions d. Nursing home admissions e. Outpatient visits All data obtained from VA databases All outcomes summed over 6-month time intervals: 6 months before start of intervention, start of intervention to 6 months after start, and 6-12 months after intervention period ☐ **Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: health care cost and utilization data extracted by blinded investigator Intention-to-treat analysis (ITT): yes Withdrawals/dropouts adequately described: no withdrawals - database data available regardless of participation in intervention Treatment adherence: NR; reported no difference in outcomes for those who completed study vs. those who did not Treatment integrity: monitored by doctoral-level investigators **Study Quality: Fair**

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Study, Year Funding Source Medical Condition Intervention Type	Sample Characteristics	Inclusion/Exclusion Criteria	Intervention Comparator Length of Follow-up	Outcomes Assessed	Study Quality
Wright, 2001[67] Funding Source: Foundation Condition: Alzheimer's disease **KQ1 ☒ KQ2 ☐** **Intervention Type:** Educational; skill-based; emotional; problem solving	N=93 Age (years): 77.4 Gender (% male): 24 Race/ethnicity (%): NR Marital Status (%): NR Education (%): NR Veterans (%): NR Recruitment Method: NR Family Characteristics: Relationship to patient: *Spouse 45%; adult daughters 38%; other relative 17%* Age (years): 59.5 Gender (% female): 76 Race/ethnicity (%): *white 68.6; African-American 31.4* Education (years): 12 (mean) Veterans (%): NR	Inclusion: Alzheimer's disease patient admitted to and about to be discharged from behavioral ICU; had primary caregiver living in same household and within an 80 mile radius of the hospital Exclusion: NR	Intervention (n=68): targeted at caregiver; case management & counseling/ education; conducted in-home (2 weeks, 6 weeks, 12 weeks post-discharge) and by phone (6 and 12 months post-discharge); unclear if manualized Comparator (n=25): Usual care; caregivers received phone calls on same time schedule for data collection only (no counseling or case management) Length of Follow-up: none (12 month treatment)	***Physical functioning:*** a. # deceased 12 months post baseline b. Blessed Dementia Rating Scale ***Symptom control/ management:*** a. CMAI (Cohen-Mansfield Agitation Inventory) ***Utilization:*** a. % Institutionalized at 12 months post baseline b. # days at home prior to institutionalization (mean, SD, range) All outcomes proxy report and assessed during intervention at 2 weeks, 6 weeks, 12 weeks, 6 and 12 months (post baseline) **☒ Negative caregiver outcomes reported**	Allocation concealment: unclear Blinding: no Intention-to-treat analysis (ITT): no Withdrawals/dropouts adequately described: no Treatment adherence: NR Treatment integrity: NR **Study Quality: Poor**

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Table 10. Memory-Related Disorders – Physical Functioning

Study, Year Interventions	Physical Condition	Baseline Functional Level	IADL or ADL Scale	Baseline	Post-Treatment (SD)	Follow-up* (time assessed)
Brodaty, 2009[59] 1) Donepezil + standard services + psychological caregiver intervention (n=26) 2) Donepezil + standard services (n=26)	Alzheimer's disease	GDS = 4.5 (0.55) MMSE = 20.7 (5.27) ADCS-ADL = 58.1 (13.03) ADAS-Cog = 26.8 (10.79) RMBPCL =10.98 (7.94)	Death, percent		NR	1) 46% (12/26) 2) 54% (14/26) Mean follow-up: 5.4 years, up to 8.5 years
Burgener 1998[65] 1) Educational and behavioral intervention (n=11) 2) Education only (n=12) 3) Behavioral only (n=12) 4) Comparison group (n=12)	Alzheimer's disease or multi-infarct dementia	Baseline mean MMSE=8.9 (moderate to severe)	Composite (OARS, IADL, SCS) (higher score=better self-care ability)	1) 11.8 2) 12.5 3) 8.8 4) 14.6 (Standard deviations not provided)	NR	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
Chang 1999[71] 1) Nurseline cognitive-behavioral (n=34) 2) Placebo telephone calls (n=31)	Dementia	Significant dressing and eating problems; MMSE<21	ADL subscale of Functional Rating Scale for the Symptoms of Dementia (higher score = poorer function)	1) 4.6 (2.9) (n=33) 2) 4.9 (3.0) (n=30)	Reported no significant difference over time and no group x time interaction (data not provided)	NR
Gerdner 2002[69] 1) Progressively Lowered Stress Threshold (PLST) training program 2) Routine information, community referrals, case management, and support groups	Alzheimer's disease or a related disorder	Moderate to severe cognitive impairment	Subscale from The Memory and Behavior Problems Checklist 1989R (PR)	NR	NR	NR *Authors report rate of increase in ADLs (B=0.33, p < 0.01) did not vary by treatment group*

