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Interventions to Support Caregivers or Families of Patients with TBI, PTSD, or Polytrauma: A Systematic Review

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted health care topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and health care of Veterans. QUERI provides funding for four ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- Develop clinical policies informed by evidence;
- Implement 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.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

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

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This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the **Durham VA Medical Center, Durham, NC**, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (*eg*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

STAKEHOLDERS AND TECHNICAL EXPERT PANEL

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The list of stakeholders and members of the Technical Expert Panel (TEP) who provided input to this report follows.

Stakeholders

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Technical Expert Panel

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CORRIGENDUM

In this updated report (February 13, 2018), we made the following changes:

1. Correctly attributed the findings on caregiver burden to Moriarty et al 2016 instead of Winter et al 2016. These publications reported results from the same study, but the findings about caregiver burden were published by Moriarty and colleagues.
2. As a result of study details published in Moriarty et al 2016, we updated the risk of bias of the overall study from unclear to low. This contributed to a change in the strength of evidence from low to moderate for the meta-analyses that included results published by Winter et al 2016: overall patient function, physical function, and caregiver psychological symptoms. These strength of evidence ratings have been updated.
3. We added Hanks et al 2012 to the meta-analysis for patient physical function after realizing that it had been erroneously omitted; we have updated the results from that meta-analysis throughout the report.

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INTRODUCTION

Family members perform a significant service caring for Veterans with severe physical, mental, and cognitive impairments. In the United States, 1.1 million family members provide care for Veterans who served in the military since September 11, 2001,[1] a population characterized by high rates of physical injury, including musculoskeletal problems and associated pain, polytrauma,[2] traumatic brain injury (TBI), and traumatic mental health conditions such as posttraumatic stress disorder (PTSD). Beyond the most commonly reported tasks of helping with essential daily activities, such as grocery shopping or managing finances, and helping the Veteran cope with stressful situations, caregivers fill an important role in helping Veterans engage with their health care.[1] Depending on the injuries and health conditions, for some families the need for intensive family caregiving support can last for decades.[1] Further, caregiving can have negative implications for caregiver physical and mental health,[3,4] employment,[5,6] and financial security.[7-9] Family caregivers of post-9/11 Veterans differ from the general population of caregivers in that they are younger and thus more likely to be actively managing work and raising children while performing caregiving tasks. Systematic support and training that takes into account individual contexts, preferences, and needs may help family caregivers to facilitate Veteran recovery processes at home.[10]

Generally, there is a need for health care systems to recognize the role that family caregivers play and for evidence-based strategies to include them as part of the health care team.[10,11] Such support may be critical not only to optimize the well-being and functioning of family members, but also to ensure that individual recovery processes are supported consistently and with high-quality care from the health care team and family members in the home. In recognition of the role that family caregivers play in helping Veterans in their recovery process, the US Congress signed into law the Caregivers and Veterans Omnibus Health Services Act of 2010, which established the Program of Comprehensive Assistance for Family Caregivers (PCAFC) in the Department of Veterans Affairs. This program provides unprecedented support for family caregivers of Veterans seriously injured during military service on or after September 11, 2001. Covered services include a financial stipend, access to health care, skills training, education about VA resources and services, respite care, and travel support. Demand for the program has far exceeded expectations, with more than 32,000 caregivers approved since May 2011.

Systematic reviews have shown that some caregiver supportive services can improve caregiver outcomes, primarily by reducing caregiver burden and mental distress,[12,13] and improve care recipient function.[13] Yet this research has focused most frequently on care recipients with cognitive or memory disorders and other illnesses such as cancer.[12] Given the demand for PCAFC services, there is a need to better understand the impact of caregiver interventions on care recipient populations with long-term, disabling conditions that are common among Veterans, including PTSD, TBI, and polytrauma. In particular, the number of Veteran service users in 2015 with a PTSD diagnosis represented 10% of all users (*ie*, 600,000 of 5.7 million users), and very little is known about how to best support these Veterans through family engagement.[14] It is possible that intervention mechanisms operate differently among these populations due to their life stage, duration of expected caregiving needs, and care recipient symptoms.

WHO ARE THE FAMILY CAREGIVERS?

A family caregiver may be defined as “any relative, partner, friend or neighbor who has a significant personal relationship with, and provides a broad range of assistance for, an older person or an adult with a chronic or disabling condition.”[15] These individuals may be primary or secondary caregivers and live with, or separately from, the person receiving care.

In the mental health caregiving literature, particularly among younger care dyads, family members frequently do not identify themselves as a “caregiver.” This reflects the reality that there is no perfect term. Other terms that are relevant are “informal caregivers” to indicate this care is not from trained, health care professionals and is typically unpaid. Other terms are “care partners,” “companions,” “close others,” and “carers.” For the remainder of this paper we use the term “family caregiver” to refer more generically to persons who either provide unpaid hands-on care or help navigate the health care system.

PURPOSE OF THE REVIEW

This evidence synthesis describes the volume of published literature evaluating family caregiving interventions for patients with polytrauma, TBI, and PTSD and the effects of these interventions and strategies on caregiver and care recipient (patient) outcomes. Our eligibility criteria are purposefully broad to include interventions that focus exclusively on caregivers and those that focus on patients but incorporate a family member or caregiver. For the purposes of this report, we use the term “family caregiving interventions” to mean interventions that are patient-focused and involve caregivers or families of patients (care recipients) with TBI, PTSD, and polytrauma. We anticipate the report will be used by the VA Caregiver Support Program to refine or expand existing educational opportunities, for example training that is provided as part of the eligibility process, for this important and prevalent population by shedding light on characteristics of effective caregiver support programs and corresponding characteristics of the populations who benefit. Further, providing a comprehensive inventory of the common measures that others have used to quantify recovery, emotional well-being, and other outcomes of function will advance our understanding of how to evaluate caregiver interventions among this population of individuals with trauma-associated injury.

METHODS

TOPIC DEVELOPMENT

This evidence report was commissioned to describe the published literature on family caregiving interventions for patients with selected trauma-related illnesses, and to examine the effects of caregiver support programs on both caregivers and care recipients. The report is intended to inform the VA Caregiver Support Program and to identify future research needs to inform the program's practices and policies.

The Key Questions (KQs) for this systematic review were developed after a topic refinement process that included a preliminary review of published peer-reviewed literature, consultation with internal partners and investigators, and consultation with content experts and key stakeholders at the VA Caregiver Support Program and the VA Office of Mental Health.

The final KQs were:

KQ 1: For which patient groups (*ie*, patients with posttraumatic stress disorder, traumatic brain injury, or polytrauma) that receive interventions that involve family members has the impact on care recipient outcomes been assessed?

KQ 2: What effects do programs or strategies that involve family caregivers have on care recipient and caregiver outcomes? Outcomes of interest include caregiver burden and psychological symptoms; care recipient functional status, psychological symptoms, quality-of-life indicators, disease-specific symptoms, independence, health care utilization; and family economic status, family functioning, and clinical eligibility for specific programs or services.

We followed a standard protocol for this review, and each step was pilot-tested to train and calibrate study investigators. The PROSPERO registration number is CRD42017053516.

SEARCH STRATEGY

In consultation with an expert librarian, we conducted searches of MEDLINE® (via PubMed), CINAHL, and PsycINFO. We evaluated the bibliographies of systematic or nonsystematic reviews, and contacted content experts to identify additional relevant studies. We used a combination of MeSH keywords and selected free-text terms to search titles and abstracts. All citations were imported into 2 electronic databases (for referencing, EndNote® Version X7, Thomson Reuters, Philadelphia, PA; for data abstraction, DistillerSR; Evidence Partners Inc., Manotick, ON, Canada). The exact search strategies used are in Appendix A.

STUDY SELECTION

Using prespecified inclusion/exclusion criteria (Table 1), the titles and abstracts of articles included in existing reviews and identified through our primary search were reviewed independently by 2 reviewers for potential relevance to the KQs. Articles included by either reviewer underwent full-text screening. At the full-text screening stage, 2 independent reviewers were required to agree on a final inclusion/exclusion decision. Disagreements were resolved by discussion or by a third investigator. Articles meeting eligibility criteria were included for data abstraction. In brief, we included randomized trials and quasi-experimental studies evaluating a broad range of family caregiving interventions for patients with polytrauma, PTSD, or TBI that reported patient-centered outcomes. Interventions could be designed to support the caregiver or family member, or designed to support the patient with involvement or support from the family member (*eg*, couples therapy).

Table 1. Inclusion and Exclusion Criteria

Study Characteristic	Inclusion Criteria	Exclusion Criteria
Population	Adults ≥18 years of age with any of the following conditions: · Polytrauma (includes both physical only and physical + mental) · Posttraumatic stress disorder (PTSD) · Traumatic brain injury (TBI) Patients may be diagnosed with an eligible illness using criterion-based definitions (*eg*, DSM), validated screening/severity measures (*eg*, patient checklist), or clinical diagnosis. In addition to an eligible condition, patients must have functional cognitive, psychosocial, or other impairments that limit their ability to independently perform functions of daily life.	· Care recipients: <18 years of age or with developmental disorders (*eg*, autism), schizophrenia, bipolar disorder, schizoaffective disorder, psychotic disorder, or dementia · Studies enrolling mixed samples with <70% of participants having an eligible condition · Caregivers: Home-based care provided by a caregiver who does not have a preexisting relationship with care recipient
Interventions	Interventions that train family caregivers or support family caregiving or involvement by individuals who have a preexisting relationship (*eg*, family, friend) with the care recipient Interventions to support family caregiving may consist of 1 or more of the following: · Caregiver training (*eg*, skills training to manage patient behavior) · Illness education · Dyadic or family therapy · Information about the health care system and community resources or social/emotional support (*eg*, mindfulness training, support groups, marital therapy) · Day-to-day practical support (*eg*, in-home respite care, instrumental support) · Financial assistance (*eg*, stipends that allow a family member to stay home) Interventions to train or support family caregivers may be delivered in person or by telephone. In-home respite care provides planned short-term and time-limited breaks for family caregivers of individuals with	· Caregiving interventions using remote technologies (*eg*, interactive voice response systems, medication reminders, smart homes, telehealth/video-based clinical appointments not for the purpose of caregiver training or vitals-monitoring systems) · Direct caregiving by a clinician or allied health care professional (*eg*, home health care service) · Peer support programs or therapy (*eg*, cognitive behavioral therapy) for the care recipient only · Interventions or programs that occur primarily outside the home (*eg*, adult day services); as defined by the Department of Health and Human Services, adult day services provide an organized program in a community group setting to promote social, physical, and emotional well-being, with certification required for all adult day service providers

Study Characteristic	**Inclusion Criteria**	**Exclusion Criteria**
	severe chronic illness in order to support and maintain the primary caregiving relationship.	
Comparators	Any comparator including waitlist, usual care, attention control, or active comparator	No comparator except for interrupted times series, which does not require a comparator
Outcomes	Care recipient primary outcomes: · Functional status or health care quality of life—defined as global quality of life and further conceptualized to include functional status, including physical functioning (*eg*, activities of daily living), general psychological functioning (*eg*, psychological well-being), social functioning (*eg*, social well-being), and ability to live independently. · Psychological outcomes including depressive symptoms or anxiety symptoms using standardized assessments · Disease-specific symptoms (*eg*, patient checklist for PTSD) · Adverse effects Caregiver primary outcomes: · Caregiver burden (*eg*, Zarit Burden Scale) · Psychological outcomes including depressive symptoms or anxiety symptoms using standardized assessments · Adverse effects Family functioning (*eg* marital functioning, relationship quality) · Household economic status · Care recipient health care utilization including outpatient, emergency department, inpatient, institutional, total	Studies that do not plan to report any included outcomes; however, studies that plan to report an included outcome but give cursory results (*eg*, p=NS) were included
Timing	Studies reporting outcomes at ≥28 days (approximately 1 month) following initiation of family caregiving intervention	Studies reporting outcomes at <28 days
Setting	Community settings	Institutional settings (*eg*, skilled nursing facility)
Study design	· Randomized controlled trials · Cluster-randomized trials · Nonrandomized cluster trials	Case reports, case-series, and cross-sectional studies and all studies without a comparator

Study Characteristic	Inclusion Criteria	Exclusion Criteria
	· Controlled before-and-after studies with at least 2 intervention sites and 2 control sites · Interrupted time series design	
Publication type	· English-language only · Peer-reviewed articles · Published from 1995 forward	· Non-English articles · Abstracts only · Letters to the editor · Editorials · Dissertations

DATA ABSTRACTION

Data from published reports were abstracted into a customized DistillerSR database by one reviewer and overread by a second reviewer. Disagreements were resolved by discussion or by a third investigator. Data elements included descriptors to assess applicability, quality elements, intervention/exposure details, and outcomes. Key characteristics abstracted included patient descriptors, caregiver characteristics, intervention characteristics, comparator, and outcomes of interest (Appendix B). We abstracted outcomes at end of treatment and for the longest follow-up reporting comparative data. Multiple published reports from a single study were treated as a single study, prioritizing results based on the most complete and appropriately analyzed data. When critical data were missing or unclear in published reports, we requested supplemental data from the study authors. Key features relevant to applicability included the match between the sample and target populations (*eg*, age, community resources, or Veteran status).

