

Table 5. Study Descriptive Information - Bipolar Disorder Studies

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Clarkin, 1998 <sup>94</sup> Government, Foundation	N = 46 randomized N = 33 analyzed <u>Gender</u> : 54% male <u>Age</u> : 47.7 years <u>Race/ethnicity</u> : NR <u>Marital status</u> : NR <u>Education</u> : NR  Veterans: NR  <i>Family Characteristics</i> : significant other of opposite sex  <i>Recruitment Method</i> : patients consecutively admitted to inpatient and outpatient services were considered for inclusion	<u>MH Condition</u> : major affective disorder or bipolar disorder, manic, depressed, or mixed <u>Assessed by</u> : Interview using Schedule for Affective Disorders and Schizophrenia <u>SO</u> : spouse or partner of opposite sex, married or living together ≥ 6 months <u>Inclusions</u> : 21 to 65 years old; admission diagnosis of major affective disorder or bipolar disorder, manic, depressed, or mixed; married or living with significant other of opposite sex ≥6 months <u>Exclusions</u> : organic brain syndrome, current primary diagnosis of alcohol or drug abuse, pregnancy, contraindications to use of lithium or carbamazepine	1) Medical manage- ment + marital inter- vention (N=18)  2) Medical manage- ment only (N=15)  <u>Randomized</u> : N=46  <u>Analysis</u> : Baseline: N = 33 Post-treatment (Final 11 months): N=33	<u>Format</u> : marital therapy <u>Manualized</u> : Yes <u>Session</u> : 25 (one weekly for first 10; then bimonthly) <u>Txt Length</u> : 11 months <u>Approach</u> : psychoeduca- tional  NOTE: all patients received standardized medications in each of 3 classes: mood stabilizers, antidepressants, and antipsychotics	<u>Patient Outcomes</u> : Symptoms a. SADS-C  Functioning a. Global Assessment Scale  <u>Intermediate Outcomes</u> : a. Medication Adherence using study developed scale (1-6 rating, poor to excellent)  <u>Family Outcomes</u> : None  <u>Outcome timeframe</u> : Baseline Post-treatment (Final): 11months	<u>Allocation concealment</u> : Unclear  <u>Blinding</u> : Unclear  <u>Intention to treat analysis</u> : No  <u>Withdrawals adequately described</u> : No  <u>Treatment Integrity</u> : audio tapes of marital intervention sessions were sampled for adherence to procedures outlined in manual  <u>Study Quality</u> : <b>Poor</b>

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Miklowitz, 2000 <sup>90</sup> Government, Foundation	N = 101 randomized N = 79 analyzed Gender: 37% male Age: 35.6 yrs Race/ethnicity: White 84% Marital Status: 55% married or cohabiting Education: NR  Veterans: NR  <i>Family Characteristics:</i> 37% parents, 55% spouses, 7% siblings, 1% adult offspring  <i>Recruitment Method:</i> Recruited from 4 psychiatric inpatient units or referred to study as outpatients.	<u>MH Condition:</u> Bipolar I disorder, manic, mixed, or depression <u>Assessed by:</u> Structured Clinical Interview for DSM-III-R <u>SO:</u> "close relatives" including parents, spouses, siblings <u>Inclusions:</u> DSM-II-R diagnosis of bipolar I disorder, manic, mixed, or depressed episode in previous 3 months; age 18-60 yrs; no neurologic disorder or developmental disability; no DSM-III-R drug or alcohol disorders in previous 6 months; living with or in regular contact (4+ hrs/wk) with close relative; willing to commit to pharmacotherapy with mood stabilizers or antipsychotic medications; English speaking; patient and relative willing to consent <u>Exclusions:</u> no additional criteria reported	1) Family-focused treatment with pharmacotherapy (N=31)  2) Crisis management with pharmacotherapy (N=70) ("treatment as usual" condition with 2 home-based family education sessions, emergency counseling as needed, minimum of monthly telephone call to monitor status)  Randomized: N=101  Analysis: Baseline: N=101 Long term (Final): 12 months: N=79	<u>Format:</u> Family-focused (family or marital) <u>Manualized:</u> Yes <u>Session:</u> up to 21 sessions, 1 hour, in the family's home <u>Txt Length:</u> 9 months <u>Approach:</u> psychoeducation, communication skills, problem definition and solution	<u>Patient Outcomes:</u> Symptoms a. SADS-C b. Relapse c. Survival  <u>Intermediate Outcomes:</u> a. Medication Compliance  <u>Family Outcomes:</u> None  <u>Outcome timeframe:</u> Baseline Long Term (Final): 12 months	<u>Allocation concealment:</u> Unclear  <u>Blinding:</u> Yes (medication intensity and compliance ratings)  <u>Intention to treat analysis:</u> No  <u>Withdrawals adequately described:</u> Yes  <u>Treatment Integrity:</u> audio tapes reviewed for adherence  <b>Study quality: Good</b>
Miklowitz, 2003 <sup>5</sup> Government, Foundation	Same as Miklowitz 2000 <sup>90</sup>	Same as Miklowitz 2000 <sup>90</sup> <u>MH Condition:</u> <u>Assessed by:</u> <u>SO:</u> <u>Inclusions:</u> <u>Exclusions:</u> Same as Miklowitz 2000 <sup>90</sup>	Same as Miklowitz 2000 <sup>90</sup> 1) Family-focused treatment with pharmacotherapy (N = 22 completed 2 years)  2) Crisis management with pharmacotherapy (N = 43 completed 2 years)	Same as Miklowitz 2000 <sup>90</sup>	Same as Miklowitz 2000 <sup>90</sup>  2 year outcomes	Same as Miklowitz 2000 <sup>90</sup>

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
<p>Miklowitz, 2007<sup>92</sup></p> <p>Government</p> <p>All patients were enrolled in Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) study</p> <p>NOTE: included patients in 26-wk trial of mood stabilizer + placebo or mood stabilizer + antidepressant (RAD) and willing to be randomized to psychosocial treatment; initiated study (PAD) with patients ineligible for pharmacotherapy trial due to previous poor response to agents</p>	<p>N = 293 randomized N = 293 analyzed</p> <p>Gender: 41% male</p> <p>Age: 40.1 yrs</p> <p>Race/ethnicity: Caucasian 94% African American 4% Native American &lt;1% Asian/Pacific Islander 1% Other 1%</p> <p>Marital Status: Married 33% Unmarried 37% Separated 31%</p> <p>Veterans: NR</p> <p><i>Family Characteristics:</i> Not specified – “typically spouses, parents, or siblings”</p> <p><i>Recruitment Method:</i> Referrals from Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)</p>	<p><u>MH Condition:</u> Bipolar I or II disorder and current major depressive episode</p> <p><u>Assessed by:</u> Structural Clinical Interview for DSM-IV and Mini-International Neuropsychiatric Interview</p> <p><u>SO:</u> Family members</p> <p><u>Inclusions:</u> 18+ years; DSM-IV criteria for current bipolar I or II disorder and a current major depressive episode; current treatment with mood stabilizer or willing to start treatment; no current psychotherapy (or willing to discontinue or taper); English speaking, able to consent</p> <p><u>Exclusions:</u> require immediate treatment for DSM-IV substance or alcohol abuse or dependence disorder (except nicotine); pregnant or planned pregnancy in next yr; history of intolerance, nonresponse, or medical contraindication to paroxetine or bupropion; required initiation or dose changes of antipsychotic medications</p>	<p>1) Family-focused treatment (FFT)* (N=26)</p> <p>2) Interpersonal and social rhythm therapy (IPSRT) (N=62)</p> <p>3) Cognitive behavior therapy (CBT) (N=75)</p> <p>4) Collaborative care (CC) – control group (N=130)</p> <p>NOTE: All patients received pharmacotherapy</p> <p>*Assignment to FFT possible only if willing family members</p> <p>Randomized: N=293</p> <p>Analysis: Baseline: N=293 Long term (Final): 12 months: N=293</p>	<p>1) <u>Format:</u> FFT <u>Manualized:</u> Yes <u>Session:</u> up to 30 50-min sessions <u>Txt Length:</u> 9 months <u>Approach:</u> psychoeducation, communication enhancement, problem solving</p> <p>2) <u>Format:</u> IPSRT <u>Manualized:</u> Yes <u>Session:</u> up to 30 50-min sessions <u>Txt Length:</u> 9 months <u>Approach:</u> Social Rhythm Metric for stable social