Evidence-based Synthesis Program

QUERI

Family Involved Psychosocial Treatments for Adult Mental Health Conditions: A Review of the Evidence

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Prepared by:
Evidence-based Synthesis Program (ESP) Center
Minneapolis VA Medical Center
Minneapolis, MN
Timothy J. Wilt, MD, MPH, Director

Investigators:
Principal Investigator:
Laura Meis, PhD

Co-Investigator:
Joan Griffin, PhD

Research Associates:
Maureen Carlyle, MPH
Nancy Greer, PhD
Agnes Jensen, BS
Roderick MacDonald, MS
Indulis Rutks, BS

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PREFACE

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

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

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

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

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

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EVIDENCE REPORT

INTRODUCTION

Since 2008, the President has signed two new laws establishing or expanding VA authority to provide family services for Veterans' mental health care. The first law, Public Law 110-387: Veterans' Mental Health and Other Care Improvements Act of 2008, was signed into law on October 10, 2008. Section 301 of the Act amends title 38 of United States Code (U.S.C.) § 1701(5)(B) and 38 U.S.C. § 1782(a) and (b). This law expands VA authority to provide enhanced family mental health services, such as consultation, professional counseling, marriage and family counseling, and training to families of patients with Service Connected and Non-Service Connected injuries or conditions when 1) no Veteran treatment would otherwise occur without the family member's involvement, 2) the Veteran's treatment would be less or not effective without family member's involvement, 3) or, the treatment can be delivered most efficiently when the family member is included in treatment. The second law, Public Law 111-163: Caregivers and Veterans Omnibus Health Services Act, signed in May, 2010, allows, among other things, the VA authority to provide these same services to family caregivers of Veterans and directs the VA to provide additional benefits (e.g., financial stipends and health care benefits) to a select group of eligible caregivers, namely those providing essential care to Veterans injured in Operation Iraqi Freedom (OIF) and Operation Enduring Freedom (OEF). Of note, current eligibility criteria for VA family-related services do not extend to close friends or intimate partners who do not reside with the Veteran. These new laws, along with the VA's adoption in primary care of Patient-Aligned Care Teams, or a patient-centered medical home model, recognize the important role families have on a treatment team and their influence over a patient's care and related outcomes. Synthesis of the scientific literature on the effectiveness of involving family or intimate partners (referred to hereafter as family, encompassing both intimate partners, spouses, and other family members) in psychosocial interventions to treat or improve a broad range of mental health conditions, family problems, marital strain, and physical health conditions, including an examination of both patient outcomes and caregiver and family outcomes, is essential to shaping the VA's provision of family involved care but beyond the scope of a single review. The focus of the present review is on one of these vital areas for synthesis: the effectiveness of family involved interventions in treating mental health conditions. This synthesis is intended to help clarify the evidence for potential best practices within the VA in family involved mental health care to guide both policy and clinical practice. While these family or couple interventions likely also affect caregivers, the focus of this review is specifically on patient outcomes (versus caregiver or family member's personal functioning), including patients' family functioning.

TYPES OF FAMILY TREATMENTS FOR MENTAL HEALTH CONDITIONS

While individual psychotherapies for mental health problems have long been the standard for mental health care, family problems are pronounced among patients with mental health conditions. Among OEF/OIF Veterans recently returning from deployment, interpersonal problems have been identified as increasing at a greater rate than any other health-related problem,[1] and relationship distress in intimate relationships can facilitate or hinder treatment seeking.[2] Consequently, family involvement has been explored for a number of conditions,

including depression,[3] substance use,[4] bipolar disorder,[5] schizophrenia,[6] panic disorder with agoraphobia,[7] and posttraumatic stress disorder (PTSD).[8] Family interventions for mental health conditions can take multiple forms, as outlined by Baucom and colleagues,[9] and may fall across any given category or combination of categories.

Partner or Family Assisted Treatment[9]

In this case, family member(s) act as surrogate therapists or coaches to help the patient. Typically, the family aids the patient in completing out-of-session homework within a cognitive-behavioral treatment, and relationships between the patient and family are not a focus of treatment. This category of family involvement capitalizes on prior work establishing robust associations between social support, instrumental support, and treatment adherence across multiple medical conditions.[10]

Disorder Specific Couple or Family Treatment[9]

For interventions taking this approach, family behavior and relationships that are theorized to fuel disorder symptoms are addressed. Family relationships are targeted only to the extent to which they directly influence the patient's disorder or treatment. Such interventions, especially for schizophrenia or bipolar disorder, often target expressed emotions (EE) or related constructs. EE includes family members' expressed criticism, hostility, and emotional over-involvement toward the patient and is tied to poor medication adherence, including among patients with schizophrenia,[11] and greater relapse rates and symptom severity among patients with schizophrenia, eating disorders, depression, PTSD, and bipolar disorder,[12-15] EE likely reflects disturbances within the entire family system, including family organization, emotional climate, and transactions.[16] Supported mechanisms underlying EE include a family member's attributions of patient's negative behavior to controllable factors, personal factors, and beliefs that the patient is not making appropriate efforts at self-improvement.[16, 17]

Additionally, behavior patterns between family and patients and specific to a given disorder can be conceptualized as maintaining the condition, with reciprocal associations postulated between mental health symptoms and family functioning.[18, 19] For example, environmental contingencies have been theorized to maintain use for substance use disorders[20] and avoidance of trauma cues for individuals with PTSD.[21] Additionally, for those with substance use disorders, relationship distress may increase substance use cravings, reinforce the use of substances to cope with distress,[19] or even motivate patients to remain sober due to fears of relationship dissolution.[22]

General Marital OR Family Treatment[9]

Interventions taking this approach directly address general family or relationship distress, under the assumption that improving family functioning will reduce patient stressors and improve patient functioning.[9]

PRESENT STUDY

With one known exception,[9] prior reviews have focused on a discrete number of mental health conditions at a time (i.e., a review of family treatments for depression). To the best of our knowledge, the most recent comprehensive review that included family involved interventions for any mental health condition was published in 1998.[9] A comprehensive review is called for to update

the evidence, to serve VA needs, and to facilitate comparisons of the evidence across conditions. Additionally, such a review can highlight family interventions for mental health conditions that may not have been addressed in recent prior reviews due to too few RCTs to warrant a disorder specific review (i.e., sexual functioning disorders, PTSD). Prior reviews are potentially less relevant to VA populations due to their focus on studies conducted both nationally and internationally. Studies conducted outside the US (i.e., family interventions within Eastern societies) may be less relevant to US Veterans, given important cultural differences in family structure and function. Finally, given the VA's interest in including families in order to improve the quality of care provided in the VA, an important question to address is the comparative efficacy of family involved interventions versus individual-only treatment approaches.

In the only known comprehensive review of family involved psychosocial treatments for mental health conditions, Baucom and colleagues[9] established categories for evaluating the efficacy of a couple/family intervention, based upon Chambless and Hollon's[23] definition of empirically supported treatments (i.e., "clearly specified psychological treatments shown to be efficacious in controlled research with a delineated population," p. 7). They define an *efficacious* treatment as one in which the intervention has demonstrated superiority over waitlist control in studies conducted by two independent research teams. An *efficacious and specific* intervention has demonstrated superiority in at least two studies conducted by independent research teams over a placebo, nonspecific, or alternative intervention. They modify these labels with *possibly* (i.e., possibly efficacious and possibly efficacious and specific) when the above criteria are met by a single study. Using these criteria, the conclusions from the 1998 review are outlined in Table 1.

Table 1. Empirically Supported Couple and Family Treatments for Mental Health Conditions (Baucom 1998[9])

Mental Health Condition	Intervention	Efficacy Status
Schizophrenia	Behavioral Family Therapy[24-28]	1
	Supportive Family Therapy[29 30-32]	1
	Family systems[33]	3
Alcohol Use Disorders	Community Reinforcement Approach[34-36]	3
	Behavioral Marital Therapy[37, 38]	3
Female orgasmic disorder	Sexual skill training for primary female orgasmic disorder[39, 40]	3
	Masters and Johnson for female orgasmic disorders[41]	3
Mixed female sexual dysfunctions	Behavioral Marital Therapy + Masters and Johnson[42]	3
Female hypoactive sexual desire	Marital + orgasm consistency training[43]	3
Depression	Behavioral Marital Therapy[44, 45]	4
Obsessive Compulsive Disorder	Family-assisted exposure therapy[46]	4
	Partner-assisted exposure therapy[47, 48]	4
Agoraphobia	Partner-assisted exposure therapy[49-53]	4
	Partner-assisted Cognitive-Behavioral Therapy[54]	4
	Partner-assisted exposure + couple communication training[55]	4

Efficacy Status:
1 = Efficacious & Specific; superior to placebo, nonspecific, or alternative intervention in at least two studies conducted by independent research teams.
2 = Efficacious; superior to waitlist in RCTs conducted by two independent research teams.
3 = *Possibly* Efficacious & Specific; criteria met for efficacious and specific from a single study.
4 = *Possibly* Efficacious; criteria met for efficacious from a single study.[9, 23]

Baucom and colleagues[9]concluded that family involved treatments for schizophrenia were clearly efficacious for reducing relapse rates. These family treatments often incorporated elements from all three types of approaches to family involvement (family assisted interventions, disorder specific interventions, and family/couple therapy). These findings are largely consistent with larger reviews of empirically supported treatments.[23] Chambless and Ollendick[56] reviewed the American Psychiatric Association's Task Force and various other work groups' recommendations for psychosocial interventions considered efficacious and possibly efficacious, using similar criteria and including family treatments. Their review largely overlaps with Baucom and colleagues'[9] conclusions, with a few exceptions. First, one group[57] identified behavioral marital therapy as efficacious for depression among patients with marital discord and a second[58] identified behavioral marital therapy as possibly efficacious for depression. Second, multiple work groups identified the Community Reinforcement Approach and behavioral couple therapy for alcohol use disorders as either efficacious or possibly efficacious.

OBJECTIVES

The present study provides an update to prior work conducted by Baucom[9] and others[56]by examining the effectiveness of family involved psychosocial treatments in US samples for mental health conditions. Due to our focus solely on mental health conditions and US studies, our findings are not intended to be a strict replication and extension of Baucom and colleagues'[9] prior review. We conducted a systematic review of randomized controlled trials (RCTs) of psychosocial interventions, addressing a mental health condition through a family intervention. Given prior work already conducted in this area, we focused on only those studies conducted after 1995. To optimize relevance to Veterans and the VA, in addition to a focus on US studies, we limited our review to improvements in patient functioning, including patient symptoms and family/couple functioning (primary outcomes) and treatment adherence, treatment attendance, patient satisfaction, and social support for patients (intermediate outcomes). Figure 1 provides our analytic framework, depicting our population, interventions, comparators, and outcomes of interest. We were interested in reviewing the evidence of the efficacy of family involved interventions (compared to no psychosocial intervention), as well as the degree to which family involved interventions are superior to an alternative individually-focused or family involved intervention (i.e., specificity).

We sought to address two specific questions:

Key Question #1. What is the efficacy of family involved interventions in improving outcomes for adult patients with mental health conditions [i.e., how do family involved psychosocial treatments compare to no psychosocial treatment: (a) waitlist/no treatment or (b) medication management only]?

Key Question #2. What is the effectiveness of family involved interventions compared to alternative interventions in improving outcomes for adult patients with mental health conditions [i.e., how do family involved interventions compare to (a) any individually-oriented psychosocial intervention or (b) any alternative family involved intervention]?

Figure 1. Analytic Framework


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                                          ┌──────────────────────────────┐
                                          │                              │
                                          │                              ▼
                    Intervention:         ┌─────────────────────┐    ┌──────────────────────────────┐
┌──────────────┐    Family involved care  │ Intermediate Patient│    │ Final Outcomes               │
│  Population   │                          │ Outcomes            │    │ Patient Outcomes: Symptom    │
│ Adults and    │───────────────────────▶ │ Treatment attendance/│───▶│ improvement, functional      │
│their          │                         │ adherence, social    │    │ improvement, quality of      │
│family members │    Comparators:         │ support for          │    │ life, length of stay,        │
└──────────────┘                          │ patients, patient    │    │ discharge                    │
                    KQ1. No psychotherapy  │ satisfaction         │    │ disposition, utilization     │
                    or placebo            │ with care            │    │                              │
                                          └─────────────────────┘    │ Family Outcomes: Family      │
                    KQ2. Individually-                                │ functioning, relationship/   │
                    oriented                             ╭────────╮   │ couples functioning          │
                    treatment/usual                      │ Adverse│   └──────────────────────────────┘
                    care/alternative family              │ Effects│
                    treatment                            ╰────────╯
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Intervention: Family involved care

Comparators:

KQ1. No psychotherapy or placebo

KQ2. Individually-oriented treatment/usual care/alternative family treatment

Population Adults and their family members

Intermediate Patient Outcomes
Treatment attendance/ adherence, social support for patients, patient satisfaction with care

Final Outcomes
Patient Outcomes: Symptom improvement, functional improvement, quality of life, length of stay, discharge disposition, utilization

Family Outcomes: Family functioning, relationship/couples functioning

Adverse Effects

METHODS

TOPIC DEVELOPMENT

This project was nominated by Sonja Batten, PhD, Office of Mental Health Services. The key questions and scope were refined with input from a technical expert panel.

SEARCH STRATEGY

We searched MEDLINE (Ovid) and PsycINFO for randomized controlled trials (RCTs) and systematic reviews published from 1980 to November, 2011 using standard search terms. We limited the search to articles involving adolescents and adults and published in the English language. Search terms included: family, couples, home nursing, legal guardians, couple therapy, family therapy, and marital therapy. The search strategies are presented in Appendix A.

We obtained additional articles from systematic reviews, reference lists of pertinent studies, and suggestions from members of our technical expert panel.

STUDY SELECTION

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

- RCT conducted in the United States or systematic review or meta-analysis of RCTs.
- Study involves a patient age 18 and over with a DSM-III or DSM-IV **mental health** condition.[59, 60]
- Intervention must involve family members or caregivers of the adult patient (patient may or may not be present for the intervention).
- Study reports intermediate patient outcomes or final outcomes of interest as outlined in the analytic framework (Figure 1).
- Control group must be used; control group may be no treatment/placebo or an alternative active treatment (e.g., usual care, individually-oriented treatment, or another family/couple-oriented intervention).
- Study published in a peer-reviewed publication after 1995.

DATA ABSTRACTION

We abstracted the following study characteristics for each included study: author, date of publication, funding source, sample characteristics (gender, age, race/ethnicity, marital status, education, Veteran status, family characteristics, and recruitment method), inclusion and exclusion criteria (mental health condition, how the condition was assessed, family/caregivers involved, specific inclusion and exclusion criteria), treatment groups, intervention characteristics

(format, whether manualized, number of sessions, treatment length, approach, and treatment integrity), outcomes assessed (list of patient, family/couple, and intermediate outcomes assessed), and study quality (allocation concealment, blinding, analysis approach, description of withdrawals). We extracted final outcomes (patient outcomes and family/couple functioning measures) and intermediate outcomes, by mental health condition, for each treatment arm, where reported, and noted whether the analysis included all patients randomized or study completers only. Final patient outcomes of interest were: symptom improvement, global functioning, quality of life, length of stay, disposition at discharge, and health care utilization. The family/couple functioning outcome of interest in all studies was global function or satisfaction. We also were interested in intimate partner violence, communication skills and relationship conflict, observational data of communication skills among couples, and sexual satisfaction. Sexual satisfaction was abstracted under patient symptom improvement for studies of treatment for sexual dysfunction and as a measure of couples functioning in the studies of treatment for substance abuse. Intermediate outcomes of interest were treatment attendance, adherence, social support for the patient, and satisfaction with care. We assessed outcomes at a number of different time points in order to determine initial and persistent changes in behavior. When available, we examined behavior at baseline, after treatment (post-treatment), short-term follow-up (up to 6 months), and long-term follow-up (up to 12 months or longer) across treatment arms. All abstraction was done by trained research personnel and verified by a second research associate under the supervision of the Principal Investigator.

QUALITY ASSESSMENT

We assessed study quality of included trials (all were randomized, controlled trials) according to the following criteria: 1) adequate allocation concealment, 2) blinding of key study personnel, 3) analysis by intention-to-treat, and 4) reporting of number of withdrawals/dropouts by group assignment.[61] We also considered whether the treatment protocol was manualized and whether the quality and consistency of the treatment protocol was evaluated (i.e., treatment integrity) as part of the quality assessment for individual studies. Studies were rated as good, fair, or poor quality. A rating of good generally indicated that the treatment was manualized and integrity was assessed. In addition, the trial reported adequate allocation concealment, blinding, analysis by intent-to-treat, and reasons for dropouts/attrition. Studies were generally rated poor if the treatment was neither manualized nor assessed for quality, the method of allocation concealment was inadequate or not defined, blinding was not defined, analysis by intent-to-treat was not utilized, and reasons for dropouts/attrition were not reported and/or there was a high rate of attrition.

DATA SYNTHESIS

We constructed evidence tables showing the study characteristics and results for all included studies, organized by clinical condition. We critically analyzed studies to compare their characteristics, methods, and findings. We compiled a summary of findings for each key question and drew conclusions based on qualitative synthesis of the findings or pooled analyses where feasible.

RATING THE BODY OF EVIDENCE

We assessed the overall strength of evidence using the method reported by Owens et al.[62] The overall evidence was rated as: (1) high, meaning high confidence that the evidence reflects the true effect; (2) moderate, indicating moderate confidence that further research may change our confidence in the estimate of effect and may change the estimate; (3) low, meaning there is low confidence that the evidence reflects the true effect; or (4) insufficient, indicating that evidence either is unavailable or does not permit a conclusion.

PEER REVIEW

A draft version of this report was reviewed by members of our technical expert panel and VA clinical leadership. Their comments and our responses are presented in Appendix C. Responses were also incorporated into the final report.

RESULTS

LITERATURE FLOW

We reviewed 2,469 titles and abstracts from the electronic search. After applying our initial inclusion/exclusion criteria at the abstract level, 2,025 references were excluded. We retrieved 444 full-text articles for further review and another 397 references were excluded. Inclusion criteria added at the full-text review stage included limiting the scope of the review to patients with mental health conditions and articles published after 1995. Four articles were identified by hand search. We therefore identified a total of 51 references for inclusion in the current review representing 39 unique projects. We grouped the studies by mental health condition and addressed the key questions for each condition. Table 2 details the number of publications and number of unique projects per condition.

Table 2. Number of Publications and Number of Unique Trials for Each Mental Health Condition

Mental Health Condition	Publications	Unique Trials
Substance Use Disorders	26	22
Schizophrenia Spectrum	8	4
Bipolar	10	6
Depression	1	1
Eating Disorders	1	1
Nicotine Dependence	1	1
Posttraumatic Stress Disorder (PTSD)	2	2
Sexual Dysfunction	2	2
Total	**51**	**39**

Figure 2 details the exclusion criteria and the number of references excluded at the abstract and full-text review stages.

Figure 2. Literature Flow Diagram

Search results =

2,469 references

Pulled for full text review =

444 references

Included = 51 references

(39 unique studies)

Identified by hand search/author
correspondence =
4 references

Excluded = 2,025 references

Study not conducted in the US. = 315
Not adult population = 361
Not a peer reviewed, randomized trial = 291
Not a condition of interest, or study is about prevention = 281
Intervention is not counseling, therapy, education,
  or family based treatment involving a family member = 587
No patient outcomes of interest = 172
Not a mental health diagnosis = 17
Paper published prior to 1990 = 1

Excluded = 397 references

Study not conducted in the U.S. = 121
Not adult population = 9
Not a peer reviewed, randomized trial = 34
Not a condition of interest, or study is about prevention = 17
Intervention is not counseling, therapy, education,
  or family based treatment involving a family member = 33
No patient outcomes of interest = 48
Not a mental health diagnosis = 78
Paper published prior to 1990 = 36
Paper published 1990 – 1995 = 21

OVERVIEW OF TRIALS

Substance Use Disorders

The largest set of studies that met our criteria was from the substance use disorder (SUD) literature. Detailed descriptions of the study characteristics and outcomes are provided in Appendix D, Tables 1 to 4. We found twenty-six papers that met our criteria for substance use disorders, representing twenty-two unique RCTs. As summarized in Table 3 below, the 22 RCTs were nearly split between trials for treatment of alcohol (n=11) and drug use (n = 9) and two studies included treatment for either alcohol or drug use.[63, 64] Most studies (16 of 22) verified the SUD by a structured interview using DSM criteria.[60]

Population Studied

Subject and intervention characteristics are summarized in Tables 3 and 4. There were a total of 1623 patients studied, ranging from 29 to 184 participants in a single trial. Samples sizes for treatment conditions were small. Over 60% of the twenty-two trials (n=14) had an intervention condition arm with 30 or fewer subjects. The average patient and family member were each 38

years old. Patients were racially diverse (69% non-white, on average) and typically male (77%) with a female participating family member or intimate partner (76%). All subjects were married or cohabitating in all but four of the trials reporting marital status. Two trials[4, 65] were conducted with Veteran samples; none reported whether the family member was a Veteran. Eleven trials limited their participants to men,[4, 63, 65-73] including five alcohol use disorder (AUD) trials,[4, 65, 71-73] five drug use disorder trials,[66-70] and one trial that included those with drug use or alcohol use disorders.[63] Three trials limited patients to women.[74-76] These included two AUD trials[74, 75] and one drug use disorder trial.[76] The remaining seven trials included both men and women.[64, 77-82] Of these, two were AUD trials,[79, 81] four were drug use disorder trials,[77, 78, 80, 82] and one trial included subjects with either alcohol or drug dependence.[64]

Table 3. Summary of Baseline Characteristics, Substance Use Disorders Studies (22 trials)

Characteristics	Number/mean (range)	Number of trials reporting
Total number of patient/family dyads randomized	1623 (29-184)	19
Total number of patients from dyads analyzed	1589 (28-184)	19
Total number of family randomized for family only studies (patient not involved in intervention)	252 (32-130)	3
Total number of family only analyzed (patient not involved in intervention)	252 (32-130)	3
Marital status, % married	82% (17-100%)	16
Patient gender, % male	80%	20
Family member gender, % female	76%	17
Race, % non-white patients	31.5% (2-59.5%)	18
Veterans, %	100	2
Age of patients, years	38.0 (27.7-47.8)	19
Age of family members, years	37.8 (28.8-55.3)	13

Although we had a broad definition of family for inclusion in our review, most of the studies examined the effects of including a spouse or romantic partner in treatment. Of the twenty-two trials, 15 included a spouse or partner (wife/female partner = 10; husband/male partner = 3; either husband or wife/romantic partner = 3) of the subject.[4, 63, 65-67, 69-76, 78, 79] Seven trials did not restrict to wives or partners, allowing adult children, partners, or friends to participate.[64, 68, 77, 80-83] One of these trials specified any family member who was *not* a spouse or partner was eligible.[82]

Inclusion of Patients with Comorbid Conditions

Rates of co-occurring conditions among participants were not typically reported. However, in 15 trials, individuals with co-occurring serious mental health conditions defined as an organic mental, paranoid, psychotic disorders or schizophrenia, were typically excluded from participation. Patients at risk of harming oneself or others, including those with suicidal/homicidal ideation or history of domestic violence were excluded in three trials and one study reported excluding anyone with a psychiatric condition that may affect informed consent for treatment.

Intervention

By far the most commonly investigated family involved intervention (17 of 22 trials) was behavioral couples, marital, or family therapy (BCT/BMT/BFT), a dyadic (one patient and one family member/intimate partner), disorder-specific, couple/family treatment, designed to address a SUD through 1) cognitive behavioral strategies to promote abstinence, involving the family

member, and 2) traditional behavioral couple therapy techniques to enhance communication, problem solving skills, and relationship satisfaction.[9] For simplicity, we use BCT in this review to refer to behavioral couple therapy for SUDs that includes either a spouse or an unmarried intimate partner (BCT or BMT). BFT refers to the same intervention, but including other family members. BCT/BFT were typically delivered in an outpatient setting, and with only two exceptions,[4, 64] participants were recruited from outpatient settings, the community, or the media, rather than following an inpatient stay. The length of the intervention varied, ranging from 10 to 56 weeks. The other psychological interventions reviewed included motivational enhancement treatment with psychoeducation and couple therapy (Helping Other Partners Excel or HOPE)[70] and community reinforcement training with families (i.e., CRAFT), an intervention delivered solely to the families of patients with SUDs to enhance communication, build skills, and develop coping strategies that would encourage the family's loved one to enter treatment.[80, 81, 83] HOPE and CRAFT were conducted in outpatient settings, and treatments ranged from 2 to 24 weeks.