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Study, Year Interventions	Physical Condition	Baseline Functional Level	IADL or ADL Scale	Baseline	Post-Treatment (SD)	Follow-up* (time assessed)
Gitlin, 2010[10] 1) COPE (n=117) 2) Comparator (n=120)	Dementia	MMSE score <24; needed help with daily activities or had behavioral symptoms	Overall functional dependence (15-item modeled after the FIM; higher score=greater independence)	1) 3.0 (1.2) (n=102) 2) 2.8 (1.3) (n=107)	1) 3.7 (1.3) (n=102) 2) 3.3 (1.3) (n=107) **p=0.02 between groups** Cohen *d*=0.21	NR
			Net % improved overall functional dependence	NA	1) 49% 2) 29% Difference net improvement (95% CI): 19.2 (2.7, 36.0); **p=0.02**	NR
			IADL dependence subscale (8 items, higher score=greater independence)	1) 1.8 (1.0) (n=102) 2) 1.8 (1.0) (n=107)	1) 2.8 (1.2) (n=102) 2) 2.5 (1.1) (n=107) **p=0.007 between groups** Cohen *d*=0.43	NR
			Net % improved IADL dependence	NA	1) 62% 2) 44% Difference net improvement (95% CI): 17.9 (1.9, 34.0) **p=0.03**	NR
			ADL dependence subscale 8 items, higher score =greater independence)	1) 4.3 (1.7) (n=102) 2) 4.1 (1.8) (n=107)	1) 4.6 (1.6) (n=102) 2) 4.3 (1.7) (n=107) p=0.21 between groups	NR
			Activity engagement (high score indicates greater engagement	1) 1.9 (0.4) (n=102) 2) 2.0 (0.4) (n=107)	1) 2.0 (0.4) (n=102) 2) 1.9 (0.4) (n=107) **p=0.03 between groups** Cohen *d*=0.26	NR
			Net % improved Activity engagement	NA	1) 13% 2) -2.0% Difference net improvement (95% CI): 14.6 (-8.8, 38.0); p=0.22	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	IADL or ADL Scale	Baseline	Post-Treatment (SD)	Follow-up* (time assessed)
Gitlin, 2003[73] (REACH) 1) Environmental Skill-Building Program (ESP) (n=89) 2) Resource information plus usual care (n=101)	Dementia	MMSE <24; baseline mean MMSE=12 (moderate)	ADL requiring assistance-mobility subdomain of FIM (scale 1-6; higher score=greater independence)	1) 4.1 (1.9) (n=89) 2) 4.2 (1.9) (n=101)	6 Months 1) 3.7 (1.7) (n=89) 2) 3.8 (1.9) (n=101) p=0.93 between groups	NR
			IADLs requiring assistance (scale 1-6; higher score=greater independence)	1) 1.9 (1.0) (n=89) 2) 1.9 (1.1) (n=101)	6 Months 1) 1.7 (0.8) (n=89) 2) 1.6 (0.9) (n=101) p=0.69 between groups	NR
Gitlin, 2001[57] 1) Home environment program (n=100) 2) Usual care (n=102)	Dementia	"Minimal" ADL Dependency (mean 3.1/6) "High" IADL Dependency (mean 5.5/6)	ADL dependence (modified FIM - scale 1-6; higher score=greater dependence)	1) 2.9 (1.5) (n=93) 2) 3.2 (1.4) (n=78)	3 months 1) 3.2 (1.6) (n=93) 2) 3.6 (1.4) (n=78) p=0.60 between groups; adj mean diff=-0.06 (95%CI -0.3, 0.18)	NR
			IADL dependence (modified FIM - scale 1-6; higher score=greater dependence)	1) 5.4 (0.6) (n=93) 2) 5.6 (0.5) (n=78)	**1) 5.5 (0.6) (n=93)** **2) 5.8 (0.4) (n=78)** **p=0.03 between groups**; adj mean diff=-0.13 (95%CI -0.24, -0.01)	NR
Logsdon, 2010[63] 1) Early Stage Memory Loss (ESML) (n=96) 2) Wait List (WL) (n=46)	Dementia	Early stage Alzheimer's and dementia; (inclusion criteria was MMSE ≥ 18; but mean for enrolled patients was 23.4)	SF-36 Physical Component	1) 42.0 (11.8) (n=96) 2) 43.9 (11.0) (n=46)	1) 41.4 (11.0) (n=92) 2) 42.0 (11.1) (n=44) **p=NR, ns**	NR
Martin-Cook, 2005[60] 1) Caregiver skills training (n=24) 2) Wait List (n=23)	Dementia (primarily Alzheimer's disease)	Baseline mean MMSE=19.4 (moderate)	Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory-MCI version (ADCS-MCI) (score 0-69, higher score=greater functioning)	**1) 35.2 (SE=3.1) (n=24)** **2) 31.7 (SE=3.3) (n=23)** **p=0.03**	7 weeks (2 weeks post-tx) **1) 39.1 (SE=3.2) (n=24)** **2) 31.1 (SE=3.3) (n=23)** **p=0.03**	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	IADL or ADL Scale	Baseline	Post-Treatment (SD)	Follow-up* (time assessed)
Mittelman, 2006 [52] 1) Multi-component intervention (n=203) 2) Usual care (n=203)	AD	Global Deterioration Scale baseline of 4 = 33%; 5 to 7 = 67% (moderate to moderately severe)	Older Americans Resources and Services (OARS) Physical Health rating (1-10; higher score indicates worse health)	1) 2.20 (0.72) (n=203) 2) 2.17 (0.73) (n=203) p=NR	NR	NR
			Global Deterioration Scale (GDS) (1-7, higher score indicates worse functioning)	GDS = 4 1) 72/203 (35.5%) 2) 64/203 (31.5%) p=NR GDS = 5 1) 91/203 (44.8%) 2) 77/203 (37.9%) p=NR GDS = 6 or 7 1) 40/203 (19.7%) 2) 62/203 (30.5%) p=NR	NR	NR
Teri, 2003[12] 1) Reducing Disability in Alzheimer's Disease (n=76) 2) Routine medical care (n=77)	Alzheimer's disease	Baseline MMSE = 16.8 *moderate to severe*	SF-36 physical health component (higher score indicates better functioning)	1) 62.2 (36.6) 2) 67.9 (35.1)	1) 72.1 (33.0) (n=68) 2) 50.7 (39.1) (n=72) p<0.001	21 months post-tx 1) 60.0 (41.1) (n=45) 2) 57.4 (40.2) (n=44) p=0.01 p<0.01 (longitudinal, all post-tx assessments)
			Sickness Illness Profile: Mobility (higher score indicates worse functioning)	1) 16.3 (19.2) 2) 14.2 (13.8)	1) 16.0 (17.1) (n=68) 2) 15.2 (17.1) (n=72) p=0.17	21 months post-tx 1) 18.9 (17.1) (n=45) 2) 21.0 (18.8) (n=44) p=0.01 p=0.02 (longitudinal, all post-tx assessments)
			# of restricted activity days and days spend in bed in past 2 weeks	1) 0.6 (2.2) 2) 0.4 (4.5)	1) 0.1 (0.4) 2) 0.6 (2.5) p<0.001	21 months post-tx 1) 0.9 (3.2) 2) 0.0 (0.3) p=NR p=0.45 (longitudinal, all post-tx assessments)
Wright 2001[67] 1) Education and counseling (n=68) 2) Usual care (n=25)	Alzheimer's disease	Moderate loss of memory; enrolled following in-patient treatment for agitation	% Deceased	NA	12 months 1) 11% (7/61) 2) 22% (5/23) p=ns	NR

*Last follow-up reported only if > 6 months post-treatment
[1]Standard error
ES=effect size; NR=not reported; ns=not statistically significant

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Table 11. Memory-Related Disorders – Cognitive Function

Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Gitlin, 2003[73] (REACH) 1) Environmental Skill-Building Program (ESP) (n=89) 2) Resource information + usual care (n=101)	Dementia	MMSE <24; baseline mean MMSE=12 (moderate)	RMBPC – memory subscale	1) 4.9 (1.5) 2) 4.6 (1.6)	6 months 1) 4.6 (1.5) 2) 4.6 (1.6) p=0.12 between groups Adj mean diff=-0.27 (95%CI -0.60, 0.07)	NR
Gonyea, 2006[64] 1) Behavioral 2) General information (Number randomized not reported)	Alzheimer's disease	Mild to moderate (MMSE 10 or higher)	Neuropsychiatric Inventory (higher scores=greater impairment)	1) 22.9 (13.0) (n=40) 2) 21.7 (12.9) (n=40)	1) 16.4 (10.1) (n=40) 2) 19.4 (12.3) (n=40)	NR
Jirovec, 2001[58] 1) Intervention – scheduled toileting (N=77) 3) Control "friendly" monthly call only (N=41) Note: 2 intervention groups (visits conducted every 2 or 6 months, were combined for analysis due to no differences between groups)	Memory impairment	NR	Short Portable Mental Status Questionnaire (SPMSQ) (higher score=greater cognitive impairment)	1) 6.6 (2.2) (n=44) 2) 6.7 (2.1) (n=30) p=NR, ns	1) 6.7 (2.1) (n=44) 2) 7.1 (2.3) (n=30) p=NR, ns	NR
Martin-Cook, 2005[60] 1) Caregiver skills training (n=24) 2) Wait List (n=23)	Dementia (primarily Alzheimer's disease)	Baseline mean MMSE=19.4 (moderate)	Neuropsychiatric Inventory (NPI) (score range 1-114, higher score=poor functioning)	1) 13.6 (SE=2.5) (n=24) 2) 12.5 (SE=2.6) (n=23) p=NR	7 weeks (2 weeks post-tx) 1) 12.6 (SE=2.5) (n=24) 2) 12.0 (SE=2.6) (n=23) p=NR (ns)	NR
			Mini-mental state examination (MMSE)	1) 19.4 (SE=1.4) (n=24) 2) 19.0 (SE=1.5) (n=23) p=NR	7 weeks (2 weeks post-tx) 1) 20.8 (SE=1.5) (n=24) 2) 18.6 (SE=1.5) (n=23) p=NR (ns)	NR
McCurry 2005[61] 1) Nighttime Insomnia Treatment and Education for Alzheimer's Disease (NITE-AD; n=17) 2) Supportive contact control (n=19)	Alzheimer's disease	Community-dwelling and ambulatory; dementia for 5.8 years on average; Mini-Mental State Exam of 11.8 on average	RMBPC – ***Memory***** (Average frequency of behaviors over past week)	1) 3.3 (0.6) (n=17) 2) 2.9 (1.0) (n=19)	1) 3.1 (0.6) (n=13) 2) 2.6 (0.9) (n=16)	1) 3.2 (0.6) (n=11) 2) 2.6 (0.8) (n=12) (6 months)
Ostwald, 1999[50] 1) Minnesota Family Workshop (MFW), n=72 2) Workshop wait list, n=45	Dementia	Signs of mild to severe dementia	Mini-mental state examination (MMSE)	1) 17.6 (7.1), n=45 2) 19.8 (6.9), n=29 p=NR	1) 17.4 (7.3), n=45 2) 18.9 (7.6), n=29 Intervention effect: p=0.32 Intervention by time: p=0.45	

Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Quayhagen, 2000[62] 1) Cognitive stimulation (n=21) 2) Dyadic counseling (n=29) 3) Dual supportive seminar (n=22) 4) Early day care (n=16) 5) Wait list (n=15)	Dementia (possible or probably Alzheimer's disease, or cardio vascular multi-infarct)	Mild to moderate	Problem solving-composite of Geriatric Coping Schedule and conceptualization factor from DRS (higher score=better problem solving)	1) 66.4 (SE=2.7) 2) 64.5 (SE=2.6) 3) 66.4 (SE=2.6) 4) 66.6 (SE=4.9) 5) 67.5 (SE=4.7) p=ns	3 months (1 month post-tx) (n=103) 1) 72.3 (SE=3.8)‡ 2) 65.2 (SE=3.2) 3) 66.8 (SE=3.2) 4) 65.8 (SE=3.1) 5) 64.9 (SE=6.3) p=0.073 (‡p=0.009 for 1st intervention over time)	NR
			Immediate Memory - composite of Logical Memory I and Visual Reproduction 1 from Wechsler Memory Scale – Revised (WMS-R) and memory factor of Dementia Rating Scale (DRS)	1) 41.2 (SE=3.5) 2) 39.5 (SE=2.7) 3) 37.8 (SE=3.1) 4) 40.3 (SE=4.4) 5) 39.0 (SE=4.2) p=ns	3 months (1 month post-tx) (n=103) 1) 43.5 (SE=4.4) 2) 39.2 (SE=2.6) 3) 37.6 (SE=3.1) 4) 41.3 (SE=3.8) 5) 38.3 (SE=5.2) p=ns	NR
			Delayed Memory - composite of WMS-R Logical Memory II and Visual Reproduction II	1) 6.9 (SE=1.9) 2) 7.1 (SE=1.9) 3) 6.9 (SE=2.4) 4) 8.6 (SE=3.5) 5) 5.9 (SE=2.9) p=ns	3 months (1 month post-tx) (n=103) 1) 10.1 (SE=2.5) 2) 7.8 (SE=1.9) 3) 7.6 (SE=2.3) 4) 9.6 (SE=4.0) 5) 6.3 (SE=3.2) significant time main effect (p=0.03) due to improvement in group 1; "less change" in other groups	
			Verbal Fluency: Composite of 2 recalled word scales and initiation factor score on DRS	1) 65.9 (SE=5.5) 2) 60.2 (SE=3.4) 3) 61.6 (SE=3.9) 4) 63.4 (SE=4.9) 5) 61.4 (SE=5.7) p=ns	3 months (1 month post-tx) (n=103) 1) 70.1 (SE=6.3) 2) 58.7 (SE=3.5) 3) 60.6 (SE=4.5) 4) 63.2 (SE=4.4) 5) 59.9 (SE=7.7) p=ns	

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Teri, 1997[70] 1) Behavior Therapy-Pleasant Events (BT-PE) (n=23) 2) Behavior Therapy-Problem-solving (BT-PS) (n=19) 3) Usual care (n=10) 4) Wait list (n=20)	Alzheimer's disease and depression	Baseline MMSE = 16.5	Mini Mental Status Exam	1) 15.8 (7.8) 2) 15.7 (7.4) 3) 16.8 (5.4) 4) 17.9 (7.9) Group differences=ns	Mean change 1) -0.9 (3.1) 2) -1.0 (2.9) 3) 0.1 (4.1) 4) -0.7 (3.6) Group differences=ns	
			DRS (Dementia Rating Scale)	1) 105.8 (30.7) 2) 106.8 (24.2) 3) 111.2 (14.5) 4) 112.1 (22.0) Group differences=ns	Mean change 1) -5.0 (11.9) (n=16) 2) -1.3 (8.2) (n=9) 3) 2.6 (15.3) (n=8) 4) 3.6 (6.3) (n=14) Group differences=ns	
Teri, 2005[66] 1) STAR Caregivers (n=47) 2) Routine medical care (n=48)	Alzheimer's disease	Baseline MMSE = 14 *moderate*	RMBPC – Memory subscale	1) 3.0 (0.7) 2) 3.0 (0.8)	6 months **1) 2.8 (0.8) (n=32)** **2) 3.1 (1.0) (n=31)** **p=0.031** (longitudinal, adjusted for baseline values, includes 2 & 6 month assessments)	NR

*Last follow-up reported only if > 6 months post-treatment

**Data obtained from author

ES=effect size; NR=not reported; ns=not statistically significant

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Table 12. Memory-Related Disorders – Quality of Life – Global Functioning