rhythms, problem resolution, rehearsed strategies</p> <p>3) <u>Format:</u> CBT <u>Manualized:</u> Yes <u>Session:</u> up to 30 50-min individual sessions <u>Txt Length:</u> 9 months <u>Approach:</u> psychoeducation, life events scheduling, cognitive restructuring, problem-solving, detection and intervention for mood episodes, interventions for comorbidities</p> <p>4) <u>Format:</u> CC <u>Manualized:</u> Yes <u>Session:</u> 3 50-min individual sessions <u>Txt Length:</u> 6 weeks <u>Approach:</u> psychoeducation</p>	<p><u>Patient Outcomes:</u> 1) Recovery 2) Time to recovery Clinical Monitoring Form - depression and mania items used to define recovery (≤2 moderate symptoms for ≥8 of the previous weeks) and compute time to recovery and total time in recovery over 1 year of observation</p> <p><u>Intermediate Outcomes:</u> Attendance</p> <p><u>Family Outcomes:</u> None</p> <p><u>Outcome timeframe:</u> Baseline Long Term (Final): 12 months</p>	<p><u>Allocation concealment:</u> Unclear</p> <p><u>Blinding:</u> unclear</p> <p><u>Intention to treat analysis:</u> Yes</p> <p><u>Withdrawals adequately described:</u> Yes</p> <p><u>Treatment Integrity:</u> audio tapes rated for adherence to treatment</p> <p><u>Study quality:</u> <b>Good</b></p>

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Miklowitz, 2007 <sup>95</sup>  NOTE: Data from subset of patients from Miklowitz 2007 with baseline assessment with LIFE-RIFT) tool	N = 152 Gender: 41 % male Age: 41.1 yrs Race/ethnicity: White 95% Marital Status: Married 31% Unmarried 37% Separated 32%  Veterans: NR  Family Characteristics: Husbands Children:	Same as Miklowitz 2007 <sup>92</sup>  MH Condition: Assessed by: SO: Inclusions: Exclusions:	1) Psychosocial Treatment (combined FFT, IPSRT, and CBT groups) (N=84)  2) Collaborative Care (CC) (N=68 )	Same as Miklowitz 2007 <sup>92</sup>	<u>Patient Outcomes:</u> a. Functioning (LIFE-RIFT total score)  <u>Intermediate Outcomes:</u> None  <u>Family Outcomes:</u> a. Relationship functioning & satisfaction domains (LIFE-RIFT)  <u>Outcome timeframe:</u> Baseline Long term (Final): 9 months	Same as Miklowitz 2007 <sup>92</sup>
Miller, 2004 <sup>89</sup>  Government	N = 92 randomized N = 92 analyzed Gender: 43% male Age: 39 years Race/ethnicity: NR Marital Status: Married 67% Never married 15% Separated/divorced/Widowed 18% Education (years): 13  Veterans: NR  Family Characteristics: Spouses 62% Parents 17% Other adults 21%  Recruitment Method: In-patients, partial hospital patients, and outpatients from a university-affiliated psychiatry clinic	MH Condition: Bipolar I disorder mood episode (mania, major depression, or mixed) Assessed by: Structured Clinical Instrument for DSM-III-R-Patient Version SO: patient and family members Inclusions: current bipolar I disorder mood episode; no DSM-III-R alcohol or drug dependence within 12 months of enrollment; age 18-65 yrs; living with or in regular contact with relative or significant other; English speaking Exclusions: no additional criteria reported	1) Pharmacotherapy + family therapy (N=33) 2) Pharmacotherapy + multifamily psychoeducational group (MFG) therapy (N=30) 3) Pharmacotherapy alone (N=29)  Randomized: N=92  Analysis: Baseline: N=92 Long term (Final): 28 months: N=92	1) Format: Family therapy Manualized: Yes Session: 6 to 10 50-min sessions Txt Length: NR* Approach: Problem Centered Systems Therapy of the Family 2) Format: MFG therapy (4-6 patients and family members > 12 yrs) Manualized: Yes Session: 6 90-min sessions Txt Length: 6 weeks* Approach: Psychoeducational 3) Format: Pharmacotherapy Manualized: Yes Session: weekly for 1 mo then every 3 months Txt Length: NR* Approach: medication adjustment, support, encouragement	<u>Patient Outcomes:</u> Symptoms a. Recovery (defined as 2 consecutive months scores of <7 on HAM-D and <6 on BRMS)  <u>Intermediate Outcomes:</u> a. Pharmacotherapy sessions attended  <u>Family Outcomes:</u> None  <u>Outcome timeframe:</u> Baseline Long Term (Final): 28 months	<u>Allocation concealment:</u> Unclear  <u>Blinding:</u> Yes (rating of pharmacotherapy)  <u>Intention to treat analysis:</u> Yes  <u>Withdrawals adequately described:</u> No  <u>Treatment Integrity:</u> Treatments monitored and evaluated at weekly meetings of study clinicians and investigators  <u>Study Quality:</u> Fair