CATEGORIZATION OF THE INTERVENTIONS

Disease symptoms, treatment side effects, and consequences of disease progression are often the target of patient-centered interventions. Because both the interventions and targets of the interventions were unique and differed by condition, we used a general framework to categorize the interventions. We defined major intervention categories by grouping intervention components identified by existing reviews and that we expected might be related to the outcomes of interest within patients assessed for PTSD, TBI and polytrauma. We did not exclude any types of intervention categories. Our 5 major intervention categories were (1) skills training for caregivers (*eg*, change or manage patient behavior, communicate with care recipient), (2) education for caregivers (*eg*, illness education, tailored advice, planning for events), (3) interventions that provide support or counseling for family members related to their caregiving role (*eg*, counseling, stress management), (4) interventions to enhance support for caregivers (*eg*, social support), and (5) unique interventions with unique intervention targets.[16] We categorized the intervention target as caregiver focused, patient focused, or dyadic.

QUALITY ASSESSMENT

Quality assessment was done by the researcher abstracting or evaluating the included article; this initial assessment was overread by a second, highly experienced reviewer. Disagreements were resolved between the 2 reviewers or, when needed, by arbitration from a third reviewer.

We used the key quality criteria described by the Cochrane Effective Practice and Organization of Care Review Group for RCTs and nonrandomized studies.[17] For RCTs, nonrandomized studies, and controlled before-after studies, these criteria are: adequacy of randomization and allocation concealment; comparability of groups at baseline; blinding; completeness of follow-up and whether incomplete data were addressed appropriately; protection against contamination; and selective outcome reporting. For interrupted time series studies, these criteria were: the independence of the intervention from other changes; prespecification of the shape of the intervention; whether the intervention was likely to affect data collection; blinded outcome assessment; whether incomplete data were addressed appropriately; and selective outcome reporting.[17] We assigned a summary risk of bias (ROB) score (low, unclear, or high) to individual studies. Summary ROB was defined using Cochrane guidance: “low bias” as unlikely to alter the results seriously, “unclear bias” as raising some doubts about the results, and “high bias” as bias that may alter the results seriously.[18]

DATA SYNTHESIS

We summarized the primary literature by abstracting relevant data from the eligible studies. For KQ 1, we described the breadth and types of studies conducted. We developed summary tables and figures to describe the literature, using number of studies over time, types of study designs, types of interventions, and descriptions of the types of outcomes reported. For KQ 2, summary tables describe the key study characteristics of the included studies such as study design, patient demographics (including age and condition), and details of the intervention and comparator. We categorized outcomes into caregiver outcomes (*eg*, caregiver burden), care recipient outcomes (*eg*, functional status), and household outcomes (*eg*, relationship quality, economic status). A table of outcome measures abstracted for this review is included in Appendix C.

We then determined the feasibility of completing a quantitative synthesis (*ie*, meta-analysis) to estimate summary effects. Feasibility depended on the volume of relevant literature, conceptual homogeneity of the studies, and completeness of results reporting. For all analyses, we focused on studies at low or moderate ROB. We aggregated outcomes when there were at least 3 studies with the same outcome, based on the rationale that 1 or 2 studies do not provide adequate evidence for summary effects. We planned to evaluate the consistency of effects by elements of the intervention, United States versus other countries, spouse versus non-spouse caregivers (or caregiver recipient relationship), and randomized versus nonrandomized design, but there were too few studies for these subgroup analyses.

Continuous outcomes were summarized using the standardized mean difference because studies used different measures for the same construct (*eg*, Patient Health Questionnaire and Beck Depression Inventory for depression severity). Although we focused on analyzing the follow-up measures, we used change from baseline in a few instances where baseline values differed substantially between the treatment arms. Standard deviation of change used the reported baseline and follow-up standard deviations and accounted for correlation between the baseline and follow-up measures. We used the Knapp Hartung approach to adjust the standard errors of the estimated summary coefficients in the random effects analyses.[19,20] Sensitivity analyses omitted studies judged high ROB. We evaluated for statistical heterogeneity using visual inspection and Cochran's Q and I^2 statistics. Publication bias was not assessed using funnel plots because we did not have >10 studies in an analysis.

When quantitative synthesis was not feasible, we analyzed the data qualitatively. We gave more weight to the evidence from higher quality studies with more precise estimates of effect. A qualitative synthesis focuses on documenting and identifying patterns of the intervention across outcome categories. We analyzed potential reasons for inconsistency in treatment effects across studies by evaluating differences in the study population, intervention, comparator, and outcome definitions.

RATING THE BODY OF EVIDENCE

The strength of evidence for each KQ was assessed using the approach described in the Agency for Healthcare Research and Quality's *Methods Guide*.[21] We limited the Grading of Recommendations Assessment, Development and Evaluation (GRADE) ratings to primary outcomes identified by the stakeholder and Technical Expert Panel as critical to decision-making: functional status, disease-specific symptoms, caregiver burden, and adverse effects. In brief, this approach requires assessment of 4 domains: risk of bias, consistency, directness, and precision (Table 2).

Table 2. Strength of Evidence Required Domains

Domain	Rating	How Assessed
Quality (risk of bias)	Good Fair Poor	Assessed primarily through study design (randomized controlled trial vs observational study) and aggregate study quality
Consistency	Consistent Inconsistent Unknown/not applicable	Assessed primarily through whether effect sizes are generally on the same side of "no effect," the overall range of effect sizes, and statistical measures of heterogeneity
Directness	Direct Indirect	Assessed by whether the evidence involves direct comparisons or indirect comparisons through use of surrogate outcomes or use of separate bodies of evidence
Precision	Precise Imprecise	Based primarily on the size of the confidence intervals of effect estimates, the optimal information size, and considerations of whether the confidence interval crossed the clinical decision threshold for using a therapy

Additional domains were used when appropriate: coherence, dose-response association, impact of plausible residual confounders, strength of association (magnitude of effect), and publication bias. These domains were considered qualitatively, and a summary rating was assigned after evaluation in the GRADE Pro software (https://gradepro.org/) and discussion by 2 reviewers as high, moderate, low, or very low strength of evidence. In some cases, high, moderate, or low ratings were impossible or imprudent to make. In these situations, a grade of insufficient was assigned. This 4-level rating scale consists of the following definitions:

- High—High confidence that the true effect lies close to that of the estimate of the effect.
- Moderate—Moderate confidence in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low—Limited confidence in the effect estimate. The true effect may be substantially different from the estimate of the effect.
- Very low—Very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

PEER REVIEW

This report was reviewed by technical experts and clinical leadership. A transcript of their comments and our responses is provided in Appendix D.

RESULTS

REPORT ORGANIZATION

The results are organized into 3 sections: literature flow, KQ 1 results, and KQ 2 results. In the results sections for key questions, we describe the key findings, followed by detailed descriptions of the included studies. For KQ 2, which describes the effects of the interventions, we organize the outcomes by condition and within condition, by care recipient, caregiver, and household outcomes.

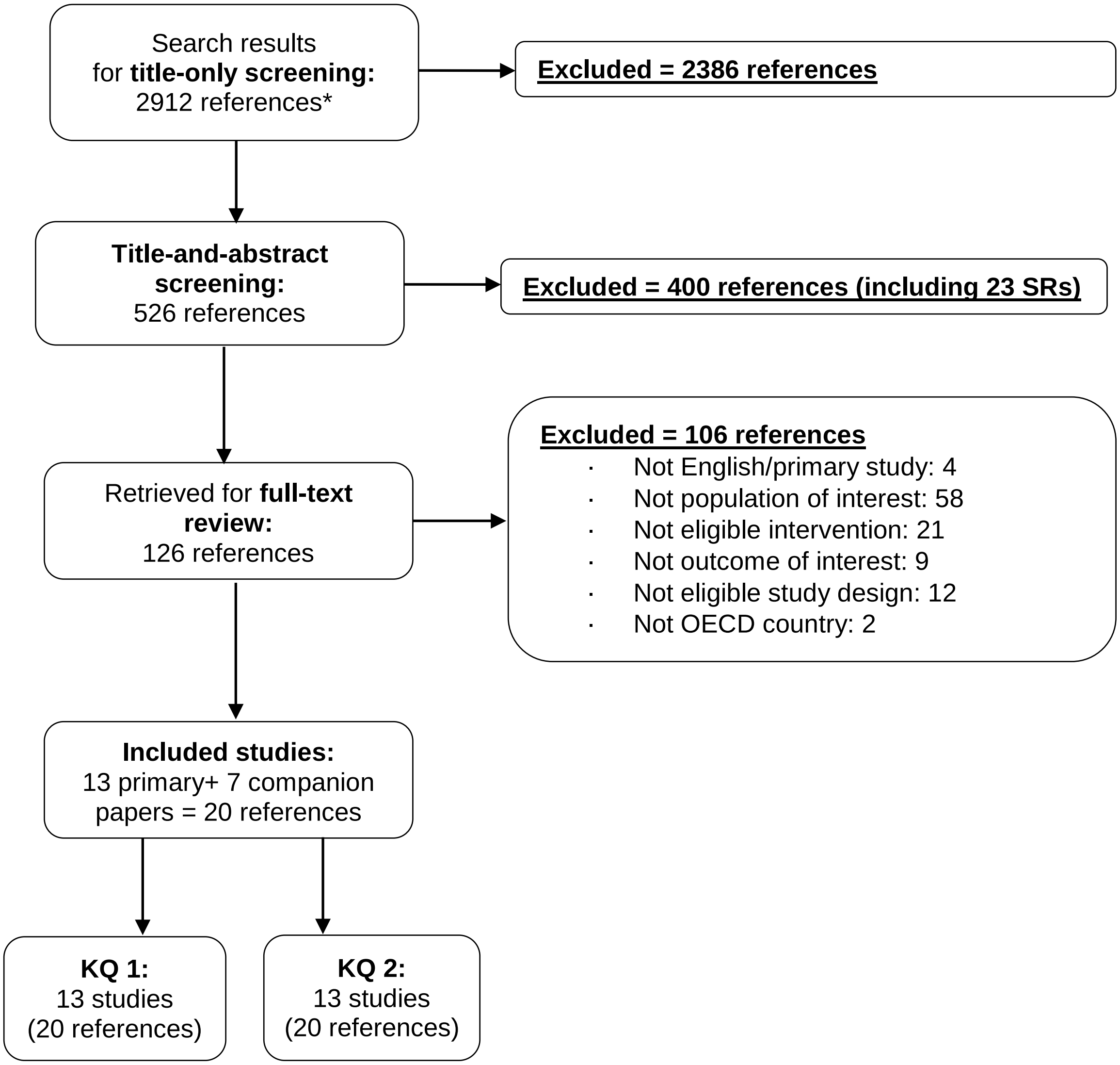
LITERATURE FLOW

Figure 1 shows the flow of articles through the literature search and screening process. The literature search identified 2837 unique citations from a combined search of MEDLINE (via PubMed (n=1319)), PsycINFO (n=149), and CINAHL (n=1369). An additional 73 articles were identified from manual searches of bibliographies and current literature published after the search date, for a total of 2912 unique citations. After applying inclusion and exclusion criteria at the title-only screening level, 526 were promoted to full-abstract screening. After applying criteria at the full-abstract level and removal of 23 systematic reviews, the citations were culled down to 126 articles for full-text review. Of these, 19 were retained for data abstraction (13 primary papers and 6 companion papers).

Among the 13 included primary studies, 10 were randomized controlled trials (RCTs), 2 were nonrandomized trials, and 1 was an interrupted time series design. All 13 primary studies were applicable to both KQs and most were conducted in the United States (n=10).