Table 4. Summary of Heterogeneity, Substance Use Disorders Studies (22 trials)

		Number of trials reporting
Subjects diagnosed with:	Alcohol use disorders only	11
	Drug use disorders only	9
	Either drug or alcohol use disorders	2
Diagnosis verified by structured interview:	Yes	16
	Not reported	6
Family intervention with:	Wife/female intimate partner	11
	Husband/male intimate partner	3
	Husband/wife or male/female intimate partner	2
	Any identified family member	5
	Anyone but spouse	1
Family intervention compared to:	Waitlist	0
	Drug treatment only	2
	Treatment as usual or individual treatment(s)	14
	Other family treatment (s)	6
Subject gender:	Men	12
	Women	3
	Both men and women	7

Comparison Interventions and Study Designs

Family involved treatments were compared to one (11 trials[4, 64, 66-68, 70, 76, 79, 80, 82, 84-86]), two (9 trials[63, 65, 71-74, 77, 81, 83, 86, 87]), or three (2 trials[69, 78]) comparison interventions. Comparison interventions included 1) medical observation only (1 trial[64]); 2) individual treatment(s) only (10 trials[66-68, 70, 75-77, 79, 80, 82]); 3) individual and alternative family involved treatment(s) (8 trials[63, 69, 71, 73, 74, 78, 81, 83]); or 4) only an alternative family involved treatment (3 trials[4, 65, 72]).

Comparison to Medical Observation

As noted, one study compared a family involved treatment to medical observation only and was reviewed for Key Question 1. In this study, authors tested the effect of a family intervention on

the utilization of continuing care after patients were discharged following hospital admission for alcohol detoxification. Male and female participants admitted to an inpatient detoxification unit for alcohol use (with or without comorbid drug dependence) and a family member were randomized into either treatment as usual (consisting of assisting the patient with withdrawal symptoms, monitoring risks for developing serious problems during withdrawal, but no family involvement) or a brief family intervention. The family intervention included two meetings with participants and family members (either a spouse or parent) to review continuing care plans both prior to and after discharge and develop strategies for successful outcomes. This intervention was delivered by phone and in-person, depending on what was most convenient for the family member.

Comparison to Individual Treatment Only

Fifteen trials compared family involved treatments to individual behavioral treatment.[63, 66-71, 73-79, 82] These trials were reviewed to assess evidence for Key Question 2A.

Seven of the fifteen trials were two-armed trials that directly compared BCT to individual cognitive-behavioral therapy (ICBT).[66-68, 75, 76, 79, 82] An additional six trials compared BCT to ICBT and another family involved treatment(s) or variation of BCT. Three of the six trials[63, 73, 74] compared BCT to ICBT plus a psychoeducational program serving as an attention control condition. Two of these trials had the same psychoeducational program (Psychoeducational Attention Control Treatment or PACT)[63, 74] while the other was slightly different, but had common strategies and education targets with the PACT treatment.[73] Two other trials also included a comparison of BCT to ICBT and PACT, but also included a fourth arm to compare standard BCT to a briefer version of the therapy (B-BCT).[69, 78] Another three-arm trial[71] compared BCT to ICBT, but also a variation of BCT that included a parent training intervention. Results from these trials that compared a family involved intervention to an individual treatment were used to assess evidence for Key Question 2A.

The remaining two trials[70, 77] did not use BCT, but instead another family involved treatment. One was three-arm trial that included male and female participants with a substance abuse diagnosis who were assigned either to 1) naltrexone with ICBT; 2) naltrexone, ICBT, plus contingency management (incentives for participants to remain in treatment); 3) naltrexone, ICBT, contingency management, and reciprocal relationship counseling for the patient and a family member, friend, spouse, or child.[77] The second non-BCT trial was a two-armed trial that compared group motivational enhancement therapy with psychoeducation and couple therapy (Helping Other Partners Excel, HOPE) to a counselor-led drug treatment support group for men with drug use disorders.[70]

Comparison to Alternative Family Treatment(s) Only

Six trials compared family involved treatments to one or more alternative family treatments.[4, 65, 72, 80, 81, 83] Evidence from these trials were used to assess evidence for Key Question 2B. Two of these trials[4, 72] compared Behavioral Marital Therapy (BCT) to BCT plus a relapse prevention condition. O'Farrell and colleagues [4] conducted a two armed trial that directly compared these two conditions; the trial by McCrady et al.[72] was a three-armed trial that compared BCT to BCT plus relapse prevention or to BCT plus a self-help group for family members. Another trial that

compared family involved treatments was also by O'Farrell et al.[65] In that two-armed trial, a combination of BCT and ICBT was compared to BCT and interactional treatment, a therapy approach that does not pre-plan therapy sessions, but instead focuses on mutual support, sharing of feelings, and problem solving through discussion. The remaining three studies were unique in that they targeted the family members of patients with a drug use disorder, not the patient with the disorder, directly.[80, 81, 83] Each of these three trials compared a family intervention to alternative treatments for families. In Kirby and colleges two-armed trial,[80] family members (spouses, parents, siblings) were randomized into either a 12-step self-help group counseling program or a community reinforcement training (CRT) which included individual counseling for a family member to enhance communication, build skills, and develop coping strategies that were specific to the subject's drug use disorder. The other two trials were similar. A variation of the community reinforcement training, called the community and reinforcement and family training (CRAFT) was tested. Like Kirby et al.,[80] both compared CRAFT to a 12-step self-help group counseling program. In the trial by Meyers et al.,[83] these two conditions were also compared to a CRAFT plus aftercare, which consisted of additional group therapy with family members for 6 months after the CRAFT intervention. In the trial by.[81] CRAFT and the self-help conditions were compared to a Johnson Institute intervention, where families confront the alcoholic about their abuse and describe their own experiences and observations about the abuse in order to encourage treatment engagement.

Outcomes

The most common patient outcomes reported were self-reported days of abstinence within a specified period of time, self-reported quantity and/or frequency of substance use, and initiation of treatment (utilization of care). The degree of symptom relief was commonly measured by the percentage of days abstinent (PDA) from alcohol or drugs or the percentage of heavy drinking days (PDHD), typically using the Time-Line Follow Back procedure (TLFB).[88] Tables 5 and 6 provide an overview of our findings. The most frequently reported family outcome was family or couple functioning, most often measured by the Dyadic Adjustment Scale (DAS). Length of time that participants were followed for assessments was variable, but typically included at the least a post-treatment or short-term assessment and in many cases assessments every 3 months for 12 months after treatment termination.

Table 5. Main Findings, Substance Use Disorders Studies (Alphabetical Order by First Author)

Study, Year Interventions	Patient Outcomes[a]		Family Outcomes			
	Symptoms	**Utilization**	**Family Functioning**	**Couple Functioning**	**Intimate Partner Violence**	**Communication/ Conflict**
Carroll, 2001[77] 1) Counseling for significant other+ ICBT+Contingency Management + Naltrexone vs. 2) ICBT + Contingency Management + Naltrexone vs. 3) ICBT and Naltrexone	Cond. 1) vs. 2): *Post: ns* Cond. 1)& 2) vs. 3): *Post: ns*		Cond. 1) vs. 2): *Post: +*			
Fals-Stewart, 1996,[66] 2000,[84] 2002[85] 1) Behavioral couple therapy vs. 2) Individual treatment - behavioral therapy	**(1996)** *Post: ns* *Short term: ns* *Long term: ns* **(2000)** *Long term: +*			Marital Happiness Scale : **(1996)** *Post: +* *Short term: ns* *Long term: ns* **(2000)** *Long term: +* % days separated: *Post: +* *Short term: +* *Long term: ns*	**(2002)** *Long term: +*	**(1996)** *Post: +* *Short term: ns* *Long term: ns*
Fals-Stewart, 2001[67] 1) Behavior Couple Therapy treatment package vs. 2) Individual based methadone maintenance (standard treatment)	*Post: +*			*Post: +*		
Fals-Stewart, 2003[68] 1) Naltrexone + Behavioral Family Therapy vs. 2) Naltrexone + individual based therapy	*Post: +* *Long term: +*		*Long term: +*			
Fals-Stewart, 2005[69] 1) Standard Behavioral couple therapy vs. 2) Individual based therapy vs. 3) Brief Behavioral couple therapy vs. 4) Psychoeducational attention control treatment	Cond. 1) vs. 2)[b] *Post: ns* *Short term: ns* *Long term: +* Cond. 3) vs. 2) *Post: +* *Short term: +* *Long term: +* Cond. 1) vs. 4) *Post: ns* *Short term: +* *Long term: +* Cond. 3) vs. 4) *Post: ns* *Short term: ns* *Long term: ns*			Cond. 1) vs. 2)[b] *Post: +* *Short term: +* *Long term: +* Cond. 3) vs. 2) *Post: +* *Short term: +* *Long term: +* Cond. 1) vs. 4) *Post: +* *Short term: +* *Long term: +* Cond. 3) vs. 4) *Post: +* *Short term: +* *Long term: +*		

Study, Year Interventions	Patient Outcomes[a]		Family Outcomes			
	Symptoms	Utilization	Family Functioning	Couple Functioning	Intimate Partner Violence	Communication/ Conflict
Fals-Stewart, 2006[74] 1) Behavioral couple therapy vs. 2) Individual based therapy vs. 3) Psychoeducational attention control treatment	Cond. 1) vs. 2) *Post*: *ns* *Short term*: *ns* *Long term*: *ns* Cond.1) vs. 3) *Post*: *ns* *Short term*: *ns* *Long term*: *ns*			Cond. 1) vs. 2) *Post*: + *Short term*: + *Long term*: + Cond.1) vs. 3) *Post*: + *Short term*: + *Long term*: + Cond. 2) vs. 3) *Post*: *ns* *Short term*: *ns* *Long term*: *ns*	Cond. 1) vs. 2) *Long term*: + Cond.1) vs. 3) *Long term*: +	
Fals-Stewart, 2008[78] 1) Standard Behavioral couple therapy vs. 2) Individual based therapy vs. 3) Brief Behavioral couple therapy vs. 4) Psychoeducational attention control treatment	Cond. 1) vs. 2)[b] *Post*: + *Short term*: + *Long term*: + Cond.1) vs. 3) *Post*: *ns* *Long term*: *ns* Cond. 3) vs. 2) *Post*: *ns* *Long term*: + Cond. 3) vs. 4) *Post*: *ns* *Long term*: +			Cond. 1) vs. 2)[b] *Post*: + *Short term*: + *Long term*: + Cond.1) vs. 3) *Post*: *ns* *Long term*: *ns* Cond. 3) vs. 2) *Post*: + *Long term*: + Cond. 3) vs. 4) *Post*: + *Long term*: +		
Fals-Stewart, 2009[79] 1) Behavioral Couple Therapy vs. 2) Individual based treatment	*Post*: *ns* *Short term*: + *Long term*: +			*Post*: + *Short term*: + *Long term*: +		
Jones, 2011[70] 1) HOPE: Helping Other Partners Excel vs. 2) Usual care	*Short term*: -			*Short term*: -		
Kelley, 2002[63] 1) Behavior Couple Therapy vs. 2) Individual Behavioral Therapy vs. 3) Psychoeducational attention control treatment	Cond. 1) vs. 2) & 3) *Post*: + *Short term*:+ *Long term*: +			Cond. 1) vs. 2) & 3) *Post*: + *Short term*: + *Long term*: +		
Kirby, 1999[80] 1) Individual counseling and Psychoeducation vs. (community reinforcement training intervention) 2) Self help (Narcotics Anonymous)	*Post*: *ns*	*Post*: *ns*	*Post*: *ns*			

Study, Year Interventions	Patient Outcomes[a]		Family Outcomes			
	Symptoms	Utilization	Family Functioning	Couple Functioning	Intimate Partner Violence	Communication/ Conflict
Lam, 2009[71] 1) Behavioral Couple Therapy vs. 2) Individual based treatment vs. 3) Parent Skills with Behavioral Couple Therapy	Cond. 1) vs. 2)[b] *Post*: ns *Short term*: ns *Long term*: ns Cond. 1) vs. 3) *Post*: ns *Short term*: ns *Long term*: ns Cond. 2) vs. 3) *Post*: ns *Short term*: ns *Long term*: ns			Cond. 1) vs. 2)[b] *Post*: + *Short term*: ns *Long term*: ns Cond. 1) vs. 3) *Post*: ns *Short term*: ns *Long term*: ns Cond. 2) vs. 3) *Post*: ns *Short term*: ns *Long term*: ns	Cond. 1) vs. 2) *Post*: ns *Short term*: ns *Long term*: ns Cond. 1) vs. 3) *Post*: ns *Short term*: ns *Long term*: ns Cond. 2) vs. 3) *Post*: ns *Short term*: ns *Long term*: ns	
McCrady, 1996,[72] 1999,[86] 2004[87] 1) Alcohol focused spouse involvement + behavioral marital therapy (ABCT) vs. 2) ABCT+ AA/Al Anon vs. 3) ABCT + relapse prevention	**(1996)** Cond. 1) vs. 2) *Post*: ns Cond. 1) vs. 3) *Post*: ns Cond. 2) vs. 3) *Post*: ns **(1999)** Cond. 1) vs. 2) *Short term*: ns Cond. 1) vs. 3) *Short term*: ns Cond. 2) vs. 3) *Short term*: ns **(2004)** Cond. 1) vs. 2) *Long term*: ns Cond. 1) vs. 3) *Long term*: ns Cond. 2) vs. 3) *Long term*: ns			**(1999)** Cond. 1) vs. 2) *Short term*: ns Cond. 1) vs. 3) *Short term*: ns Cond. 2) vs. 3) *Short term*: ns **(2004)** Cond. 1) vs. 2) *Long term*: ns Cond. 1) vs. 3) *Long term*: ns Cond. 2) vs. 3) *Long term*: ns		

Study, Year Interventions	Patient Outcomes[a]		Family Outcomes			
	Symptoms	Utilization	Family Functioning	Couple Functioning	Intimate Partner Violence	Communication/ Conflict
McCrady, 2009[75] 1) Alcohol Behavior Couple Therapy vs. 2) Alcohol Behavior Individual Therapy	% PDA[c] *Post*: ns *Long term*: ns % PDHD *Post*: ns *Short term*: ns *Long term*: ns % complete abstinence *Short term*: ns *Long term*: ns % no drinking *Short term*: ns *Long term*: ns	*ns*		+		
Meyers, 2002[83] 1) Community Reinforcement and Family Training (CRAFT) vs. 2) Al-Anon or Narcotics Anonymous facilitation therapy vs. 3) CRAFT + aftercare	Cond. 1) vs. 2) *Short term*: ns *Long term*: ns Cond. 1) vs. 3) *Short term*: ns *Long term*: ns Cond. 2) vs. 3) *Short term*: ns *Long term*: ns	Cond. 1) vs. 2) *Short term*: + Cond. 1) vs. 3) *Short term*: ns Cond. 1) vs. 3) *Short term*: +				
Miller, 1999[81] 1) CRAFT vs. 2) Al-Anon vs. 3) Johnson Institute intervention		Cond. 1) vs. 2) *Short term:* + *Long term:* + Cond. 1) vs. 3) *Short term:* + *Long term:* + Cond. 2) vs. 3) *Short term:* ns *Long term:* ns	Cond. 1) vs. 2) *Short term:* ns Cond. 1) vs. 3) *Short term:* ns Cond. 2) vs. 3) *Short term:* ns			Cond. 1) vs. 2) *Short term:* ns Cond. 1) vs. 3) *Short term:* ns Cond. 2) vs. 3) *Short term:* ns
O'Farrell (1998a)[4] 1) Behavioral Couple Therapy + Relapse Prevention vs. 2) Behavioral Couple Therapy	*Post:* ns *Short term:* + *Long term:* + *Final:* ns			*Post:* ns *Short term:* ns *Long term:* ns *Final:* ns		*Post:* ns *Short term:* ns *Long term:* ns *Final:* ns

	Patient Outcomes[a]		Family Outcomes			
Study, Year Interventions	**Symptoms**	**Utilization**	**Family Functioning**	**Couple Functioning**	**Intimate Partner Violence**	**Communication/ Conflict**
O'Farrell (1998b)[65] 1) Behavioral Marital Therapy vs. 2) Interactional Couple Therapy vs. 3) Individual treatment only				Cond. 1) vs. 2) *Post: ns* Cond. 1) vs. 3) *Post: ns* Cond. 2) vs. 3) *Post: ns*		
O'Farrell (2008)[64] 1) Brief Family Treatment Intervention vs. 2) Treatment as usual	*Short term: ns*	*Post: +* *Short term: ns*				
O'Farrell (2010)[82] 1) Behavioral Family Counseling + Individual Based Treatment vs. 2) Individual Based Treatment	PDA : *Post: ns* *Short term: ns* PDPSU: *Post: ns* *Short term: ns*		*Post: ns* *Short term: ns*			
Walitzer, 2004[73] 1) Behavior Couple Therapy (alcohol-focused) vs. 2) Individual group counseling vs. 3) Alcohol focused spouse involvement in behavior change	Mean days abstinent: Cond. 1) vs. 2) *Post: ns* *Short term: ns* *Long term: ns* Cond. 3) vs. 2) *Post: +* *Short term: ns* *Long term: ns* Mean days heavy drinking: Cond. 1) vs. 2) *Post: +* *Short term: +* *Long term: ns* Cond. 3) vs. 2) *Post: +* *Short term: +* *Long term: ns*			1) vs. 2) *Post: ns* *Short term: ns* *Long term: ns* Cond. 3) vs. 2) *Post: ns* *Short term: ns* *Long term: ns*		
Winters, 2002[76] 1) Behavior Couple Therapy vs. 2) Individual Behavioral Therapy	*Post: +* *Short term: +* *Long term: ns*			*Post: +* *Short term: ns* *Long term: ns*		

Note: Symbols denote differences between condition 1 and condition 2 unless otherwise noted: + effects favor condition 1; − effects favor the comparator treatment; = no differences; *ns* = differences between conditions are non-significant (p > 0.05). Post refers to post-treatment assessment; short-term refers to the last assessment conducted within 6 months of treatment ending; long term refers to the last assessment conducted within 12 months of treatment ending; final refers to the last assessment conducted after 12 months of treatment ending

[a]No patient outcomes reported for global functioning.
[b]Mean comparisons not conducted by author, but in secondary analysis for this review.

[c]After adjusting for relationship functioning, both short and long term.

Table 6. Intermediate Findings, Substance Abuse Disorder Studies (Alphabetical Order by First Author)

Study, Year Interventions	Intermediate Outcomes		
	Attendance	Adherence	Satisfaction
Carroll, 2001[77] 1) Counseling for significant other+ ICBT+ Contingency Management + Naltrexone vs. 2) ICBT + Contingency Management + Naltrexone vs. 3) ICBT and Naltrexone	Cond. 1) & 2) vs. 3): + Cond. 1) vs. 2): *ns*	Naltrexone adherence: Cond. 1) & 2) vs. 3): *ns* Cond. 1) vs. 2): *ns*	
Fals-Stewart, 1996,[66] 2000,[84] 2002[85] 1) Behavioral Couple Therapy vs. 2) Individual treatment - behavioral therapy	*ns*		*ns*
Fals-Stewart, 2001[67] 1) Behavior Couple Therapy treatment package vs. 2) Individual based methadone maintenance (standard treatment)	*ns*		*ns*
Fals-Stewart, 2003[68] 1) Naltrexone + Behavioral Family Therapy vs. 2) Naltrexone + individual based therapy	+	Naltrexone adherence: +	*ns*
Fals-Stewart, 2005[69] 1) Brief Behavioral Couple Therapy 2) Standard Behavioral Couple Therapy vs. 3) Individual based therapy vs. 4) Psychoeducational attention control treatment	*ns*		*ns*
Fals-Stewart, 2006[74] 1) Behavioral Couple Therapy vs. 2) Individual based therapy vs. 3) Psychoeducational attention control treatment	*ns*		*ns*
Fals-Stewart, 2008[78] 1) Brief Behavioral Couple Therapy vs. 2) Standard Behavioral Couple Therapy vs. 3) Individual based therapy vs. 4) Psychoeducational attention control treatment	*ns*		*ns*
Fals-Stewart, 2009[79] 1) Behavioral Couple Therapy vs. 2) Individual based treatment	*ns*		*ns*
Kelley, 2002[63] 1) Behavior Couple Therapy vs. 2) Individual Behavioral Therapy vs. 3) Psychoeducational attention control treatment	*ns*		

Study, Year Interventions	Intermediate Outcomes		
	Attendance	Adherence	Satisfaction
Kirby, 1999[80] 1) Individual counseling and Psychoeducation vs. (community reinforcement training intervention) 2) Self help (Narcotics Anonymous)	+		
Lam, 2009[71] 1) Parent Skills with Behavioral Couple Therapy vs. 2) Behavioral Couple Therapy vs. 3) Individual based treatment	*ns*		
McCrady, 1996,[72] 1999,[86] 2004[87] 1) Alcohol focused spouse involvement + behavioral marital therapy (ABCT) vs. 2) ABCT + AA/Al Anon vs. 3) ABCT + relapse prevention	*ns*	Patient homework completed *ns* (1996) + (1999)	
McCrady, 2009[75] 1) Alcohol Behavior Couple Therapy vs. 2) Alcohol Behavior Individual Therapy	+		
Meyers, 2002[83] 1) Community Reinforcement and Family Training (CRAFT) vs. 2) CRAFT + aftercare vs. 3) Al-Anon or Narcotics Anonymous facilitation therapy	*ns*		
Miller, 1999[81] 1) CRAFT vs. 2) Johnson Institute intervention vs. 3) Al-Anon	*Cond. 1) vs. 2): +* *Cond. 3) vs. 2): +*		
O'Farrell, 1998a[4] 1) Behavioral Marital Therapy + Relapse Prevention vs. 2) Behavioral Marital Therapy		Anti-abuse contract: *Post: ns Short term: ns* *Long term + Final: ns*	
O'Farrell, 2010[82] 1) Behavioral Family Counseling + Individual Based Treatment vs. 2) Individual Based Treatment	+		
Walitzer, 2004[73] 1) Behavior Couple Therapy (alcohol-focused) vs. 2) Individual group counseling vs. 3) Alcohol focused spouse involvement in behavior change	*ns*		
Winters, 2002[76] 1) Behavior Couple Therapy + Individual Behavioral Therapy vs. 2) Individual Behavioral Therapy	*ns*		*ns*

Note: Symbols denote differences between condition 1 and condition 2 unless otherwise noted: + effects favor condition 1; − effects favor the comparator treatment; *ns* = differences between conditions are non-significant (p > 0.05)

Bipolar Disorder

We included 6 unique RCTs (10 publications) of family interventions for subjects with bipolar disorder. Detailed descriptions of the study characteristics and outcomes are provided in Appendix D, Tables 5 to 8. Subject and intervention characteristics are summarized in Tables 7 and 8. Table 9 is an overview of our findings.

Population Studied

Baseline characteristics of the study subjects are summarized in Table 7. There were a total of 625 subjects; two trials had less than 50 subjects and 3 trials had more than 100 subjects. The mean age in all 6 studies was less than 50 years. The majority of subjects were white, less than half were male, and approximately half were married. No study specifically enrolled Veterans.