Study, Year Interventions	Physical Condition	Baseline Functional Level	Quality of Life Assessment Scale	Baseline	Post-Treatment	Follow-up* (time assessed)
Belle, 2006[55] 1) Multicomponent (n=323) 2) Attention control (check-in calls) (n=319)	Alzheimer's or related disorders	NR; required to have diagnosed disease	Single question – Did participation in this project help improve care recipient's life?	NA	**"A great deal"** **1) 40.4% (n=323)** **2) 16.3% (n=319)** **RR=2.47 [1.86, 3.27]**	NR
Gitlin, 2010[10] 1) Care of Persons with Dementia in their Environments (COPE) (n=117) 2) Comparator (n=120)	Dementia	MMSE score <24; needed help with daily activities or had behavioral symptoms	Quality of Life–Alzheimer's Disease scale (12 items, scale 1-4; higher scores indicated better quality of life)	1) 2.1 (0.4) (n=102) 2) 2.1 (0.5) (n=107)	1) 2.2 (0.5) (n=102) 2) 2.1 (0.5) (n=107) p=0.06 between groups Cohen's *d*=0.14	NR
Gitlin, 2008[74] 1) Tailored Activity Program (TAP) (n=30) 2) Wait list (N=30)	Dementia	MMSE <24; able to feed self and participate in ≥ 2 self-care activities; baseline mean MMSE=12 (moderate)	12-item Quality of Life-Alzheimer's Disease (QOL-AD) scale; score is mean response (1=poor, 4=excellent)	1) 2.2 (0.3) (n=27) 2) 2.0 (0.4) (n=29)	4 Months 1) 2.4 (0.4) (n=27) 2) 2.1 (0.5) (n=29) p=0.095 between groups	NR
Logsdon, 2010[63] 1) Early Stage Memory Loss (ESML) (n=96) 2) Wait list (WL) (n=46)	Dementia	Early stage Alzheimer's and dementia; (inclusion criteria was MMSE ≥ 18; but mean for enrolled patients was 23.4)	Quality of Life-Alzheimer's Disease (QOL-AD) (13-item measure, with a higher score indicating greater improvement)	1) 39.0 (6.0) (n=96) 2) 38.8 (5.6) (n=46)	1) 39.6 (5.3) (n=92) 2) 37.8 (6.3) (n=44) **p<0.01; β=1.74** **Effect size=0.44** # improved by group: 1) 48% 2) 30% p<0.05	NR
Teri, 2005[66] 1) STAR Caregivers (n=47) 2) Routine medical care (n=48)	Alzheimer's disease (possible or probable)	Baseline mean MMSE=14 (moderate)	13-item Quality of Life-Alzheimer's Disease (QOL-AD) (higher score=better QOL)	1) 27.8 (5.5) 2) 28.3 (4.9)	6 months **1) 28.4 (5.4) (n=32)** **2) 28.2 (4.6) (n=34)** **p=0.031** (longitudinal, adjusted for baseline values, includes 2 & 6 month assessments)	NR
Wright, 2001[67] 1) Education and counseling (n=68) 2) Usual care (n=25)	Alzheimer's disease	Moderate loss of memory; enrolled following in-patient treatment for agitation	Blessed Dementia Rating Scale (scale 0-17; higher score=more severe dementia)	1) 7.87 (3.47), n=68 2) 9.62 (3.38), n=25 p=0.03 Used as covariate to explain agitation; correlation with agitation (r=0.40, p<0.0001)	"Over time" (unclear if 12 months) 1) 10.5 2) 12.4 (SD not reported) Correlation with agitation (r=0.21, p=ns)	NR

*Last follow-up reported only if > 6 months post-treatment
[1]Scale of -3 to +3; higher score indicates better well-being
ES=effect size; NR=not reported; ns=not statistically significant

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Table 13. Memory-Related Disorders – Symptom Management/Control

Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
Belle, 2006[55] 1) Multicomponent (n=323) 2) Attention control (check-in calls) (n=319)	Alzheimer's or related disorders	NR; required to have diagnosed disease	3 questions for memory, depression, and disruption; scale of 1 (substantial improvement) to 5 (substantial decline); total 3 to 15 with higher score indicating greater decline		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 not reported)	NR
Bourgeois, 2002[72] 1) Patient-change 2) Self-change 3) Visitation control (Number randomized not reported)	Alzheimer's disease	MMSE score of 20 or less	Behave-AD *Total Score* (max score of 75, higher score=perception of more severe problems)	1) 16.9 (10.2) (n=18) 2) 18.4 (7.7) (n=18) 3) 18.6 (8.8) (n=15)	1) 15.2 (10.1) 2) 13.5 (6.3) 3) 18.4 (10.8) **Group 2 vs Group 3: p<0.05** All other p values, NR, ns	1) 17.5 (10.4) 2) 14.8 (10.5) 3) 23.1 (11.4) **Group 2 vs Group 3: p<0.01** All other p values, NR, ns
			Behave AD - *Aggressivity/ Activity Disturbance Subscale*	1) 6.4 (4.3) (n=18) 2) 5.8 (2.5) (n=18) 3) 6.7 (3.0) (n=15)	1) 5.4 (4.2) 2) 5.3 (3.4) 3) 6.9 (3.3) All p values, NR, ns	1) 5.6 (3.8)* 2) 5.2 (3.6)** 3) 8.4 (2.4) **Group 1 vs Group 3: p<0.05** **Group 2 vs Group 3: p<0.01** All other p values, NR, ns
			Behave AD *Psychosis/ Delusion Subscale*	1) 4.6 (4.0) (n=18) 2) 6.9 (6.3) (n=18) 3) 6.9 (5.0) (n=15)	1) 4.8 (4.0) 2) 4.8 (4.3) 3) 5.8 (5.4) All p values, NR, ns	1) 6.8 (5.1) 2) 5.5 (6.3) 3) 7.6 (7.1) All p values, NR, ns
			Frequency of Problem Behaviors (weekly average)	1) 2.5 (1.9) (n=12) 2) 2.0 (0.8) (n=16) 3) 1.7 (0.9) (n=15)	1) 1.3 (2.1) 2) 2.0 (0.7) 3) 2.0 (0.8) **Group 1 vs Group 3: p<0.05** All other p values, NR, ns	1) -0.2 (3.4) 2) 1.5 (1.9) 3) 1.9 (1.2) **Group 1 vs Group 3: p<0.01** All other p values, NR, ns