A search of clinicaltrials.gov for caregiving and our 3 conditions of interest produced 72 entries, 58 of which were not applicable; 14 entries may produce applicable results in the future, but all interventions are along the same lines as studies included in our report. Only 1 entry addressed polytrauma, but it was an observational study that would not meet our criteria. There was no evidence of publication bias.

Figure 1. Literature Flow Diagram



* Search results from CINAHL (1369), PubMed (1319), PsycINFO (149), and manual (75).

KEY QUESTION 1: For which patient groups (*ie*, patients with posttraumatic stress disorder, traumatic brain injury, or polytrauma) that receive interventions that involve family members has the impact on care recipient outcomes been assessed?

Key Points

- We identified 13 studies evaluating caregiving interventions for family caregivers of patients with PTSD or TBI, 10 of which assessed the impact on care recipient outcomes.
- Most studies enrolled caregivers of patients with TBI (n=9).
- No studies enrolled patients assessed to have polytrauma.
- The most commonly reported care recipient outcomes were physical or mental functional status and psychological status (*eg*, depression severity).[22-28]

Detailed Findings for KQ 1

We identified 13 studies that assessed patient-focused psychological or rehabilitation treatments with family member involvement for patients with PTSD or TBI (Table 3). Nine studies evaluated interventions for caregivers of patients with TBI.[22-30] Four studies evaluated interventions for caregivers of patients with PTSD.[31-34] One TBI study also examined PTSD diagnoses and found frequent comorbidity (67%).[28] We did not identify any intervention studies for caregivers of patients with polytrauma.

Table 3. Evidence Profile for Family Caregiving Studies (n=13)

	TBI Studies (n=9)	**PTSD Studies (n=4)**
Study designs	6 RCTs 2 nonrandomized trials 1 interrupted time series	3 RCTs 1 cluster RCT
Study years	1995, 2005 (2 studies), 2008, 2012, 2013, 2015, 2016 (2 studies)	1999, 2008, 2012, 2015
Number of patients	1,148	324
Number of caregivers (studies NR)	673 (2 studies NR)	97 (2 studies NR)
Mean patient age (range) reported in # of study arms (studies NR)	38.7 (30.3-44.6) reported in 18 study arms (2 studies NR)	38.0 (32.6-46.7) reported in 9 study arms
Mean caregiver age (range) reported in # studies	48.6 (41.2-51.8) reported in 6 studies	34.5 (32.2-40.7) reported in 2 studies
Intervention Setting	Care recipients living in the community	Care recipients living in the community
Patients are Veterans	1 study	3 studies
Countries	USA (6), Canada (1), United Kingdom (1), Australia (1)	USA (4), Canada (1)[a]

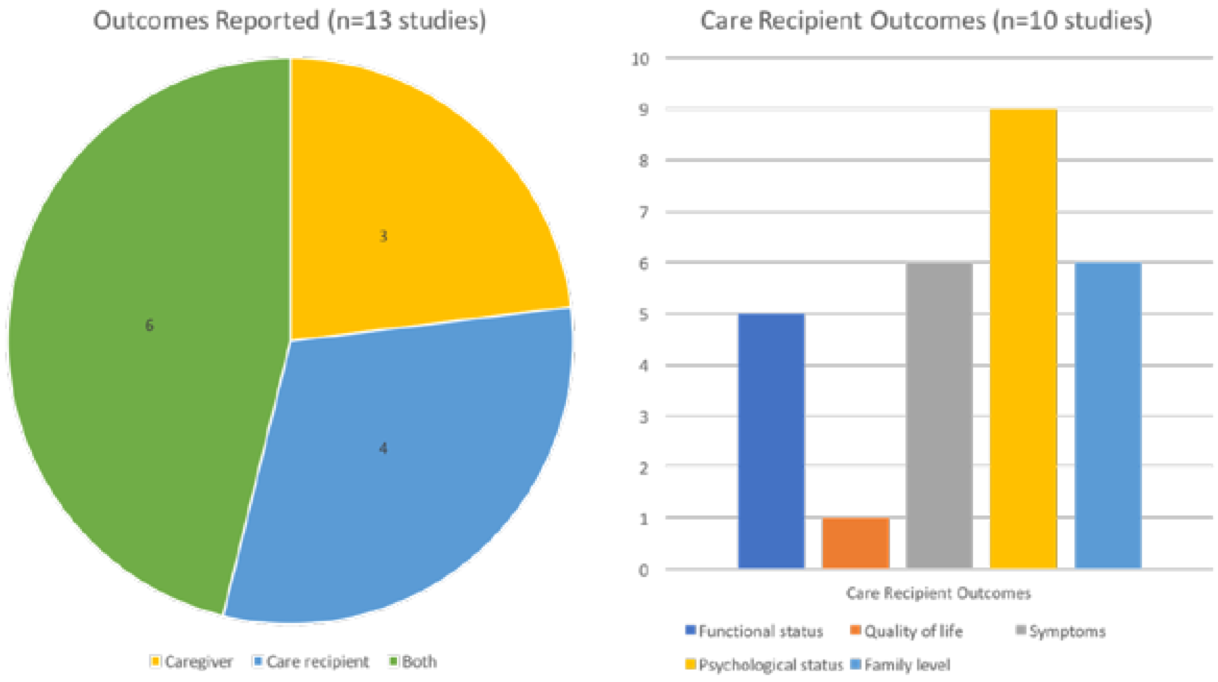
[a] One study was conducted in both the United States and Canada.

Studies were conducted between 1995 and 2016, with the majority (77%) since 2005. Among the 12 multiarm studies (1 study was a single-arm interrupted time series design[22]), 10 studies had 2 arms, and 2 studies had 3 arms, for a total of 14 comparisons with patient-focused, family-involved interventions. Interventions were compared with waitlist or inactive comparators in 5 studies, usual care in 4, and active comparators in 4 studies. One study was an interrupted time series design and the 1 arm was its own comparator. The intervention target was both caregiver and care recipient in 6 studies, only the care recipient in 3 studies, and only the caregiver in 4 studies. Delivery type was one-on-one in 9 studies, group in 3 studies, and both in 1 study.[30] In-person was used as the mode of delivery in 10 studies, and in 7 of those it was the only mode used. Phone was used in 5 interventions, usually in combination with in-person or written communication. Eight different disciplines were used for the interventionist. The only disciplines occurring more than once were psychologist (n=4) and social worker (n=2). Frequency and duration varied greatly. Frequency of sessions ranged from 3 to 16, but in the 3-session intervention study, the intervention was 10 hours in duration. The duration of other sessions ranged from 30 minutes to 2.5 hours. The duration of entire interventions ranged from 10 weeks to 2 years, with a median of 14 weeks; 2 studies did not report the intervention duration.[26,27]

Studies included 2 of the prespecified intervention components on average (range 1-4). The majority of interventions included illness education (n=12, 92%) and skills training (n=9, 69%). Seven studies included another type of component, usually help with resource navigation (n=3) or written materials such as homework or handouts (n=3) to complement illness education. Five studies (38%) included a therapy aspect: behavioral family therapy, couples therapy, problem-solving therapy, or individual therapy sessions,[26,30,33,34] and another 3 studies included an aspect such as emotional support in caregiver groups.[22,24,32] There were no studies that offered financial assistance or other practical assistance, such as respite care, as part of the intervention.

The outcomes reported are summarized in Figure 2. Three studies reported outcomes for caregivers only,[22,26,29] 4 studies reported outcomes for care recipients only,[23,30-32] and 6 studies reported both caregiver and care recipient outcomes.[24,25,27,28,33,34] Three studies reported family-level outcomes including family functioning; none reported household economic status.[24,33,34] The most commonly reported outcomes included psychological status in 9 studies, caregiver burden in 3 studies, quality of life in 3 studies, and family functioning in 3 studies. No studies reported on any type of adverse events or clinical eligibility for specific programs or services. A variety of measurement instruments were utilized for each outcome category. A table of outcome measures abstracted for this review is included in Appendix C. Timing of outcome measurement varied widely across studies, as intervention duration ranged from 2.5 months to 1 year (and up to 2 years in a subset of 1 study).

Figure 2. Frequency of Outcomes Reported in Caregivers and Care Recipients (left) and Care Recipients Only (right)



KEY QUESTION 2: What effects do programs or strategies to support or train family caregivers have on care recipient and caregiver outcomes?

Key Points

- Interventions that included family caregivers did not improve overall functional status, physical functional status, emotional/social function status, or psychological symptoms for the *TBI care recipient*. However, these outcomes were reported in only a few studies, and the 95% CI did not exclude a moderate effect (low to very low strength of evidence [SOE]).
- Interventions that included family caregivers showed positive effects for psychological symptoms of the *TBI caregiver*[25,26,28] (moderate SOE).
- Qualitative synthesis demonstrated a consistent pattern of small beneficial effects of the interventions on *TBI caregiver burden*; however, only 1 of the 3 studies found a statistically significant effect of the intervention on caregiver burden.[35]
- Two forms of couples therapy for PTSD showed consistent improvements in PTSD-related symptoms and some other psychological symptoms for *PTSD care recipients*; patient-reported, but not partner-reported, relationship quality improved (moderate SOE).
- There is preliminary evidence from 1 study that caregiver involvement may improve mental health treatment-seeking and engagement for refugees with PTSD.[32]

- The evidence is insufficient to determine if evidence-based treatment for PTSD, with additional augmentation by family-based skills building intervention, improves *PTSD caregiver* or *care recipient* outcomes; however, one evidence-based couples-based treatment for PTSD (cognitive behavioral conjoint therapy [CBCT]) found a significant positive effect of the intervention on psychological symptoms for partners who were in the distressed range at pretreatment.[36]
- *Care recipient* independence, adverse effects, clinical eligibility for specific programs or services, and household economic status were not examined in any identified study.

Next, we present detailed findings for KQ 2 beginning with TBI studies, followed by PTSD studies, and then quality of evidence for both.

Detailed Findings for TBI

Nine studies evaluated the effect of patient-focused interventions that included family caregivers on outcomes for patients with TBI and their caregivers.[22-30] Six studies were RCTs.[23-28] Except for a single 4-arm trial,[24] all trials had 2 comparison arms. Of the 3 nonrandomized studies, 2 used a controlled pre-post design,[29,30] and 1 used an interrupted time series design.[22] Across the 9 studies, 100% of patients were classified as having TBI. Only 1 study assessed comorbid PTSD.[28] In total, there were 1,148 care recipients and 673 family caregivers. One study included only Veteran participants.[28] Mean participant age ranged from 30.3 to 44.6 years. Definitions of TBI varied but included self-report of a head trauma,[22,24,29,30] the Glasgow Coma Scale,[23,27] and the VA Criteria for TBI.[28] Recruitment settings included inpatient,[23,25] outpatient,[28,30] rehabilitation units,[24,27] and community settings.[22,26,29]

Interventions and modalities (Appendix B) varied across studies and ranged from less structured mentored telephone calls[24] to specific therapeutic interventions.[25,26,28,29] However, common intervention strategies included family illness education, skills-building for TBI recovery, problem-solving, and psychosocial support. Of the 4 studies evaluating specific therapeutic interventions, 1 RCT used the Veterans' In-home Programme (VIP) intervention,[28] which included 6 in-home visits and 2 follow-up telephone contacts with an occupational therapist that focused on patient and family members problem-solving environmental challenges in the home. Two studies used problem-solving therapy.[25,26] One study with high risk of bias (ROB) used the Brain Injury Family Intervention, a structured family therapy treatment program based on principles of cognitive behavioral therapy to enhance family function.[29] Another high ROB study paired peer mentors with TBI patients and their family caregiver to discuss topics of relevance for families with a TBI survivor.[24] Other studies used group illness education approaches for family caregivers and care recipients[22,27,30]; these group sessions covered topics such as managing cognitive and behavioral problems associated with TBI, emotional coping skills, communication, and goal-setting. One low ROB study used motivational interviewing for problem-solving related to patient-identified and family caregiver-identified issues.[23]

Group, individual, and telephone modalities were used across and within studies. Five studies used in-person components,[24,26,28-30] 5 studies delivered part of the intervention over the telephone,[23-26,28] and 3 delivered content through group sessions.[22,27,30] The number of planned sessions ranged from 4[27] to 17.[24] Planned session duration varied from 10 hours per weekend[22] to

30-45 minute phone calls[23,24]; total planned intervention duration across all sessions ranged from fewer than 10 hours to 35 hours.