Table 7. Summary of Baseline Characteristics, Bipolar Disorder Studies

Characteristic	Mean (range) except as noted	Number of trials reporting*
Total number of patients randomized	Total=625 (40-293)	6
Gender, % male	42 (37-54)	6
Age of subjects, years	38 (26-48)	6
Race, % white	87 (60-94)	4
Veterans, %	NR	0
Marital status, % married	52 (15-67)	5

*6 trials were presented in 10 articles

Five studies examined family involved interventions with patients with either bipolar I mood disorder, (3 studies[89-91]) or bipolar I or II mood disorder (2 studies[92, 93]). One study did not specify a bipolar type but included patients with "major affective disorder or bipolar disorder, manic, depressed, or mixed."[94] In five studies, the intervention targeted patients with these disorders,[89-92, 94] while the sixth directly targeted the caregivers of individuals with either condition.[93] Two studies enrolled participants predominantly while they were inpatients,[89, 90] while the remaining studies enrolled participants predominantly while they were outpatients. Few requirements for participating family members were reported. In one study, the family member was a spouse or intimate partner.[94] One study required that caregivers (family or other individual in close contact, supporting the patient financially, or involved in their treatment) had to have at least one physical or mental health problem.[93]

Inclusion of Comorbid Conditions

Rates of co-occurring conditions among participants were not typically reported. However, the five studies that enrolled patients[89-92, 94] excluded individuals with a current alcohol or drug dependence disorder. Individuals with other co-occuring mental health diagnoses were not explicitly excluded although two studies did exclude patients with organic central nervous system disorder.[91, 94] In two studies, the patient had to be either taking[91, 92] or willing to take[92] mood stabilizing medications.

Intervention

The interventions included general marital or family therapy,[89, 94] disorder-specific family therapy,[90-92] and a combination of disorder-specific family intervention and family-assisted treatment.[93] In the study by Clarkin et al.,[94] the intervention was manualized psychoeducational marital therapy delivered by social workers with experience in family treatment.[94] It is unclear whether the

intervention was delivered to individual or multiple couples. In the study reported by Miller et al.,[89] the family therapy program, titled Problem Centered Systems Therapy of the Family, was a 6 to 10 session intervention with a patient and his or her family members, focused on problem solving, communication, roles, affective responsiveness, affective involvement, and behavior control. Several studies[90-92] provided Family-Focused Treatment (FFT), a 9-month psychoeducation program (up to 21 sessions) providing education on bipolar disorder, communication training, and problem-solving skills training delivered to individual patients and their family members. Perlick et al.[93] provided a variant of FFT referred to as Family-Focused Treatment-Health Promoting Intervention (FFT-HPI), a 12-15 session psychoeducational intervention focused on enhancing caregiver skills for managing their relative's illness, defining self-care goals, resolving barriers to patient care and self-care, examination of core beliefs, and problem solving. It is unclear whether the caregivers met individually or in a group. FFT-HPI was explicitly developed to address both patient symptoms and health behaviors of the caregiver. Treatment periods generally ranged from 6 weeks to 9 months. All interventions were delivered in outpatient settings.

Comparison Interventions and Study Design

Comparator groups included medication only (2 trials[89, 94]), individual therapy plus medication (2 trials[91, 92]), multifamily group therapy with medication (1 trial[89]), crisis management with medication (1 trial[90]), ICBT with medication (1 trial[92]), collaborative care with medication (1 trial[92]), and health education.[93]

Table 8. Summary of Heterogeneity, Bipolar Disorder Studies

		Number of trials reporting*
Subjects diagnosed with:	Bipolar I only	3
	Bipolar II only	0
	Bipolar I or Bipolar II	2
	Not specified	1
Diagnosis verified by structured interview		6
Subjects recruited:	Shortly after episode (hospitalization not reported)	1
	While admitted to inpatient or outpatient services	4
	Not reported	1
Family intervention with:	Intimate partner only	1
	Any single family member	1
	Any combination of family members	4
	One couple/family at a time	6**
	Groups of families	1**
Family intervention compared to:	Waitlist	0
	Another treatment	6
Subject gender:	Men	0
	Women	0
	Both men and women	6

*6 trials were presented in 10 articles
**Miller (2004) compared an intervention with one family at time to a multifamily group intervention (represented in both counts)

Outcomes

Five studies assessed subject symptoms using established rating scales[89-91, 93, 94] with one study reporting recovery status,[89] and one study reporting relapse,[91] rather than the actual symptom scores. One study assessed clinical status based on DSM-IV criteria.[92] Global family functioning was reported in one study.[95] Two studies reported measures of global patient function,[94, 95] and two reported hospitalization data.[89, 91] Five studies reported intermediate outcomes related to treatment attendance or medication adherence.[89-92, 94] Three studies reported post-treatment results following 5 months,[93] 9 months,[95] or 11 months[94] of treatment. One study reported results at 12 months, 3 months after treatment programs lasting up to 9 months.[92] Another reported results at 28 months or 22 months after a 6 month treatment program.[89] One study reported data following treatment (9 months) and 3 months post-treatment (12 months total)[90] with 24 month follow-up in a subsequent publication.[5] Finally, one study reported results after an active treatment year (9 months treatment program) and after an additional follow-up year.[91]

Table 9. Main Findings, Bipolar Disorder Studies (Alphabetical Order by First Author)

Study, year Interventions	Patient Improvement			Family/Couple Improvement[a]
	Symptoms	Global Functioning	Utilization	Family Functioning
Clarkin, 1998[94] 1) Medication management + marital intervention vs 2) Medication management only	*ns*	+		
Miklowitz, 2000,[90] 2003[96] 1) Family focused + medication vs 2) Crisis management + medication	+ Survival without relapse: +			
Miklowitz, 2007[92, 95] 1) Family focused therapy vs 2) Inter-personal and social rhythm therapy vs 3) Cognitive behavioral therapy 4) Collaborative care	# months well[b]: *ns* Recovery[c]: +			
Miller, 2004,[89] Solomon, 2008,[97] Miller, 2008[98] 1) Medication + family therapy vs 2) Medication + multiple-family group therapy vs 3) Medication only	Recovery[d]: *ns*		*ns*[e]	
Perlick, 2010[93] 1) Family focused, health promoting vs 2) Health education	+			
Rea, 2003[91] 1) Family focused + medication vs 2) Individual therapy + medication	Relapse, rehospitalization: active treatment year: *ns* post-treatment year: +			

[a]No family outcomes reported for couples' global functioning, intimate partner violence, communication or conflict.
Note: For comparison of condition 1) to condition 2) except where noted + effects favor the intervention; – effects favor the comparator treatment; *ns* = differences between conditions are non-significant (p > 0.05).
[b]Conditions 1, 2, and 3 significantly different from 4; condition 1 not significantly different from 4
[c]Conditions 1, 2, and 3 significantly different from 4; condition 1 also significantly different from 4
[d]No differences between any treatments
[e]Condition 1 not significantly different from condition 3; results reported only for subgroup of patients who recovered

Schizophrenia Spectrum Disorders

For schizophrenia spectrum disorders, 4 unique studies (8 publications) met inclusion criteria for the current review. Detailed descriptions of the study characteristics and outcomes are provided in Appendix D, Tables 9 to 12. Participant and intervention characteristics are summarized in Tables 10 and 11.

Population Studied

Baseline characteristics of the study subjects are summarized in Table 10. There were a total of 810 participants, with data analyzed for 595 of these participants. The mean age in all studies was less than 35 years. The majority of subjects were male and predominantly white. No study excluded patients based on gender. Current marital status was reported in two of four trials, and most subjects were not married (90%). No study reported subjects' Veteran status. Each of the four studies included participation from the subject and any family member; Mueser et al.[99, 100] expanded that definition to include any person in a "caring but non-professional relationship" with subject (e.g., clergy). None of the four studies required the subject and participating family member to reside together; however, two of the studies[99-103] required a minimum four hours per week contact between them.

Inclusion of Comorbid Conditions

Each of the four studies included subjects with a range of schizophrenia spectrum disorders, as verified by structured interview. The complexity of clinical presentation included in the above trials varied. Schooler and colleagues[24, 104] employed the most restrictive inclusion/exclusion criteria, excluding participants with liver damage, chronic organic brain syndrome, or substance dependence,[24, 104] but participants with substance abuse disorders were not excluded (unless diagnosed with schizophreniform disorder). A second trial also did not explicitly exclude participants who met criteria for a substance abuse disorder.[101-103] Both Mueser et al.[99, 100] and McFarlane et al.[29] explicitly studied complicated cases by requiring eligible subjects to have either an active substance abuse disorder,[99, 100] or a 'complicating' factor,[29] including lack of consistent treatment participation, history of violence or suicidality, arrests, criminal convictions, homelessness, moderate to severe substance abuse, or frequent hospitalization. McFarlane et al.[29] however, did exclude acutely violent or suicidal participants, or participants with a major medical illness or physical addiction that required hospitalization, until they were stabilized. Participants were not excluded for any other comorbid mental health diagnosis or co-occurring problem.

Table 10. Summary of Baseline Characteristics, Schizophrenia Spectrum Disorder Studies

Characteristics	Mean (range) except as noted	Number of trials reporting
Total number of subjects randomized	810 (68-528)	4
Total number of subjects analyzed	595 (68-313)	4
Gender, % male	69 (65-77)	4
Age of subjects, years	31 (30-34)	4
Race, % white	74 (71-78)	2
Veterans, %	NR	0
Marital status, % married	10 (6-13)	2

Intervention

All interventions were two years in length, with the exception of Mueser et al.[99, 100] Mueser and colleagues[99, 100] compared a brief treatment lasting 2-3 months to an intervention lasting 9-18 months. All of the studies were conducted in an outpatient setting; however, two of the four studies recruited subjects after an acute psychotic episode or hospitalization,[24, 29] while the other two recruited subjects from community mental health agencies.[99-103]

Two of the interventions[29, 101-103] utilized multi-family groups. Multi-family groups combine disorder specific family intervention (emphasizing improvement of communication) with general family therapy goals (formal problem solving) and building of a social support network. The subject was included in the multi-family groups. Psychoeducation was a component to both interventions, to better understand the subjects' mental illness and engage family members in the subjects' recovery. McFarlane and colleagues[29] examined Asserted Community Treatment (ACT), which included an initial family education and engagement component, one home visit, and multi-family groups.

Schooler and colleagues assigned subjects to either Applied Family Management (AFM) or Supportive Family Management (SFM).[24, 104] Both AFM and SFM included an initial psychoeducational workshop, case management, and monthly support group meetings for both subjects and families over a two year period. The more intensive AFM added behavioral single family treatment conducted in the home. Subjects who stabilized (16-24 weeks) were further randomized into three double blind medication dosages of fluphenazine decanoate (continuous moderate or 'standard' dose, continuous low dose, or targeted dose only when symptomatic) and entered a two year maintenance phase.

Mueser et al.[99, 100] utilized both the disorder specific and general family therapy approaches in their Family Intervention for Dual Disorders, which combines behavioral single family therapy with a family education component through the 9-18 month intervention. A multi-family support group was available after the active intervention up to the 36 month point.

A commonality with all interventions was that even if an initial "family only session" was provided, the subject was present and included in subsequent family therapy sessions.

Table 11. Summary of Heterogeneity, Schizophrenia Spectrum Disorder Studies

		Number of trials reporting
Subjects diagnosed with:	Schizophrenia only	0
	Schizoaffective disorder only	0
	A range of possible schizophrenia spectrum disorders	4
Diagnosis verified by structured interview		4
Subjects recruited:	Following a recent hospitalization	2
	From community mental health setting	2
Family intervention with:	Intimate partner only	0
	Any single family member	4
	Any combination of family members	0
	One couple/family at a time	0
	Groups of families	0
Family intervention compared to:	Waitlist	0
	Another treatment	4
Subject gender:	Both men and women	4

Comparison Interventions and Study Design

In one study, with follow up for one year post-treatment,[101-103] the comparison condition was standard care which consisted of individual case management and medication management services.

Three interventions[24, 29, 99, 100, 104] compared more to less intense family intervention. In McFarlane et al. (1996), the intervention and comparison groups both participated in manualized Asserted Community Treatment (described above), but the comparison group did not include multi-family groups. Additional family interaction with the treatment team occurred throughout the two year intervention only in the event of a crisis. Schooler et al.[24] included case management and monthly family group meetings in the comparison condition (Supportive Family Management) throughout the two year intervention. Mueser et al.[99, 100] provided only brief psychoeducation (2-3 months) in the comparison group; however, a multi-family support group was available after the active intervention up to the 36 month point.

Outcomes

Patient outcomes assessed included hospitalization,[24, 29, 102, 103] service utilization,[102, 103] symptom severity,[101] global functioning,[29] and time to relapse/rescue medication (medication added with prodromal relapse signs and discontinued after stabilization).[24] Mueser and colleagues[100] reported on numerous dual diagnosis patient outcomes including substance use, psychiatric functioning, problem solving, and knowledge of disease. Family outcomes were assessed in two studies[29, 104] using the Social Adjustment Scale and the Patient Rejection Scale.[104] All studies reported outcomes post-treatment, with the exception of McDonell and colleagues,[103] who reported one year-post-treatment outcomes, and Mueser and colleagues,[100] who included 36 month outcomes. Table 12 is an overview of our findings.

Table 12. Main Findings, Schizophrenia Spectrum Disorder Studies (Alphabetical Order by First Author)

Study, year Interventions	Patient Improvement			Family/Couple Improvement	
	Symptoms	Global Functioning	Utilization	Family Functioning	Couple Functioning
Dyck, 2000,[101] 2002,[102] McDonell, 2006[103] 1) Multiple Family Group vs. 2) Standard Care	+		State Hospitalization: + Any Hospitalization: *ns* Crisis/urgent care: *ns*		
McFarlane, 1996[29] 1) Assertive Community Treatment + Multiple Family Group vs 2) Assertive Community Care + Crisis Care only	*ns*	*ns*	*ns*	*ns*	
Mueser, 2009[99] and in press[100] 1) Family Intervention for Dual Disorders vs 2) Family Psychoeducation	Schizophrenia symptoms: + substance use: *ns*	+			
Schooler, 1997[24] 1) Applied Family Management vs 2) Supportive Family Management	*ns*		*ns*	SAS/Social: NS PRS + SAS Friction: +	SAS/Sexual: *ns*

Note: For comparison of condition 1) to condition 2) except where noted + effects favor the intervention; − effects favor the comparator treatment; *ns* = differences between conditions are non-significant (p > 0.05).
SAS = Social Adjustment Scale (family friction, social/leisure and sexual/romance factors); PRS = Patient Rejection Scale

Posttraumatic Stress Disorder

There were two studies which met our search criteria examining family involved interventions for PTSD. Detailed descriptions of the study characteristics and outcomes are provided in Appendix D, Tables 13 to 16.

Population Studied

The two studies included a total of 233 participants. All patients in the trial conducted by Glynn and colleagues[8] were recruited from the Los Angeles VA (either inpatient or outpatient care). Participants for Weine[105] trial were recruited from the community. For Glynn and colleagues[8] (N = 36) the average patient was 47 years old, 45% were white, and all participants were Vietnam Veterans with combat-related PTSD (100% male). Ninety percent participated in the family intervention with their wife or intimate partner. For Weine and colleagues[105] (n = 197), all patients were Bosnian refugees, screening positive for PTSD, and not currently in mental health treatment. The average patient was 38 years old, most were married (82%), and half were male (48%). Veteran status was not reported. All adult family members were invited to participate and descriptive information on family members' relationship to patients was not described. Most family members were female (60%) with mean age of 36 years.

Inclusion of Comorbid Conditions

Glynn and colleagues[8] excluded participants with a number of conditions, including organic brain disorder, psychotic disorders, severe dissociative conditions, current substance dependence, or overt physical aggression to self or others in the past year. Weine[105] excluded participants with active psychosis, substance intoxication or withdrawal, or an acute confusional state. Participants were not excluded for any other comorbid mental health diagnosis or co-occurring problem.

Intervention

The family involved treatment condition in Glynn and colleagues' trial[8] included 9 weeks of exposure therapy (18 sessions) followed by PTSD-specific behavioral family therapy, which included psychoeducation about PTSD, anger management, and communication training (disorder-specific family treatment;[9] 34 sessions). Weine and colleagues[105] examined a 9 session (16 week) family involved support group intended to increase the access of Bosnian refugees with PTSD to mental health services (Coffee and Family Education and Support; CAFES; disorder specific family therapy[9]). Both trials were delivered through outpatient treatment.

Comparison Interventions and Study Design

Glynn and colleagues[8] compared the family involved treatment (exposure therapy with BFT) to two conditions: 1) exposure therapy alone (18 sessions, 9 weeks) or 2) wait list followed by behavioral family therapy (16 sessions) for interested dyads. Weine and colleagues[105] compared CAFES to a no treatment control group.

Outcomes

Primary outcomes relevant for the present study examined by Glynn and colleagues[8] included a composite of symptoms of PTSD assessed through structured clinical interview and self-report, social adjustment, and rates of treatment dropout. Outcomes were assessed at post-treatment and 6 months post-treatment. Weine and colleagues[105] examined the number of mental health visits attended by participants who screened positive for PTSD at 6, 12, and 18 months post-treatment. Main findings are reviewed in Table 13.

Table 13. Main Findings, Post Traumatic Stress Disorder Studies (Alphabetical Order by First Author)

Study, year Interventions	Patient Improvement			Family/Couple Improvement[a]	
	Symptoms	Global Functioning	Utilization	Family Functioning	Couple Functioning
Glynn, 1999[8] 1) Exposure Therapy + Behavioral family therapy vs. 2) Exposure Therapy vs. 3) Wait list	ns	ns			+
Weine, 2008[105] 1) Coffee and Family Education and Support vs. 2) No treatment control			+		

Note: For comparison of condition 1) to condition 2) except where noted + effects favor the intervention; − effects favor the comparator treatment; ns = differences between conditions are non-significant (p > 0.05).
[a]No family outcomes reported for intimate partner violence, communication or conflict.

Sexual Functioning Disorders

There were two studies which met our search criteria examining family involved interventions for sexual functioning disorders. Detailed descriptions of the study characteristics and outcomes are provided in Appendix D, Tables 17 to 20. Main outcomes are summarized in Table 14.

Population Studied

The two studies included a total of 97 participants. For both studies, all patients were males with erectile dysfunction (ED) who participated with their female intimate partner. Both samples were highly similar in terms of age (Aubin et al.,[106] mean age = 52 years; Banner et al.,[107] mean age = 57years) and race (Aubin:[106] 86% white; Banner:[107] 85% white). For the trial conducted by Aubin and colleagues,[106] eight-six percent were married. Rates of marriage were not reported by Banner and colleagues.[107] Veteran status was not reported in either study.

Inclusion of Comorbid Conditions

Both studies included only participants in heterosexual relationships of at least 6 months (Banner,[107]: 6 months; Aubin[106]: 12 months) and whose intimate partners did not have a sexual functioning disorder. Aubin and colleagues[106] included participants with ED, regardless of the etiology of the condition (50% not due to a medical condition; findings not stratified by etiology of ED). They excluded participants who reported a history of gender identity disorder, screened positive for depression, reported intimate partner violence, reported an extra-marital affair in the last year, discussed separation in the last year, and reported sexual dysfunction among intimate partners. Banner and colleagues[107] only included patients whose ED was not due a medical condition. They also excluded patients diagnosed with a number of medical conditions which could cause ED, participants with significant mental health conditions, and participants whose intimate partner had one of a number of sexual functioning disorders.

Intervention

The family involved treatment Aubin and colleagues[106] examined consisted of 12 weeks (8 sessions) of medication (Sildenafil) plus outpatient sex therapy that included a combination of existing couple and sex therapy techniques including communication skills, sensate focus, sexual fantasy training, and cognitive restructuring. Banner and colleagues[107] examined medication (Sildenafil) plus cognitive-behavioral sex therapy. They assigned participants to either medication plus cognitive-behavioral sex therapy or medication only for four weeks. At four weeks, they then provided cognitive-behavioral sex therapy to those in the medication only condition with continuing symptoms. Due to contamination across conditions after 4 weeks, only outcome data at 4 weeks are presented.

Comparison Interventions and Study Design

Aubin and colleagues[106] compared the family involved treatment to 12 weeks of medication management (Sildenafil), including 8 brief, typically individual, 15 minute, medication pick up visits to discuss any medical concerns. Banner and colleagues[107] compared the family involved intervention to medication management (Sildenafil) that included a pre-treatment information session.

Outcomes

Primary outcomes for both studies included the International Index for Erectile Function (IIEF)[108] and the Dyadic Adjustment Scale (DAS)[109] although DAS findings were not reported by Banner and colleagues.[107] Aubin and colleagues[106] also assessed relationship functioning using the Personal Assessment of Intimacy in Relationships scale (PAIR),[110] as well as treatment satisfaction through the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS).[111] Assessments were conducted at post-treatment and 2 months after treatment completion. Banner and colleagues[107] also assessed patient global functioning through the Beck Depression Inventory,[112] and Beck Anxiety inventory.[113]

Table 14. Main Findings, Sexual Functioning Disorders Studies (Alphabetical Order by First Author)

Study, year Interventions	Patient Improvement[a]		Family/Couple Improvement[b]
	Symptoms	Global Functioning	Couple Functioning
Banner, 2007[107] 1) Sildenafil + couple sex therapy vs 2) Sildenafil + couple sex therapy for treatment non-responders	*ns*		
Aubin, 2009[106] 1) Sildenafil + couple sex therapy vs 2) Sildenafil only	*ns*		*ns*

Note: For comparison of condition 1) to condition 2) except where noted + effects favor the intervention; − effects favor the comparator treatment; *ns* = differences between conditions are non-significant (p > 0.05).
[a]No patient outcomes were reported for health care utilization.
[b]No studies reported family/couple outcomes for intimate partner violence, communication, or conflict.

Other Conditions

We identified one trial each of family involved interventions for depression, eating disorders, and smoking cessation. The findings are summarized in Table 15. Subject characteristics treatment descriptions and outcomes are presented in Appendix D, Tables 21 to 24.

Depression

The depression study[114] included 35 heterosexual couples in which the woman was diagnosed with depression and the male partner was non-depressed. The mean age of the women was 43.2 years; the mean age of the men was 45.0 years and 94.3 percent of the couples were married. Eighty-eight percent of the sample were non-Hispanic white, 5.6 percent were Hispanic, 3.1 percent were black, and 3.1 percent were Asian. Couples were excluded if there was infidelity in the past 6 months or more than two acts of aggression in the past year. Couples were mildly to moderately distressed with severely discordant couples excluded. The women could be receiving other treatment for depression if they had been in individual psychotherapy for at least 12 weeks or on a stable dose of psychotropic medication for at least 8 weeks. The intervention was brief, problem-focused couple therapy for depression with wait list control as the comparator. Outcomes included measures of depression and relationship satisfaction. Thirty couples completed the 5 week treatment conducted in an outpatient setting. Three month follow-up data were obtained for twenty-seven couples.

Eating Disorders

Overweight women with binge eating disorder were the focus of the study by Gorin et al.[115] Women were excluded if they engaged in purging behaviors more than once per month or met diagnostic criteria for anorexia nervosa, bulimia nervosa, or eating disorder of no specific origin. They also could not be receiving concurrent treatment for weight loss, including appetite suppressants. The women were required to have a spouse or cohabiting partner willing to participate in treatment but marital status was not reported. The mean age of the women was 45.2 years, and 86 percent of the sample was Caucasian. The intervention was group CBT for binge eating disorder with involvement of the spouse or intimate partner. The goal was for both partners to understand binge eating disorder, identify coping resources, agree about a plan of action, and feel confident in their ability to address binge eating disorder (i.e., a disorder specific couple intervention.)[9] The comparators were standard group CBT and wait list control. The primary outcomes were binge eating frequency assessed with both a 7 day calendar recall and the Eating Disorder Examination Questionnaire (EDEQ).[116, 117] The treatment phase was 12 weeks with an additional 6 month follow-up; participants were outpatients.

Nicotine Dependence

The smoking cessation study[118] targeted women, pregnant for 20 weeks or less, who were current smokers or recent quitters. The women were required to be living with an intimate partner and willing to have the partner contacted regarding participation in the study. The mean age of the women was 24 years, 77 percent were white, and 96 percent were married. It was reported that 77% of the women had tried to quit smoking, with a mean of 3 prior attempts. Fifty-two percent of partners were smokers. The intervention was individual counseling calls by a health advisor with partners assisting in a coaching capacity (partner-assisted treatment[9]). The comparators were individual counseling and usual care. Outcomes of interest were support for cessation, general support, and smoking status. The patients were followed to 12 months post-partum, and the study was conducted on an outpatient basis.