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
Burgener 1998[65] 1) Educational and behavioral intervention (n=11) 2) Education only (n=12) 3) Behavioral only (n=12) 4) Comparison group (n=12)	Alzheimer's disease or multi-infarct dementia	Baseline mean MMSE=8.9 (moderate to severe)	Dementia Behavior Disturbance Scale (DBDS) (higher score=increased level of difficult behavior)	1) 28.4 2) 36.8 3) 25.9 4) 25.6 (SD not reported)	NR	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
Burns, 2003[51] 1) Behavior Care (n=85) 2) Enhanced Care (n=82)	Alzheimer's disease and related disorders	Medical diagnosis or <24 on MMSE and limitations in ADLs/IADSLs	Revised Memory and Behavior Problems Checklist (RMBPC) (0 to 96, higher score=greater bother)	1) 19.6 (11.6) (n=37) 2) 11.8 (12.7) (n=39) p=0.007	1) 14.8 (10.2) (n=37) 2) 9.2 (12.8) (n=38) group effect: p=0.92 group x time interaction: p=0.98	NR
Camberg, 1999[11] 1) SimPres audio tape 2) Placebo audio tape 3) Usual care Crossover trial, n=54	Alzheimer's disease	Average MMSE = 5.1(4.4) – severe cognitive impairment	SCMAI agitated behaviors scale –lower score = more positive well-being (weekly staff surveys)	NR	1) 25.5 2) 27.1 3) 25.1 All 3 groups: F=3.9, df 2616, p=0.021 Group 1) vs 2) p=0.134 Group 1) vs 3) p=0.714 Group 2) vs 3) p=0.017	NR
Chang, 1999[71] 1) Nurseline cognitive-behavioral (n=34) 2) Placebo telephone calls (n=31)			Functional Rating Scale for the Symptoms of Dementia (14 items scores 0-3; higher score = poorer function; <21 able to stay at home longer)	Overall Function 1) 18.4 (8.9) 2) 18.5 (8.4) Behavior Subscore 1) 13.6 (9.0) 2) 13.8 (6.4)	**1) 19.5 (8.6)** **2) 20.0 (9.0)** **p=0.03 over time (interaction p=ns)** **1) 14.9 (6.3)** **2) 15.1 (6.5)** **p=0.02 over time (interaction p=ns)**	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
Gerdner 2002 1) Progressively Lowered Stress Threshold (PLST) training program 2) Routine information, community referrals, case management, support groups	Alzheimer's disease or a related disorder	Moderate to severe cognitive impairment	The Memory and Behavior Problems Checklist (PR)	NR	NR	NR For non-spouse caregivers: 1) *B* = 0.00, ns 2) *B* = 0.77, *p* < .01 (increase in behavior problems) For spouse caregivers: 1) *B* = 0.18, ns 2) *B* = 0.18, ns
Gitlin, 2010[75] 1) Advanced Caregiver Training (ACT) (n=137) 2) Control (n=135)	Dementia	MMSE score <24	# problem behaviors at baseline (ABID) Frequency of problem behaviors/month (RMBPC)	1) 9.4 (3.7) (N=117) 2) 9.9 (4.0) (N=122) p=0.34 1) 12.1 (13.4) (N=117) 2) 13.5 (11.7) (N=122) p=0.21	NR NR	NR NR
			Targeted behavior improved (Selected one problem behavior to target for improvement)	NA	1) 67.5% (N=117) 2) 45.8% (N=122) **p=0.002**	NR
			Targeted behavior stayed the same	NA	1) 14.0% (N=117) 2) 22.5% (N=122)	
			Targeted behavior worsened	NA	1) 18.4% (N=117) 2) 31.7% (N=122)	
Gitlin, 2010[10] 1) COPE (n=117) 2) Comparator (n=120)	Dementia	MMSE score <24; needed help with daily activities or had behavioral symptoms	Agitated Behavior in Dementia scale – higher score indicates greater number and frequency of agitated behaviors	1) 11.0 (14.6) (n=102) 2) 9.8 (10.7) (n=107)	1) 6.7 (10.6) (n=102) 2) 5.5 (8.0) (n=107) p=0.59 between groups	NR
Gitlin 2008[74] 1) Tailored Activity Program (TAP) (n=30) 2) Wait list (N=30)	Dementia	MMSE <24; able to feed self and participate in ≥ 2 self-care activities; baseline mean MMSE=12 (moderate)	Frequency of occurrence of 24 behaviors; caregivers indicated occurrence (yes or no) and, if yes, frequency in past month	1) 30.5 (30.3) (n=27) 2) 41.5 (70.5) (n=29)	**4 months** **1) 18.8 (17.6) (n=27)** **2) 60.8 (85.3) (n=29)** **d=0.72; p=0.009 between groups**	NR
			Number of behaviors occurring	1) 8.0 (3.8) (n=27) 2) 7.5 (4.5) (n=29)	4 months 1) 7.2 (4.1) (n=27) 2) 7.7 (3.7) (n=29) p=0.249 between groups	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
Gitlin 2003[73] (REACH) 1) Environmental Skill-Building Program (ESP) (n=89) 2) Resource information + usual care (n=101)	Dementia	MMSE <24; baseline mean MMSE=12 (moderate)	Modified RMBPC - number of disruption-related behaviors (higher score=occurrence of increased number of behaviors)	1) 2.1 (1.6) 2) 2.2 (1.8)	6 months 1) 1.9 (1.6) 2) 2.0 (1.9) p=0.74 between groups	NR
Gitlin 2001[57] 1) Home environment program (n=100) 2) Usual care (n=102)	Dementia	"Minimal" ADL Dependency (mean 3.1/6) "High" IADL Dependency (mean 5.5/6)	Total number of problem behaviors (from 29-item MBPC + 4 related behaviors) (higher score=greater number of problem behaviors)	1) 20.3 (5.4) (n=93) 2) 18.7 (6.3) (n=78)	3 months 1) 17.2 (7.7) (n=93) 2) 14.4 (9.8) (n=78) p=0.11 between groups Adj mean diff=1.85 (95%CI -0.42, 4.13)	NR
Jirovec, 2001[58] 1) Intervention – scheduled toileting (N=77) 2) Control "friendly" monthly call only (N=41) Note: 2 intervention groups (visits every 2 or 6 months) combined for analysis due to no differences between groups	Memory impairment	NR	% Urinary Incontinence (UI) (incontinent episodes divided/ total voiding episodes)	1) 43% (23%) (n=44) 2) 47% (31%) (n=30) p=NR, ns	1) 37% (28%) (n=44) 2) 49% (36%) (n=30) p=NR	NR
			# patients whose incontinence decreased	NA	1) 28/44=64% 2) 15/30=50% **Z=-1.83, p<0.05**	
McCallion, 1999[68] 1) FVEP (Family Visit Education Program) (n=32) 2) Usual Care (UC) (n=34)	Dementia	Severe impairment – weighted mean MMSE=6.9	MOSES (Multidimensional Observation Scale for Elderly Subjects)	Self-care 1) 24.7 (5.1) 2) 24.0 (5.6) Disorientation 1) 28.6 (6.3) 2) 25.6 (6.2) Irritability 1) 16.7 (6.2) 2) 14.6 (4.7) Withdrawal 1) 23.1 (4.2) 2) 22.4 (5.4)	Self-care 1) 25.0 (5.7) 2) 24.8 (5.8) p=NR, ns **Disorientation** **1) 29.0 (7.8)** **2) 24.5 (7.5)** **p=0.046** Irritability 1) 17.2 (7.3) 2) 14.0 (4.7) p=NR, ns Withdrawal 1) 23.4 (5.4) 2) 21.9 (5.4) p=NR, ns	NA

Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
McCallion, 1999[68] (continued)			Cohen-Mansfield Agitation Inventory CMAI Nursing staff report: Likert scale rating resident's behavior over 2 week period Trained study observer version: # behavior observations/20 minute period, while patient was visiting with family member	(n's by group=NR) Physically aggressive behavior *Nurse Staff:* 1) 12.5 (7.1) 2) 10.6 (4.6) *Study observer:* 1) 0.0 (0.0) 2) 0.0 (0.0) Physically non-aggressive behavior *Nurse Staff:* 1) 14.3 (7.6) 2) 10.6 (5.6) *Study observer:* 1) 0.5 (1.4) 2) 0.3 (1.2) Verbally agitated behavior *Nurse Staff:* 1) 10.6 (9.6) 2) 11.6 (7.7) *Study observer:* 1) 1.7 (3.2) 2) 0.5 (1.2)	(n's by group=NR) Physically aggressive behavior *Nurse Staff:* 1) 11.7 (6.1) 2) 9.7 (3.2) p=NR, ns *Study observer:* 1) 0.3 (1.5) 2) 0.0 (0.0) p=NR, ns Physically non-aggressive behavior *Nurse Staff:* 1) 12.5 (7.2) 2) 10.6 (5.2) p=NR, ns *Study observer:* 1) 1.4 (4.4) 2) 1.1 (6.0) p=NR, ns Verbally agitated behavior *Nurse Staff:* 1) 13.9 (8.6) 2) 10.6 (7.5) p=NR, ns *Study observer:* 1) 1.9 (3.8) 2) 0.9 (2.0) p=NR, ns	NA

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
McCurry 2005[61] 1) Nighttime Insomnia Treatment and Education for Alzheimer's Disease (NITE-AD; n=17) 2) Supportive contact control (n=19)	Alzheimer's disease	Community-dwelling and ambulatory; dementia for 5.8 years on average; Mini-Mental State Exam of 11.8 on average	RMBPC – ***Disruption****** (Average frequency of behaviors over past week)	1) 1.1 (0.7) (n=17) 2) 1.0 (0.5) (n=19)	1) 0.8 (0.6) (n=13) 2) 0.8 (0.6) (n=16)	1) 0.9 (0.6) (n=11) 2) 0.7 (0.6) (n=12) (6 months)
			RMBPC – ***Memory****** (Average frequency of behaviors over past week)	1) 3.3 (0.6) (n=17) 2) 2.9 (1.0) (n=19)	1) 3.1 (0.6) (n=13) 2) 2.6 (0.9) (n=16)	1) 3.2 (0.6) (n=11) 2) 2.6 (0.8) (n=12) (6 months)
			Sleep activity: Night wake time (hours)	1) 1.9 (1.4) (n=17) 2) 1.6 (1.3) (n=19)	1) 1.1 (0.9) (n=13) 2) 1.6 (1.0) (n=16) p<0.05	**1) 1.2 (0.8) (n=11) 2) 1.8 (1.8) (n=12) (6 months) p=0.03**
			Number of night awakenings	1) 12.4 (11.6) (n=17) 2) 9.9 (7.9) (n=19)	1) 7.1 (6.4) (n=13) 2) 11.3 (7.6) (n=16) p=0.09	**1) 8.2 (7.1) (n=11) 2) 12.2 (11.3) (n=12), p=0.01**
			Percentage of time asleep (sleep hrs/time in bed)	1) 79.9 (12.4) (n=17) 2) 83.1 (11.1) (n=19)	1) 87.6 (9.4) (n=13) 2) 83.9 (9.0) (n=16) p=0.19	1) 85.9 (9.3) (n=11) 2) 82.4 (16.2) (n=12), p=0.12
			Wake index (wakes/hour)	1) 2.6 (5.4) (n=17) 2) 1.4 (1.1) (n=19)	1) 0.9 (0.8) (n=13) 2) 1.5 (1.1) (n=16) p=0.14	**1) 1.1 (1.1) (n=11) 2) 1.5 (1.4) (n=12) p=0.03**
			Duration of night awakenings (minutes)	1) 8.2 (1.7) (n=17) 2) 7.6 (1.1) (n=19)	1) 8.0 (2.0) (n=13) 2) 7.9 (1.2) (n=16) p=0.26	**1) 8.0 (2.0) (n=11) 2) 8.3 (1.6) (n=12) p=0.04**
Mittelman 2004[54] 1) Multicomponent intervention (n=203) 2) Usual care (n=203)	Alzheimer's disease	Global Deterioration Scale baseline of 4 = 33%; 5 to 7 = 67% (moderate to moderately severe)	Frequency of Problem Behaviors - Memory Behavior Problems Checklist (MBPC) (sum of 5 point Likert scale for 29 troublesome behaviors; higher score indicates greater frequency	**1) 41.2 (18.3) (n=203) 2) 46.7 (19.4) (n=203) p=0.004**	NR	NR; p=NR but "virtually no differences reported" Growth model: Group 1) vs 2) t=0.19, p=0.8469 Group x time: t=-0.04, p=0.9695
Ostwald, 1999[50] 1) Minnesota Family Workshop (MFW) (n=72) 2) Workshop wait list (n=45)	Dementia	Signs of mild to severe dementia	RMPBC – disruptive behavior subscale	1) 6.8 (5.8), n=52 2) 5.3 (4.1), n=31 p=NR	1) 6.2 (5.3), n=52 2) 4.9 (3.5), n=31 Intervention effect: p=0.43 Intervention by time: p=0.08	

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Problem Behavior	Baseline	Post-Treatment	Follow-up* (time assessed)
Quayhagen 2000[62] 1) Cognitive stimulation (n=21) 2) Dyadic counseling (n=29) 3) Dual supportive seminar (n=22) 4) Early day care (n=16) 5) Wait list (n=15)	Dementia (possible or probably Alzheimer's disease, or cardio vascular multi-infarct)	Mild to moderate	MBPC part A (Zarit et al., 1985)	1) 21.8 (SE=3.2) 2) 22.0 (SE=2.4) 3) 24.8 (SE=3.5) 4) 27.8 (SE=4.2) 5) 25.4 (SE=5.1) p=ns	3 months (1 month post-tx) (n=103) 1) 22.3 (SE=3.7) 2) 22.0 (SE=2.7) 3) 25.2 (SE=3.6) 4) 30.5 (SE=4.5) 5) 25.9 (SE=5.4) p=ns	NR
Robison 200753** 1) Partners in Caregiving in the Special Care Unit Environment (PIC-SCU) (n=209) 2) Control unit (n=179)	Dementia	All institutionalized at specialized skilled nursing facilities	Cohen-Mansfield Agitation Inventory (CMAI) (5 point scale, 1 = resident never engages in specific behavior, 5 = manifests behavior on average several times/hour). *7 of 14 behaviors on CMAI reported; remaining 7 behaviors not shown (treatment group showed more improvement than control group, however, differences between groups non-significant)* *repeated measures analyses (not single time point comparisons)*	N=561 total (n by group NR); all p=NR Cursing or verbal aggression 1) 1.84 2) 1.74 Other aggression, self-abuse, or sexual advances 1) 1.35 2) 1.23 Inappropriate dress or disrobing 1) 1.41 2) 1.20 Constant requests for attention or help 1) 1.76 2) 1.63 Grabbing people, destroying property 1) 1.46 2) 1.49 Pacing, wandering 1) 1.35 2) 1.23 Restlessness 1) 2.05 2) 1.80	NR	NR
Wright 200167 1) Education and counseling (n=68) 2) Usual care (n=25)	Alzheimer's disease	Moderate loss of memory; enrolled following in-patient treatment for agitation	Cohen-Mansfield Agitation Inventory (CMAI) (higher score=greater agitation)	1) 65.9 (21.9) 2) 74.1 (21.4) p=0.13	1) NR 2) NR Controlling for dementia rating - group x time p=0.52	NR

*Last follow-up reported only if > 6 months post-treatment

**Note: Unit of intervention is the facility special care unit – not individual family members. N's above reflect family members of residents living on the unit that participated. CMAI outcome reported for ALL patients on randomized units, regardless of whether or not the patient's family members participated in intervention.