Comparison interventions included active control (education[26]), inactive control (treatment as usual[23-25,28]) and waitlist controls.[27,29,30] One study was an interrupted time series and thus individuals served as their own control over time.[22] One trial[24] describes 4 arms, but reports outcomes for only 1 comparison: mentored patients and caregivers versus patients and caregivers without mentoring.

Using the Cochrane Risk of Bias Criteria,[18] ROB was judged low for 3 studies,[23,25,28] unclear for 2 studies,[22,26] and high for 4 studies.[24,27,29,30] Table 4 summarizes findings for TBI studies.

Table 4. Summary of Findings for TBI Studies

Study Target	N Enrolled Veterans?	Study Design Comparison	Mean Age in Years (SD) % Female	Outcomes Reported	Overall Risk of Bias
Acorn, 1995[22] Caregiver	33: 19 caregivers 14 care recipients Unclear	Interrupted time series Illness education and social support (before and after)	Caregiver 50 (range 26-69) 74% Care recipient 34 (range 15-60) 29%	Caregiver Quality of life Psychological (well-being) Care recipient NR	Unclear
Bell, 2005[23] Care recipient	171 Unclear	RCT Illness education and resource access vs treatment as usual	Caregiver NR Care recipient 35 (15.0) %NR	Caregiver NR Care recipient Quality of life Functional status (physical and mental) Psychological (mood)	Low
Hanks, 2012[24] Care recipient	158: 62 caregivers 96 care recipients Yes	RCT Illness education, social support, and resource access vs treatment as usual	Caregiver 51.0 (12.0) 45% Care recipient 39.7 (17.5) 10.5%	Caregiver Family function Psychological (mood) Care recipient Functional status (physical and mental) Psychological (mood) Aggregate Family function	High
Kreutzer, 2015[29] Caregiver	154 Unclear	Nonrandomized Illness education, skills training, and homework vs waitlist	Caregiver 51.2 (IQR 40.6-62.1) 72.2% Care recipient 41.5 (IQR 25.6-52.3) %NR	Caregiver Burden Care recipient NR	High

Study Target	N Enrolled Veterans?	Study Design Comparison	Mean Age in Years (SD) % Female	Outcomes Reported	Overall Risk of Bias
Powell, 2016[25] Caregiver	153 Unclear	RCT Illness education and skills training vs treatment as usual	Caregiver 49.6 (13.5) 82.3% Care recipient 42.3 (20.2) 24.8%	Caregiver Quality of life Psychological (mood) Care recipient Quality of life Functional status (mental)	Low
Rivera, 2008[26] Caregiver	67 Unclear	RCT Therapeutic aspects and skills training vs education control	Caregiver 51.1 (12.2) 92.5% Care recipient 36.9 (14.5) 25.3%	Caregiver Burden Quality of life (satisfaction) Psychological (mood) Care recipient NR	Unclear
Sinnakaruppan, 2005[27] Caregiver and care recipient	99: 50 caregivers 49 care recipients Unclear	RCT Illness education, skills training, and handouts vs waitlist	Caregiver NR 78.6% Care recipient 44.1 (10.3) 21.9%	Caregiver Psychological (mood) Care recipient Functional status (physical and mental) Psychological (mood)	High
Togher, 2013[30] Caregiver and care recipient	44 Unclear	Nonrandomized Illness education, therapeutic aspect, and skills training vs waitlist or patient-only treatment	Caregiver 49.7 (13.6) 79.3% Care recipient 35.2 (12.3) 13.8%	Caregiver NR Care recipient Disease-specific (TBI symptoms)	High
Winter, 2016[28] Moriarty, 2016[35] Care recipient	162: 81 caregivers 81 care recipients Yes	RCT Illness education, skills training, and resource access vs enhanced treatment as usual	Caregiver 41.6 (12.6) 93.8% Care recipient 40.1 (13.1) 13.6%	Caregiver Psychological (mood) Burden Care recipient Functional status (physical and mental) Psychological (mood)	Low

Abbreviations: IQR=interquartile range; NR=not reported; RCT=randomized controlled trial; SD=standard deviation; TBI=traumatic brain injury

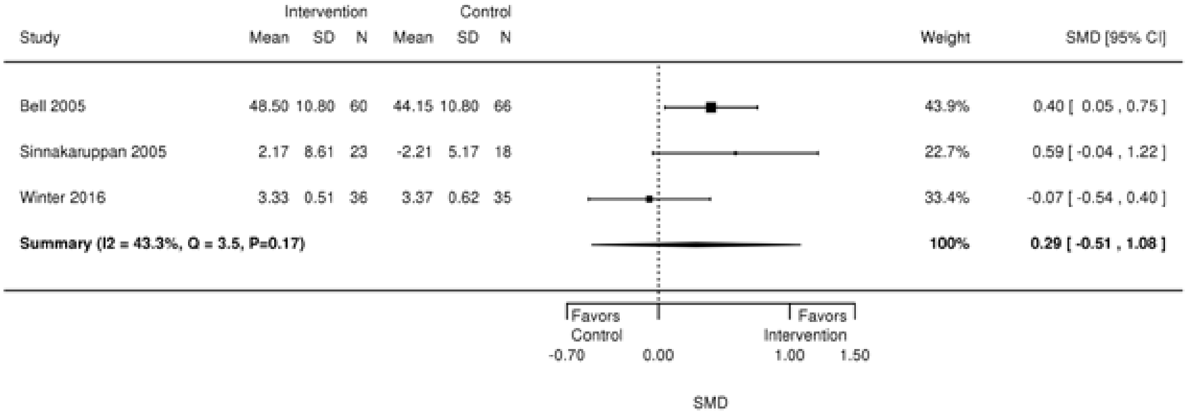
TBI: Care Recipient Outcomes

Quantitative Summary

Meta-analyses were conducted for 4 patient-level outcomes. These analyses included 5 RCTs[23-25,27,28] (455 patients) and were conducted for overall functional status, physical functional status, social/emotional function status, and psychological symptoms. Interventions evaluated across the 5 RCTs included the Veteran's In-home Program (VIP), consisting of in-home visits and telephone contacts with the family member to implement coping strategies,[28] group illness education,[27] telephone counseling using motivational interviewing for problem solving that targeted both family caregivers and care recipients,[23] problem-solving therapy with TBI family caregivers,[25] and patient and significant other mentoring on topics such as disease education and relationship skills (*ie*, building trust, problem-solving, goal-setting).[24] The number of contacts across interventions was similar. For the meta-analyses, data from the last assessment time point was used, and this time point generally coincided with end of treatment, except for 2 studies for which only data from a 3-month post-intervention follow-up was available,[23,27] and 1 study for which only data from 1 month after the intervention was reported.[24] One study did not define the length of the intervention.[27] Assessment time points ranged from 4 months[28] to 12 months.[23,26]

Overall functional status. Outcome measures for overall functional status included the Patient Competency Rating Scale (PCRS),[28] the Functional Independence Measure (FIM),[27] and the SF-36 Physical and Mental Subscales averaged across patients.[23] There was no effect of the interventions on overall functional status of patients with TBI (SMD 0.29, 95% CI -0.51 to 1.08, I^2=43.3%, Q=3.5, p=0.17) (Figure 3). However, confidence intervals were broad and do not exclude a moderate effect of the intervention. Heterogeneity was moderate, but not statistically significant (I^2=43.3%, Q=3.5, p=0.17); it is possible that the social and emotional functional status subscales in the measures of overall functional status did not represent similar constructs. Also, interventions varied in content, delivery, and format.

Figure 3. Forest Plot of Overall Functional Status for TBI Care Recipients



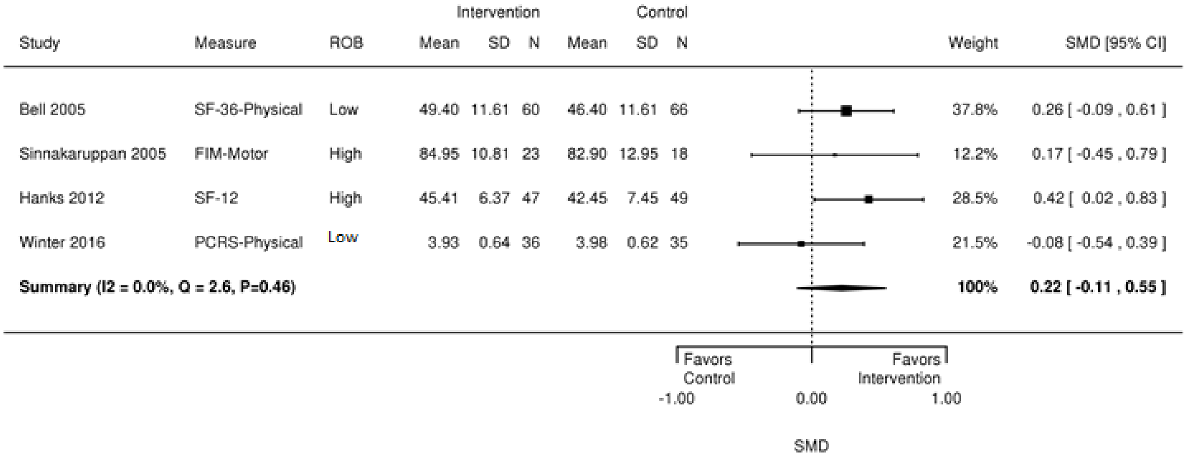
	Intervention			Control				
Study	Mean	SD	N	Mean	SD	N	Weight	SMD [95% CI]
Bell 2005	48.50	10.80	60	44.15	10.80	66	43.9%	0.40 [0.05 , 0.75]
Sinnakaruppan 2005	2.17	8.61	23	-2.21	5.17	18	22.7%	0.59 [-0.04 , 1.22]
Winter 2016	3.33	0.51	36	3.37	0.62	35	33.4%	-0.07 [-0.54 , 0.40]
Summary (I2 = 43.3%, Q = 3.5, P=0.17)							**100%**	**0.29 [-0.51 , 1.08]**

Abbreviations: CI=confidence interval; SD=standard deviation; SMD=standardized mean difference

Physical functional status. Outcome measures for physical functional status included the physical function subscale from the PCRS,[28] the motor subscale from the FIM,[27] the SF-12,[24] and the SF-36 physical function subscale.[23] Results showed no effect of interventions for family caregivers and patients on the overall functional status of patients with TBI (SDM 0.22 95% CI -0.11 to

0.55, I^2=0%, Q=2.6, p=0.46) (Figure 4). However, confidence intervals were broad and do not exclude a moderate effect of the intervention.

Figure 4. Forest Plot of Physical Functional Status for TBI Care Recipients



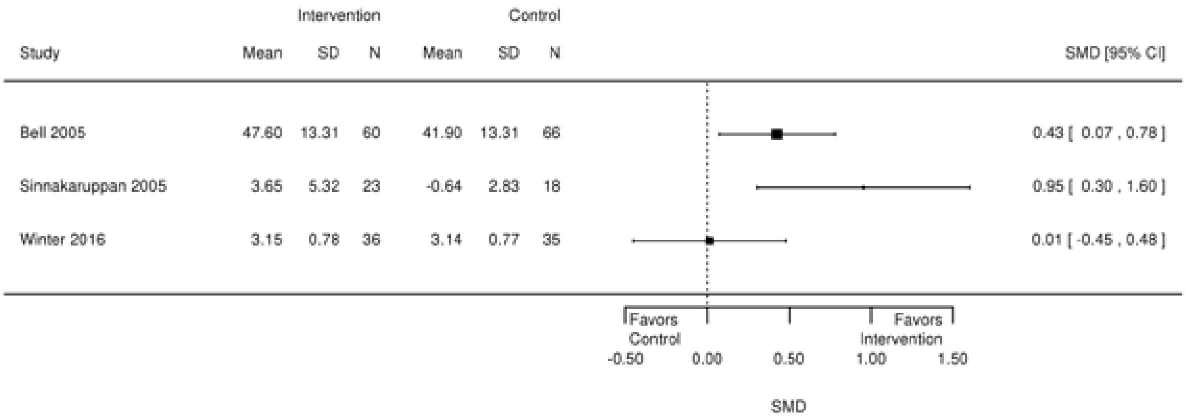
Study	Measure	ROB	Intervention Mean	Intervention SD	Intervention N	Control Mean	Control SD	Control N	Weight	SMD [95% CI]
Bell 2005	SF-36-Physical	Low	49.40	11.61	60	46.40	11.61	66	37.8%	0.26 [-0.09 , 0.61]
Sinnakaruppan 2005	FIM-Motor	High	84.95	10.81	23	82.90	12.95	18	12.2%	0.17 [-0.45 , 0.79]
Hanks 2012	SF-12	High	45.41	6.37	47	42.45	7.45	49	28.5%	0.42 [0.02 , 0.83]
Winter 2016	PCRS-Physical	Low	3.93	0.64	36	3.98	0.62	35	21.5%	-0.08 [-0.54 , 0.39]
Summary (I2 = 0.0%, Q = 2.6, P=0.46)									**100%**	**0.22 [-0.11 , 0.55]**

Abbreviations: CI=confidence interval; SD=standard deviation; SMD=standardized mean difference

One study reported 2 measures for patient physical function: the FIM functional independence measure and a functional status composite from the Functional Status Examination (FSE).[23] Results from the FIM were included in the meta-analysis reported above. The between-group mean difference from the FSE favored the intervention, but similar to the FIM, results were not statistically significant (2.1, 95% CI -0.6 to 4.7).