Table 15. Main Findings, Depression, Eating Disorders, and Smoking Cessation Studies

Study, year Interventions	Patient Improvement			Family/Couple Improvement[a]	
	Symptoms	Global Functioning	Utilization	Family Functioning	Couple Functioning
DEPRESSION: Cohen, 2010[114] 1) Brief Couple Therapy vs. 2) Wait list control	+				+
EATING DISORDERS: Gorin, 2003[115] 1) Group Cognitive Behavioral Therapy (CBT) with spouse vs. 2) Group CBT vs. 3) Wait list control	*ns*[b]	*ns*[b]			*ns*[b]
SMOKING CESSATION: McBride, 2004[118] 1) Partner assisted + woman-only care vs 2) Woman-only care vs 3) Usual care	*ns*[b]				

Note: For comparison of condition 1) to condition 2) except where noted + effects favor the intervention; − effects favor the comparator treatment; *ns* = differences between conditions are non-significant (p > 0.05).
[a]No family outcomes reported for intimate partner violence, communication or conflict.
[b]No differences across all treatment conditions

RESULTS BY KEY QUESTION

KEY QUESTION #1. What is the efficacy of family involved interventions in improving outcomes for adult patients with mental health conditions [i.e., how do family involved psychosocial treatments compare to no psychosocial treatment: (a) waitlist/no treatment or (b) medication management only]?

Substance Use Disorders

Detailed descriptions of the outcomes are provided in Appendix D, Tables 2 to 4.

As noted above, no studies that we reviewed compared a family involved intervention to waitlist, but one study directly compared family treatment to medication-only care. O'Farrell and colleagues[64] tested the effect of a family intervention on the utilization of continuing care. Male and female subjects admitted to an inpatient detoxification unit for alcohol use (with or without comorbid drug dependence) and a family member were randomized into either treatment as usual, consisting of assistance with withdrawal symptoms, monitoring risks for developing serious problems during withdrawal, but no family involvement, or a brief family intervention. The family intervention included meeting with subjects and family members (either a spouse or parent) to review continuing care plans both prior to and after discharge. This intervention was delivered by phone and in-person, depending on what was most convenient for the family member. Three months post-discharge, there were no significant differences between conditions

in the percent of days using alcohol or drug use. However, those in the brief family condition were twice as likely to enter continuing care programs compared to the usual care group (r = 0.36; medium effect). The authors did not report any family functioning outcomes.

Bipolar Disorder

None of the studies we identified included a wait-list control or no-treatment arm; two studies included a medication only arm.[89, 94] Outcomes are presented in Appendix D, Tables 6 to 8. In one study, it was noted that the psychiatrist provided support, encouragement, and direct advice as needed but avoided the use of psychotherapy.[89] Clarkin and colleagues[94] reported on change in symptoms when medication management plus marital therapy was compared to medication management only. The symptom change in scores over time did not differ significantly for the two treatment groups. However, they did find greater improvement in post-treatment medication adherence (p = 0.008) following marital therapy. Additionally, significantly improved global functioning was also reported (change in Global Assessment Scale, GAS, of 8.6 points in the marital therapy group compared to a change of 1.0 point in the medication only group).

The second study, evaluating Problem Centered Systems Therapy of the Family (PCSTF), reported no differences in recovery, median time to recovery, or relapse after recovery between subjects receiving medication plus family therapy (PCSTF) or multi-family group therapy (MFG) and subjects receiving medication only. There were also no differences in recovery or relapse when level of family impairment was considered. However, there were significant family impairment by treatment interactions for the number of depressive episodes per year, percentage of time in episode, and percentage of time in a depressive episode, indicating family therapy resulted in an improved course of illness for participants with high family impairment.[89, 98] Compared to medication management, the disorder specific psychoeducational family therapy (MFG) led to 1.4 fewer depressive episodes per year (d = 1.0), 14% percent less time in a mood episode (d = 0.82), and 1.7 fewer mood episodes, yearly (d = 0.92). The general family therapy (PCSTF) led to 0.9 fewer depressive episodes per year (d = 0.70) than medication management, additional comparisons between these groups for impaired families were non-significant.

No significant difference in number of medication sessions attended for the entire study population were reported, but significantly greater number of sessions were attended among those in PCSTF than the medication only group when only subjects who recovered were analyzed.[89, 97, 98]

Summary

No studies compared a family intervention to no intervention. Of two studies that compared marital or family therapy to medication only, marital therapy was associated with improved overall functioning and better medication adherence but not with improvement in symptoms. Problem Centered Systems Therapy of the Family was not found to be associated with recovery. However both PCSTF and MFGs were associated with improved depression over medication management only for patients in distressed families. No studies reported a family or couple function outcome.

Schizophrenia Spectrum Disorders

No studies compared a family intervention to no treatment or medication only.

Posttraumatic Stress Disorder

Each of the two studies of family involved interventions for PTSD compared the family involved intervention to a waitlist control. Results are presented in Appendix D, Tables 14 to 16. Glynn and colleagues[8] found that those assigned to either exposure therapy plus behavioral family therapy or exposure therapy alone reported fewer post-treatment PTSD symptoms than waitlist controls, however this difference eroded with time (differences non-significant at 6 month follow-up) and differences between groups on social adjustment were non-significant at each time point. Additionally, those who participated in exposure therapy plus behavioral family therapy were more likely to drop out of treatment than waitlist controls.[8] However, Weine and colleagues[105] found the patients of family members who participated in a family support group (i.e., CAFES) were significantly more likely attend mental health care treatment (the primary study outcome) than no treatment controls. Weine and colleagues[105] also collected data relevant to our key questions on PTSD symptoms and depression. However, differences on these variables across conditions were not presented. Also, the role of family distress in predicting treatment response was not examined.

Sexual Functioning Disorders

Two studies compared a family involved intervention to a medication only condition.[106, 107] Outcomes are reported on Appendix D, Tables 18 to 20. Findings suggested that sex therapy plus medication resulted in greater satisfaction with treatment[106] and cognitive-behavioral sex therapy plus medication did not result in greater erectile functioning on continuous scale scores. Differences were provided in rates of patient exceeding cutoffs indicating clinical improvement of erectile functioning (48% in the sex therapy condition and 29% in the medication only condition), but significance tests of these differences were not provided.[107] All other results indicated non-significant differences between conditions on couple functioning.[106]

Other Conditions

Findings from studies of depression, eating disorders, and smoking cessation are presented in Appendix D, Tables 22 to 24.

Depression

We identified one trial of couple therapy for depression that met our inclusion criteria.[114] Briefly, 35 heterosexual couples (94% of whom were married) were randomly assigned to Brief Couple Therapy (18 couples) or wait list control (17 couples). In each couple, the female was diagnosed with depression; male partners could not meet diagnostic criteria for depression. While single time point, univariate analyses at the 3 month follow-up demonstrated significant differences only in HAM-D[119] and not Beck Depression Inventory 2nd Edition (BDI-II) scores,.[120] analyses using hierarchical linear modeling found that BDI-II (d = 0.54) and HAM-D (d = 0.72) scores decreased significantly over the course of the study (both p < 0.01, mean follow-up of 24.2 weeks). It was reported that 67% of women in the treatment group improved (a 50% or greater reduction in BDI-II or HAM-D scores) compared to 17% in the control group and that 47% of

the treatment group showed full recovery (BDI-II score below 11 and HAM-D score below 6) compared to 8% of the control group. Scores for marital satisfaction, as measured by the Dyadic Adjustment Scale (DAS),[109] did not differ between treatment and control using the univariate approach. However, using hierarchical linear modeling, greater improvements in marital satisfaction were observed for treatment couples than control couples (p < 0.01). At the 3 month follow-up, the average participant in couple therapy reported relationship adjustment in the satisfied range (above 97.5;[121] mean = 102.1) while those in the waitlist condition reported scores indicating clinically significant relationship distress for the average participant (mean = 92.4).

Summary

One trial met our inclusion criteria and compared disorder-specific brief couple therapy to wait-list control. When examined over time through hierarchical linear modeling, brief couple therapy was associated with greater improvements in symptoms and greater marital satisfaction, though at any given time point, there were no significant differences in depression symptoms or marital satisfaction.

Eating Disorders

We included one study of family involved treatment of eating disorders that included a wait-list control.[115] The study enrolled women ages 18 to 65 years who were diagnosed with binge eating disorder. Participants were randomized to group CBT with spouse involvement, standard CBT, or wait-list control. Wait-list control results were only available at the end of the 12 week treatment period. There was no direct test for differences between the CBT with spouse group and wait-list controls. Data from the two CBT groups were combined and the "active CBT" group was found to have higher post-treatment self-reported abstinence rates (p = 0.02) and greater reductions in self-reported number of days binged (p=0.04) than the waitlist condition. However, scores on the EDEQ,[116, 117] administered as a confirmatory measure of binge eating frequency, did not differ significantly.

Summary

Group CBT for binge eating disorder with spouse involvement was not directly compared to wait-list control. Active CBT (i.e., CBT with spouse or individually) subjects had better symptom improvement than wait-list controls.

KEY QUESTION #2. What is the effectiveness of family involved interventions compared to alternative interventions in improving outcomes for adult patients with mental health conditions [i.e., how do family involved interventions compare to (a) any individually-oriented psychosocial intervention or (b) any alternative family involved intervention]?

Substance Use Disorders

Overview

The remaining 21 SUD trials (25 papers) in our review addressed Key Question 2. Outcomes data are presented in Appendix D, Tables 2 to 4. The majority of studies that addressed Key Question 2 were aimed at three different time points in the trajectory of treatment: treatment

initiation or initial engagement, attendance or adherence, and treatment response. Results, therefore, were first organized by these stages. Trials providing data on treatment response are organized by common outcomes of interest: substance use or abstinence, relationship adjustment, and intimate partner violence. Within these categories, we then reviewed studies that addressed any SUD, including an alcohol use disorder (AUD) or a drug use disorder. Lastly, we reviewed the studies that compared different types of family interventions and then results by various sub-groups of interest, including Veteran status, gender, and family composition.

Studies by Fals-Stewart

Fifteen studies compared family involved treatment to an individual treatment. Of these, ten (67%) were either written by Dr. William Fals-Stewart[66-69, 74, 78, 79, 84, 85] or based on data he collected.[63, 71, 76] In 2010, Dr. Fals-Stewart was criminally charged by the State of New York with fraud that allegedly occurred during a scientific misconduct hearing held to review evidence about whether Dr. Fals-Stewart fabricated data in some of his federally-funded studies.[122] Dr. Fals-Stewart died in 2010 soon after criminal charges were filed, and because of his death, associated legal proceedings never reached a conclusion. While his studies have not been retracted by any journal, given the nature of the potential misconduct, we present findings both with and without Dr. Fals-Stewart's work.

Initiation

Three studies examined family interventions to improve patient initiation to SUD treatment.[80, 81, 83] These studies were unique in that they did not directly involve the person with the AUD or drug use disorder in the intervention. Each trial compared one family involved intervention to at least one other alternative family involved intervention (KQ2B). No trials reviewed included an individually-oriented treatment for the subject with an AUD or drug use disorder as a comparator (KQ2A). Consequently, we can make no conclusions regarding the comparative efficacy between family involved interventions versus individually-oriented interventions, targeting patients only, in promoting treatment initiation. All three trials examined community reinforcement training with families (i.e., CRAFT). CRAFT was developed to enhance communication, build skills, and develop coping strategies that would encourage the family's loved one to enter treatment. Kirby and colleagues[80] randomized 30 family members (spouses, parents, siblings) of someone with a drug use disorder into either 1) an earlier version of CRAFT, community reinforcement training (CRT), or 2) a 12-step self-help group counseling program. Miller and colleagues[81] randomized 130 family members of alcoholics into either 1) a version of the CRAFT intervention refined for families of alcoholics, 2) the Johnson Institute intervention, where families confront the alcoholic about their abuse and describe their own experiences and observations about the abuse in order to encourage treatment engagement, or 3) Alcoholics-Anonymous (Al-Anon), a self-help group for families of alcoholics. Meyers et al.[83] randomized 90 family members with a drug-abusing loved into either 1) CRAFT, 2) CRAFT plus 6 months of post-intervention group counseling sessions, or 3) Al-Anon/Narcotics-Anonymous (Narc-Anon), a 12-step program for family and friends of drug users. Across all three studies, the CRAFT intervention was significantly better at promoting initiation of treatment than the non-CRAFT approaches. Miller and colleagues[81] also found that parents were more likely to persuade drinkers into treatment than spouses. Initiation of treatment, however, was narrowly defined. For example, in Kirby and colleague's study,[80] treatment initiation

was defined as whether the drug user entered counseling or drug abuse treatment or attended a self-help group. Miller et al.[81] defined initiation as completing an initial 4-hour assessment and at least one treatment session and Meyers et al.[83] viewed a patient completing a baseline assessment and scheduling a substance use treatment session as treatment initiation. These findings suggest that CRAFT may be a useful intervention for promoting treatment engagement, but evidence is limited about whether it is effective in improving treatment attendance or adherence.

Attendance and Adherence (KQ2A and KQ2B)

Eighteen of our twenty-one trials (86%) reported outcomes on treatment attendance. Ten trials reported no statistically significant differences across treatment conditions. Six, however, reported significantly better attendance for those in family involved interventions.[68, 75, 77, 80-82] Four of these six were drug us disorder trials; the other two were AUD trials. All six addressed Key Question 2A, since all compared attendance in a family involved treatment to attendance in an individual treatment. Three compared BFT or BCT to ICBT[68, 75, 82] and another compared reciprocal relationship counseling to ICBT. In two of these trials, patient treatment attendance was significantly better for those in family involved treatments than for those enrolled in only individual treatment (5-8 more session attended; patients were male opioid users only[68] or men and women with any substance use problem[82]). However, McCrady and colleagues[75] found those in ICBT were significantly more likely to complete treatment than those in BCT (24% versus 44% completed; patients were all female alcohol use disorder patients).

In the two other trials, both of which used CRAFT-type interventions[80, 81] the subject in the intervention with the AUD or drug use disorder was not the target for the intervention; therefore, family attendance to intervention sessions was measured. Family members were more likely to attend CRAFT sessions than either a self-help group[80] or the Johnson Institute training sessions.[81] However, there was no evidence to suggest that family attendance to intervention sessions for any of the three family interventions examined affected the primary outcome, patient initiation of treatment.

Two studies[68, 77] of patients receiving outpatient treatment reported differences in adherence to naltrexone (a medication to reduce substance use cravings). Both studies compared medication adherence for those randomized into family involved treatment versus those in individual treatment. Findings were mixed. Carroll and colleagues[77] did not find a significant difference in doses of naltrexone taken by condition, but Fals-Stewart and colleagues[68] did find superior medication adherence in BCT versus ICBT. With only two studies reporting medication adherence data, there is little evidence to suggest that family treatment significantly improves abstinence supporting medication adherence among individual with an SUD.

Treatment Response

As noted, fifteen of the twenty-one AUD and drug use disorder trials that addressed Key Question 2 examined if outcomes from family involved treatments differed from outcomes of at least one individual based treatment.[63, 66-71, 73-79, 82] We first review this evidence across all studies and then separately for studies addressing AUD and drug use disorder symptoms.

The most common symptom-related outcomes were related to either abstinence or days of heavy use, most frequently collected using subject or family members' self-report of abstinence, typically using the Time Line Follow Back (TLFB).[88] These reports were then converted into the percent of days

an individual was abstinent (percent days abstinent; PDA) from substances or the percent of days that alcohol or drugs were heavily used (percent days of heavy drinking; PDHD) during the period assessed. Only six used urine tests to assess reliability of self-reported abstinence or use. Participants were typically assessed post-treatment and at three months, six months, nine months, and twelve months after treatment and asked to recall their use since the last assessment. A few studies continued follow-up assessments up to 18 months after treatment. Researchers often used survival analyses and growth curve modeling to assess factors associated with cumulative PDA or time to relapse. For our report we categorize follow-up assessments into three time points: post-treatment, short-term follow up (within 6 months post-treatment), and long-term follow up (at least 12 months post-treatment).

Substance Use Disorder Symptoms (Key Question 2A)

BCT Trials. Thirteen of the fifteen trials compared BCT/BFT to ICBT.[63, 66-69, 71, 73-76, 78, 79, 82] Nine of these trials used PDA from alcohol or drug use as a primary outcome. All but one[79] also included sample sizes for each condition. Consequently, for the remaining eight trials we were able to pool data and compare unadjusted weighted means in order to assess the evidence for these two conditions. Data from the pooled analysis examining PDA among these eight studies are presented below in Figure 3. Note that for one study (Kelley, 2002) we present data separately for the drug use and alcohol use populations. Although results from each individual study did not consistently show significant differences across conditions, on average, we found a 4% difference in mean days abstinent between BCT to ICBT at post-treatment. This translates into 1.2 fewer days of drinking or drug use per month (30 day month) or 14.6 days per year for those in BCT/BFT. At short-term follow up (within 6 months of treatment completion), the mean difference in days abstinent was 11%, a statistically significant difference across conditions. This equates to 3.3 fewer days of drinking/drug use per month (30 day month) or 40 fewer days per year for those in BCT/BFT. This difference is even greater at long-term-follow up (within 12 months of treatment completion), increasing to nearly 12%, which equates to 3.6 fewer days of drinking/drug use per month (30 day month) or nearly 44 fewer days per year for those in BCT/BFT. The proportion of those abstinent decreased in both groups with each subsequent follow up, but those in the BCT/BFT condition showed less of a decrease in PDA than those in ICBT, suggesting the effects of the intervention eroded more slowly for those in BCT/BFT. Although not part of the pooled analysis, this trend is repeated in all but one of the studies used in the pooled analysis.[63] Using survival analyses and growth curve modeling, all of these studies report a significantly slower rate of relapse for the BCT/BFT condition than for ICBT.

Of the studies not included in the pooled analysis, three used outcomes specific to alcohol use that are described in more detail below,[69, 73, 75] and one used an addiction severity index to assess change,[67] also described below.

Alternatives to BCT Trials. Two of the fifteen trials did not compare BCT/BFT to ICBT.[70, 77] Carroll et al.[77] found no significant differences in the PDA from cocaine or opioid use between those who received naltrexone and reciprocal relationship counseling versus those who received ICBT and naltrexone. Jones et al.,[70] however, found that subjects in HOPE, the motivational and psychoeducational group intervention with couple therapy, actually had higher heroin use at short-term follow up, compared to a counselor-led drug treatment support group for men with drug use disorders. The inconsistency of these data for non-BCT trials provides little evidence to support non-BCT interventions for improving abstinence, especially for drug use disorders.

Figure 3. Differences between BCT and ICBT: Percent Days Abstinent for Alcohol and Drug Use

Study or Subgroup	Couple/Marital			Individual			Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
	Mean	SD	Total	Mean	SD	Total			
1.1.1 Post-treatment									
Fals-Stewart 1996	95.4	15.4	40	91.1	14.1	40	12.3%	4.30 [-2.17, 10.77]	
Fals-Stewart 2006	96.3	16.3	46	93.6	17.7	46	10.7%	2.70 [-4.25, 9.65]	
Fals-Stewart 2008	94.1	13.4	46	88.3	13	46	17.7%	5.80 [0.40, 11.20]	
Kelley 2002 (Drug)	85.9	22.7	22	81.8	26.2	21	2.4%	4.10 [-10.58, 18.78]	
Kelley 2002 (EtOH)	90.2	21.9	25	86.6	17.4	22	4.1%	3.60 [-7.65, 14.85]	
Lam 2009	92.3	15.2	10	88.3	16.7	10	2.6%	4.00 [-10.00, 18.00]	
McCrady 2009	80.5	27.7	50	74.2	35	52	3.5%	6.30 [-5.92, 18.52]	
O'Farrell 2010	71.1	37	15	43.6	41.9	14	0.6%	27.50 [-1.35, 56.35]	
Winters 2002	94.2	6.4	36	90.2	8	36	46.1%	4.00 [0.65, 7.35]	
Subtotal (95% CI)			290			287	100.0%	4.43 [2.16, 6.70]	
Heterogeneity: Tau² = 0.00; Chi² = 3.12, df = 8 (P = 0.93); I² = 0%									
Test for overall effect: Z = 3.82 (P = 0.0001)									
1.1.2 Short-term followup (6 months)									
Fals-Stewart 1996	81.5	28.6	40	70.4	24.5	40	11.9%	11.10 [-0.57, 22.77]	
Fals-Stewart 2006	85.9	18.1	46	75	20.3	46	26.3%	10.90 [3.04, 18.76]	
Fals-Stewart 2008	84.1	26.5	46	70.3	27.1	46	13.6%	13.80 [2.85, 24.75]	
Kelley 2002 (Drug)	77.6	25.8	22	63.6	42.3	21	3.7%	14.00 [-7.06, 35.06]	
Kelley 2002 (EtOH)	80.6	27.2	25	71.4	26.2	22	7.0%	9.20 [-6.08, 24.48]	
Lam 2009	85.1	20.7	10	78.2	22.6	10	4.5%	6.90 [-12.09, 25.89]	
McCrady 2009	75.7	34.3	50	61.4	39.5	52	7.9%	14.30 [-0.04, 28.64]	
O'Farrell 2010	57.7	40.4	15	46.4	32	14	2.3%	11.30 [-15.14, 37.74]	
Winters 2002	81.9	16.3	31	71.9	17.9	32	22.8%	10.00 [1.55, 18.45]	
Subtotal (95% CI)			285			283	100.0%	11.21 [7.17, 15.24]	
Heterogeneity: Tau² = 0.00; Chi² = 0.81, df = 8 (P = 1.00); I² = 0%									
Test for overall effect: Z = 5.45 (P < 0.00001)									
1.1.3 Long-term followup (12 months)									
Fals-Stewart 1996	73.2	29.8	40	65.1	26.9	40	10.9%	8.10 [-4.34, 20.54]	
Fals-Stewart 2003	59.6	26.4	62	49.3	28.4	62	18.1%	10.30 [0.65, 19.95]	
Fals-Stewart 2006	79.3	29.7	46	60.2	20.9	46	15.3%	19.10 [8.61, 29.59]	
Fals-Stewart 2008	74.1	25.8	46	60.2	27.3	46	14.3%	13.90 [3.05, 24.75]	
Kelley 2002 (Drug)	66.9	35.6	22	53.4	24.8	21	5.1%	13.50 [-4.77, 31.77]	
Kelley 2002 (EtOH)	70.9	25.6	25	60.4	22.4	22	9.0%	10.50 [-3.22, 24.22]	
Lam 2009	77.8	20.2	10	70.2	18.6	10	5.8%	7.60 [-9.42, 24.62]	
McCrady 2009	75.4	34.7	50	63.1	37.6	52	8.6%	12.30 [-1.73, 26.33]	
Winters 2002	74.2	22.2	33	65.4	26.1	35	12.8%	8.80 [-2.70, 20.30]	
Subtotal (95% CI)			334			334	100.0%	11.93 [7.82, 16.04]	
Heterogeneity: Tau² = 0.00; Chi² = 3.00, df = 8 (P = 0.93); I² = 0%									
Test for overall effect: Z = 5.69 (P < 0.00001)									

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Favors Individual   Favors Couple/Marital

Test for subgroup differences: Chi² = 14.59, df = 2 (P = 0.0007), I² = 86.3%

Horizontal bars for each study represent the study's confidence interval. Confidence intervals extending below 0 indicate non-significant differences. Size of box or diamond reflects sample size.

Fals-Stewart Studies. Given that six of the eight studies included in the pooled analyses were either first-authored by Dr. Fals-Stewart or were based on data he collected, we also conducted the pooled analyses using the two studies that did not include Dr. Fals-Stewart's studies[75, 82] (forest plots shown in Appendix E; Figures 1a and 1b). In this analysis, at post-treatment, there was not a significant mean difference in PDA between those in BCT and ICBT. At the short term follow-up, however, those in BCT had a significantly higher mean PDA than those in ICBT. The difference in mean PDA was 13.6%, which equates to 4 fewer days of drinking/drug use per month or nearly 50 fewer days per year for those in BCT/BFT. Only the McCrady et al.[75] study measured long term outcomes, and there was no significant difference between BCT and ICBT during that follow-up period.