***Data obtained from author

[1]Univariate analyses of covariance, with baseline measures of HbA1c, FBP and diabetes knowledge as covariates (no significant differences between groups at baseline)

ES=effect size; NR=not reported; ns=not statistically significant

Table 14. Memory-Related Disorders – Patient Depression/Anxiety

Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Gitlin 2008[74] 1) Tailored Activity Program (TAP) (n=30) 2) Wait list (N=30)	Dementia	MMSE <24; able to feed self and participate in ≥ 2 self-care activities; baseline mean MMSE=12 (moderate)	Cornell Scale for Depression in Dementia (CSDD); sum of combined ratings of patient and caregiver (0=not present, 2=severe)	1) 9.2 (5.1) (n=27) 2) 8.1 (4.5) (n=29)	4 Months 1) 9.0 (4.6) (n=27) 2) 8.7 (4.7) (n=29) p=0.34 between groups	NR
Logsdon, 2010[63] 1) Early Stage Memory Loss (ESML) (n=96) 2) Wait list (WL) (n=46)	Dementia	Early stage Alzheimer's and dementia; (inclusion criteria MMSE ≥ 18; mean for enrolled patients was 23.4)	Geriatric Depression Scale (GDS) (higher score indicates higher level of depression)	1) 5.3 (3.5) (n=96) 2) 5.3 (3.4) (n=46)	1) 5.1 (3.5) (n=92) 2) 5.9 (4.0) (n=44) **p<0.01; β=-1.34** **Effect size=0.36**	NR
McCurry 2005[61] 1) Nighttime Insomnia Treatment and Education for Alzheimer's Disease (NITE-AD; n=17) 2) Supportive contact control (n=19)	Alzheimer's disease	Community-dwelling and ambulatory; dementia for 5.8 years on average; Mini-Mental State Exam of 11.8 on average	Revised Memory and Behavior Problems Checklist (RMBPC) – depression (average frequency of behavior over 1 week)	1) 1.1 (0.6) (n=17) 2) 0.8 (0.6) (n=19) ns	**1) 0.8 (0.6) (n=13)** **2) 0.7 (0.7) (n=16)** **Comparisons between pre to post-treatment change scores** **p=0.04**	**6 months** **1) 0.9 (0.7) (n=11)** **2) 0.9 (0.9) (n=12)** **p=0.007**
			Cornell Depression Scale*** (8+=mild depression; 12+= moderate depression)	1) 9.2 (5.0) (n=17) 2) 7.1 (2.6) (n=19)	1) 7.1 (3.8) (n=13) 2) 6.2 (3.0) (n=16)	1) 7.5 (6.0) (n=11) 2) 7.5 (4.2) (n=12)
McCallion, 1999[68] 1) FVEP (Family Visit Education Program) (n=32) 2) Usual Care (UC) (n=34)	Dementia	Severe impairment – weighted mean MMSE= 6.9	MOSES (Multidimensional Observation Scale for Elderly Subjects) – Depression subscale	1) 19.2 (7.3) 2) 14.6 (6.0) (n by group=NR)	1) 20.8 (7.8) 2) 15.1 (6.6) (n by group=NR) p=NR, ns	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
McCallion, 1999[68] (continued)			CSDD (Cornell Scale for Depression in Dementia) - subscales (higher score indicates greater level of depression)	(n by group=NR) Mood-related signs 1) 2.9 (2.1) 2) 2.2 (1.7) Behavioral disturbance 1) 1.3 (1.0) 2) 1.5 (1.3) Physical signs 1) 0.9 (1.2) 2) 0.9 (1.6) Cyclic functions 1) 1.2 (1.4) 2) 1.9 (1.7) Ideational disturbance 1) 0.5 (1.1) 2) 0.2 (0.6	(n by group=NR) **Mood-related signs** **1) 2.6 (2.1)** **2) 2.7 (1.6)** **p=0.003** Behavioral disturbance 1) 1.4 (1.6) 2) 1.4 (1.2) p=nr, ns **Physical signs** **1) 0.5 (1.1)** **2) 1.1 (1.8)** **p=0.024** **Cyclic functions** **1) 0.9 (1.4)** **2) 1.0 (1.3)** **p=0.020** **Ideational disturbance** **1) 0.4 (1.1)** **2) 0.4 (1.0)** **p=0.040**	NA
Teri, 1997[70] 1) Behavior Therapy-Pleasant Events (BT-PE) (n=23) 2) Behavior Therapy-Problem-solving (BT-PS) (n=19) 3) Usual care (n=10) 4) Wait list (n=20)	Alzheimer's disease and depression	Baseline MMSE = 16.5 (moderate)	Hamilton Depression Rating Scale	1) 16.3 (5.3) 2) 16.0 (4.0) 3) 14.1 (4.0) 4) 14.5 (3.5) Group differences=ns	Mean change 1) -5.3 (4.0) 2) -3.8 (2.3) 3) -0.3 (4.7) 4) 0.3 (3.5) 1 > 3 & 4, p<0.01 2 > 3 & 4, p<0.01 1 vs 2=ns	6 months, groups 1 and 2 combined but not compared controls
			Cornell Scale for Depression in Dementia	1) 14.8 (4.2) 2) 15.1 (3.5) 3) 13.9 (4.6) 4) 14.0 (4.2) Group differences=ns	Mean change 1) -4.2 (4.5) 2) -3.7 (3.8) 3) 0.0 (2.0) 4) 0.1 (3.5) 1 > 3 & 4, p<0.01 2 > 3 & 4, p<0.01 1 vs 2=ns	NR

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Study, Year Interventions	Physical Condition	Baseline Functional Level	Assessment Tool	Baseline	Post-Treatment	Follow-up* (time assessed)
Teri, 1997[70] (continued)			Beck Depression Inventory	1) 15.5 (7.1) 2) 21.7 (7.9) 3) 17.9 (9.2) 4) 17.1 (8.4) Group differences=ns	Mean change 1) -1.3 (6.3) 2) -4.5 (4.5) 3) 1.9 (5.8) 4) 0.5 (3.5) 1 > 3 & 4, p<0.01 2 > 3 & 4, p<0.01 1 vs 2=ns	NR
			Clinically significant improvement**	NR	1) 52% 2) 68% 3) 20% 4) 20% Overall p<0.005	NR
Teri 2003[12] 1) Reducing Disability in Alzheimer's Disease (n=76) 2) Routine medical care (n=77)	Alzheimer's disease	Baseline MMSE = 16.8 (moderate)	Cornell Scale for Depression in Dementia (higher score indicates greater impairment)	1) 5.7 (3.9) (n=76) 2) 5.8 (4.5) (n=77)	1) 5.2 (3.6) (n=72) 2) 6.2 (3.8) (n=68) **p=0.02**	21 months post-treatment 1) 6.4 (4.5) (n=44) 2) 7.4 (5.0) (n=45) p=0.10 (longitudinal)
			Hamilton Depression Rating Scale (higher score indicates greater impairment)	NR	Only patients with CSDD≥ 6 at baseline: Post-tx (n=NR) 1) improved 2.0 (4.9) 2) declined 0.6 (5.1) Adj mean difference: **2.21 (95% CI, 0.22-4.20), p=0.04**	Only patients with CSDD≥ 6 at baseline: 21 months post-treatment, values NR; Adj mean difference: **2.14 (95% CI, 0.14-4.17), p=0.04**

