e-Table: Randomized controlled trials of pharmacotherapy and psychotherapy for borderline personality disorder (BPD)*

Trial	Study subjects and outcome measures	Study arms and duration	Results	Comments	Funding source
Soloff et al[36]	*Subjects:* 108 inpatients (76% women) aged 16–36 yr (42 with BPD and 66 with BPD and schizotypal personality disorder) *Outcome measures:* Depression (HRS, BDI); global severity (GAS, SCL-90); anxiety, anger-hostility (SCL-90, IMPS, BDHI); psychoticism (SSI, SCL-90, IMPS); impulsivity (Ward Scale, BIS, SRTIC); and borderline psychotherapy (BSI)	• Phenelzine 60 mg/d (n = 38) • Haloperidol 4 mg/d (n = 36) • Placebo (n = 34) *Duration:* Washout wk followed by 5 wk of treatment and 16 wk of continued treatment for patients responding to medication	All groups improved on measures of depression, anxiety, anger-hostility and impulsivity. Some statistically significant differences between the 3 arms were found for some of the multiple outcomes tested	High dropout rates in all groups, especially among patients who experienced neuroleptic side effects (hypersomnia and leaden paralysis). Given the multiple outcomes measured, the finding of some statistically significant differences is not unexpected	US National Institute of Mental Health
Cowdry et al[37]	*Subjects:* 16 women aged 23–42 yr referred by private psychotherapists *Outcome measures:* Clinical change rated by physicians and patients using modified Bunney-Hamburg rating scale and 7-point scale similar to CGI; changes in dyscontrol, assessed from physician and patient reports of angry outbursts, physical violence, self-damaging behaviour, and suicide threats and attempts	• Alprazolam 1–6 mg/d • Carbamazepine 200–1200 mg/d • Trifluoperazine hydrochloride 2–12 mg/d • Tranylcypromine sulfate 10–60 mg/d • Placebo *Duration:* 2 wk of dose adjustment, 4 wk of treatment, 1 wk of tapering, and ≥ 1 wk drug free before starting next drug	Physicians rated patients as significantly improved relative to placebo while receiving tranylcypromine and carbamazepine. Patients rated themselves as significantly improved relative to placebo only while receiving tranylcypromine	Given the large number of comparisons in this study, the finding of some statistically significant differences is not unexpected	US National Institute of Mental Health
Zanarini et al[38]	*Subjects:* 28 women aged 18–40 yr recruited through newspaper ads who met criteria for BPD *Outcome measures:* SCL-90 subscales measuring anxiety, depression, paranoia, anger-hostility and interpersonal sensitivity	• Olanzapine 2.5 mg (n = 19) • Placebo (n = 9) Doses adjusted in both groups according to perceived response and side effects *Duration:* 6 mo	Olanzapine group showed statistically significant improvement on all components of SCL-90 scale except depression	Authors did not use intention-to-treat analysis. Only 8 subjects in olanzapine group and 1 subject in placebo group completed the study	Eli Lilly
Zanarini et al[39]	*Subjects:* 45 women aged 18–40 yr recruited through newspaper ads who met criteria for BPD *Outcome measures:* Depression (MADRS) and impulsive aggression (OAS-M)	• Fluoxetine 10 mg (n = 14) • Olanzapine 2.5 mg (n = 16) • Fluoxetine 10 mg plus olanzapine 2.5 mg (n = 15) *Duration:* 8 wk	Olanzapine was more effective than fluoxetine in treating both symptom areas studied. Combination treatment was also superior to fluoxetine but not to olanzapine	Results presented using regression models. All groups improved over time on both outcome measures	Eli Lilly
Bogenschutz et al[40]	*Subjects:* 40 patients (25 female) aged 18–60 yr recruited from community and outpatient clinics *Outcome measures:* CGI-BPD and global CGI; impulsive aggression (OAS-M and AIAQ); depression (HAM-D); anxiety (HAM-A); global symptom severity (SCL-90); global functioning (GAF); alcohol use (ASI); movement disorders (AIMS, BAS, SAS)	• Olanzapine 2.5–20 mg as titrated over time (n = 16) • Placebo (n = 19) *Duration:* 12 wk	Olanzapine group showed significantly greater improvement than placebo group on CGI-BPD and global CGI; secondary measures did not show significant difference at end point, although some (GAF, AIAQ and HAM-D) showed significant differences at 8 wk	Only 23 patients completed the trial. Results for global scale presented only in graphs, without confidence intervals. Authors did not perform intention-to-treat analysis	Eli Lilly

Salzman et al[41]	*Subjects:* 22 patients recruited through newspaper ads *Outcome measures:* Global mood and functioning, anger and depression (HAM-D, GAS, PDRS, POMS, OAS-R)	• Fluoxetine 20 mg/d titrated to maximum of 60 mg/d (*n* = 13) • Placebo (n = 9) *Duration:* 13 wk	Both groups showed some improvement. Secondary analyses showed clinically and statistically significant decrease in anger in fluoxetine group	Multiple secondary analyses done despite the finding of no significant differences between study groups in any of the primary outcome measures except self-reported mood	Not stated