Emotional/social functional status. Outcome measures for social/emotional functional status included the emotional function subscale from the PCRS,[28] the cognitive subscale from the FIM,[27] and the SF-36 mental function subscale.[23] Results showed high statistical heterogeneity (I^2=63.3%, Q=5.4, p=0.07), and thus we do not report a summary estimate of effect (Figure 5). The median intervention effect was 0.43 (SDM range 0.95 to 0.01). We examined the studies qualitatively to identify potential sources for the observed heterogeneity and believe that the measures of social and emotional functional status measured dissimilar constructs. For example, the FIM measured cognitive functional status while the SF-36 measured psychological symptoms and social participation. Refer to the “Overall functional status” paragraph above for more discussion.

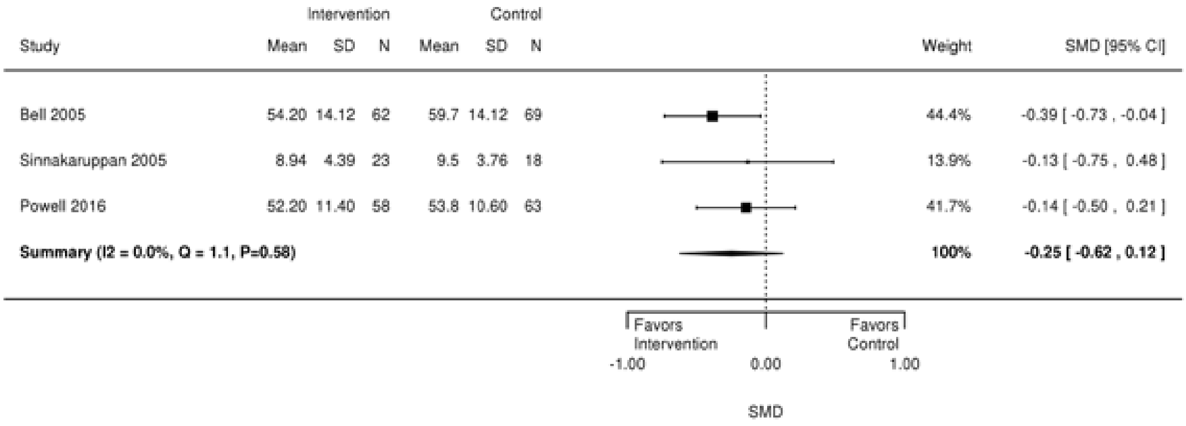
Figure 5. Forest Plot of Emotional/Social Functional Status for TBI Care Recipients



Abbreviations: CI=confidence interval; SD=standard deviation; SMD=standardized mean difference

<u>Psychological symptoms.</u> Outcome measures for psychological symptoms included the Brief Symptom Inventory (BSI) total score[23,25] and the average of the anxiety and depression subscales of the Hospital Anxiety and Depression Scale (HADS).[27] Results demonstrated no effect of interventions for family caregivers on TBI care recipient psychological symptoms (SDM -0.25, 95% CI -0.62 to 0.12, I^2=0.00; Q=1.1, p=0.58) (Figure 6). While not significant, the direction of the results favors the intervention.

Figure 6. Forest Plot of Psychological Symptoms for TBI Care Recipients



Abbreviations: CI=confidence interval; SD=standard deviation; SMD=standardized mean difference

Two studies not included in a meta-analysis because of differences in study design or outcome measure examined the association between a family intervention and family caregiver psychological symptoms post-intervention using the General Well Being Scale[22] and the BSI.[24] The study that used an interrupted time series design found no significant pre-post change in the score (scores from the 3 post-intervention time points were averaged together).[22] The other study also found no effect of the intervention on care recipient psychological symptoms (Cohen's d=0.31, p=0.21, n=62) at end of treatment (12 months).[24]

One study had consistently strong intervention effects on the patient outcomes of interest.[23] We examined this study qualitatively to understand whether components of the intervention or the study sample drove these effects. We were unable to identify a definitive reason for these differences. The intervention reported was the least intensive, both in regard to delivery format and number/frequency of contacts, and the patient was the primary target of the intervention. In addition, the intervention addressed immediate concerns using motivational interviewing and problem-solving techniques. Therefore, it is possible that the heightened emphasis on the patient, as opposed to the family caregiver, and the focus on addressing current problems drove the observed effects.

Qualitative Summary

Outcomes from studies without an RCT design or without a sufficient number of studies to do a meta-analysis are described qualitatively below. These studies reported changes in functional status, quality of life, and TBI symptoms. Care recipient outcomes related to independence, health service use, and adverse effects were not reported.

<u>Quality of life.</u> Two studies evaluated the effect of interventions involving family caregivers on care recipient quality of life.[23,25] One study used the Life Satisfaction Scale and found no intervention effect at end of treatment (6 months).[25] The other study found significant between-group mean differences from the EuroQoL and the Perceived Quality of Life (PQOL) scale favoring the intervention (mean difference from EuroQOL=0.10, 95% CI 0.02 to 0.19; mean difference from PQOL=8.8, 95% CI 1.7 to 15.9).[23]

<u>TBI symptoms.</u> Several studies evaluated improvements in TBI symptoms as a result of the interventions. One study found that participation in the intervention was associated with statistically significant improvements in communication skills, specifically casual interaction (p=0.01) and purposeful interaction (p=0.03) as measured by the Measure of Participation in Conversation (MPC).[30] Another study showed small statistically significant between-group differences favoring the intervention at end of treatment (3 months) on TBI dysexecutive and memory problems using the Behavioral Assessment of the Dysexecutive Syndrome scale (p=0.048) and Rivermead Behavioral Memory Test-profile (-2.55, 95% CI -4.97 to -0.13, p=0.04, n=31).[27] The intervention included a heavy emphasis on providing information about TBI symptoms and on developing coping skills for patients and caregivers. A third study also reported positives changes in patient identified target symptoms as a result of the intervention (Cohen's d=0.66, 95% CI 0.18 to 1.09).[28]

<u>Psychological symptoms.</u> One study examined care recipient psychological symptoms using the BSI and found no between-group difference related to intervention participation (Cohen's d=0.24, p=0.24, n=96).[24]

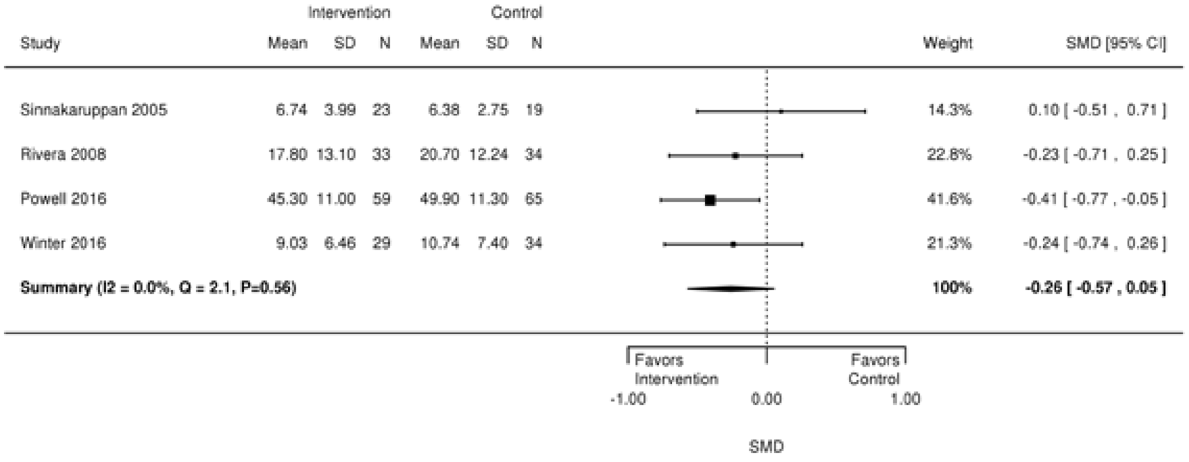
TBI: Family Caregiver Outcomes

Quantitative Summary

A meta-analysis for 1 family caregiver-level outcome (caregiver psychological status) was conducted. This meta-analysis used data from 3 RCTs[25,26,28] (254 patients) that evaluated problem-solving therapy with family caregivers[25,26] and VIP.[28] The number of contacts across interventions ranged from 8 to 12.

<u>Caregiver psychological symptoms.</u> Outcome measures included the Center for Epidemiological Studies-Depression scale (CES-D),[26,28] the BSI-18,[25] and the average of the HADS depression and anxiety scales to measure caregiver psychological symptoms[27] (Figure 7). Results (296 patients) found no benefit of the intervention on caregiver psychological outcomes (SDM -0.26, 95% CI -0.57 to 0.05, I^2=0.0, p=0.56).

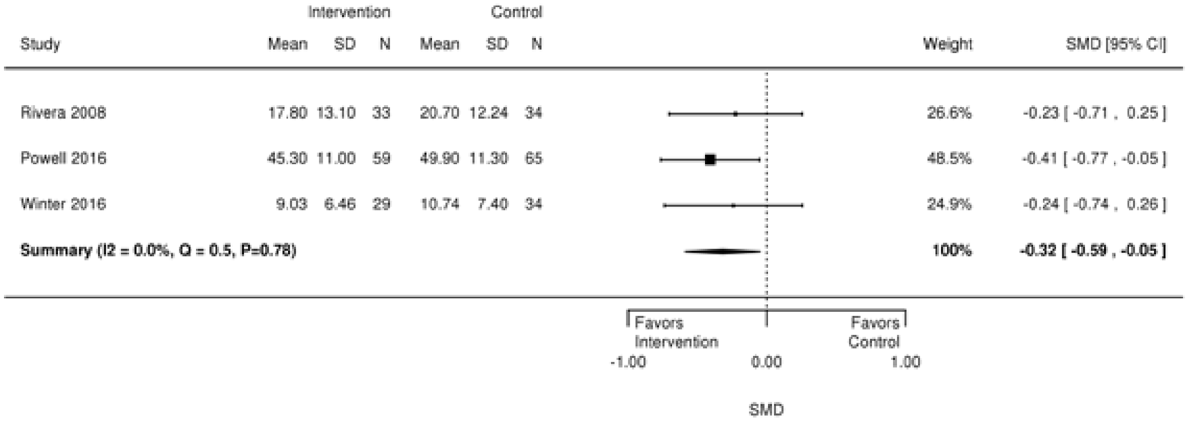
Figure 7. Forest Plot of Psychological Symptoms for TBI Caregivers



Abbreviations: CI=confidence interval; SD=standard deviation; SMD=standardized mean difference

We conducted a sensitivity analysis that omitted a study rated high ROB that used 8 sessions of group illness education targeting both family caregivers and care recipients[27] (Figure 8). These more rigorous results found a positive effect of the interventions for family caregivers and patients on the overall functional status of patients with TBI (SDM -0.32, 95% CI -0.59 to -0.05, I^2=0.0, Q=0.5, p=0.78). The SOE for this meta-analysis was rated as moderate.

Figure 8. Forest Plot of Sensitivity Analysis of Psychological Symptoms for TBI Caregivers



Abbreviations: CI=confidence interval; SD=standard deviation; SMD=standardized mean difference

Qualitative Summary

Studies also reported changes in family caregiver quality of life, burden, and psychological symptoms. Adverse effects were not reported.

