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A naturalistic longitudinal study of extended inpatient treatment for adults with borderline personality disorder: An examination of treatment response, remission and deterioration

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Abstract

Background: Experts express reluctance to hospitalize patients with borderline personality disorder (BPD) for more than a few days, arguing that extended inpatient care leads to deterioration and adverse events. To date, there is no empirical support for these assertions. **Aims:** The current study examined the assumption of iatrogenic effects among BPD adults. **Methods:** Clinically significant and reliable change in symptoms, functional capacities, and adverse events were quantified for both inpatients with BPD (n=245) and a well-matched inpatient reference (n=220) sample. Latent growth curve (LGC) models were used to evaluate moderators of the trajectory of PHQ-9 depression scores over the course of hospitalization. **Results**: Large effect size improvements were observed in depression, anxiety, suicidal ideation and functional disability among patients with BPD (Cohen's $d \geq 1.0$) and those in the reference sample (Cohen's $d \geq .80$). Clinical deterioration and adverse events were rare (occurring in no more than 1.1% of BPD and reference patients on any outcome) with no difference across patient cohorts. BPD diagnosis failed to influence the trajectory of continuous depression severity. Rather, trait emotion dysregulation was associated with initial depression severity. **Conclusions:** Twenty-five years ago it was assumed that adults with BPD could not benefit from psychiatric treatment. Today there are a number of effective evidence-based outpatient treatments for BPD, but beliefs about extended inpatient treatment have changed little. Current results indicate that extended inpatient treatment can result in significant and clinically meaningful symptomatic and functional improvement in BPD patients without iatrogenic effects.

Key words: Borderline personality disorder, extended hospitalization, iatrogenic effects

Borderline personality disorder (BPD) is the most extensively studied personality disorder (1-3); however, knowledge gaps persist, especially in the area of inpatient treatment course and outcome. This gap is particularly problematic because 1. Adults with BPD utilize inpatient and emergency department services at a higher rate than any other psychiatric group and far more than individuals with depression (4), and 2. Psychiatry is polarized over the utility of extended hospitalization for adults with BPD. Many BPD experts warn against hospitalizing patients with BPD for more than a few days due to concerns that extended hospitalization will lead to significant deterioration (5-9). Dawson and MacMillan warn clinicians never to hospitalize borderline patients (5), while Paris strongly advises against hospitalization, concluding that hospital admissions are designed to treat episodic mood disorders and psychosis, but not persistent mood or suicidal conditions (9). Paris has a point—the vast majority of short-term psychiatric units in the US and Canada are designed for stabilization and may not be suitable for BPD patients; however, the tautology carelessly extends beyond acute hospital units and ignores the existence of extended hospital programs in European countries and the US. Further, such provocative proclamations appear to be based purely on anecdotal evidence, given the absence of published scientific evidence of functional variations during the course of extended hospital treatment, or in particular demonstrating deterioration in functioning in patients with BPD. Complicating matters, practice guidelines (10-12) specifically include indications for hospitalization (in the context of stepped-care based on least restrictive, cost-effective care for current functional impairment). The American Psychiatric Association *Practice Guideline for the Treatment of Patients with Borderline Personality Disorder* (10) advances a set of indications for extended hospitalization:

1. Persistent and severe suicidality, self-destructiveness, or nonadherence to outpatient treatment or partial hospitalization, 2. Comorbid refractory axis I disorder (e.g., eating disorder, mood disorder) that presents a potential threat to life, 3. Comorbid substance abuse or dependence that is severe and unresponsive to outpatient treatment or partial

> hospitalization, 4. Continued risk of assaultive behavior toward others despite brief hospitalization, and 5. Symptoms of sufficient severity to interfere with functioning, work, or family life that are unresponsive to outpatient treatment, partial hospitalization, and brief hospitalization (pg. 13).

While the APA guideline for extended hospitalization is logical and consistent with the stepped-care model, the advice appears based on clinical wisdom, to prevent further deterioration and/or death, rather than based on evidence that extended hospitalization is an effective intervention for individuals diagnosed with BPD.