Coccaro et al[42]	*Subjects:* 40 patients recruited by outpatient referral or self-referral through public service announcements *Outcome measures:* Aggression and Irritability subscales of OAS-M; physician-rated CGI-I and patient-rated AIAQ	• Fluoxetine 20–60 mg/d (*n* = 27) • Placebo (*n* = 13) *Duration:* 2-wk single-blind placebo lead-in phase followed by randomization and 12-wk follow-up	Sustained reduction in scores on OAS-M Aggression and Irritability subscales with fluoxetine relative to placebo; fluoxetine was superior to placebo in proportion of subjects showing improvement on CGI-I; no difference between groups in self-reported AIAQ measures	Of 64 patients entered in 2-wk placebo lead-in phase, only 40 were eligible for randomized treatment phase. Only 14 patients in fluoxetine group and 9 in placebo group completed the trial. The authors did not use intention-to-treat analysis	US National Institute of Mental Health and Eli Lilly
Rinne et al[43]	*Subjects:* 38 women aged 18–50 yr recruited from outpatient clinics, community mental health centres and through newspaper and Internet ads *Outcome measures:* Subscales (rapid mood shift, impulsivity and aggression) of BPD Severity Index	• Fluvoxamine 150 mg/d (*n* = 20); titrated to maximum of 250 mg/d after wk 10 • Placebo (*n* = 18) *Duration:* 6 wk	No statistically significant differences between groups except for subscale of rapid mood shift	Of 125 subjects screened, 78 met the diagnostic criteria; only 38 were entered in the trial. The authors did not use intention-to-treat analysis	DeGeestgronden Institute of Mental Health Care, Stichting tot Steun of Vereniging Bennekom, National Fund for Mental Health and Solvay Pharma
Hollander et al[44]	*Subjects:* 52 patients aged 18–65 yr (54% female) with history of aggression causing distress or impairment in work or interpersonal relationships *Outcome measures:* Aggression subscale of OAS, and YMRS, BIS and HAM-D	• Divalproex, mean dose 1325 mg/d (*n* = 20) • Placebo (*n* = 32) *Duration:* 12 wk	Tabular data for primary end points not shown. In subgroup analyses Divalproex was superior to placebo in reducing impulsive aggression	Primary outcomes were unclear and not shown. The number of patients completing the 12-wk trial was not given	Abbott Laboratories
Frankenburg et al[45]	*Patients:* 30 women aged 18–40 yr with BPD and bipolar II disorder recruited through newspaper ads *Outcome measures:* SCL-90 scales measuring interpersonal sensitivity, anger-hostility and depression; OAS–M	• Divalproex, dose adjusted to achieve serum level between 50 and 100 mg/L (*n* = 20) • Placebo (*n* = 10) *Duration:* 6 mo	Based on last completed end-point measure, there were greater changes in outcome scores in divalproex group than in placebo group	Only 7 patients in divalproex group and 4 in placebo group completed the study. Based on the data for patients completing the study, the results must be regarded as showing no difference between the study groups	Abbott Laboratories
Links et al[46]	*Subjects:* 17 patients (16 women) aged 18–45 yr recruited from psychiatric services *Outcome measures:* HAM-D, CSD, anger and suicidal components of SADS–Change questionnaire; therapist assessment of drug therapy	• Lithium, mean dose 986 mg/d; • Desipramine, mean dose 162 mg/d; • Placebo *Duration:* total 22 wk (3 cycles, each composed of 2-wk dose adjustment, 4 wk of treatment, 1 wk of tapering, 1 wk drug free before starting next cycle)	No statistically significant changes in scores for each study drug relative to placebo. Therapists rated lithium significantly superior to placebo	Fewer than 14 subjects completed at least 1 of the crossover trials	Ontario Ministry of Health and Long-term Care

Zanarini et al[47]	*Subjects:* 30 women aged 18–40 yr recruited through newspaper ads who met criteria for BPD *Outcome measures:* OAS-M, MADRS	• Ethyl-eicosapentaenoic acid (E-EPA, an omega-3 fatty acid), 1000 mg/d (*n* = 20) • Placebo (*n* = 10) *Duration:* 8 wk	Improvement from baseline in both outcome measures significantly greater in E-EPA group than in placebo group	Low dropout rates	Not stated
Linehan et al[50]	*Subjects:* 44 women aged 18–45 yr who met criteria for BPD and who had at least 2 incidents of parasucide in past 5 yr, with 1 incident occurring during 8 wk preceding enrolment *Outcome measure:* History of parasuicide behaviour (PHI), history of medical and psychiatric treatment (THI), current suicide ideation (Scale for Suicide Ideators), depression (BDI), hopelessness (BHS), reasons for living (RLI–SCS)	• Cognitive dialectical behaviour therapy (*n* = 22) • Usual care in community (*n* = 22) *Duration:* 12 mo	Subjects receiving dialectical behaviour therapy had significantly fewer incidents of parasuicide than those receiving usual care	A pretreatment phase of assessment was required; some potential subjects dropped out during this phase	National Institute of Mental Health