Alcohol Use Disorder Symptoms (Key Question 2A)

Of the fifteen studies that family treatment to individually-oriented treatment, seven trials examined AUDs.[63, 69, 71, 73-75, 79] Kelley et al.[63] included subjects with both AUD and drug use disorders and stratified data by disorder.[63]

BCT. All but one of the seven trials compared BCT to an individual treatment.[73] Five included measures of PDA[63, 71, 74, 75, 79] and three included measures of PDHD[69, 75, 79] during the follow-up period of interest using the TLFB procedure.[88] As noted previously, one trial[79] did not include sample sizes for each condition and was not included in the pooled analysis. As shown in Appendix E, Figure 2, pooled analyses demonstrated no significant difference in PDA between BCT and ICBT post-treatment. However, at both short- and long-term follow up, those in BCT had significantly more PDA than those in individual treatments. Those in BCT, on average, had nearly 11% more days abstinent (3.3 more days abstinent per month; 40 fewer days per year) than ICBT at 6 months and 12.5% more days abstinent at 12 months (3.8 days per month; 45.6 per year). Although there were far fewer studies, this same pattern was found for PDHD: there was no significant difference in PDHD between BCT and ICBT post-treatment, but at both short- and long-term follow up, those in BCT had a significantly lower PDHD than those in ICBT (Appendix E, Figure 3). On average, we found that those in BCT had 10.2% fewer days of heavy drinking than those in ICBT at 6 months (3 days per month; 37 days per year) and nearly 14% fewer days at 12 months (4 days per month; 51 days per year). It should be noted that one of these studies, a trial conducted by McCrady and colleagues,[75] included both PDA and PDHD outcomes, and was the only study not based on data collected by Dr. Fals-Stewart. In that study, neither PDA nor PDHD showed a significant difference across treatment conditions.

One study not included in the pooled analysis was by conducted by Walitzer et al.[73] It was not included because neither the comparator nor the outcomes were similar to the pooled studies. Instead of comparing BCT to ICBT, BCT was compared to individual group counseling and a combination of abstinence, light drinking days, and heavy days of drinking per month were assessed at post-treatment, short-term follow-up, and long-term follow up. Means days abstinent or days light drinking were not significantly different across conditions. The mean days of heavy drinking at post-treatment and short-term follow-up, however, were significantly different, with fewer subjects in the BCT condition drinking heavily compared to individual group counseling. Long-term outcomes were not significantly different across conditions.

Alternatives to BCT. We did not find any studies that met our criteria that tested differences between alternative family treatments to BCT or BFT and individual treatment for AUDs.

Drug Use Disorder Symptoms (Key Questions 2A and 2B)

Of the fifteen studies that compared family treatment to individually-oriented treatment, eight trials examined drug use disorders.[63, 66-68, 70, 76-78] One of these trials[66] had three papers included in our review.[66, 84, 85] A trial conducted by O'Farrell and colleagues[82] included those with drug use disorders and alcohol dependence.[82] Of the eight trials that examined drug use disorders, all but two compared BCT to ICBT. One of the two alternative interventions to BCT and ICBT, described in detail below, compared a combination of motivational enhancement therapy (MET), psychoeducation, and couple therapy to a weekly, counselor-led support group for drug users,[70] The second trial compared a program that included naltrexone, contingency management, and

group CBT with reciprocal relationship counseling to a similar program but without reciprocal relationship counseling.[77]

BCT. Five of the eight studies examined BCT and included measures of PDA using the TLFB.[63, 66, 68, 76, 78, 88] As shown in Appendix E, Figure 4, pooled analyses demonstrated a significant difference in PDA between BCT and ICBT for the four studies that included post-treatment assessments and short-term follow ups. Five studies included outcomes at the long-term follow up and these findings were also consistent with earlier time points. We found that, on average, those in BCT/BFT had nearly 4.5% more days abstinent (1.3 days per month; 16 days per year) than ICBT at post-treatment. At 6 months, they had, on average, 11.5% more days (3.5 days per month; 45.4 days per year) and at 12 months they had 10.4% more days abstinent (3 days per month; 38 days per year). All of these studies were conducted by or had data collected by Dr. Fals-Stewart, making it impossible to examine the effects of treatment among non-Fals-Stewart studies.

Alternatives to BCT. As noted, two studies did not compare BCT to ICBT. In the first study, 62 opioid-dependent male partners of pregnant women received either psychoeducation and support in individual group sessions (usual care) or an intervention program called Helping Other Partners Excel (HOPE), which included pregnancy and SUD psychoeducation for couples and motivational enhancement therapy, case management, and contingency management for symptom reduction for subjects.[70] Results showed that, at short-term follow up, those in the HOPE condition had spent more days in outpatient treatment and fewer days on public assistance than those in usual care. However, although days of heroin use were significantly lower for both conditions compared to baseline, these gains were not sustained at the same rate. Those in the HOPE condition, in fact, had significantly more days of heroin use at short-term follow up than those in usual care. Because of the multi-factorial intervention, however, it was not clear if any one part of the intervention reduced the intervention's effectiveness.

In the second non-BCT study, Carroll and colleagues[77] examined male and female subjects with a drug use diagnosis who were assigned either to 1) naltrexone (a medication to reduce cravings for alcohol or drugs) plus group CBT, 2) naltrexone, group CBT, plus contingency management (incentives for subjects to remain in treatment), or 3) naltrexone, group CBT, contingency management, and reciprocal relationship counseling for the patient and a family member, friend, spouse, or child. There were no significant differences in the number of naltrexone doses taken or PDA from cocaine or opioid use between those in the naltrexone-only group and the group that included relationship counseling. The authors did find, however, that those participating in the relationship counseling condition reported significantly improved family functioning over time, as assessed by the Addiction Severity Index, compared to the other two groups.

Alternative Comparison Conditions. Although the majority of studies examining symptom reduction compared BCT to ICBT, six trials included additional conditions which were also compared to BCT and ICBT. These additional conditions included BFT with parenting skills training (1 trial[71]); a psychoeducational attention control treatment (PACT) as an additional comparison condition in trials with BCT and ICBT treatment groups (4 trials[63, 69, 74, 78]); and, an alternative form of BCT.[65] Two additional trials, one for AUDs and one for SUDs, compared standard BCT with a briefer version of the treatment.[41,69]

In the parenting skills study, Lam and colleagues[71] examined a sample of 30 married fathers with an AUD and found, although all three groups showed significant improvement at 12-months compared to baseline, neither attendance rates nor PDA at baseline, post-treatment, or 12-months post-treatment were significantly different across conditions (BCT, ICBT, BCT + parent skills training). Nor did the authors find any significant reductions in interpersonal violence, dyadic adjustment, or relationship satisfaction related to treatment condition.

Across the four studies that compared PACT to BCT and ICBT, the authors found that the pattern of differences between BCT and PACT was similar to the pattern of differences between BCT and ICBT. Specifically, across each study, there were no significant differences between BCT and PACT in PDA at post-treatment, but by 12 months, the difference in PDA between conditions was significant compared to those in PACT. Similar findings were reported for the effect of treatment on couple functioning. Significantly greater improvements in couple functioning were found for those in BCT than those in PACT at post-treatment and at short- and long-term assessments. Two of the studies that included a PACT condition also included both a standard and brief version of BCT.[69, 78] In both of these studies, the standard and brief versions showed significant differences in PDA compared to ICBT and PACT, but few differences between the two versions.

One study examined the effect of different family involved treatments on symptom reduction.[65] BCT was compared to interactional treatment, a therapy approach that does not pre-plan therapy sessions, but instead focuses on mutual support, sharing of feelings, and problem solving through discussion. In this study, which included 36 participants with an AUD, PDA or PDHD were not reported, but relationship functioning, measured as sexual satisfaction was. The data show that subjects in the two treatment conditions did not significantly differ in their reports of sexual satisfaction.

Effectiveness of Interventions on Relapse Prevention for AUDs and Drug Use Disorders (KQ2B)

Two studies, by McCrady and colleagues[72] and O'Farrell and colleagues,[4] specifically compared BCT to BCT plus relapse prevention. McCrady and colleagues compared 1) BCT, 2) BCT with enhancements to prevent relapse (BCT/RP), and 3) BCT plus Al-Anon in their clinical trial of 90 men with AUDs and their spouses/female partners. Relapse prevention training included strategies to anticipate risky situations and identify potential signs for relapse. The addition of relapse prevention to BCT did not significantly increase participant's time before relapse or improvements in relationship functioning at 6 or 18 months after treatment. However, in a sample of 59 male alcoholics and their female spouses, O'Farrell and colleagues[4] found that those who received BCT plus relapse prevention had more PDA at 6 and 12 months than those who received BCT alone. At 18 months after treatment, those assigned to BCT plus relapse prevention reported 13.2% more days abstinent than those in BCT (4.0 more days per month or 48.2 more days per year). However, differences were no longer significant at the 30 month follow-up. Those with the most severe drinking and poorest couple functioning at baseline reported the greatest benefit from BCT plus relapse prevention. Finally, those with the lowest severity of marital problems at baseline were more likely to maintain complete abstinence through 18 months.

No studies specifically examined relapse prevention for those with drug use disorders.
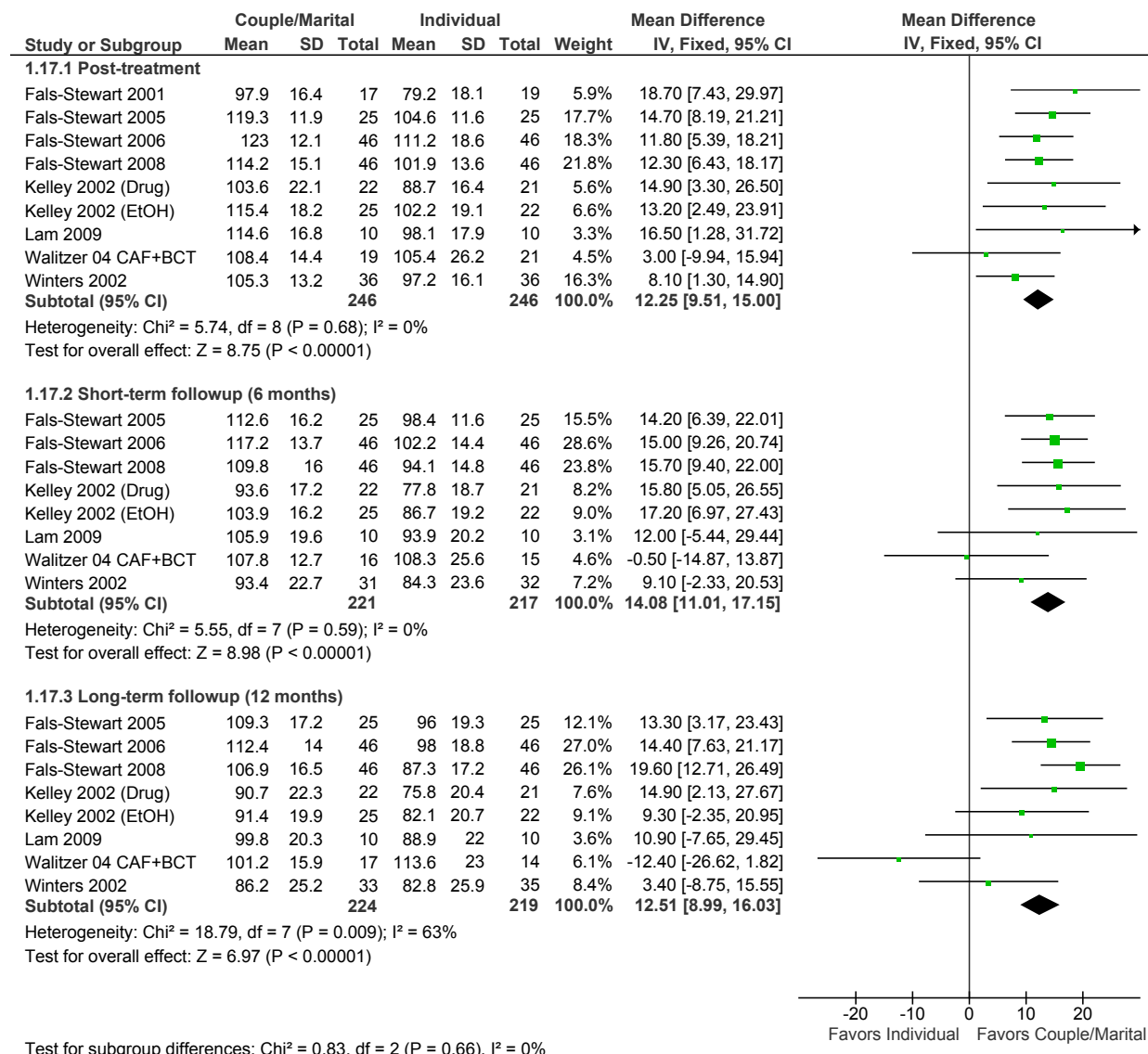
Family Functioning (Family Involved versus Individual Treatment; KQ2A)

The primary family outcome in studies that met our inclusion criteria was family or couple functioning. Twenty-one of the twenty-two trials, including both drug use disorder and AUD trials, reported either family or relationship functioning outcomes. Multiple instruments were used to measure functioning, but the most prevalent was the Dyadic Adjustment Scale (n=9) followed by the Marital/Relationship Happiness Scale (n=4) and the family/relationship sub-scale of the Addiction Severity Index (n=3).

BCT. Overall, nine trials reported differences in relationship adjustment between individuals participating in BCT versus ICBT using the Dyadic Adjustment Scale (DAS) at post-treatment, short-term follow-up, and long-term follow-up assessments. We pooled data to analyze the effect of treatment conditions on DAS scores but, as previously reported, one trial[79] did not include sample sizes for each condition and, therefore, was not included in the pooled analysis. Pooled analyses that included unadjusted weighted means are presented in Figure 4. Again, we reported separate findings for drug use and alcohol use subjects in the 2002 study by Kelley et al. Findings were consistent with findings for PDA. At post-treatment, on average there was a 12% difference in DAS scores, with those receiving BCT having significantly higher couple and family functioning than those in ICBT. The total weighted mean post-treatment for BCT was 112.7 and for ICBT, 100.5, both of which are above the threshold of 97.5 used as a screen for relationship distress (scores range from 0 – 151; Christenson et al.[121]). At short-term follow up (within 6 months of treatment completion), those in BCT had scores 14% higher than those in ICBT, with a total weighted mean of 106.8 for BCT and 93.5 (below the threshold indicating relationship distress) for ICBT. At 12 months, BCT scores were 12.5% higher than ICBT, and while weighted mean scores for BCT remained above 97.5 (mean = 101.2), scores for ICBT were below (mean = 90), consistent with couples experiencing clinically meaningful relationship distress.

Of the trials comparing BCT to ICBT not included in the pooled analysis,[66, 68, 75, 82] all measured different elements of relationship distress, including marital adjustment,[66] family functioning,[68] separation,[75] and relationship happiness,[82] yet none reported significant differences across conditions.

Figure 4. Differences between BCT and ICBT: Relationship Adjustment for AUD and Drug Use Disorder Studies

Study or Subgroup	Couple/Marital			Individual			Weight	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
	Mean	SD	Total	Mean	SD	Total			
1.17.1 Post-treatment									
Fals-Stewart 2001	97.9	16.4	17	79.2	18.1	19	5.9%	18.70 [7.43, 29.97]	
Fals-Stewart 2005	119.3	11.9	25	104.6	11.6	25	17.7%	14.70 [8.19, 21.21]	
Fals-Stewart 2006	123	12.1	46	111.2	18.6	46	18.3%	11.80 [5.39, 18.21]	
Fals-Stewart 2008	114.2	15.1	46	101.9	13.6	46	21.8%	12.30 [6.43, 18.17]	
Kelley 2002 (Drug)	103.6	22.1	22	88.7	16.4	21	5.6%	14.90 [3.30, 26.50]	
Kelley 2002 (EtOH)	115.4	18.2	25	102.2	19.1	22	6.6%	13.20 [2.49, 23.91]	
Lam 2009	114.6	16.8	10	98.1	17.9	10	3.3%	16.50 [1.28, 31.72]	
Walitzer 04 CAF+BCT	108.4	14.4	19	105.4	26.2	21	4.5%	3.00 [-9.94, 15.94]	
Winters 2002	105.3	13.2	36	97.2	16.1	36	16.3%	8.10 [1.30, 14.90]	
Subtotal (95% CI)			**246**			**246**	**100.0%**	**12.25 [9.51, 15.00]**	

Heterogeneity: Chi² = 5.74, df = 8 (P = 0.68); I² = 0%
Test for overall effect: Z = 8.75 (P < 0.00001)

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	
1.17.2 Short-term followup (6 months)									
Fals-Stewart 2005	112.6	16.2	25	98.4	11.6	25	15.5%	14.20 [6.39, 22.01]	
Fals-Stewart 2006	117.2	13.7	46	102.2	14.4	46	28.6%	15.00 [9.26, 20.74]	
Fals-Stewart 2008	109.8	16	46	94.1	14.8	46	23.8%	15.70 [9.40, 22.00]	
Kelley 2002 (Drug)	93.6	17.2	22	77.8	18.7	21	8.2%	15.80 [5.05, 26.55]	
Kelley 2002 (EtOH)	103.9	16.2	25	86.7	19.2	22	9.0%	17.20 [6.97, 27.43]	
Lam 2009	105.9	19.6	10	93.9	20.2	10	3.1%	12.00 [-5.44, 29.44]	
Walitzer 04 CAF+BCT	107.8	12.7	16	108.3	25.6	15	4.6%	-0.50 [-14.87, 13.87]	
Winters 2002	93.4	22.7	31	84.3	23.6	32	7.2%	9.10 [-2.33, 20.53]	
Subtotal (95% CI)			**221**			**217**	**100.0%**	**14.08 [11.01, 17.15]**	

Heterogeneity: Chi² = 5.55, df = 7 (P = 0.59); I² = 0%
Test for overall effect: Z = 8.98 (P < 0.00001)

Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI	
1.17.3 Long-term followup (12 months)									
Fals-Stewart 2005	109.3	17.2	25	96	19.3	25	12.1%	13.30 [3.17, 23.43]	
Fals-Stewart 2006	112.4	14	46	98	18.8	46	27.0%	14.40 [7.63, 21.17]	
Fals-Stewart 2008	106.9	16.5	46	87.3	17.2	46	26.1%	19.60 [12.71, 26.49]	
Kelley 2002 (Drug)	90.7	22.3	22	75.8	20.4	21	7.6%	14.90 [2.13, 27.67]	
Kelley 2002 (EtOH)	91.4	19.9	25	82.1	20.7	22	9.1%	9.30 [-2.35, 20.95]	
Lam 2009	99.8	20.3	10	88.9	22	10	3.6%	10.90 [-7.65, 29.45]	
Walitzer 04 CAF+BCT	101.2	15.9	17	113.6	23	14	6.1%	-12.40 [-26.62, 1.82]	
Winters 2002	86.2	25.2	33	82.8	25.9	35	8.4%	3.40 [-8.75, 15.55]	
Subtotal (95% CI)			**224**			**219**	**100.0%**	**12.51 [8.99, 16.03]**	

Heterogeneity: Chi² = 18.79, df = 7 (P = 0.009); I² = 63%
Test for overall effect: Z = 6.97 (P < 0.00001)

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Favors Individual   Favors Couple/Marital

Test for subgroup differences: Chi² = 0.83, df = 2 (P = 0.66), I² = 0%

Horizontal bars for each study represent the study's confidence interval. Confidence intervals extending below 0 indicate non-significant differences. Size of box or diamond reflects sample size.

Alternatives to BCT. Two trials[70, 77] did not compare BCT to ICBT. Both included measures of relationship functioning. In the trial conducted by Carroll et al.,[77] those randomized to naltrexone plus CBT plus relationship counseling had significantly higher reports of family functioning post-treatment, as assessed by the Addiction Severity Index sub-scale, than those in the CBT plus naltrexone only condition. In the trial conducted by Jones et al.,[70] however, there were no significant differences in couple functioning, as measured by the Partner Support Questionnaire and the Relationship Assessment Form, across conditions, either during or after treatment.

Family Functioning - Alcohol Use Disorder Studies (KQ2A)

<u>BCT</u>. Seven trials examined treatments for AUDs and six used the DAS as a measure of couple or family functioning. All six compared BCT to ICBT. We pooled data from all but one of these studies;[79] a study that did not provide sample sizes by condition. At post-treatment, there was a significant difference in DAS scores (12.5, p<0.001), with those in BCT reporting significantly higher couple and family functioning (Appendix E, Figure 5). Weighted means at post-treatment were 117.8 for BCT and 106.2 for ICBT, both above the clinical cut-point for relationship distress. This same pattern persisted at short-term follow up: those in BCT had scores nearly 14% higher than those in ICBT (p<0.001), although the weighted means were lower than post-treatment (BCT, mean = 111.4 and ICBT, mean = 98.6). At 12 months, scores were nearly 10% higher (p<0.001), with weighted means indicating that, while BCT patients were still in the satisfied range on relationship adjustment, those in IBCT were, on average, reporting relationship adjustment scores consistent with relationship distress (BCT, mean = 104.9; ICBT, mean = 95.7). Only one of these studies, a study by Walitzer et al (2004), was not first-authored by and did not use data collected by Dr. Fals-Stewart. Although a small study (N = 64 across 3 treatment conditions), this one study did not show any significant differences in DAS scores across conditions.

Two studies that compared BCT to ICBT were not included in the pooled analysis. One, as noted, was due to sample sizes not being available.[79] In this analysis, however, the authors reported that compared to ICBT, those in BCT had significantly higher DAS scores at post-treatment, short-term follow-up, and long-term follow-up. The other was a study by McCrady et al.[75] that assessed separation rates. At long-term follow up, there was no significant difference in separation rates across conditions.

<u>Alternatives to BCT</u>. We did not find any studies that met our inclusion criteria, tested differences in family functioning among patients with only AUDs, and compared a non-BCT/BFT family treatment to individual treatment.

Family Functioning - Drug Use Disorder Studies (KQ2A)

<u>BCT studies</u>. Eight trials examined treatments for drug use disorder s.[63, 66-68, 70, 76-78] Of those, six compared BCT to ICBT [63, 66-68, 76, 78] and four of the six[63, 67, 76, 78] used the DAS to assess relationship functioning. As with AUDs, we pooled data from those trials that included an assessment of DAS and found that those in BCT had significantly higher family functioning at post-treatment, short-term follow-up, and long-term follow-up (Appendix E, Figure 6). Four studies reported post-treatment DAS scores and those in BCT had scores nearly 12% higher than those in ICBT. Weighted mean scores at post-treatment were lower than those for AUD, with the average BCT score being 107.3 and the average for IBCT being 94.7 (consistent with a positive screen for relationship distress). Three studies reported data for short- and long-term outcomes. For short-term, those in BCT conditions had 14.5% higher scores than those in ICBT. The weighted mean score at short-term follow up for BCT was consistent with relationship satisfaction (above the clinical threshold for relationship distress; mean = 101.1), but this was not the case for ICBT, with scores indicating the average participant was experiencing relationship distress (mean = 87.5). The difference across conditions at the long-term follow-up was even larger. Those in BCT or BFT had DAS scores over 15.5% higher of than those in ICBT at least

one year after treatment, although the weighted mean DAS scores had declined with time with both groups now falling within the clinically distressed range on relationship adjustment (BCT, mean = 96.6; ICBT, mean = 83.4). All of the studies in the pooled analysis used data from, or were first-authored by, Dr. Fals-Stewart.

Two studies, both conducted by Fals-Stewart and colleagues,[66, 68] compared BCT to ICBT, assessing relationship functioning through alternate measures. In Fals-Stewart et al.'s 1996 trial,[66] the Locke Wallace Marital Adjustment Test (MAT) was used to assess couple functioning. No significant differences were reported across conditions at any follow up. Likewise, in the Fals-Stewart and colleagues[68] trial, using the Addiction Severity Index to assess family functioning, no significant differences were found across conditions at post-treatment.

Alternatives to BCT. As previously reported, the trials conducted by Jones et al.[70] and Carroll et al.[77] did not compare BCT, but alternatives to BCT. The Carroll et al.[77] trial found significant differences in family functioning, with the family treatment having better outcomes than the individual treatment. Jones et al.,[70] however, found no significant differences in couple functioning across conditions.

Intimate Partner Violence

BCT. Three studies, 2 examining subjects with AUDs and 1 with drug use disorders, assessed whether BCT compared to ICBT reduced intimate partner violence among those with a drug use disorder .[71, 74, 85] Lam found no significant changes across conditions at any time point. In Fals-Stewart et al.'s[85] paper, violent behaviors are reported, but tests of association by condition were not. In Fals-Stewart and colleagues'[74] study, however, those in BCT reported significantly less physical aggression at long-term follow up than those who participated in ICBT.