Quality of life. One study examined family caregiver quality of life at end of treatment using the Bakas Caregiving Outcomes Scale.[25] The mean difference in scores between the intervention and treatment as usual control group was not statistically significant (mean difference 2.3, 95% CI -1.9 to 6.6, N=124). Another study used the Satisfaction with Life Scale (SWLS) to measure caregiver quality of life and found no effect over time (Cohen's d= -0.14, p=0.52, n=67) at end of treatment (12 months).[26]

Caregiver burden. Three trials examined caregiver burden, but due to the high ROB of 1 study,[29] we did not conduct a meta-analysis. Two studies used the Zarit Burden Scale to examine changes in family caregiver burden as a result of the intervention.[26,29] One found no significant between-group effect over time (Cohen's d=0.30, p=0.79) at end of treatment (12 months).[26] The other study also found no within-group difference over time as a result of the intervention at end of treatment (22 weeks) (SMD 0.35, 95% CI -0.11 to 0.80.[29] A third study used the burden subscale of the Modified Caregiver Appraisal measure to examine intervention effects on caregiver burden and found a statistically significant positive effect of the intervention on caregiver burden at end of treatment (4 months) (Cohen's d=0.311, p=0.018, n=63).[35] These effects are consistent in direction and magnitude of effect across all 3 studies.

TBI: Household Outcomes

Quantitative Summary

There were not enough studies that examined household-level outcomes to conduct a meta-analysis.

Qualitative Summary

Studies reported changes in family function, but household economic status was not examined as an outcome in any study.

Family function. One study with high ROB examined changes in family function as a result of the intervention.[24] This study evaluated changes in the Family Assessment Device score between intervention and control groups and found no significant effect (Cohen's d=0.25, p=0.23, n=62) at end of treatment.

Detailed Findings for PTSD

Four RCTs (336 patients) evaluated patient-focused PTSD treatments with a family member involved or included and reported on family member outcomes. Three studies included Veteran participants.[31,33,34] Mean participant age ranged from 33 to 47 years. All patients in the studies had a PTSD diagnosis, confirmed by a structured clinical interview (Clinician-Administered PTSD Scale),[31,33,34] or supported by a symptom scale score (PTSD Symptom Scale).[32] Patients were recruited from outpatient and community settings. Consistent with most literature on PTSD, the term "caregiver" was not utilized as this is a role more often recognized in support of patients with other disorders that more commonly fall under the "serious mental illness" category, requiring longer-term support. In 2 studies[33,34] of couples' treatment, the caregiver was defined as an intimate partner or cohabiting opposite-sex partner. In another study, 89% of family participants were spouses/partners and the remainder siblings or parents.[31] One study did not describe the level or extent of family participation.[32]

Interventions varied substantially across studies and precluded meaningful meta-analyses. One 3-arm trial compared the effect of augmenting prolonged exposure (PE) therapy with a behavioral family therapy (BFT), a family-based skills-building intervention, for Veterans with chronic combat-based PTSD to PE alone and waitlist arms.[31] Two studies compared couples-based therapies (CBCT-PTSD and structured approach therapy [SAT]) to waitlist[33] or a family education control.[34] Another study evaluated the effect of a multiple-family group intervention, Coffee and Family Education and Support (CAFES), education sessions aimed at increasing access to mental health care on a community population of Bosnian refugees living in the United States, via a 2-arm RCT.[32] Interventions ranged from 9 to 16 sessions and were delivered in person over 12 weeks to 6 months. All interventions included an illness education component, 3 utilized formal therapies,[32-34] 3 incorporated a skills-building strategy,[32,33] and 1 used a social support strategy.[31] Two companion studies[36,37] reported on secondary analyses evaluating partner outcomes the CBCT-PTSD study.[33] Table 5 summarizes findings for PTSD studies.

Table 5. Summary of Findings for PTSD Studies

Study Target	N Enrolled Veterans?	Study Design Comparison	Mean Age in Years (SD) % Female	Outcomes Reported	Overall Risk of Bias
Glynn, 1999[31] Care recipient	42 Yes	Cluster RCT Illness education vs waitlist or directed therapeutic exposure	Caregiver NR Care recipient 46.7 (3.1) %NR	Caregiver NR Care recipient Psychological (mood) Functional status (mental) Disease-specific (PTSD symptoms)	High
Monson, 2012[33] Caregiver and care recipient	40: 20 caregivers 20 care recipients Yes	RCT Illness education, therapeutic aspect and skills training vs waitlist	Caregiver 37.8 (11.3) 32% Care recipient 46.7 (3.1) 25%	Caregiver Psychological (mood) Care recipient Psychological (mood) Functional status (mental) Disease-specific (PTSD symptoms) Aggregate Family function (reported by both caregiver and care recipient)	Unclear
Sautter, 2015[34] Caregiver and care recipient	114: 57 caregivers 57 care recipients Yes	RCT Illness education, therapeutic aspect, and skills training vs PTSD family education	Caregiver 32.3 (7.8) 98% Care recipient 33.2 (6.6) 2%	Caregiver Psychological (mood) Care recipient Psychological (mood) Disease-specific (PTSD symptoms) Aggregate Family function (reported by both caregiver and care recipient)	Unclear

Study Target	N Enrolled Veterans?	Study Design Comparison	Mean Age in Years (SD) % Female	Outcomes Reported	Overall Risk of Bias
Weine, 2008[32] Caregiver and care recipient	197 care recipients; family was targeted also, but no reported demographics No	RCT Illness education, therapeutic aspect, social support, skills training and resource access vs treatment as usual	Caregiver NR Care recipient 37.7 (NR) 50.2%	Caregiver NR Care recipient Psychological (mood) Disease-specific (PTSD symptoms) Mental health service utilization	High

Abbreviations: NR=not reported; PTSD=posttraumatic stress disorder; RCT=randomized controlled trial; SD=standard deviation

PTSD: Care Recipient Outcomes

All studies reported patient outcomes in response to including family members in the intervention. Both couples-based interventions (SAT and CBCT-PTSD)[33,34] showed consistent patterns of improved PTSD symptoms at the end of treatment as measured by clinician interview (mean difference on CAPS ranged 23.2 to 27.6) or patient-reported symptoms (mean difference on the PTSD Checklist ranged 8.4 to 11.8). Improved PTSD symptoms exceeded the threshold for clinically meaningful improvement. Other psychological symptoms, including patient-reported anxiety and depressive symptoms, showed a pattern of greater improvement with the intervention. Interpersonal relationships as reported by the patient also improved. One high ROB study found that the multiple-family group sessions increased the number of mental health visits among refugees with PTSD.[32]

PTSD: Family Caregiver Outcomes

Two studies[33,34] (companions[36,37]) reported caregiver outcomes. Using structured approach therapy (SAT), neither self-reported depressive symptoms nor anxiety symptoms improved significantly compared to family education. In a secondary analysis of couples-based treatment for PTSD (CBCT-PTSD),[33] partners who were in the distressed range at pretreatment reported significant improvements in depression and anxiety symptoms.[36]

PTSD: Household Outcomes

Only 2 studies reported limited family function outcomes.[33,34] Interpersonal relationships as reported by the partner did not improve in either study (moderate SOE). In a secondary analysis of the study by Monson et al,[33,37] CBCT-PTSD improved relational functioning posttreatment in partners who reported clinically-distressed levels of psychological functioning pretreatment.[37] Household economic status was not examined as an outcome in any study.

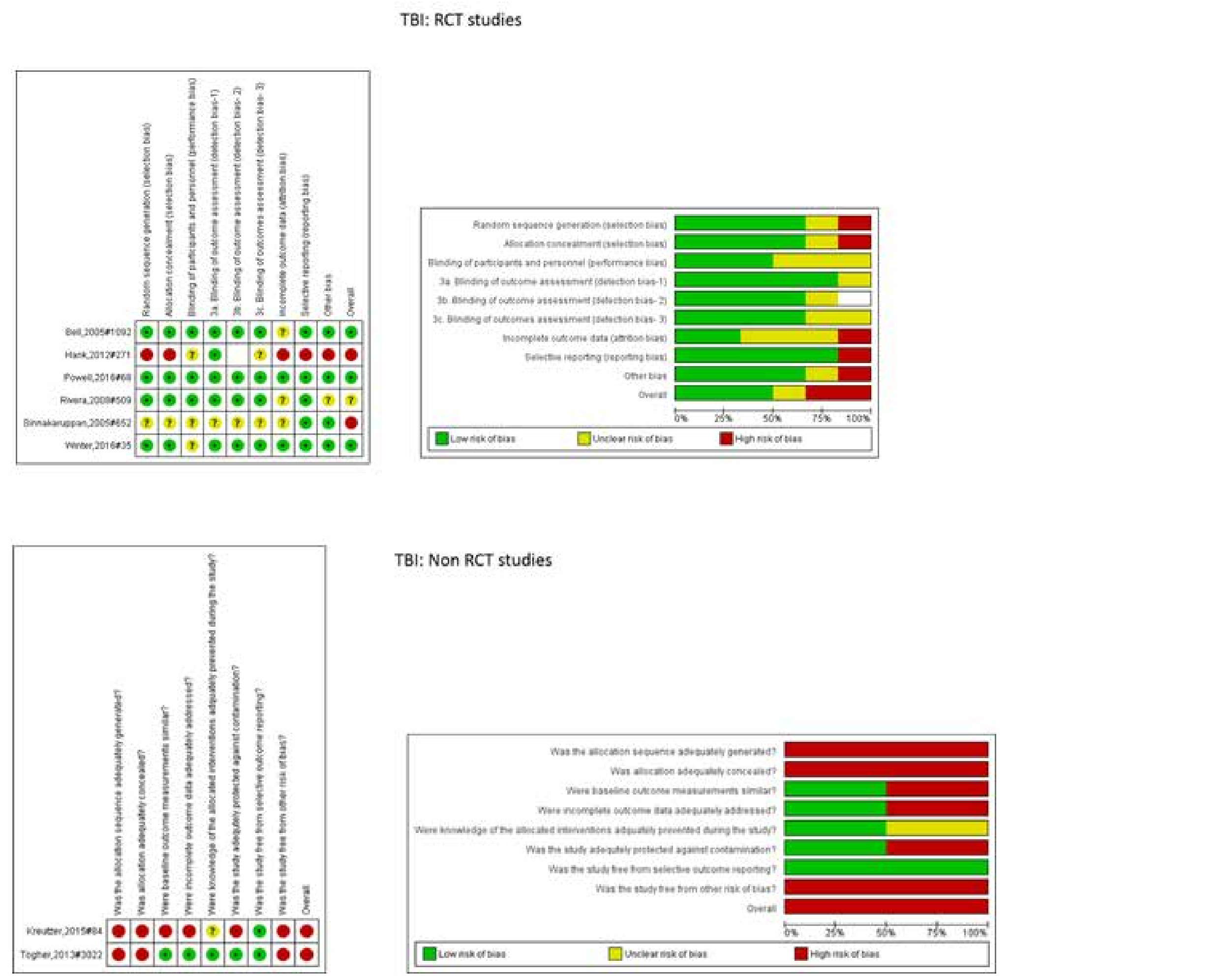
Quality of Evidence for Key Question 2

Risk of Bias for TBI Studies

We evaluated ROB for all TBI studies. The plots for the RCTs (n=6) and nonrandomized studies (n=2) are displayed in Figure 9. Of the 6 RCTs, 3 were considered to be low ROB,[23,25,28] 1 was unclear ROB,[26] and 2 were high ROB.[24,27] Problems noted were lack of blinding of participants, personnel, and outcome assessors and incomplete reporting of outcome data.