Bohus et al[51]	*Subjects:* 60 women aged 18–44 yr who met criteria for BPD and had at least 1 suicide attempt or at least 2 self-injurious acts within 2 yr before enrolment *Outcome measures:* LPC, SLC-90, HAM-A, STAI, BDI, HAM-D, STAXI, DES, GAF, IIP	• 3-mo inpatient dialectical behaviour therapy program (*n* = 40) • Nonspecific outpatient care while on waiting list for inpatient dialectical behaviour therapy (*n* = 20) *Duration:* 4 mo	Inpatient program was significantly superior to outpatient care on all outcome measures except dissociation and anger	9 patients in inpatient group did not complete 3-mo program. All subjects received medications as needed. Assignment to inpatient therapy was not random	German Research Foundation and Borderline Personality Disorder Research Foundation
Simpson et al[52]	*Subjects:* 25 women with BPD (mean age 35 yr) recruited from 5-day dialectical behaviour therapy program involving partial hospitalization *Outcome measures:* BDI, STAI, OAS-M, DES, STAXI, GAF	• Fluoxetine 40 mg/d (*n* = 12) • Placebo (*n* = 13) All patients received dialectical behavior therapy *Duration:* 12 wk	No statistically significant difference between groups in any outcome measure	Multiple primary outcomes	Brown University Medical School and Eli Lilly
Verheul et al[53]	*Subjects:* 64 women aged 18–70 yr referred by psychologists or psychiatrists from addiction treatment and psychiatric services; also, referrals by general practioners and self-referrrals possible if a psychologist or psychiatrist was willing to provide usual care *Outcome measures:* treatment retention rates; BPD Severity Index, LPC	• 12-mo dialectical behaviour therapy (*n* = 31) • Usual care (*n* = 33) *Duration:* 1 yr	Patients receiving dialectical behaviour therapy were more likely than those in usual care group to remain in therapy and less likely to engage in self-mutilating behaviour. No other outcome measures were statistically significant	Results presented only in graphs, without confidence intervals	ZAO Health Insurance Company
Bateman et al[54]	*Subjects:* 44 patients aged 16–65 yr receiving care for BPD in inner-city psychotherapy unit *Outcome measures:* Acts of self-harm (SSHI); patient reports of global severity of symptoms (SLC-90), depression and anxiety (BDI, STAI), social adjustment and interpersonal problems (Social Adjustment Scale–self-report, IIP–circumflex version)	• Partial hospitalization with weekly individual and group psychotherapy (*n* = 22) • Usual care (*n* = 22) *Duration:* 18 mo	Significantly fewer acts of self-harm in partial hospitalization group than in the usual care group. Self-reported measures of depression, anxiety, global severity of symptoms and social adjustment were all significantly improved in partial hospitalization group	Low dropout rate. Patients permitted to take medications during the trial	Not stated

Note: AIAQ = Anger, Irritablity and Assault Questionnaire, AIMS = Abnormal Involuntary Movement Scale, ASI = Addiction Severity Index, BAS = Barnes Akathisia Scale, BDHI = Buss–Durkee Hostility Inventory, BDI = Beck Depression Inventory, BHS = Beck Hopelessness Scale, BIS = Barratt Impulsiveness Scale, BSI = Borderline Syndrome Index, CGI = Clinical Global Improvement, CGI-BPD = Clinical Global Impressions scale modified for borderline personality disorder, CGI-I = Clinician Global Impression Rating of Improvement, CSD = Carroll Scale for Depression, DES = Dissociations Experiences Scale, GAF = Global Assessment of Functioning, GAS = Global Assessment Scale, HAM = Hamilton Rating Scale, HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression, IIP = Inventory of Interpersonal Problems, IMPS = Inpatient Multidimensional Psychiatric Scale, LPC = Lifetime Parasuicide Count, MADRS = Montgomery–Asberg Depression Rating Scale, OAS-M = Modified Overt Aggression Scale, OAS-R = Overt Aggression Symptom checklist, PDRS = Personality Disorder Rating Scale, PHI = Parasuicide History Interview, POMS = Profile of Mood States, RLI–SCS = Reasons for Living Inventory – Survival and Coping Scale, SADS = Schedule for Affective Disorders and Schizophrenia, SAS = Simpson–Angus Scale, SCL-90 = Symptom Checklist-90 items, SRTIC = Self-Report Test of Impulse Control, SSHI = Suicide and Self-Harm Inventory, SSI = Schizotypal Symptom Inventory, STAI = State-Trait Anxiety Inventory, STAXI = State-Trait Anger Expression Inventory, THI = Treatment History Interview, YMRS = Young Mania Rating Scale.
*DSM diagnostic criteria for BPD were used in all of the studies, although the specific requirements varied slightly across the studies. All but 1 study (reference 51) was a randomized controlled trial.