*Last follow-up reported only if > 6 months post-treatment; [1]higher score indicates higher level of emotion; [2]higher score indicates poorer adjustment
**% no longer meeting criteria for major depression (if major depression at pre-treatment) or no longer meeting criteria for minor or major depression (if minor depression at pre-treatment)
***Data obtained from author
ES=effect size; NR=not reported; ns=not statistically significant

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Table 15. Memory-Related Disorders – Hospitalization or Institutionalization

Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Hospitalization or Institutionalization	Baseline	Post-Treatment	Follow-up* (time assessed)
Bass, 2003[56] 1) Care consultation (N=109) 2) Usual care (N=73)	Dementia, Alzheimer's disease, memory loss	Not reported	# Emergency Department Visits past 12 months (range 0-5 for total sample)	1) 0.4 (1.0) (n=NR) 2) 0.4 (0.9) (n=NR)	1) 0.5 (1.0) (n=NR) 2) 0.7 (1.1) (n=NR) p=NR, ns	NR
			# Hospital Admissions past 12 months (range 0-4 for total sample)	1) 0.2 (0.6) (n=NR) 2) 0.3 (0.6) (n=NR)	1) 0.2 (0.6) (n=NR) 2) 0.3 (0.6) (n=NR) p=NR, ns	NR
			# Physician Visits past 12 months (range 0-27 for total sample)	1) 2.9 (2.8) (n=NR) 2) 2.9 (2.6) (n=NR)	1) 5.2 (4.0) (n=NR) 2) 5.2 (4.5) (n=NR) p=NR, ns	NR
Belle, 2006[55] 1),Multicomponent (n=323) 2) Attention control (check-in calls) (n=319)	Alzheimer's or related disorders	NR; required to have diagnosed disease	Institutionalization (permanent as reported by caregiver)	NR	1) 4.3% (n=261) 2) 7.2% (n=257) p=0.118 (no difference between groups for any racial/ethnic group)	NR
Brodaty, 2009[59] 1) Donepezil + standard services + psychological caregiver intervention (n=26) 2) Donepezil + standard services (n=26)	Alzheimer's disease	GDS=4.5 (0.55) MMSE=20.7 (5.27) ADCS-ADL=58.1 (13.03) ADAS-Cog=26.8 (10.79) RMBPCL=10.98 (7.94)	Admitted to nursing home	NR	NR	1) 27% (7/26) 2) 23% (6/26) Mean follow-up = 5.4 years, up to 8.5 years
Mittelman, 2006 [52] 1) Multicomponent intervention (n=203) 2) Usual care (n=203)	Alzheimer's disease	Global Deterioration Scale baseline of 4 = 33%; 5 to 7 = 67% (moderate to moderately severe)	Nursing Home (NH) Placement		NR	At 18 years: 1) 49% (99/203) 2) 55% (111/203) p=0.23
			Median Time to NH placement; Model predicted mean time; Hazard Ratio (HR) with 95% confidence interval			At 18 years: 1) 1,766 days (n=203) 2) 1,181 days (n=203) Univariate unadjusted: HR=0.71 [95%CI 0.54, 0.94], p=0.015 Multivariate baseline adjusted: HR=0.72 [95%CI 0.54, 0.96], p=0.024

Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Hospitalization or Institutionalization	Baseline	Post-Treatment	Follow-up* (time assessed)
Teri, 2003[12] 1) Reducing Disability in Alzheimer's Disease (n=76) 2) Routine medical care (n=77)	Alzheimer's disease	Baseline MMSE = 16.8 (moderate)	# patients institutionalized	NR	NR	21 months post-tx For any reason: 1) 21/76 (28%) 2) 22/77 (28%) p=0.84 Due to behavior problems of pt: 1) 4/76 (5%) 2) 11/77 (14%) p=NR Pt impairment/illness: 1) 4/76 (5%) 2) 4/77 (5%) p=NR Due to increased ADL impairment: 1) 5/76 (7%) 2) 6/77 (8%) p=NR Due to ill health or death of caregiver: 1) 8/76 (10%) 2) 1/77 (1%) p=NR
Wray, 2010[49] 1) Telephone Education Program (n=83) 2) Usual care (n=75)	Dementia	At least moderate level	Total admissions	1) 0.4 (0.9) 2) 0.3 (0.9)	1) 0.4 (0.9) 2) 0.5 (0.9) Time effect: p=0.02 (baseline to intervention period; no difference between groups; no interaction)	1) 0.4 (0.9) 2) 0.2 (0.5)
			Acute admissions	1) 0.2 (0.6) 2) 0.2 (0.6)	1) 0.2 (0.7) 2) 0.2 (0.6) p=ns	1) 0.2 (0.9) 2) 0.1 (0.6) p=ns
			ICU admissions	1) 0.0 (0.1) 2) 0.0 (0.0)	1) 0.0 (0.2) 2) 0.0 (0.2) p=ns	1) 0.0 (0.2) 2) 0.0 (0.0) p=ns
			Nursing home admissions	1) 0.2 (0.7) 2) 0.1 (0.4)	1) 0.1 (0.4) 2) 0.2 (0.6) p=ns	1) 0.2 (0.5) 2) 0.1 (0.3) p=ns

Study, Year Interventions	Physical Condition	Baseline Functional Level	Measure of Hospitalization or Institutionalization	Baseline	Post-Treatment	Follow-up* (time assessed)
Wray, 2010[49] (continued)			Outpatient visits	1) 12.5 (13.5) 2) 14.6 (16.5) p=ns	1) 11.2 (12.9) 2) 14.1 (16.5) p=ns	1) 12.4 (14.8) 2) 13.4 (17.4) Time effect: p=0.03 (baseline to follow-up; no difference between groups; no interaction)
Wright, 2001[67] 1) Education and counseling (n=68) 2) Usual care (n=25)	Alzheimer's disease	Moderate loss of memory; enrolled following in-patient treatment for agitation	% Institutionalized	NR	12months 1) 28% (17/61) 2) 22% (5/23) p=ns	NR
			# days at home before institutionalization	NA	NR	12 months post baseline: 1) 121 (107.6) Range: 5-362 2) 126 (110.5) Range: 5-360 p=0.891

*Last follow-up reported only if > 6 months post-treatment

ES=effect size; NR=not reported; ns=not statistically significant

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