Alternatives to BCT. We were unable to locate studies meeting our inclusion criteria that examined intimate partner violence outcomes among patients with a SUD that examined alternatives to BCT.

Family Functioning (Comparisons among Different Family Treatments; KQ2B)

Six trials compared family involved treatments to one or more alternative family treatments.[4, 65, 72, 80, 81, 83] All but Meyers and colleagues[83] reported outcomes associated with family or couple functioning. Because study designs and measures used were different across studies, these data were not pooled. Of the two trials that tested variations of the CRAFT intervention,[80, 81] neither reported significant differences in couple or family functioning across conditions at any follow up assessment. McCrady et al.,[87] a 1996 trial of BCT versus BCT + Al/Anon versus BCT + relapse prevention, reported no significant long-term differences in marital happiness across conditions. O'Farrell et al.,[4] a study of BCT versus BCT + relapse prevention, also did not find any significant differences in marital happiness post-treatment or in the short- or long-term follow-up across conditions. However, using repeated measures analysis of covariance to assess the effects of the intervention over time (as opposed to one specific time point), they found that couples randomized to BCT with relapse prevention had greater marital satisfaction over longer periods of time than those randomized to BCT only. In O'Farrell et al.'s[65] trial that analyzed data on sexual satisfaction, no significant differences were found across conditions. No evidence from any of the trials we reviewed, therefore, show that one family involved treatment improves relationship functioning more than another.

Sub-Groups of Interest

Veterans. As noted, only two studies reported Veterans as study participants.[4, 65] In both studies, all participants were Veterans. In one of these studies, comparing BCT to BCT plus relapse prevention, researchers found that the addition of relapse prevention to BCT resulted in more PDA at 6 and 12 months than those who received BCT alone (see above for further discussion). In the other study, also by O'Farrell et al.,[65] there were no differences in sexual satisfaction, a common problem associated with AUDs, between those randomized to BCT and those receiving interactional treatment. With the inconsistency of these findings, there is little evidence about whether BCT is effective with Veteran populations. No evidence exists to evaluate whether Veterans respond differently to BCT than non-Veterans. However, the average PDA reported for Veteran BCT participants in the one trial reporting this information[4] found PDAs (post-treatment: 98.0%; short-term follow-up: 87.6%; long-term follow-up: 82.7%), that were comparable, if not better, than average rates of PDA reported in the AUD trials included in our pooled analyses (post-treatment: 80.5-96.3%; short-term follow-up: 75.7-85.9%; long-term follow-up: 70.9-79.3%).

Women. Overall, four studies examined women with drug use disorders or AUDs.[74-76, 79] One examined drug use disorders in both men and women, but did not stratify the results by gender.[82] McCrady and colleagues[75] found that women in the ICBT group were significantly more likely to attend treatment sessions and complete all sessions than those in the BCT group. Additionally, women with an additional Axis I disorder had significantly higher PDA with BCT than ICBT, women with poor relationship functioning at baseline reported greater declines in substance use when assigned to BCT than ICBT, and women in BCT with drinking behavior that was influenced by their spousal or romantic relationship prior to treatment reported greater declines in substance use than those assigned to ICBT. Women with the best relationship functioning at baseline also had a slower decrease over time in PDA. In growth curve models, Fals-Stewart[74] found that women in BCT increased their alcohol use at a slower rate than women in ICBT or PACT at 12 months, but not post-treatment.

Three of the four studies that limited participation to women reported PDA and two reported mean DAS scores; therefore, we pooled these results (Appendix E, Figures 7 and 8). In order to compare women to men, we also pooled data from trials comparing BCT to ICBT that were limited to men and assessed PDA (4 trials) and DAS (3 trials) (Appendix E, Figures 9 and 10). At each follow-up, women in BCT had significantly greater PDA than those in ICBT. At post-treatment, women in BCT had nearly 4% greater PDA than women in ICBT. This equates to 1.2 fewer days per month (30 day month) or 14.6 days per year. At short-term follow up this difference was 11%, or 3.3 days a month or 40 days per year, and at long-term follow up, the difference increased to almost 14% (4.2 days per month or 51 days per year). The mean difference between BCT and ICBT at post-treatment and short-term follow up was nearly the same for men, but at long-term follow up, the difference between conditions was less for men than women, with almost a 10% difference between BCT and ICBT (3 days per month or 36.5 days per year).

For DAS, women in BCT were also significantly more likely to have higher scores than women in ICBT. At post-treatment, women in BCT had over 10% higher scores than women in ICBT. Weighted mean scores at post-treatment were 115.2 for BCT and 105.1 for ICBT. At short term

follow up, women in BCT had 14% higher scores than women in ICBT, with weighted mean scores of 107.6 for BCT and 94.9 for ICBT, with ICBT patients meeting the clinical cutoff consistent with relationship distress. At long term follow up mean DAS scores for women in BCT were nearly 12% higher than for women in ICBT. Weighted mean scores at long term treatment were 101.5 for BCT and for ICBT, 91.4. ICBT patients at the long term follow-up assessment had scores that met the clinical cutoff consistent with relationship distress. For men, the difference in mean scores across conditions was greater, but overall weighted means were lower. At post-treatment, men in BCT had over 14.5% higher scores than men in ICBT. Weighted mean scores at post-treatment were 110.7 for BCT and 96.1 for ICBT. At short term follow up, however, men in BCT had a nearly 16% higher score than men in ICBT, with a weighted mean score of 100.3 for BCT. For ICBT, the weighted mean score was 84.5. At long term follow up, mean DAS scores for men in BCT were 11.7% higher than for men in ICBT. Weighted mean scores at long term treatment were 92.6 for BCT and for 80.9 for ICBT. Men in ICBT conditions had DAS scores at each follow up that met clinical criteria for relationship distress; men in BCT conditions, however, had scores that met the clinical cutoff consistent with relationship distress only at long-term follow up.

Intimate Partner versus Family Involvement. As noted, most of the studies in our review included spouses or romantic partners of someone with an AUD or drug use disorder. Of the seven trials that included family members and did not restrict participation to wives or intimate partners, three were the CRAFT interventions that targeted the family member of individuals with a drug use disorder to encourage the drug use disorder patient's treatment initiation,[80, 81, 83] and one targeted family members as a means of encouraging patients completing hospitalization for substance use detoxification to initiate continuing care and treatment.[64] Although data were typically not stratified by relationship status, Miller and colleagues,[81] as previously noted, did find that parents were better at encouraging drinkers to engage in treatment than spouses. All four studies did show that interventions targeting families broadly, and not restricted to spouses, were effective at promoting treatment initiation. Three other studies[68, 77, 82] that did not restrict therapy to spouses compared a family involved to an individually-oriented treatment. Two trials compared BFT to ICBT.[68, 82] Findings from these two studies, however, were not consistent. Fals-Stewart and colleagues[68] found that, compared to ICBT, participants in BFT attended significantly more sessions, took naltrexone on more days ICBT, and had significantly higher PDA for opioids, cocaine, alcohol and all drugs combined at 12 months post-treatment. They also had significantly longer periods of abstinence from opioids during treatment and higher family functioning at 12 months post-treatment. O'Farrell and colleagues,[82] however, found that, although participants with an SUD in the BFT condition attended more sessions than those in ICBT, subjects did not have greater PDA from drinking or other illicit drugs or fewer days using their primary substance than those in ICBT at post-treatment or 6-month follow up. Similarly, Carroll and colleagues,[77]as described above, found no significant differences in the number of naltrexone doses taken or PDA from cocaine or opioid use between those in the naltrexone and CBT group therapy conditions than those who received naltrexone, group CBT, contingency management, and reciprocal relationship counseling.

Same Sex Couples. One study examined the impact of family involved treatment on same sex couples. Fals-Stewart and colleagues[79] compared BCT to ICBT among men (n=52) and women (n=48) in same sex relationships who were entering outpatient treatment for an AUD.

Subjects were randomized into 20 weeks of BCT or 20 weeks of ICBT only. The authors found that there were no significant differences in attendance across conditions nor was there any difference post-treatment in percent days of heavy drinking (PDHD). However, for both groups at 6- and 12-month follow-up assessments, those in BCT had significantly fewer PDHD, and at 12-months, using growth curve modeling, both men and women in the BCT condition increased their heavy days of drinking at a significantly slower rate than those in ICBT only. Findings were similar on for couple functioning. Both men and women in the BCT condition reported better couple functioning at post-treatment, 6-month follow-up, and 12-month follow-up. Growth curve modeling showed faster improvements in relationship adjustment (DAS scores) during treatment and slower declines in relationships adjustment over the 12-months after treatment completion among BCT than ICBT participants.

Summary

In contrast to Key Question 1, there is more evidence to address the second key question, **what is the effectiveness of family involved interventions compared to alternative interventions in improving outcomes for adult patients with mental health conditions** *[i.e., how do family involved interventions compare to (a) any individually-oriented psychosocial intervention or (b) any alternative family involved intervention]?* The majority of studies addressing Key Question 2 are aimed at the three different time points in the trajectory of treatment: treatment initiation or engagement, attendance, and treatment response. As with the results, the discussion focuses on the evidence at these stages and then discusses some of the methodological considerations for this set of studies.

Initiation

The largest amount of evidence on treatment initiation came from the three studies that assessed CRAFT. While these studies varied in quality, their consistency suggests that CRAFT is efficacious at promoting treatment initiation for people with SUDs, but there is little evidence on whether that engagement is sustained or if that engagement leads to reduced patient symptoms. Evidence from O'Farrell and colleagues[64] also supports the finding that active family involved interventions improve patient engagement.

Attendance and Adherence

We found some evidence from five trials to suggest that family treatment improves treatment attendance in AUD and drug use disorder trials. Ten trials, however, did not show any differences in attendance by condition. The evidence, therefore, is inconsistent on whether family involved treatments improve session attendance. Likewise, there was conflicting evidence, based on two studies, on whether family treatment significantly improved medication adherence.

Effectiveness of Interventions on Treatment for AUD and Drug Use Disorder Symptoms

Although results from individual studies that assessed whether treatment that included families as active participants improved abstinence or reduced substance use behaviors were not consistent, results from pooled analyses showed that, across studies, family involved treatments, specifically BCT or BFT, resulted in a significantly higher proportion of days abstinent than ICBT. These differences were consistent and persistent across all time points, but the short-term

effect appeared to be strongest. These same patterns were seen when data from AUD and drug use disorder trials were stratified. These findings are largely consistent with a recent prior review of BCT for SUDs which reported 'robust' findings that BCT was better than control conditions in reducing the frequency of use (d = 0.45), reducing the consequences of use (d = 0.50), and improving relationship satisfaction (d = 0.51).[123]Powers and colleagues[123] included non-US studies and child-focused studies of BCT.

However, when the only two studies not either conducted or first-authored by Dr. Fals-Stewart (both targeted at AUDs) were examined separately in pooled analyses, these patterns differed slightly. There were no differences between BCT and ICBT at post-treatment or long-term, but there were significant differences in the short-term. Because all of the drug use trials included were either first-authored by or used data collected by Dr. Fals-Stewart, we have no evidence, outside of his work, on trials that met our inclusion criteria, to compare BCT to ICBT for drug use disorders. Therefore, although there is compelling evidence to suggest that BCT is effective at improving PDA, especially for periods within 6 months of treatment completion, questions remain about its effectiveness immediately post-treatment and for long-term abstinence or harm reduction.

Effectiveness of Interventions on Treatment for Family Outcomes (Couple and Family Functioning)

Like findings on abstinence and reduction of drug or alcohol use behaviors, active family treatments for SUDs showed better short- and long-term improvements in couple functioning than individual treatments in pooled analyses, although for individual studies these differences were not always statistically significantly, especially at later time points (e.g., 12 months). Passive attention control treatments that included families were not significantly different from ICBT, but they were significantly different from BCT, with BCT showing significant improvements in couple functioning. Some evidence from three studies of variable quality (1 poor, 1 fair, and 1 good quality) suggests BCT also reduces intimate partner violence.

Effectiveness of Interventions on Relapse Prevention for AUDs and Drug Use Disorders

Our findings showed mixed results in treatments that added additional relapse prevention treatment to standard BCT, with one study[72] failing to show significant differences in AUD between those assigned to BCT and those assigned to BCT with relapse prevention and another study[4] demonstrating a significant increase in PDA for those assigned to BCT plus relapse prevention versus those in standard BCT at both short-term and long-term assessments. In the latter study, those with the most severe drinking and poorest couple functioning at baseline benefitted the most from BCT plus relapse prevention. The interaction between marital happiness and relapse was also considered in the former study, but this relationship was not significant. No studies addresses relapse for those in drug use disorder trials.

Sub-Groups of Interest

<u>Veterans</u>. Two studies of the 22 studies reviewed identified Veterans as participants. No direct comparisons between Veterans and non-Veteran samples were found among studies that met our inclusion criteria. Findings from the one trial we reviewed that provided substance use outcomes with Veterans[4, 65]demonstrated comparable or better rates of PDA from alcohol use

(post-treatment: 98.0%; short-term follow-up: 87.6%; long-term follow-up: 82.7%) than average rates of PDA reported in the AUD trials included in our pooled analyses. However, without direct comparisons within trials between Veteran and non-Veteran samples and between BCT and ICBT, we can draw few conclusions on whether treatment response for Veterans differs from treatment response for non-Veterans.

Intimate Partners versus Other Family Members. While the data are limited, it appears that treatments involving family members, including those who are and are not intimate partners, are successful in increasing SUD treatment initiation among those with SUDs. Once in treatment, however, the data are mixed (one study supported BFT over ICBT or medication only,[68] another found non-significant differences between BFT and ICBT[77]). Only one study[82] limited participation to non-intimate partners. While subjects in the BFT arm were more likely to attend treatment than those in ICBT in this trial, there were no significant differences across conditions in PDA or PDHD across any time point.

Women. Pooled analyses showed little difference by gender in the overall effect of BCT compared to ICBT. One study by McCrady and colleagues,[75] however, found women with psychological comorbidities had significantly higher PDA with BCT than ICBT, those with poor relationship functioning at baseline responded better to BCT than ICBT, and those with the best relationship functioning at baseline had smaller differences over time in PDHD.

Bipolar Disorder
Overview

We identified 2 studies that addressed KQ2A, comparing family treatment to individual therapy.[91, 92] Three studies addressed KQ2B comparing a family therapy with a different family intervention.[89, 90, 93] Outcomes are presented in Appendix D, Tables 6 to 8.

Treatment Response: Symptoms

Comparisons with traditional individual-oriented therapies (KQ2A; 2 trials)

FFT. One study reporting symptoms compared FFT to alternative, empirically supported individual therapies (cognitive behavioral therapy or interpersonal and social rhythm therapy), with clinical status assessed at follow-up visits.[92] Based on DSM-IV criteria, the odds of being well in any given study month were greater for patients in any one of three intensive therapy groups (one of which was FFT) compared to the control condition, individually-oriented collaborative care. However, when the authors stratified the intensive therapy group by type of therapy, there was no difference between family-focused therapy and collaborative care. No significant differences between conditions were reported,[92] suggesting FFT may perform similarly to other empirically supported, intensive interventions in improving symptoms of bipolar disorder.

Relapse and recovery outcomes were reported in two studies comparing FFT to individual therapy. No significant differences in recovery or time to recovery were observed between FFT and either of two other intensive, individual therapy control groups (cognitive behavioral therapy or interpersonal and social rhythm therapy). Both the combined intensive therapy group and the FFT group alone (secondary analysis) were significantly better than individually-oriented

collaborative care.[92] A second study found no difference in number of subjects with one or more relapses during one year of active treatment but 32% lower rates of relapse and 48% lower rates of hospitalization in the FFT group compared to the individually-focused treatment group during the year after treatment.[91]

Comparisons with alternative family therapies (KQ2B; 3 trials)

FFT. Another study reported symptoms when FFT was compared to another therapy with some family involvement. A significant treatment versus time interaction was observed for symptoms scores at both 12 and 24 months follow-up, indicating FFT results in greater improvement in symptoms than participants in a "crisis management" group (modeled after standard community care with 2 family psychoeducation sessions).[90, 96] There was also a significant difference between FFT and crisis management participants in the percentage of subjects who survived one year without relapse (71% vs. 47%) when study dropouts were excluded. Using the intent-to-treat sample, relapse at 24 months was significantly lower in the FFT group.[90, 96] Relapse rates at 24 months after randomization were 35% for FFT participants and 54% for crisis management participants. Patients in crisis management relapsed an average of 20 weeks sooner than FFT participants.

Relapse and family functioning interactions. This same trial found no main effect of family distress or a treatment by family distress interaction for relapse among patients randomized to FFT or crisis management.[90] Differences in percent relapsed were noted for participants with parental relatives (fewer relapses in participants from low expressed emotion parental homes compared to those from high expressed emotion parental homes) but not spousal relatives.[90]

FFT-HPI. Participants whose caregivers received FFT-HPI had significantly fewer symptoms of depression (5.6 points on the HAM-D; d = 0.67, medium effect) and mania (4.2 points on the YMRS; d = 0.34, small effect), indicating greater symptom relief, than patients whose caregivers received health education only.[93]

Problem Centered Systems Therapy for the Family (PCSTF). Miller and colleagues (2004) failed to find differences in recovery between a general family therapy (PCSTF; 10 to 15 sessions focused on comprehensive assessment, problem identification, and task-oriented problem solving) and an alternative family therapy (disorder-specific multifamily groups [MFGs]).[89] The multifamily psychoeducational group therapy (6 sessions with 4 to 6 patients and their family members) focused on providing information about bipolar disorder, coping strategies for living with a family member with a mood disorder, and a forum to discuss differences in patients' and family members' perspectives on bipolar disorder. Among patients who recovered, the frequency of mood episode recurrence did not differ among the treatment groups but frequency of hospitalization was lower in the multifamily therapy group (5%) versus family therapy conducted with one family at a time (31%) or medication only (38%).[97]

Treatment Response: Family or Couple Functioning

Comparisons with traditional individual-oriented therapies (KQ2A; 1 trial)

FFT. Family or couple function was evaluated in one study. Significantly greater improvements in relationship functioning and satisfaction were found among subjects receiving intensive psychosocial treatment (family or individual) than those receiving individually-focused usual care.[95]

Comparisons with alternative family therapies (KQ2B). No trials.

Treatment Attendance and Medication Adherence

FFT

Attendance at therapy sessions was reported in two studies. FFT was not significantly different from multifamily therapy[89] or from other individually-oriented intense treatments.[92] A study of FFT compared to individual care reported no difference in medication adherence.[91] Family therapy (compared to crisis management with a limited family component)[90] resulted in greater medication adherence following treatment.

Summary

Two studies reported greater recovery at 12 months[92] or lower relapse at 24 months[91] based on symptom assessment in individuals who participated in family-focused therapy compared to individually oriented treatment (KQ2A). Rehospitalization was also lower in the family-focused therapy group.[91] In addition, the odds of being classified as "well" in any given month were greater for participants in any of 3 intensive therapies (including family-focused therapy) compared to individually-focused collaborative care.[92]

Two studies reported reduced symptom scores among patients whose family participated in family-focused therapy[90] or family-focused therapy with a health-promoting focus[93] versus an alternative family involved intervention (KQ2B). Lower relapse and longer relapse-free survival following family-focused therapy were also reported in one of the studies.[5] However, one study reported no difference in recovery at 28 months between family treatment delivered to individual families and multi-family therapy.[89] This study involved a shorter treatment interval (all treatment completed within 6 months vs. 9 months in the other two studies).

One study reported a significant difference between three intensive therapies (one of which was family-focused therapy) and individually-oriented collaborative care (KQ2A) in relationship functioning or satisfaction.[95] In two studies, problem-centered family therapy[89] and three intensive therapies (including family-focused therapy)[92] were not observed to improve treatment attendance compared to individually-focused collaborative care (KQ2A) [92] or multifamily therapy (KQ2B.)[89] Results for improvements in medication adherence were mixed with no difference in a study of family-focused therapy compared to individual therapy (KQ2A)[91] or family-focused therapy compared to crisis management with limited family involvement (KQ2B).[5]

Overall, although studies typically assessed symptoms and reported either the symptom scores or relapse/recovery based on symptom scores, few studies assessed other outcomes of interest including global functioning (2 studies), health care utilization (1 study), family outcomes (1 study), attendance (2 studies), or medication adherence (3 studies). No study reported quality of life or satisfaction with care.

Many of the studies reviewed above were cited in a systematic review of family psychosocial interventions for bipolar disorder completed by Justo et al.[124] All of the studies in their review were randomized or quasi-randomized trials that enrolled adults and involved psychoeducational interventions or psychotherapy. Overall, based on 5 studies reviewed by Justo and colleagues[124]

that compared family interventions to no intervention, two of which met eligibility for our review,[89, 94] no added effect of the family intervention to medication only was observed. In three studies that compared one family intervention to another family intervention or individual therapy, all of which were included in our review,[89-91] results were inconsistent. Of the 7 studies in the Justo et al. review, 5 were conducted in the United States. Four of the five studies were eligible for inclusion in our review.[5, 89, 91, 94] The fifth study was published in 1990 and did not meet our eligibility criteria. As reported in the Cochrane review, that study found no significant clinical improvement when a family intervention was compared to no intervention.

Schizophrenia Spectrum Disorders

Overview

Four studies addressing KQ2 met our search criteria; one comparing a family intervention to individual oriented therapies (KQ2A) and three comparing two family involved therapies (KQ2B). Data are presented in Appendix D, Tables 10 to 12.

Comparisons with Traditional Individual-Oriented Therapies (KQ2A; 1 trial)

One trial examined differences between a two-year multiple family group (MFG) intervention and standard individual mental health care (case management and medication management) within outpatient mental health service clinics.[101-103] While the present review focuses on treatment comparisons at post-treatment and after treatment completion, the length of this intervention (2 years) increases the relevance of mid-treatment findings. At mid-treatment (1 year post-baseline)**,** subjects in the MFG group showed significant improvement in negative symptoms as measured by MSANS (Modified Scale for the Assessment of Negative Symptoms),[101] with subjects in the MFG scoring, on average, one point better on a 25 point scale. At post-treatment, there were no statistical differences in hospitalization between the two groups. MFG subjects had statistically higher use of outpatient services that was attributable to greater time spent in the intervention for MFG participants.[103] At the one-year follow-up, differences between the MFG group and their standard care counterparts on overall psychiatric hospitalization rates were non-significant. However, hospitalization in state level facilities (which provide longer term care and include patients referred directly from the criminal justice system) was 12% lower (significant difference) for MFG subjects than for standard care subjects. No significant group differences were observed in outpatient service use at one year post-treatment.[103] Differences between groups on family functioning or by distressed and non-distressed families were not reported.

In another study of note (not reported in our tables), Herz and colleagues[125] studied the effectiveness of a program of relapse prevention (an early intervention treatment strategy with psychoeducation for patient and family, active monitoring of the subject for prodromal symptoms, weekly group therapy for the patient, and a biweekly multifamily group) to treatment as usual. Treatment as usual included individual supportive therapy and medication management biweekly for 15 to 30 minutes. Significant differences in relapse and rehospitalization rates were found, favoring the intervention. However, only 29% (12 of 41) of the relapse prevention patients' families <u>actually attended</u> family groups, and full results were not reported for those who attended family groups versus those who did not. Of note, only one patient from these

twelve families relapsed; however, this number is too low to draw conclusions as to the significance of the family component of the relapse prevention program. Given the lack of clarity regarding which subjects actually received family involvement in their care and the outcomes of those who received family involved care, this study did not meet eligibility criteria for our review. We elected to present findings here given their relevance.

Comparisons with Alternative Family Therapies (KQ2B; 3 trials)

One trial compared Assertive Community Treatment (ACT), which includes a family education and engagement component, to ACT plus a biweekly multi-family group.[29] Number of hospital admissions, rates of annual rehospitalization, and subjects' symptoms decreased throughout the two year intervention for participants in both groups pre-treatment to post-treatment; however, there were no significant differences between the groups. Data were not reported by treatment group and therefore are not included in appendix tables. One reported area of differing outcomes by treatment group was in employment rates. Employment rate for subjects in the MFG was significantly higher between months four and twenty (of the two year intervention); however, differences were non-significant at the final reporting point (end of the twenty four month intervention). Family outcomes (family dissatisfaction with the subject, reported friction between the subject and others) improved significantly for both groups pre- and post-treatment, but direct comparisons between the two treatment groups were not reported.