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Miller, 2008 <sup>98</sup>  Funding source not reported`	N = 91* Gender: 57% male Age: 39.5 years Race/ethnicity: NR Marital Status: NR Education: NR  Veterans: NR  Family Characteristics: NR for this analysis  *One family did not complete MCERS at baseline  Recruitment Method: Inpatients, partial hospital patients, and outpatients from a university-affiliated psychiatry clinic (96% while hospitalized)	Same as Miller 2004 <sup>89</sup> Analysis using proportional measures of long-term course of illness and based on level of family impairment according to McMaster Clinical Rating Scale (MCERS)  Additional Exclusions reported: DSM-III-R for alcohol/drug dependence in the last year; mood disorder secondary to a general medical condition; illness that contraindicates mood stabilizer use; pregnant, or not using contraception.	Same as Miller 2004 <sup>89</sup>  Baseline N = 91  High impairment: N = 60 (66%) Low impairment N = 31 (34%)  Final (28 months) N= 82 High impairment: N = 55 (67%) Low impairment N = 27 (33%)	Same as Miller 2004 <sup>89</sup> except indicates target was 10-15 family-therapy sessions (vs. 6-10)	Patient Outcomes: a. Recovery/ relapse (% who recovered and relapsed based on HAM-D and BRMS for high and low family impairment subgroups)  Intermediate Outcomes: None  Family Outcomes: None  Outcome timeframe: Baseline Long Term (Final): 28 months	Same as Miller 2004 <sup>89</sup>

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Perlick, 2010 <sup>93</sup> Government	<p><u>Patients:</u> N = 46  <u>Gender:</u> 37% male  <u>Age:</u> 34.7  <u>Race/ethnicity:</u>                      Caucasian 75%                      African American 7.5%                      Hispanic 17.5%  <u>Marital Status:</u>                      Married/cohabiting 15%                      Widowed/divorced/                      separated 30%                      Never married 55%</p> <p>Veterans: 2 caregivers                      from VA Medical Center</p> <p><u>Caregivers:</u> N = 46  <u>Gender:</u> 16% male  <u>Age:</u> 52.8 yrs  <u>Race/ethnicity:</u>                      Caucasian 77%                      African American 5%                      Hispanic 16%                      Other 2%  <u>Marital Status:</u>                      Married/cohabiting 44%                      Widowed/ divorced/                      separated 33%                      Never married 23%  <u>Family Characteristics:</u>                      Parents 70%; Spouse                      or SO 14%; Adult child                      14%; Friend or neighbor                      2%  <u>Recruitment Method:</u>                      Referred by mental                      health clinicians</p>	<p><u>MH Condition:</u> Bipolar I or II                      disorder  <u>Assessed by:</u> Structured Clinical                      Interview for DSM-IV Axis I                      Disorders  <u>SO:</u> Caregiver  <u>Inclusions:</u> age 18+; primary                      caregiver of relative with bipolar                      I or II; meet at least 3 (2 for non-                      relatives) criteria: a) spouse or                      parent, b) more frequent contact                      than any other caregiver, c) helps                      support patient financially,                      d) is contacted by treatment staff                      for emergencies, e) involved                      in patient's