Two studies did not meet RCT study design criteria and were assessed as nonrandomized trials; both were considered to be high ROB.[29,30] Problems included lack of allocation sequence generation, lack of adequately concealed allocation, and other risk. Of those studies, 1 had low ROB for similar baseline measurements, adequately addressed incomplete outcome measures, adequately prevented knowledge of allocated interventions during the study, and protection against contamination.[30] Both nonrandomized studies were low ROB for selective outcome reporting. Note that although 1 study self-identified as an RCT, the investigation was funded over a 10-year period and during the first 5 years of funding, controls were not recruited.[29] During the second 5 years, investigators were unable to recruit an equal number of control participants because many randomized to the control group were unwilling to wait 10 weeks before receiving the intervention, and for this reason we classified that study as nonrandomized.[29]

Figure 9. Risk of Bias Ratings for TBI Studies

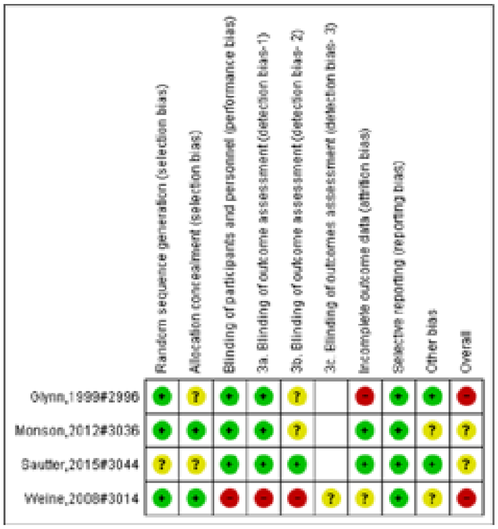


One study was an interrupted time series and was considered to have an unclear ROB.[22] Three of 6 criteria were low ROB (prespecified intervention shape; free from selective outcome reporting; free from other risks), 2 of 6 criteria were graded as unclear ROB (intervention unlikely to affect data collection, incomplete outcome data adequately addressed), and 1 of 6 items was high ROB (intervention was independent of other changes).

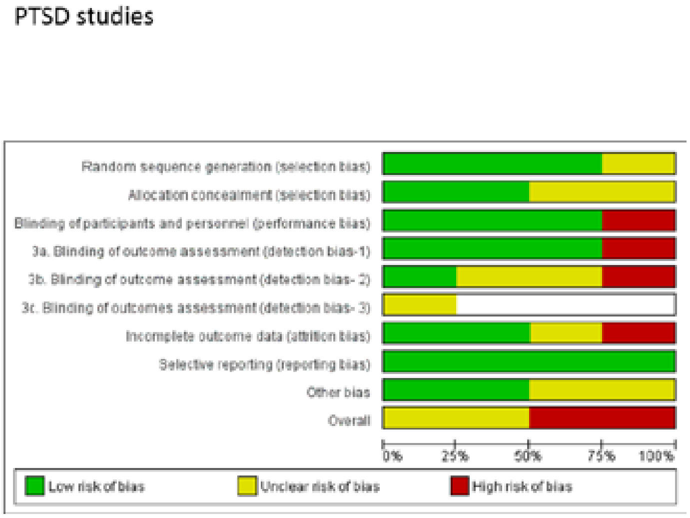
Risk of Bias for PTSD Studies

Two PTSD studies were rated as unclear ROB[33,34] and 2 as high ROB (Figure 10).[31,32] Problems included unblinded or questionable blinding of outcome assessments in 3 studies and unclear allocation concealment and incomplete outcome data due to attrition concerns in 2 studies. Regarding the latter, significant attrition (35%) was acknowledged in 1 study as a result of the increasing burden of attending 16 additional weeks of family intervention after a full course of 18 twice-weekly prolonged exposure sessions.[31] There was no evidence of selective reporting of study outcomes.

Figure 10. Risk of Bias Ratings for PTSD Studies



	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	3a. Blinding of outcome assessment (detection bias-1)	3b. Blinding of outcome assessment (detection bias- 2)	3c. Blinding of outcomes assessment (detection bias- 3)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias	Overall
Glynn,1999#2996	+	?	+	+	?		-	+	+	-
Monson,2012#3036	+	+	+	+	?		+	+	?	?
Sautter,2015#3044	?	?	+	+	+		+	+	+	?
Weine,2008#3014	+	+	-	-	-	?	?	+	?	-



SUMMARY AND DISCUSSION

Family caregiver support has been recognized as an important care component for individuals with cognitive impairments, terminal illness, chronic illness, and serious mental illness (SMI).[10,38,39] Due to recent improvements in battlefield medicine, thousands of US service members return home after combat-related trauma; however, a large proportion must live with substantial physical, social, and emotional functional impairments. Traumatic brain injury (TBI), posttraumatic stress disorder (PTSD), and polytrauma are 3 major issues facing the Veterans Health Administration (VHA) and VA users returning from the conflicts in Iraq and Afghanistan. Due to the rapid increase in the prevalence of these conditions, research about how to implement interventions to support family caregivers has lagged behind the need for such services. Interventions that do exist have adapted the approaches of family caregiver interventions for patients with other conditions, such as aging patients with dementia. In this systematic review, we extend the literature about interventions for family caregivers of patients with cognitive impairments or SMI to understand whether these interventions have beneficial effects for caregivers and patients with TBI, PTSD, and polytrauma.

Our review differs from prior reviews in several ways. This is the first systematic review to examine family caregiver interventions for patients with TBI, PTSD, or polytrauma. Other systematic reviews have examined the effectiveness of family caregiver interventions for elderly patients with cognitive and functional impairments,[13,40] patients with cancer,[40] patients with SMI,[16,41,42] and patients with mental illness more broadly.[41] The patient population included in the studies we identified had cognitive and functional impairments but were not elderly. We also found no prior reviews that examined interventions for family caregivers of patients assessed to have TBI or polytrauma. For PTSD, the review by Meis and colleagues[41] captured one of the same PTSD studies we did.[31] However, our review differed from this prior review in that we included caregiver interventions for patients with TBI and our review of PTSD studies included more recent studies and expanded the scope of the prior review that only considered studies with an RCT design.[41] Hence, our review fills an important gap in the literature. Specifically, owing to the complex physical, emotional, and social impairments that are common among patients with TBI, PTSD, and polytrauma, caregivers of these patients may have different needs than caregivers of elderly patients or patients with SMI and other mental health conditions. Given the prevalence of TBI, PTSD, and polytrauma among recently returned Veterans and the increasing impetus in VA for programs to support the role of family caregivers, our review has special implications for the VHA and VA users.

SUMMARY OF EVIDENCE BY KEY QUESTION

KQ 1—Assessment of the Impact on Care Recipient Outcomes

As expected, the existing literature is small; 13 studies meeting the prespecified review criteria were identified. Strength of evidence was low, heterogeneity across studies was high, and trials included in the meta-analyses contained few patients. Across studies, there was substantial variation in study design, intervention intensity, frequency of contacts, and how or whether disease conditions were defined. The majority of studies enrolled patients with TBI (n=9); no studies enrolled patients with polytrauma. The majority of studies applied an illness education component. Other commonly used components included skills training, social support, and therapy. We found no interventions that provided financial assistance. While individual interventions varied in delivery type, delivery mode, and intensity, most interventions aimed to address similar problems, including reducing caregiver burden, enhancing family function, improving clinical care and the home environment, improving condition-specific symptoms, and increasing family knowledge about health care resources.

KQ 2—Effects on Care Recipient and Caregiver Outcomes

The studies we examined did not show a consistent intervention effect on caregiver or care recipient outcomes. Of the 4 studies that examined family caregiver interventions for patients with PTSD, 2 evaluated couples-based therapies,[33,34] 1 evaluated the effect of augmenting prolonged exposure therapy with a family skills-building training intervention,[31] and 1 evaluated the effect of a multiple-family group education intervention on increased access to mental health care for Bosnian refugees. Couples-based therapies consistently improved PTSD symptoms.[32] From the TBI literature, quantitative meta-analyses demonstrated no effect of the interventions on overall patient function, physical function, social/emotional function, or psychological symptoms. A meta-analysis restricted to higher-quality trials[25,26,28] suggested that interventions that include family caregivers may have positive effects on caregiver psychological symptoms. Nevertheless, our findings do not preclude a moderate intervention effect for nonsignificant meta-analyses. Across meta-analyses, confidence intervals were broad, and the mean treatment effect among all studies that examined patient psychological symptoms favored the intervention. Also, qualitative findings suggest that some interventions had statistically significant effects on patient quality of life,[23] TBI symptoms (*eg*, communication, memory, and patient-identified symptoms),[27,28,30] and caregiver burden.[35] However, the results for quality of life were inconsistent, as 1 study[25] found no effect for patient or caregiver quality of life and another[26] found no effect for caregiver quality of life. While 2 of the 3 studies that examined caregiver burden did not find a statistically significant intervention effect on caregiver burden,[26,29] the effects all favored the intervention, and effect sizes were consistent across studies. Adverse effects and household economic status outcomes were not reported. Only 3 studies examined family function[31,33,34] and 1 examined mental health service use.[32]

STRENGTH OF EVIDENCE

Strength of evidence (SOE) was rated on the basis of study design, risk of bias, inconsistency, indirectness, and imprecision. (For criteria definitions, refer to the Methods section.) For TBI, the SOE was rated moderate to low for care recipient overall function, physical function, psychological symptoms, and caregiver psychological symptoms and burden. SOE was very low for care recipient mental function. SOE was not rated for adverse effects because no studies reported adverse effects, nor was SOE rated for disease-specific symptoms because the evidence was insufficient. Concerns that contributed to the low SOE were moderate to high risk of bias and imprecision that was attributed to the 95% CI not excluding a moderate effect. There were additional concerns about imprecision that may have been due to poor congruence between outcomes measures.

In Table 6 we summarize the SOE for effects of family caregiver interventions for patients with TBI. Few studies evaluated caregiver interventions for patients with PTSD and these interventions varied substantially. Because of the sparseness of evidence for these comparisons, we only rated the SOE for couples-based therapies for PTSD (Table 7).

Table 6. Strength of Evidence for Effects of Family Caregiving Interventions in TBI

Outcome	Number of RCTs (Patients)	Findings	Strength of Evidence (Rationale by Domain)
Care recipient outcomes			
Overall functional status	3 (238)	SMD 0.29 higher (0.51 lower to 1.08 higher)	Moderate Moderate ROB, consistent, direct, imprecise
Physical functional status	4 (334)	SMD 0.22 higher (0.11 lower to 0.55 higher)	Moderate Moderate ROB, consistent, direct, imprecise
Mental functional status	3 (238)	SMD 0.42 higher (0.68 lower to 1.51 higher)	Very Low Moderate ROB, inconsistent, indirect, very imprecise
Psychological symptoms	3 (293)	SMD 0.25 lower (0.62 lower to 0.12 higher)	Low Moderate ROB, consistent, direct, imprecise
Caregiver outcomes			
Psychological symptoms	3 (296)	SMD 0.32 lower[a] (0.59 lower to 0.05 lower)	Moderate Moderate ROB, consistent, direct, imprecise
Caregiver burden	3 (252)	Median effect size 0.31 (range 0.30 to 0.35) p=NS for 2 of 3 studies	Low Moderate ROB, consistent, direct, imprecise

[a] SMD and SOE rating reported are from the sensitivity analyses excluding the single high risk of bias study.
Abbreviations: RCT=randomized controlled trial; ROB=risk of bias; SMD=standardized mean difference; TBI=traumatic brain injury

Table 7. Strength of Evidence for Effects of Family Caregiving Interventions in PTSD

Outcome	Number of RCTs (Couples)	Findings	Strength of Evidence (Rationale by Domain)
Care recipient outcomes			
PTSD symptoms	2 (97)	Clinically improved symptoms by clinician interview (range 23.2 to 27.6)[a] and patient report	Moderate Unclear ROB, consistent, direct, precise
Interpersonal relationships	2 (97)	Improved as reported by the patient but not the caregiver	Low Unclear ROB, inconsistent, direct, precise

[a] Clinician-administered PTSD scale.
Abbreviations: PTSD=posttraumatic stress disorder; ROB=risk of bias

CLINICAL AND POLICY IMPLICATIONS

Clinical practice guidelines for patients with TBI, PTSD, or polytrauma offer only general recommendations regarding the role of families and caregivers.[43-45] For example, the VA/DoD clinical practice guidelines for the Management of Posttraumatic Stress Disorder and Acute Stress Reaction[45] recommends educating trauma survivors and their families about PTSD, including practical ways of coping with traumatic stress symptoms, the process of recovering, and treatment options. However, these guidelines do not make recommendations beyond education or nonspecific suggestions for family interventions. Our update of interventions to support family caregivers and patients with PTSD, TBI, or polytrauma, along with other relevant VA ESP systematic reviews,[12,40,41] should be considered by guideline panels. Given the large investment the VHA has made in caregiver support programs, it would be helpful to clinicians if guidelines addressed available programs more specifically.