The trial comparing Applied Family Management (AFM) to Supportive Family Management (SFM)[24, 104] showed no differences in the likelihood a subject would stabilize, and no significant interactions between family management and medication dosage. Rehospitalization and relapse outcomes were reported only for the 313 subjects who stabilized and only during the two years of treatment. There were no significant differences in rehospitalization, mean days to rehospitalization, time to psychotic relapse, or time to use of first rescue medication between the AFM and SFM groups overall.[24] Rehospitalization also did not significantly differ when comparing the two levels of family treatment within the three medication dosage groups. There were also no significant differences in social adjustment between the two treatment groups from baseline to post-treatment in social functioning, family relationships, or the romance/sexual factors of the social adjustment scale.[104] However, the more intensive AFM treatment was associated with significantly lower levels of rejecting attitudes by family members toward the subject (0.32 scale points at 1 year; 0.31 effect size; 1.03 scale points at 2 years; 0.30 effect size; $p < 0.01$) and significantly less family friction then the less intensive SFM intervention. However, authors note that given the non-significant differences on primary outcomes and small differences on family outcomes, differences across these treatment conditions may have limited clinical significance.

A third trial was comprised of 108 subjects with a dual diagnosis of active substance abuse or dependence and either schizophrenia, schizoaffective, or bipolar disorder.[99, 100] Patients and a family member received weekly psychoeducation in both groups, however the FPE (Family Psychoeducation) arm sessions were brief, lasting 2-3 months. In the Family Intervention for Dual Disorders (FIDD) arm, 20-30 sessions (over 18 months) were conducted and problem solving strategies and training in communication were added. Additionally, patients and family members in both groups were encouraged to attend multiple family support groups for up to 36 months. Engagement, defined as subjects participating in 2 or more sessions, was high for both groups (>80%) and not significantly different by group. Treatment exposure, defined as

attending at least 3 sessions for the FIDD group or 6 educational sessions the FPE group, did not differ between groups. Attendance in the multiple family support groups was low for both conditions (15% for FIDD and 11% for FPE; difference non-significant); these groups were discontinued three years into the study. The FIDD group Brief Psychiatric Rating Scale rating was significantly higher than the FPE group over the three year follow up period; the effect was small for total score (0.17) but moderate for the psychosis subscale (0.32). Overall subject functioning, as measured by the Global Assessment Scale, was higher in the FIDD group (p = 0.08), over the three year follow up period. In the FIDD group, the BPRS psychosis symptom reduction was much stronger for women than for men. The more intensive FIDD subjects did not show significant improvement in alcohol or drug use or percent stable days compared to their FPE counterparts, but both groups improved significantly in these areas as compared to baseline. Social problem solving skills did not improve significantly for the FIDD group as compared to the FPE group, as was hypothesized. Outcomes on the _individual_ functioning of family members, versus the family as a unit, and on how having a relationship with an individual with a mental illness affects the family member were collected; however, those outcomes are outside the scope of this review and thus are not reported here.

Results were not reported by relationship distress in trials comparing family involved therapies.

Summary and Discussion

Evidence synthesized in numerous prior reviews supports the efficacy of family interventions, typically psychoeducational family treatments, that include elements of education on the illness, family support, crisis intervention, and problem-solving skills training to improve relapse and rehospitalization rates outcomes for schizophrenia spectrum patients, compared to no intervention or medication only (KQ1).[126-130] Psychoeducational family treatments of at least 9 months, in combination with medication, have been previously recommended by existing treatment guidelines[127] with "good" evidence of leading to improved relapse rates among patients.[6, 126-128]

The Schizophrenia Patient Outcomes Research Team (PORT), funded in 1992 by the Agency for Health Care Policy and Research and the National Institute of Mental Health, issued psychosocial treatment recommendations in 1998, 2003, and 2009 which included recommendations for family based treatment. They recommend that patients with ongoing contact with their families, or who have "non-family" caregivers, should be offered psychosocial intervention that provides a combination of family education, family support, crisis intervention, and problem solving skills training,[127] regardless of level of a family's expressed emotion. Their initial recommendations were refined and expanded to include shorter interventions (less than nine months), in recognition that more complex and lengthy interventions are difficult to actually implement.[128, 129]

Research summarized in prior reviews has largely established that family psychoeducational treatments are superior to treatment as usual in reducing relapse rates.[131, 132] However, these interventions are not consistently superior to comprehensive and intensive patient-only interventions[132] and the effects of these interventions over long term follow-ups are mixed.[33, 130, 131, 133, 134] Recently a Cochrane review[126] also supported the above review findings but cautioned that these effects may be overestimated due to poor methodological quality. Also, as noted in

the Cochrane review,[126] many previous schizophrenia studies were conducted in China and other countries, so the results may not be applicable to a US. Veteran population. Family interventions for schizophrenia which met our inclusion criteria (conducted in the US since 1996 and including patient outcomes), have not included a no treatment, waitlist, or medication only comparison condition. Therefore, we cannot contribute to the body of literature establishing the general efficacy of family treatments compared to waitlist or medication management only (KQ1). While there is an important clinical need to provide some form of psychosocial intervention to patients with serious mental illness, comparisons of relatively untested programs to equally rigorous comparators complicate efforts to demonstrate the initial efficacy of untested programs.

Our findings address how family interventions compare to individually oriented care (1 trial) or other family interventions (3 trials) and include a wider breadth of patient outcomes and more complex patients with either co-occurring problems (1 trial) or co-morbid substance use disorders (1 trial) than trials conducted prior to our review period. Additionally, to address an existing gap in the literature,[9, 130] one trial examined the efficacy of family involved treatments in improving patient outcomes for patients who are relatively stable (those who have not recently suffered a psychotic relapse or hospitalization)[101-103] by recruiting participants from a community mental health setting, regardless of recent relapse or hospitalization. Dyck and colleagues[101, 102] found an intervention including multiple family groups was superior to individually-oriented treatment at the mid-treatment time point (one year after randomization) in rates of negative symptoms and rates of hospitalization. At post-treatment and long term follow-up (1 year post), the only significant difference across conditions was in rates of state-level psychiatric facility hospitalizations.[103] State-level psychiatric hospitalizations are reserved for those patients with the most severe symptoms, thus this finding may suggest that family intervention is more beneficial than individual care for those with the most severe symptoms, consistent with earlier findings.[129] Additionally, these findings are consistent with prior work suggesting erosion of treatment effects can be found across conditions at long term follow-ups.[33, 131]

Three other trials each compared a less intensive to a more intensive family intervention.[24, 29, 99, 104] Few differences were found between conditions, although improvements in both groups as compared to baseline were noted for several outcomes. This is consistent with past reviews identifying that differences among intensive interventions and among alternative family interventions with different theoretical underpinnings are largely non-significant.[130, 132] The subjects in McFarlane and colleagues[29] Assertive Community Treatment trial all showed improvement over the two year intervention, but the addition of multiple family groups yielded only one significant additional benefit, employment rates during treatment. However, these differences were also non-significant at the 24 month end point.

Schooler et al.[24] found that the addition of in-home behavioral single family therapy to a larger family-oriented treatment package did not provide significant additional benefits in subjects' need for rescue medication, relapse delay, or hospitalization. Mueser et al.,[104] examining subjects in the same study, found the more intensive family intervention lead to significantly less family friction and better attitudes towards the patient than the family-oriented treatment package delivered in clinics, without in-home BFT. There were no differences in patient social functioning between groups. Outcome data was collected only for subjects who successfully stabilized and complied with treatment, eliminating the most severely ill patients (41% of the 528 randomized), who may stand to benefit more from the more intensive family treatment.

Mueser and colleagues' trial[99, 100] enrolled subjects dually diagnosed with both schizophrenia spectrum and substance use disorders, and they expanded the definition of family to include "any caring, but non-professional relationship," including clergy and friends as well as relatives. The longer, skills oriented intervention (FIDD) was associated with greater improvements in subject psychiatric functioning and symptoms than brief (2-3 month) family psychoeducation only treatment, but did not reduce substance use. The initial success in engaging subjects and their family members in both levels of treatment suggests acceptability of family intervention for dual diagnosis patients. However, the vast majority of families (over 80%) in both study arms did not participate in multi-family groups offered between the end of the psychoeducation and skills intervention and the final data collection point (three years after randomization). How to motivate families and patients to participate in program offerings post-treatment is an area that needs further research. None of the schizophrenia studies included in our review provided results comparing distressed to non-distressed families.

Posttraumatic Stress Disorder

Overview

One study that met our criteria addressed KQ2. Relevant to KQ2A, Glynn and colleagues compared an individually-oriented treatment (exposure therapy) to that same intervention followed by PTSD-specific behavioral family therapy. Findings are presented in Appendix D, Tables 14 to 16.

Comparisons with Traditional Individual-Oriented Therapies

Differences in symptom change and social adjustment were non-significant between those who participated in exposure therapy versus exposure therapy plus BFT.[8] Additionally, Glynn and colleagues[8] collapsed all those participating in BFT with those not participating in BFT. They found greater increases in social problem solving skills over the course of treatment among those participating in BFT than those who did not participate in BFT. However, those who participated in exposure therapy plus BFT were more likely to drop out of treatment than those who participation in exposure therapy alone.[8]

No studies compared different family involved therapies. Additionally, the role of family distress in predicting differential response across conditions was not examined.

Sexual Functioning Disorders

No studies compared family interventions to traditional individual-oriented therapies or to different family interventions.

Other Conditions

Depression

No studies that met our inclusion criteria included a comparison of family involved therapy and individual or alternative family involved therapy. However, we did identify two recent Cochrane reviews that explored the role of family members in the treatment of depression. Barbato and D'Avanzo[135] included randomized controlled trials or quasi-randomized controlled trials

comparing marital therapy to other psychosocial and medication treatments or to non-active treatments.[135] The studies included heterosexual couples between the ages of 16 and 65 years with a depressed spouse (primary diagnosis by DSM-IV, International Classification of Diseases (ICD-10), or Research Diagnostic Criteria codes). Treatment was community or outpatient based. Eight trials were included; three of these were conducted in the United States (publication dates 1989-1992). The overall conclusion from the review was that there was no evidence that marital therapy was different than individual psychotherapy in terms of depressive symptoms (data from 6 studies with a total of 167 subjects) or persistence of depression (3 studies, 106 subjects) following treatment. Marital distress was lower following treatment in the marital therapy groups than in the individual therapy groups (5 studies, 137 subjects). There was no difference in the number of drop-outs (6 studies, 210 subjects). In distressed couples, there was no difference in depression outcomes (4 studies, 90 subjects) or drop-outs (4 studies, 109 subjects). Marital stress was significantly reduced (4 studies, 90 subjects). Two studies (60 subjects) that compared marital therapy to no or minimal therapy did report a reduction in depressive symptoms following treatment. The three studies from the United States, all of which compared marital therapy to individual therapy, found no difference in depressive symptoms. Two of the studies reported persistence of depression with no difference between treatment groups. The authors of the review noted small sample sizes, unclear sample representation, short follow-up periods (or assessment only at the end of treatment), and large number of drop-outs as methodological weaknesses of this literature.

The second review focused on family therapy for depression.[136] Randomized controlled trials and controlled clinical trials were included if the treatment involved 6 or more sessions of at least one hour duration and no group therapy with multiple families. Family therapy was compared to no intervention or an alternative intervention. Six studies were included in the review however two enrolled adolescents and one enrolled children. Of the three studies enrolling adults, two were conducted in the United States. In one study published in 1985, an inpatient family intervention (psychoeducation based) reduced symptoms, improved family attitude toward treatment, and improved global functioning compared to individual treatment. The results were significant only for the female patients. The second study is reviewed above.[89] Overall, the authors of the review concluded that there was insufficient evidence to assess the effectiveness of family therapy for treatment of depression. The use of psychological interventions with an evidence base was recommended.

Summary

Recent prior reviews have established that there is low[135] or insufficient[136] strength of evidence to assess whether family therapy is more effective than no treatment or waitlist in reducing symptoms of depression and increasing family functioning. An early review[9] included data from 3 studies published prior to our inclusion date. One study of behavioral marital therapy found no difference between behavioral marital therapy and individual cognitive therapy for improving depression symptoms in maritally distressed couples;[45] both interventions were superior to wait list control.[45] A second study included distressed and non-distressed couples.[44] In that study, behavioral marital therapy and individual cognitive therapy were comparable for maritally distressed couples. Cognitive therapy was superior for alleviating depression in non-maritally distressed couples. A similar result was reported in a study comparing interpersonal

psychotherapy for depression (IPT) without family involvement to IPT delivered as a couple therapy (i.e., both the patient and his or her intimate partner participate in treatment sessions).[137] The study that was eligible for and included in our review enrolled mildly to moderately distressed couples and found brief couple therapy to be superior to waitlist for reducing symptoms and improving couple function.[114]

Eating Disorders

The same study that reported outcomes for KQ1 (group CBT with spouse vs. wait list control) included a comparator active treatment group (standard CBT).[115] Results (see Appendix D, Tables 22 to 24) were reported post-treatment and at 6 month follow-up. There were no significant differences between the two active CBT groups for binge abstinence or days binged (either by 7-day recall or the EDEQ.[116, 117] Depression scores (BDI[112]) decreased for both groups but did not differ between groups. There were no differences between active CBT groups on the Rosenberg Self-Esteem Score.[138] Couple functioning (Dyadic Adjustment Scale)[109] did not differ between CBT groups post-treatment or at follow-up, however, subjects in the CBT with spouse group reported being in better agreement with their spouses regarding a plan of action for binge eating (p = 0.04). Attendance at treatment sessions was comparable.

Summary

Patient or couple functioning outcomes for women in the group CBT for binge eating disorder with spouse involvement group did not differ from results for women in the standard CBT group with the exception of better agreement on a plan for managing binge eating.

Smoking Cessation

One study of partner-assisted therapy in conjunction with individual counseling met eligibility criteria.[118] The study was conducted at an Army Medical Center and enrolled 625 women who were pregnant and their intimate partners. Partner-assisted therapy with individual counseling was compared to individual counseling alone or to usual care. Outcomes were assessed at 28 weeks of pregnancy and at 2-, 6-, and 12-months postpartum. Results are presented in Appendix D, Tables 22 to 24. No differences were observed between groups for abstinence from smoking, time to relapse, or social support (including smoking-specific support, instrumental support, or emotional support).

Summary

Abstinence from smoking, time to relapse, and social support did not differ for pregnant women who participated in partner-assisted therapy with woman-only counseling, woman-only counseling, or usual care.

SUMMARY AND DISCUSSION

This evidence synthesis summarizes the efficacy of family involved psychosocial treatments in improving the outcomes of patients with mental health conditions in the US since 1995. Two key questions were identified. Our search yielded 51 articles (39 trials), including trials of family interventions for substance use disorders (22 trials), bipolar disorder (6 trials), schizophrenia and related disorders (4 trials), PTSD (2 trials), sexual functioning disorders (2 trials), depression (1 trial), binge eating disorder (1 trial), and nicotine dependence (1 trial).

Overall, this review represents a variety of studies examining family involved treatments for mental health conditions. Trials were highly heterogeneous in terms of intervention characteristics, size, population, and findings. In many cases, the family intervention was manualized and withdrawals from the trials were adequately described. Typically, well-validated outcome measures were employed, diagnoses were verified by structured clinical interviews, and exclusion/inclusion criteria were clearly described. However, few studies included a description of allocation concealment or blinding procedures and measures used to assess the same construct were highly variable across trials. Frequently, intent to treat analyses were either not described or not employed, assessments of treatment integrity were frequently not described, and for many studies, samples were small and analyses underpowered. Additionally, many studies were conducted on mostly white and male samples, who were under 40 years old, and in all but two trials, Veteran status among participants was not reported. While post-treatment symptom severity was frequently reported, many of our other outcomes of interest were not. Most notable was the frequent absence of assessments of global family/couple adjustment, communication, conflict, observational family/couple interactions, intimate partner violence, adherence, attendance, and satisfaction with care. The substance use literature posed the largest exception to this, with studies frequently examining global family/couple adjustment, adherence, attendance, and satisfaction with care. This likely reflects the more advanced stage of development of this literature.

The majority of studies fell into either Baucom and colleague's[9] disorder specific couple/family treatment and/or partner-assisted treatment categories. The purposes of family involvement also varied and included, but were not limited to, engaging patients in care, family members acting as out-of-session coaches, psychoeducation to improve family's support for patients, and addressing family conflict that could exacerbate symptoms.

SUMMARY OF EVIDENCE BY KEY QUESTION

Key Question #1. What is the efficacy of family involved interventions in improving outcomes for adult patients with mental health conditions [i.e., how do family involved psychosocial treatments compare to no psychosocial treatment: (a) waitlist/no treatment or (b) medication management only]?

The level of development of the evidence for family involved treatments varied greatly across conditions. Consequently, family treatments for some conditions had a number of efficacy trials prior to our search timeframe (i.e., schizophrenia and substance use disorder). For these conditions, the trials reviewed were more applicable to KQ2. See Table 1 for a review of the efficacy status of family treatments for mental health conditions prior to our review.

Substance Use Disorders

One trial[64] found that among patients completing an inpatient alcohol detoxification program, a single family session and single family follow-up to help plan for continuing care (partner-assisted treatment[9]) did not result in significantly improved percent days abstinent post-intervention or greater attendance to continuing care. However, 92% of those receiving the family intervention were more likely to enter a continuing care program, a 30% improvement over patients hospitalized for substance use detoxification whose families did not participate in their aftercare planning.

Bipolar Disorder

Two trials compared a family intervention to a drug-only treatment. In one trial medication management alone was compared to medication management plus either Problem Centered Systems Therapy of the Family (PCSTF; a general family therapy[9]) or psychoeducational multifamily groups (a disorder specific family intervention[9]). There were no differences in symptoms between either family involved treatments or medication management alone.[89, 97, 98] However, compared to medication management only, patients from distressed families reported significantly lower rates of depressive episodes (psychoeducational multifamily groups: 1.4 fewer episodes per year, d = 1.0; PCSTF: 0.9 fewer episodes, d = 0.70), shorter duration of depressive episodes (psychoeducational multifamily groups: 14% less time; d = 0.82), and fewer mood episodes (psychoeducational multifamily groups: 1.7 fewer episodes, yearly, d = 0.82), suggesting a family intervention specific to bipolar disorder or a general family therapy could provide improved treatment response for patients with bipolar disorder in distressed families. In the other trial, while those assigned to psychoeducational maritial therapy (a disorder specific couple intervention) did not report greater symptom relief than those assigned to medication management only, patients in marital therapy did report better global functioning (7 points on the 100 point GAS) and medication adherence (0.53 points on a 6 point scale) than those assigned to medication management only.[94] In both cases, family functioning outcomes were not reported.

Schizophrenia

No trials.

PTSD

One trial demonstrated exposure plus Behavioral Family Therapy (a disorder specific family therapy[9]) resulted in better PTSD outcomes than waitlist;[8] however these differences eroded at follow-up and drop out was worse among those in the family treatment condition. Another trial demonstrated significantly better engagement in treatment for the patients (Bosnian refugees) of those who participated in family support groups (CAFES; a trauma-specific family therapy), than waitlist.[105] Specifically, patients' whose family members participated in CAFES attended 4 more mental health visits than waitlist controls.

Sexual Functioning

One trial[106] found subjects assigned to sex therapy plus medication reported greater satisfaction with treatment than those assigned to medication alone (disorder specific couple treat-

ment).[9, 106] Differences between conditions on erectile functioning up to two months after treatment were not significant. A second trial found no significant difference between those assigned to four weeks of cognitive-behavior sex therapy plus medication versus those assigned to medication alone after 4 weeks of treatment. Further descriptive statistics on differences between the two groups were provided at this post-treatment assessment but further formal testing was not provided.

Other Conditions Examined in Single Trials

One small trial of brief couple therapy for depression (n = 35; disorder specific couple treatment) found that couple therapy led to significantly improved depression symptoms and marital satisfaction. On continuous measures, scores on the BDI-II (d = 0.54), HAM-D (d = 0.72), and DAS (d = 0.43) were each significantly improved for participants in couple therapy compared to waitlist controls.[114] A trial of group CBT for binge eating disorder found that CBT with or without spouse involvement resulted in better symptom improvement than waitlist.[115]

Key Question #2. What is the effectiveness of family involved interventions compared to alternative interventions in improving outcomes for adult patients with mental health conditions [i.e., how do family involved interventions compare to (a) any individually-oriented psychosocial intervention or (b) any alternative family involved intervention]?

Substance Use Disorders

Twenty-one of 22 trials addressed KQ2. Fifteen trials compared family treatment to individually-oriented treatment as usual or manualized individual behavior therapy (13 of these trials examined BCT or BFT for an alcohol or substance use disorder; 2 trials examined alternative methods of family involvement in care) and 6 trials compared a family treatment to an alternative family involved treatment (3 trials examined CRAFT, a disorder-specific and partner-assisted treatment; 3 examined BCT or BFT). Findings are summarized by intervention below.

Behavioral Couple Therapy or Behavioral Family Therapy (disorder specific couple therapy[9])
Effects on substance use. BCT participants used substances for 1.2 fewer days per month (14.6 per year) at post-treatment, 3.3 days per month (40 per year) at 6 months, and 3.6 days per month (44 per year) for 12 month follow-ups. This same general pattern of results was found for studies addressing drug use only, alcohol use only, drug use disorders among men, and drug use disorders among women.

Effects on relationship adjustment. Better relationship adjustment following treatment was found among those assigned to BCT than ICBT, with 12.5% higher scores on the DAS, on average, among those who participated in BCT, one year after treatment.

Therapy with non-intimate partners (BFT). Findings are mixed for differences between ICBT and BFT, a version of BCT including non-intimate partners, with one trial finding no differences in substance use between BFT and individual treatment and a second trial finding

significantly lower rates of substance use among those in BFT than those in individual treatment at 18 months after treatment (13.2% fewer days abstinence). However, these differences eroded at 30 month follow-ups.

Brief BCT. Two trials examined both a brief version of BCT and standard BCT for substance use disorders and found both BCT and brief BCT led to significant differences in PDA compared to ICBT, but few differences were found between the standard and brief versions of BCT.

BCT with relapse prevention. Two trials added a relapse prevention intervention to BCT (2 trials[4, 72, 86, 87]) with one trial finding no differences between conditions[72, 86, 87] and the other finding greater reductions in substance use, with 13.2% fewer days of use 18 months after treatment.[4] These differences eroded and were non-significant at the 30 month follow-up. In this trial, the benefits of BCT with relapse prevention were strongest for those in the most distressed relationships and with the most severe drinking behavior.[4]

Same sex couples. One trial compared BCT to ICBT with same sex couples, finding fewer percent days heavy drinking among BCT participants at long term follow-ups and significantly slower rates of erosion in treatment effects among BCT participants (i.e., BCT participants were slower to increase their rates of heavy drinking than ICBT patients after treatment).

Veterans. Two studies examined Veterans with alcohol use disorders.[4, 65] One found no difference between BCT and a general couple therapy on sexual satisfaction.[65] Rates of substance use after treatment were not reported. The second compared BCT to BCT with relapse prevention, discussed above.[4] Veterans participating in BCT[4] demonstrated comparable or better rates of PDA from alcohol use (post-treatment: 98.0%; short-term follow-up: 87.6%; long-term follow-up: 82.7%) than average rates of PDA reported in the AUD trials included in our pooled analyses. However, direct comparisons within trials between Veteran and non-Veteran have yet to be conducted, and research has yet to evaluate BCT compared to individual therapy among Veteran samples.

CRAFT (disorder-specific and partner-assisted treatment[9])

Across 3 trials[80, 81, 83] CRAFT was found to be superior to alternative family treatments in improving patients' initiation of substance use treatment 30-48%. Trials did not provide data on differences in overall rates of session attendance or substance use.