treatment; current                      physical and mental health                      problems  <u>Exclusions:</u> no additional criteria                      reported</p>	<p>1) Family-Focused                      Treatment-Health                      Promoting Interven-                      tion (FFT-HPI) (N=25                      caregivers)</p> <p>2) Health education                      (HE) (N=21 caregivers)</p> <p>NOTE: recruited                      caregivers who were                      primary caregiver of                      relative with condition</p> <p>Randomized:                      N = 46 caregivers of                      46 patients</p> <p>Analysis:                      Baseline: N=43 care-                      givers of 40 patients                      Post-treatment (Final):                      5 months:                      N = 43 caregivers of                      40 patients</p>	<p>1) <u>Format:</u> Family focused                      (but only the caregiver was                      involved)  <u>Manualized:</u> Yes  <u>Session:</u> 12-15 sessions  <u>Txt Length:</u> approx 5                      months  <u>Approach:</u> Psychoedu-                      cation and goal setting,                      behavioral analysis of self-                      care barriers</p> <p>2) <u>Format:</u> Individual (via                      DVD)  <u>Manualized:</u>  <u>Session:</u> 8-12 sessions via                      DVD  <u>Txt Length:</u> approx 5                      months  <u>Approach:</u> health educa-                      tion</p>	<p><u>Patient Outcomes:</u>  <u>Symptom                      Improvement</u>                      a. HAM-D                      b. YMRS</p> <p><u>Intermediate                      Outcomes:</u> None</p> <p><u>Family Outcomes:</u>                      None</p> <p><u>Outcome timeframe:</u>                      Baseline                      Post-treatment                      (Final): 5 months</p>	<p><u>Allocation                      concealment:</u> Yes</p> <p><u>Blinding:</u> Yes                      (assessor and                      participants during                      administration                      of the initial                      assessment; post-                      test assessment)</p> <p><u>Intention to treat                      analysis:</u> No</p> <p><u>Withdrawals                      adequately                      described:</u> No</p> <p><u>Treatment Integrity:</u>                      Randomly                      selected treatment                      tapes rated for                      competence and                      adherence</p> <p><b><u>Study quality:</u>                      Fair</b></p>

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Rea, 2003 <sup>91</sup> Government	<p>N = 53 randomized N = 53 analyzed Gender: 43% male Age: 25.6 yrs Race/ethnicity: Caucasian 60% African American 23% Asian American 9% Other 9% Marital Status: Single 76% Married 15% Divorced 9%</p> <p>Veterans: NR</p> <p><i>Family Characteristics:</i> 74 family members (29 mothers, 22 fathers, 1 stepfather, 9 spouses, 7 siblings, 1 grandmother, 1 uncle, 4 aunts)</p> <p><i>Recruitment Method:</i> inpatients in 3 large hospitals</p>	<p><u>MH Condition:</u> Bipolar disorder, manic type <u>Assessed by:</u> DSM-III-R with confirmation by Present State Examination (PSE) with supplementary mania items <u>SO:</u> "close family member";66% had one relative to participated, 34% had multiple relatives <u>Inclusions:</u> diagnosis of bipolar disorder, manic type; age 18-45, able to give consent, currently taking mood-regulating medications; at least one close family member available to participate <u>Exclusions:</u> evidence of organic central nervous system disorder or chronic alcohol or substance abuse/dependence</p>	<p>1) Family-focused treatment with pharmacotherapy (N=28)</p> <p>2) Individually focused