Our findings are similar to those of prior high-quality systematic reviews that examined the impact of interventions for caregivers of patients with mental illness, cognitive impairment, and cancer on both caregiver outcomes[13,16,42] and patient outcomes.[40,41] These prior reviews found few high-quality studies, and there was high heterogeneity across studies. These reviews found qualitative positive effects for some interventions on outcomes.[16,41] Only 1 review[42] found quantitatively positive effects of illness education and support interventions on caregiver psychological distress. Evidence from the VA ESP systematic review that examined caregiver interventions for patients with either cancer or memory disorders did not favor family-involved interventions over usual care on functional, psychological, quality of life, symptoms control or health service use,[40] but another VA ESP systematic review that examined caregiver interventions for caregivers of elderly patients with dementia found some promise for multicomponent interventions on caregiver psychological, burden, and quality of life outcomes.[13] The findings from that review suggest that more intensive and tailored interventions occurring after a home visit are more effective. Finally, another high-quality VA ESP systematic review examined the effect of technology in supporting caregivers.[12] However, the interventions examined in that review, including handheld/tablet computers, wireless/mobile technology, iPad, m-Health, internet-based interventions, text messaging, and other informatics applications, were not similar to interventions examined in other studies, which generally involved an interventionist or peer coach/mentor. In sum, across disease conditions and types of interventions, there is no clear message about the beneficial effects of family caregiver interventions on outcomes, and in general the quality of the evidence is low. However, there is some suggestion from our review and 2 prior reviews that these interventions might have some benefit for caregiver psychological outcomes, including psychological symptoms and caregiver burden.[13,42]

The implications of our review for VA are unclear. Only 4 identified studies recruited a sample of VA users,[28,31,33,34] and it is likely that the sequela of combat-related trauma versus trauma experienced by the mostly civilian patient samples identified in this review differ. However, within VA, interest in interventions to support family caregivers as part of a wider movement to promote Veteran health is growing,[46,47] and there are likely some lessons learned about intervention delivery and outcome measurement that could inform research and implementation efforts in VA.

VA offers robust programs to support Veterans and their family caregivers through evidence-based therapies for family members of Veterans with mental illness,[46,47] family engagement interventions,[48-51] and family support interventions.[52] In addition, the VA PCAFC is a national program that supports caregivers of Veterans through the provision of a mandatory skills training, stipend, health insurance, respite care, travel support, and contact with specialized VA staff to facilitate referrals and connections. Among Veterans in PCAFC, 70% have a PTSD diagnosis and 30% have a TBI diagnosis.[53] Within PCAFC, family caregivers can choose from multiple services (except skills training and stipend, which are mandatory) and therefore it is difficult to apply the findings from this review of specific interventions to broad policy implications for PCAFC. However, specific PCAFC services (*eg*, skills training, support groups) and other family service interventions in VA, such as Homefront, a group family education program for family members of Veterans with mental illness, use similar strategies as the interventions we examined in this review, including psychosocial education, social support, and therapy. Therefore, this review has the potential to inform the content and delivery of these specific components. Unfortunately, the dearth and low quality of existing literature makes it challenging to compare and contrast optimal delivery strategies and content and their effect on outcomes. Despite this we offer some thoughts:

- While family caregiver interventions for patients with TBI, PTSD, and polytrauma may be useful, the existing interventions attempt to accomplish many goals. In fact, the goals of each study examined in this review were fairly diffuse, the intensity of the interventions substantially different, and in some cases it was unclear the degree to which family members were involved. Instead, it may be more effective to focus on 1 or 2 outcome goals and then refine content, delivery strategy, target participant (*ie*, care recipient vs caregiver), and intervention intensity to specifically address those outcomes. For example, one study focused primarily on addressing current problems with patients with TBI and involved caregivers when possible.[23] Relative to all other studies identified in this review, this phone-based intervention had the strongest effect on patient psychological and functional outcomes. Perhaps this intervention was effective because the study had a clear target: the care recipient.
- Important patient- and caregiver-centered outcomes may be difficult to quantify. Several studies have found high levels of satisfaction with the intervention, but no change in caregiver burden or psychological distress scores.[22,54,55] Relatedly, it may be necessary to rethink what constructs caregiver interventions actually impact (*eg*, success gaining information from a provider[25] or high satisfaction[22]) and identify validated measures for these outcomes that are used consistently across studies.[16] Some of the constructs being measured (*eg*, depressive symptoms) were designed for clinical populations and may not reflect the distress experienced by caregivers. Problems related to trauma are complex and multidimensional.[28] As such, intervention outcomes may not map directly onto domains of existing instruments.
- Several studies questioned whether short-term follow-up periods, such as a year or less, are sufficient to identify changes in psychological symptoms and other outcomes.[22,25] Yet, it is also possible that the interventions may have lacked the intensity and targeting needed to observe positive intervention effects no matter the length of the follow-up period.[13] For the meta-analyses presented in this review, length of time of the intervention or follow up period did not appear to be related to whether outcomes were positive or negative.

Some established literature about the impact of family members on outcomes of patients with chronic disease has identified potential behavioral mechanisms that explain these effects.[38,56,57] While the stress-vulnerability theory[58] demonstrates how and why a family caregiver would provide benefit for patients, many of the studies did not identify specific theoretical underpinnings for the intervention design. Therefore, future research should identify and apply theoretical models are needed to inform discrete study goals, intervention designs, testable hypotheses, and explanations for the observed findings. Such theoretical models would provide a benchmark for more in-depth analysis about what did and did not work and would thus move the field forward.

LIMITATIONS

This review has several limitations. Studies were limited to those from OECD countries in the Western hemisphere and articles published in English. Identifying eligible studies was difficult because structured search terms do not fully capture the broad range of eligible interventions we considered in the review. Further, the role of the caregiver depends on the condition; for example, for patients with TBI, family members are often referred to as a family caregiver because needed care may have a more clinical focus, such as help with activities of daily living. In contrast, "caregivers" of patients with PTSD are rarely conceptualized as being labeled a caregiver, but rather a supportive family member or friend. In addition, the studies typically did not give detailed eligibility criteria for the caregivers. Therefore, from these studies, it is difficult to glean much about how to target caregivers who are likely to help the Veteran. Studies for which family involvement was either causal or unplanned were not included in this review. Most studies evaluated illness education, skills-based, or therapy-based interventions. We found no studies that examined interventions to improve household economic status. There were also no policy evaluations that met our criteria for inclusion. One study that showed positive effects of the PCAFC on increased mental health, primary care, and specialty care for Veterans with PTSD did not meet EPOC study design criteria.[53] Other limitations are described below.

Publication Bias

Given the small number of studies, statistical methods to detect publication bias are not useful. Other strategies, such as searching ClinicalTrials.gov for completed but unpublished studies is theoretically appealing but in practice has not been found useful.[59]

Study Quality

We were also limited by the existing literature. We identified few studies, and most were assessed as moderate to high ROB. Study samples were small and the measures used may not have accurately captured the phenomena of interest. Use of patient- and caregiver-reported outcomes, which may be better measures of intervention effectiveness,[22,25] was rare. No studies reported adverse effects. Several studies did not clearly describe the study design, control group, and intervention procedure in order for the team to assess ROB; for example, for one study it was unclear whether the patients had been randomized or not.[24] While most control groups were "treatment as usual," how this was defined and what type of care it included was rarely defined.

Heterogeneity

Unexplained heterogeneity evident in some of our meta-analyses represents another limitation of the existing evidence. We compared interventions that varied substantially in goals, delivery, intensity, and target recipient. We found that interventions varied in intensity, frequency of contact, duration, delivery strategies, goals, and outcome measures used. Usual care comparators were not well described. In some cases, poor descriptions of the study sample and baseline severity also made it difficult to compare how sample differences contributed to the observed heterogeneity. Finally, it was difficult to determine whether the care recipient or the caregiver was the target of the intervention and how involved the family member was when the intervention focused on the patient. Studies often did not describe the planned versus the actual role of the family member in the intervention, which added a layer of complexity when trying to conduct cross-study comparisons. We also compared outcome measures that may not have measured precisely the same constructs though we attempted to pool only measures that were conceptually similar. For example, the meta-analysis of social/emotional function used measures that compared cognitive function with mental and social function. However, we carefully considered which outcome measures could be reasonably pooled and we presented standardized mean differences to show effect sizes. We also only combined studies with an RCT design and we considered qualitatively whether meta-analysis findings differed by intervention format and delivery strategy and found little evidence to suggest that variations in study format impacted observed effects across studies.

Applicability of Findings to the VA Population

Of the 13 studies, 4 (31%) were conducted specifically in Veterans, and thus are highly applicable to the Veteran population. These studies did not differ qualitatively in important ways from studies containing non-Veteran samples. All but 2 studies were conducted in North America, and the rest were conducted in other economically developed countries. Most studies were conducted after 2005. However, many of the studies enrolled patients with TBI sustained in noncombat situations. Veterans with TBI often have coexisting PTSD, and thus findings in civilian patients may not generalize well to Veterans. A caution that is applicable to trials in general is that trials tend to enroll patients who are not representative of the underlying target population, and thus interventions are often less effective when implemented in routine clinical practice.

RESEARCH GAPS/FUTURE RESEARCH

We structure our reflection of gaps in evidence by considering each element of the PICOT framework (Table 8). Although it would be possible to generate an extensive list of gaps in evidence, we restricted this list to the areas judged to be highest priority, given the current state of evidence. To facilitate future literature syntheses, we encourage investigators conducting clinical trials to include these studies in trial registries.

Table 8. Highest-priority Evidence Gaps

PICOT Domain	Evidence Gap
Population	No evidence in patients with polytrauma; sparse evidence in those with PTSD. No evidence on caregivers and patients most likely to benefit.
Interventions	Uncertainty about the relationship between outcomes and intervention dose, mode of delivery, and components. Effects of financial support have not been studied in an eligible design. Study designs are needed to incorporate patient and caregiver/stakeholder input. Need to better quantify the role of the family member, and using a dichotomy to describe the role, such as “family assisted” versus “family oriented,” would be helpful compare interventions across studies. Intervention development should be informed by conceptual models.

Comparators	Caregiver versus dyadic interventions; better descriptions of usual care are needed.
Outcomes	Few studies report care recipient outcomes. Outcome measures vary greatly across studies making synthesis difficult. Measures are needed that capture patient/caregiver reported outcomes, including intervention satisfaction and acceptability, quality of life, and changes in employment/household income.
Timing	Need randomized controlled trials of combined treatments that include economic outcomes, especially over time.

The VHA may be uniquely well-suited to addressing these gaps in evidence. Further, the population served and the resources committed give the VA the needed platform to address these gaps. The prevalence of TBI, PTSD, and polytrauma is enriched in the enrolled VA population compared with other US health care systems. Given that these interventions often represent changes in the delivery of health services, a variety of study designs, including randomized trials and quasi-experimental designs will be appropriate. In addition, the VA invested in a large caregiver support program for OEF/OIF Veterans and a partnered evaluation unit to assess the program. Findings from an evaluation of PCAFC show that participation in the program was associated with increases in mental health care, primary care, and specialty care services for all enrollees and enrollees with a PTSD diagnosis[53]; however, future research related to PCAFC evaluation should focus on specific programmatic elements and their effects on health and health service use outcomes. More broadly, identifying caregiving as a funding priority connected to specific RFAs within VA ORD would help to support investigators to conduct research that can fill the identified gaps. Specifically, RFAs that focus on caregivers or partners alone are critical to promote family resilience and unity and would provide key benefits to Veterans even if the studies do not directly address Veteran functioning.

CONCLUSION

There is a small but growing literature about family caregiver interventions for patients with trauma-based conditions, including TBI and PTSD. Overall, we identified a diverse set of interventions; the majority included a family illness education component, and many utilized skills-based curricula to promote environment modifications, improvements in condition-specific skills, caregiver self-care, and coping skills. Evidence about the impact of these interventions on patient and caregiver outcomes is inconclusive given the small literature, few patients, and the heterogeneity of intervention format, delivery, intensity, family involvement, and outcomes. Yet for several outcomes, such as caregiver burden and psychological symptoms, caregiver interventions may be a promising approach. The positive impact of caregiver interventions on caregiver distress aligns with some prior reviews across a variety of patient conditions[13,42,56]; however, there remain considerable gaps. No studies have been published that examine caregiver interventions for individuals with polytrauma; none that were eligible examined financial assistance interventions; few examined patient/caregiver reported outcomes; and study quality was low.

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