Alternatives to BCT and CRAFT

BCT versus non-disorder specific couple therapy. Two trials compared BCT to an alternative non-disorder specific couple treatment[65, 73] finding no differences between the couple interventions on substance use[73] or relationship functioning.[65, 73]

Adding additional treatment components to BCT. One trial added parenting skills training to BCT[71] and a second added attendance to AA and Al-Anon.[72, 86, 87] Both trials found no differences in symptoms or couple functioning between BCT with additional treatment components versus standard BCT.

Reciprocal relationship counseling. Carroll[77] found that the combination of reciprocal relationship counseling (disorder specific intervention[9]), contingency management, and naltrexone use was superior to contingency management plus naltrexone only in family functioning, but not in percent days abstinent or days in treatment.

Motivational and psychoeducational treatment with couple counseling for heroin users with pregnant partners. Jones and colleagues[70] found that subjects in a motivational and psychoeducational intervention that included couple therapy for male heroin users with pregnant intimate partners, actually had <u>higher</u> heroin use at short-term follow up, compared to an individual only counselor-led drug treatment support group.

Bipolar Disorder

Five RCTs provided data relevant to KQ2.

Family-Focused Therapy (FFT; 4 trials; disorder specific family treatment[9])

- FFT or an adapted version of FFT (FFT-HPI[93]) led to better symptom response than either individually-oriented care (1 trial[91]) or alternative family involved interventions (2 trials[90, 93]).

    □ FFT leads to lower rates of relapse than crisis management with limited family involvement, 24 months after randomization (35% relapse versus 54%). Patients in crisis management relapsed an average of 20 weeks sooner than those in FFT.[5, 90]

    □ FFT leads lower rates of relapse (28% versus 60%) and lower rates of hospitalization (12% versus 60%) than individual therapy one year after the end of active treatment.[91]

    □ No significant differences were found between FFT and individual therapy on medication adherence.[91]

    □ FFT-HPI leads to fewer manic (4.2 points on the YMRS; $d = 0.34$; small effect) and depression symptoms (5.6 points on the HAM-D; $d = 0.67$; medium effect) among bipolar patients than health education provided to families via DVDs.[93]

- One trial[92] found no significant differences in symptoms of bipolar disorder or family functioning between FFT and either cognitive behavioral therapy or interpersonal and social rhythm therapy, suggesting FFT may perform similarly to other empirically supported, highly intensive interventions in improving symptoms of bipolar disorder.

- Mixed findings limit conclusions that can be drawn about the role of FFT in session attendance or medication adherence.

Disorder Specific versus General Family Therapy (1 trial[89, 97, 98])

The difference in rates of recovery between general family therapy and disorder specific family therapy, delivered in multiple family groups, were non-significant.

Schizophrenia

Three trials addressed KQ2 (1 trial for KQ1 and 3 for KQ2 due to greater than 2 comparison conditions).

Multiple Family Groups (MFG; 1 trial)[101-103]

- One trial compared MFGs (disorder specific family therapy[9]), an interventions focused on psychoeducation, family functioning, and social support, to individually oriented psychosocial intervention. Results indicated that, at the one year point of a two year intervention, MFGs improved negative symptoms of schizophrenia (e.g., blunted affect, alogia, anhedonia, inattention, avolition) an average of one point on a 25 point scale and led to 12% lower rates of hospitalization at state level psychiatric hospitals than individual treatment.

- Differences in rates of hospitalization overall or at non-state level facilities, or use of crisis care, were non-significant at post-treatment and one year after treatment.

Assertive Community Treatment (ACT) With and Without a Biweekly Multi-Family Group (1 trial[29])

- No significant differences were found between groups on hospital admissions, symptoms, or family outcomes.

- Employment rates for ACT and multifamily groups were significantly different during treatment but non-significant at the final follow-up.

Applied Family Management (AFT; 1 trial[104])

- Non-significant differences were found between intensive and less intensive family interventions in symptoms or rates of hospitalization. Authors note group differences may have limited clinical significance.[104]

- A more intensive family therapy (AFM) improved family functioning (patient rejection scale) by 0.32 scale points at 1 year (medium effect size, 0.31) and 1.03 scale points (medium effect size, 0.30 effect size) at 2 year follow-up, over less intensive family interventions.

Family Intervention for Dual Disorders (1 trial; disorder specific family treatment9)

- Subjects with a comorbid substance use disorder and serious mental illness (e.g., schizophrenia, bipolar disorder) demonstrated greater improvements in psychiatric symptoms (BPRS psychosis, medium effect size, 0.32; BPRS total, small effect size, 0.17) when assigned to a longer term (9-18 months) psychoeducational family program than a brief (2-3 month) family intervention.[100]
- Differences in substance use and global functioning across conditions were non-significant

PTSD

One trial found no significant differences in PTSD outcomes between exposure therapy with Behavioral Family Therapy (disorder specific family intervention[9]) versus exposure therapy only,[8] however the family involved arm resulted in poorer rates of dropout than exposure alone.

Sexual Functioning

No trials.

Other Conditions Examined In Single Trials

There were no differences between family involved interventions and individually-oriented treatments in one trial examining smoking cessation in pregnant women[118] and a second examining binge eating disorder, with the exception of greater agreement between spouses regarding a plan of action for binge eating.[115]

EFFICACY

In Table 16 below, we summarize the efficacy status[23] and strength of evidence[62] for outcomes of interest (i.e., symptoms, family/couple functioning, and, in some cases, treatment engagement) for those family treatments demonstrating benefits over their comparators that met our review criteria. In three cases, studies demonstrated an individually-oriented, disorder specific intervention plus a family intervention led to greater improvements than waitlist/drug only conditions, but the combined treatment did not demonstrate significant gains over the individually-oriented treatment alone in the same trial.[8, 77, 115] Consequently, these trials are not included in the table below. These findings represent only studies performed in the US in the last 15 years that report on patient outcomes. Studies finding no significant differences between the treatment and the comparator at post-treatment or follow-up assessments on our outcomes of interest are not included as 'possibly efficacious studies' and, consequently, not incorporated.

STRENGTH OF EVIDENCE

In addition to identifying studies that have demonstrated efficacy or are possibly efficacious, we rated the confidence with which we draw these conclusions for the outcomes of interest (i.e., the 'strength of the evidence that underlies conclusions,' p. 513, Owens et al.[62]). Strength of evidence was considered by mental health condition, given the wide variety of interventions, techniques, and treatment targets of these interventions. In general, with the exception of behavioral couple therapy for SUDs, CRAFT for increasing treatment initiation among patients with SUDs, and Family Focused Therapy (FFT) for bipolar disorder, each intervention was typically examined in one or two trials. Additionally, the FFT studies contained highly diverse sets of comparison conditions and findings were largely mixed, limiting our confidence in the strength of evidence across these trials.

Several of the individual trials were of good or fair quality (low or medium risk of bias) but with a single, often small trial of a particular intervention for a particular outcome and imprecise estimates of effect, we have low confidence that the available evidence for the interventions examined in single trials reflect the true effect. As such, the strength of evidence for any given intervention, with the exception of BCT for drug use disorders and CRAFT for increasing treatment initiation among those with an SUD, is generally low. Specific ratings for treatments deemed efficacious or possibly efficacious are presented in Table 16. *Importantly, our strength of evidence ratings are based solely on the results of our search, which included only US studies of family involved psychosocial treatments for mental health conditions since 1995 that included patient outcomes. Also, this Table should be considered in tandem with Table 1, which identifies those interventions established as efficacious <u>prior</u> to our review, including behavioral family therapy and supportive family therapy for schizophrenia.[6, 9]*

Table 16. Family Interventions since 1996 that Improve Outcomes for US Patients with Mental Health Conditions

MH Condition	Intervention	Comparator	Outcome	Efficacy Status	Strength of Evidence
Alcohol Use Disorders	Behavioral Couple Therapy	Individual Behavioral Therapy	1) Substance Use	1	Moderate[a]
			2) Relationship Adjustment	1	Moderate[a]
			3) Intimate Partner Violence	3	Low
			4) Attendance	3	Low
	Brief family intervention to promote continuing care[64]	Treatment-as-usual	1) Substance Use	ND	Low
			2) Treatment Initiation	3	Low
	Behavioral Couple Therapy + relapse prevention[64]	Behavioral Couple Therapy	1) Substance Use	3	Low
			2) Relationship Adjustment	ND	Low
	Behavioral Family Treatment[82]	Individual Behavioral Therapy	1) Substance Use	3	Low
			2) Family Functioning	ND	Low
	CRAFT[81]	Alternative Family Treatments	1) Substance Use	ND	Low
			2) Family Functioning	ND	Low
			3) Treatment Initiation	3	Low
Drug Use Disorders	Behavioral Couple Therapy	Individual Behavioral Therapy	1) Substance Use	1	Moderate[a]
			2) Relationship Adjustment	1	Moderate[a]
			3) Intimate Partner Violence	3	Low
			4) Attendance	1	Low[b]
	Behavioral Family Treatment[68, 82]	Individual Behavioral Therapy	1) Substance Use	3	Low
			2) Family Functioning	3	Low
	CRAFT[80, 83]	Al-Anon/Nar-Anon	1) Substance Use	ND	Moderate
			2) Family Functioning	ND	Low
			3) Treatment Initiation	1	Moderate
Bipolar	Family-Focused Treatment-Health Promoting Intervention[93]	Health information DVDs reviewed by caregivers	1) Symptoms	3	Low
	Family-Focused Treatment	Crisis management with two in-home family psychoeducation sessions[5, 90]	1) Symptoms	3	Low
			2) Medication Adherence	3	Low
		Problem-focused, psychoeducational Individual therapy[91]	1) Symptoms	3	Low
			2) Medication Adherence	ND	Low
		Cognitive behavior therapy[92, 95]	1) Symptoms	ND	Low
		Interpersonal and social rhythm therapy[92, 95]	1) Symptoms	ND	Low
	Marital intervention + medication[94]	Medication only	1) Symptoms	ND	Low
			2) Global Functioning	4	Low
			3) Medication Adherence	4	Low

MH Condition	Intervention	Comparator	Outcome	Efficacy Status	Strength of Evidence
Schizophrenia	Multiple Family Groups[101-103]	Standard, Individually-oriented care	1) Symptoms	ND	Low
			2) Any Hospitalization	ND	Low
			3) State Hospitalization	3	Low
			4) MH Care Utilization	ND	Low
	Family intervention + in home behavioral family therapy (Applied Family Management[24, 104]	Family intervention	1) Symptoms	ND	Low
			2) Family Functioning	ND	Low
			3) Patient Rejection by Family	3	Low
			4) MH Care Utilization	ND	Low
			5) Attendance	ND	Low
Schizophrenia & Substance Use Disorder	Psychoeducation + skills oriented training (Family Intervention for Dual Disorder[99, 100]	Short term psychoeducation	1) Schizophrenia Symptoms	3	Low
			2) Substance Use	ND	Low
			3) Global Functioning	3	Low
			4) Medication Adherence	ND	Low
PTSD	Coffee and Family Education and Support[105]	Waitlist	1) Number of MH Visits	4	Low
Depression	Brief problem-focused couple therapy[114]	Waitlist	1) Symptoms	4	Low
			2) Relationship Adjustment	4	Low

Efficacy Status:
1 = Efficacious & Specific = superior to placebo, nonspecific, or alternative intervention in at least two studies conducted by independent research teams.
2 = Efficacious; superior to waitlist in RCTs conducted by two independent research teams.
3 = *Possibly* Efficacious & Specific; criteria met for efficacious and specific from a single study.
4 = *Possibly* Efficacious; criteria met for efficacious from a single study (Baucom, 1998;[9] Chambless & Hollon,1998[23])
ND = No significant differences found; MH = Mental health

Strength of Evidence:
High = High confidence evidence reflects true effect. The effect and confidence in the estimate of effect is unlikely to change with further research.
Moderate = moderate confidence that evidence reflects true effect. The effect and confidence of the effect may change with further research.
Low = Low confidence evidence reflects true effect. The effect and confidence of the effect will likely change with further research.[62]

[a]Seven of the nine trials comparing these conditions were written by or based on data collected by Dr. Fals-Stewart. See Substance Use Disorders Results for KQ2 for discussion.
[b]Several studies also found non-significant differences, leading to low strength of evidence.

CONCLUSIONS

Nearly half of the trials we located were examinations of family involved treatments for substance use disorders, typically BCT or BFT for substance use disorders (disorder specific couple or family therapy[9]). While findings were not without contradiction, behavioral couple therapy is superior to individual behavior therapy for improving substance use and relationship distress. CRAFT[81, 83] also increases the rates with which patients with substance use disorders initiate substance use treatment. Mixed findings indicate relapse prevention added to behavioral couple therapy may improve outcomes, especially among those with the most severe substance use and relationship distress. Finally, unlike other mental health conditions, two trials were conducted with Veterans,[4, 65] but only one trial reported substance use outcomes and compared BCT to BCT with relapse prevention (O'Farrell, 1998a), making it difficult to draw conclusions

about whether Veteran samples achieve the same benefits from BCT as other samples. More research is clearly needed examining the efficacy of family involved treatments with Veteran samples.

Findings for bipolar disorder were also mixed, with single trials demonstrating family therapy improves symptoms over medication management alone, particularly for those in distressed families, and FFT improves symptoms over alternative treatment approaches in two trials, but performs similarly to other empirically supported, individually-oriented interventions in another trial. Specifically, 1) FFT or an adapted version of FFT (FFT-HPI[93]) led to greater symptom improvements than either an individually-oriented treatment (1 trial[91]) or alternative family involved interventions (2 trials[90, 93]), 2) FFT performed similarly to other empirically supported, highly intensive, individually-oriented interventions in improving symptoms of bipolar disorder,[92] 3) for patients in distressed families, improved symptoms of depression were found for those in either a disorder specific multifamily group or general family therapy than medication management alone,[98] and 4) marital psychoeducational therapy led to greater improvements in global functioning and medication adherence, but not in symptoms, than medication management alone.

Work conducted prior to the time frame of our review has established the efficacy of behavioral family therapy and supportive family therapy for schizophrenia.[9] Given the wealth of data prior to 1996 supporting these interventions for schizophrenia, we were surprised to find only 4 US trials since that time. These trials expanded upon the work conducted in prior studies by including complex cases (i.e., multiple diagnoses or problems), but provided limited additional clarity regarding which family treatments enhance patient outcomes or if family treatments improve outcomes outside of relapse/rehospitalization rates. As noted in previous reviews,[9] schizophrenia and bipolar disorders are chronic, lifelong illnesses. Consequently, appropriate outcomes include lengthening time to relapse, improving quality of life, and enhancing family functioning, rather than success in eliminating or 'curing' symptoms. Among our outcomes of interest, one trial found rates of state-hospitalization were lower among those in multiple family psychoeducational groups than those in a shorter individually-oriented intervention of psychoeducation only.[103] A second trial found no differences on our outcomes of interest at final follow-ups for those participating in Assertive Community Training with or without a biweekly multiple family group.[29] A third trial found family therapy with an in home behavioral family therapy component resulted in less patient rejection by families than the same intervention without in-home behavioral family therapy. Differences on symptoms and rates of hospitalization were non-significant. A final trial demonstrated greater improvements in symptoms of serious mental illness and functioning, but not lower substance use, among dually diagnosed patients (serious mental illness and SUDs) assigned to a 9-18 month psychoeducational family program versus a brief (2-3 month) family intervention. However, problems with recruitment and retention of these complex patients raises concerns about the feasibility of family treatment for this group, especially long-term interventions.[100] Additional evidence from non-US trials exists supporting family treatments for schizophrenia for the prevention or delay of relapse over the past 15 years and was not included in the present review. The applicability of results to US Veterans and even US patients from studies outside the United States, particularly in China, is limited. A recent, more inclusive review of family treatments for schizophrenia concluded the quality of reporting in most these studies was poor.[126]

Family treatments for a number of additional mental health conditions were examined in one or two trials, including PTSD (2 trials), erectile dysfunction (2 trials), depression (1 trial), binge eating disorder (1 trial), and smoking cessation (1 trial). A family support group to encourage treatment engagement among Bosnian refugees with PTSD found greater rates of engagement than waitlist only participants (one trial). Additionally, support was found for brief couple therapy for depression over waitlist in improving depression and couple functioning. Results from the remaining trials included largely non-significant differences between family treatments and either individual treatment (PTSD, binge eating, smoking) or, for erectile dysfunction, medication management.

Overall, the literature indicated family involved treatments for mental health conditions were as effective as or more effective than individually-oriented psychotherapies, with two exceptions. The addition of approximately 23 weeks of disorder-specific behavioral family therapy after 9 weeks (18 sessions) of exposure therapy for PTSD lead to greater rates of treatment dropout than exposure therapy alone or waitlist.[8] Additionally, male opiod users with pregnant female partners who participated in a combination of motivational enhancement, case management, contingency management, and psychoeducational couple therapy reported greater heroin use at short-term follow-ups than patients participating in usual care. Outside of these two trials, findings either favored family involvement or demonstrated no significant differences between family interventions and comparator conditions, even when comparators were robust, active individually-oriented interventions. However, outside of the SUD literature, the number of trials testing the same intervention with the same or similar comparators was limited, leading to low confidence in the consistency of these conclusions. Additionally, many studies did not evaluate family and couple functioning after treatment, treatment adherence, or satisfaction with care. Additionally, most studies did not report Veteran status of their participants. Consequently, while the present study sought to optimize the relevance of this review to Veterans by examining only US studies, the generalizability of findings from these trials to Veterans' samples is largely unknown.

LIMITATIONS

There were several important limitations to this review. First, in order to focus on recent, high quality studies, most applicable to Veterans, our review was limited to randomized controlled trials conducted over the last 15 years. As discussed above, some family interventions were established as efficacious prior to this time frame, limiting the need for, and consequently, volume of studies addressing KQ1. Secondly, this review was also limited to studies conducted in the US only. The efficacy of family interventions has been established in many studies internationally (i.e. in China for family treatments for serious mental illness), however, their applicability to the US Veteran population or US healthcare system is not known.[129] Third, developing and advancing a psychosocial intervention such that it is appropriate for testing in an RCT is a major task requiring years of work and even further complicated by the need to recruit both patients and their families for participation. Consequently, there are numerous family involved interventions not included in our review that are in various stages of development or are currently under evaluation in RCTs (e.g., Couple therapies for PTSD,[139] Family Member Provider Outreach Program,[140] Coaching into Care,[141] REACH[142]). While our focus on RCTs is

warranted, given the VA's need for direction on which family interventions have established an evidence base, exclusions of these interventions under development is a potential limitation. Fourth, we elected to organize our findings by mental health condition, consistent with the organization of the DSM-IV. However, alternative methods of presenting findings exist. Findings could be presented comparing 'serious mental illness' (i.e., discussing schizophrenia and bipolar trials together) to other forms of mental illness or by type of intervention (family versus couple; disorder specific versus general family therapies; interventions using similar approaches, such as psychoeducational interventions). Conclusions using these alternative approaches to synthesizing findings would likely differ from those reached in this review.

Finally, interventions specifically targeting caregiver outcomes are important. However, given the VA's traditional focus on Veteran outcomes, our review included only studies which assessed participants' outcomes (including family and couple functioning). Interventions that solely seek to improve the distress and burden experienced by family members of those with mental illness are were not reviewed, and rates of improvement in the personal distress experienced by family members or caregivers were not included when reported in the trials reviewed. Our findings cannot speak to the efficacy of family interventions for mental health conditions in improving the functioning of patient's family members and caregivers.

RECOMMENDATIONS FOR FUTURE RESEARCH

There are a number of important gaps in our findings that highlight the need for future work. As discussed above, further work is needed to integrate our findings on patient outcomes with research examining how family/couple interventions effect outcomes for spouses and other family members (i.e., caregiver burden, distress, anxiety, etc). For substance use disorders, further work is needed establishing that patients' whose families participate in CRAFT have better reductions in substance use and better longer-term retention in treatment than those assigned to other interventions. Additionally, comparisons between BCT and other family involved interventions are warranted. Finally, a large number of the BCT trials reviewed were conducted within a single lab (i.e., Dr. Fals-Stewart) and further work outside of this laboratory is indicated.

A few trials found family interventions were most effective (i.e., resulted lower rates of symptoms) than comparison conditions for patients in distressed families and/or with more severe baseline symptoms (i.e., BCT with relapse prevention and family therapy for bipolar disorder). Family distress by condition interactions have also been found in studies of depression conducted prior to our review, suggesting that individuals benefit more from individual than marital therapy when in non-distressed relationships.[44, 137] If replicated, these findings could have important implications to personalizing treatment for those with greater family distress and/or more severe symptoms of mental illness. Future work should continue to test for these interactions.

With the exception of two interventions, BCT for substance use and CRAFT for the initiation of substance use treatment, in the past fifteen years, very few family treatments for improving adult mental health conditions have been investigated in more than one rigorous RCT in the US. Generally, the literature is in need of this work. Future trials are needed examining CRAFT,

BCT, and Family-Focused Therapy specifically in Veteran samples. Additionally, further work is needed to continue to establish the efficacy of interventions highlighted in Table 15 as possibly efficacious as they have demonstrated some significant improvements in patient functioning over comparison conditions in at least one trial (rated 3 or 4 on the status of their efficacy). This includes further trials of relapse prevention in addition to BCT, CRAFT for alcohol use disorders, brief BCT for substance use disorders, BFT (with non-intimate partners) for substance use disorders, family involvement to increase treatment initiation among patients hospitalized for substance use detoxification, Family-Focused Treatment-Health Promoting Intervention for bipolar disorder, Family Focused Treatment for bipolar disorder, marital therapy for bipolar disorder, in home behavioral family therapy as an addition to family treatments for schizophrenia, combined treatments for co-occurring schizophrenia and substance use disorders (Family Intervention for Dual Disorder), and support groups to promote treatment use among patients with PTSD (CAFES). Such trials are needed that use large samples, longer-term follow-ups, high quality methodologies, evaluate both patient and family outcomes, compare outcomes by 'type' of family member included (e.g., spouse, parent, sibling), and use standardized symptom measures that can facilitate comparisons across trials.

Evaluating applications of these interventions to patients with comorbid conditions (e.g., substance use and serious mental illness), non-white samples, older patients (i.e., over 65), and Veteran groups is warranted. Additionally, alternative types of family constellations (i.e., close friends, same sex couples) have received little attention among existing RCTs. For Veterans, preferences for which family members to include (i.e., intimate partners versus other family members), how these preferences vary by era (i.e., recently returning Veterans versus Vietnam/ Korean War Veterans eras), and the availability and "type" of family members interested in participating (i.e., intimate partners versus other family members) is important to inform policy decisions, especially considering that current eligibility criteria for VA family-related services does not extend to close friends or intimate partners who do not reside with the Veteran. Additionally, research is needed evaluating methods of engaging families in care. This was demonstrating in a study of schizophrenia finding that 80% of families did not participate in optional follow up family group sessions.[99, 100] Additionally, trials of family interventions for several mental health conditions were notably limited or absent from the published literature in the US in the past 15 years, including studies of family treatments for depression, PTSD and other anxiety disorders, personality disorders, eating disorders, and sexual functioning disorders, warranting further work with these conditions.

Given the intent of the ESP is to provide an objective, non-biased approach to the review topic, providing our own cost-benefit analysis of interventions is beyond scope of this review. Additionally, this information was largely absent from RCTs reviewed. Consequently, future research is needed evaluating the costs and benefits of effective interventions. This work could further consider multifamily versus single family interventions for schizophrenia, intensive versus less intensive interventions for serious mental illness, and brief versus standard length interventions for substance use and other disorders (e.g., standard BCT versus brief BCT).

Finally, with the exception of a few studies within the schizophrenia literature, limited attention was paid among studies reviewed to interventions for patients with multiple diagnoses, conditions, or problems. Future research should work to identify efficacious family treatments

for patients with commonly co-occurring conditions important to VA populations, such as PTSD and substance use disorders, serious mental illness and substance use disorders, comorbid personality disorders among patients seeking treatment for an Axis I condition. Patients were not excluded from trials due to diagnosis of a personality disorder, but findings were typically not stratified by other co-morbid conditions, preventing comparisons of treatment response by co-morbid conditions. Additionally, in the substance use literature, couples and families in which both the patient and the family member have a substance use disorder are typically excluded from trials. However, in practice, dual SUD couples and family members are not uncommon. Further work is also needed to identify evidence based practices and approaches to family involvement for patients with co-occurring intimate partner violence, suicidality, self-injury, or/ or traumatic brain injury.

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