patient treatment with pharmacotherapy (N=25)</p> <p>Randomized: N=53</p> <p>Analysis: Baseline: N=53 Post-treatment: N=53 Long term (Final): 24 months: N=29</p>	<p>1) <u>Format:</u> Family-focused or individual <u>Manualized:</u> Yes <u>Session:</u> 21 one-hour sessions over 9 months (medication management continued to 12 months) <u>Txt Length:</u>12 months<sup>a</sup> <u>Approach:</u> psychoeducation, communication enhancement training, problem-solving training</p> <p>2) <u>Format:</u> Individually focused patient treatment <u>Manualized:</u> Not stated <u>Session:</u> 21 30-min sessions over 9 months (medication management continued to 12 months) <u>Txt Length:</u>12 months<sup>a</sup> <u>Approach:</u> supportive, problem-focused, educational</p> <p><sup>a</sup>At 12 months, patients were referred to and assisted in transitioning to community providers</p>	<p><u>Patient Outcomes:</u> a. Relapse (based on BPRS and supplementary items from SADS-C) b. Rehospitalization (Patient and relative reports verified by inpatient records where possible)</p> <p><u>Intermediate Outcomes:</u> a. Medication Compliance (Psychiatrist-completed form)</p> <p><u>Family Outcomes:</u> None</p> <p><u>Outcome timeframe:</u> Baseline Post-treatment Long term (Final): 24 months</p>	<p><u>Allocation concealment:</u> Unclear</p> <p><u>Blinding:</u> Yes (outcomes)</p> <p><u>Intention to treat analysis:</u> No</p> <p><u>Withdrawals adequately described:</u> Yes</p> <p><u>Treatment Integrity:</u> Videotapes rated for therapist adherence and competence</p> <p><u>Study quality:</u> <b>Good</b></p>

Study, Year Funding Source	Sample Characteristics	Inclusion and Exclusion Criteria	Treatment Groups	Intervention	Outcomes Assessed	Quality
Solomon, 2008 <sup>97</sup> Government	<p>N = 53  <u>Gender</u>: 43% male  <u>Age</u>: 41 yrs  <u>Race/ethnicity</u>: NR  <u>Marital Status</u>: 66%                      Married or living with partner 66%                      Never married 19%,                      Separated/divorced/                      widowed 15%  <u>Education (years)</u>: 13</p> <p>Veterans: NR</p> <p><i>Family Characteristics</i>:                      NR for subgroup</p> <p><i>Recruitment Method</i>:                      Inpatients, partial                      hospital patients, and                      outpatients from a                      university-affiliated                      psychiatry clinic</p>	<p>Same as Miller 2004<sup>89</sup></p> <p>Analysis of recurrence of mood                      episodes and hospitalizations for                      53 subjects who recovered from                      intake mood episode</p>	Same as Miller 2004 <sup>89</sup>	Same as Miller 2004 <sup>89</sup>	<p><u>Patient Outcomes</u>:                      Symptoms:                      a. Frequency of                      mood episode                      recurrence (based                      on HAM-D&gt;15 or                      BRMS&gt;5)                      Utilization:                      a. Hospitalization</p> <p><u>Intermediate                      Outcomes</u>:                      None</p> <p><u>Family Outcomes</u>:                      None</p> <p><u>Outcome timeframe</u>:                      Baseline                      Long Term (Final):                      28 months</p>	Same as Miller 2004 <sup>89</sup>

NR = not reported; SO = significant other or family member included; SADS-C = Schedule for Affective Disorders and Schizophrenia-Change Version; DSM = Diagnostic and Statistical Manual of Mental Disorders; tx = treatment; BRMS = Bech-Rafaelsen Mania Scale; HAM-D = Hamilton Depression Rating Scale; LIFE-RIFT = Longitudinal Interval Follow-Up Evaluation – Range of Impaired Functioning Tool; YMRS = Young Mania Rating Scale; DVD = digital video disk; BPRS = Brief Psychiatric Rating Scale  
 \*Study patients were treated on outpatient basis for up to 28 months