Absent empirical evidence, contemporary clinicians have no way of assessing the relative merits of extended hospital care for BPD. Is it a potential iatrogenic disaster (alternatively, as some experts insist, a costly inert ingredient that postpones effective care) or can it be an effective treatment option? The current study examined symptom trajectories including remission and deterioration rates on measures of depression, anxiety, suicidal ideation, functional disability, and well-being among psychiatric inpatients with BPD (*n*=245) compared to matched reference inpatients (*n*=220). Incidents of suicide attempts and non-suicidal self-injury (NSSI) during hospitalization were compared as direct behavioral indicators of deterioration.

Hypotheses

If Iatrogenic effects are prevalent among BPD inpatients, results would indicate elevated severity of symptoms and impairment in functioning with marked spikes in symptom severity for BPD patients measured at bi-weekly intervals, and flat treatment response (higher initial symptom severity, limited improvement) relative to a reference inpatient sample. Similarly, remission rates should be substantially lower for the BPD cohort compared to a matched reference sample, particularly in light of the adverse impact that co-occurring personality disorders can have on remission rates from major depression (13), By contrast, a reference inpatient sample would be expected to evidence large effect

size reductions in symptoms, and improvement in functioning, consistent with recent studies from this inpatient setting (14-17). In the event that BPD patients evidenced equivalent rates of improvement and/or deterioration to the reference sample, we planned to explore baseline moderators of depression change (BPD diagnosis, substance use disorder, history of interpersonal trauma, emotion regulation).

Methods

Treatment Characteristics

Services were provided (June 2012-September 2015) through a specialized, extended inpatient psychiatric facility in the United States. Treatment programming was organized around a mentalization-based therapeutic model (18) that informed all aspects of care including medication management, 24-hour nursing care, psycho-educational groups, individual and group psychotherapy, addictions services, and structured interpersonal and recreational activities. Delivery of multimodal interventions was intensive with an average of 59.4 hours of available programming per week.

Procedures

Data were collected as part of the hospital's ongoing Adult Outcomes Project to assess treatment response (19). Measures were collected within 72 hours of admission and were re-administered every 14 days during hospitalization and at point of discharge. This study was approved by the Institutional Review Board of Baylor College of Medicine. Propensity score matching (PSM) was used to match 245 BPD patients receiving between two and eight weeks of inpatient care with a cohort of reference patients from this facility without BPD. A propensity score pairs subjects from the case group (BPD) with subjects from the reference group such that the overall distribution of baseline potential confounds is similar across groups (20,21). This procedure increases the probability that results are due to primary dependent variables (in this case the presence/absence of BPD) rather than baseline confounds (20). The PSM procedure identified 220 reference inpatient controls that matched

on age, gender, history of prior psychiatric hospitalization, number of psychiatric disorders, and length of hospitalization. Average length of stay (LOS) for the total sample was 40.7 days (SD= 13.9). Exclusion criteria were restricted to length of stay ≤ 14 days and ≥ 57 days (consistent with the design of the treatment program). Characteristics of the BPD and matched reference patients are provided in Table 1.

Measures

Demographic variables were assessed using a standardized patient information survey (15). Trauma-related events were assessed using a modified 14-item version (22) of the Stressful Life Events Screening Questionnaire (SLESQ-R). A large-scale psychometric study of the SLESQ-R (23) found adequate internal consistency (Ordinal alpha = .87). Psychiatric disorders including personality diagnoses were assessed using research versions of the Structured Clinical Interview for DSM-IV Disorders (SCID-I/II). The SCID-I (24) and SCID II (25) were administered by master's level researchers after reviewing pertinent psychiatric and psychosocial evaluations and consultation with the attending psychiatrist.

Patient Health Questionnaire scales for depression (PHQ-9) and generalized anxiety (GAD-7) were used to monitor symptoms over the course of hospitalization. The psychometric properties of the PHQ-9 and GAD-7 are well-established (26,27) with average internal consistencies of $\alpha = .88$ and $\alpha = .91$, respectively, across assessments in this study. Severity of suicidal ideation was assessed using the Columbia Suicide Severity Risk Scale *(*C-SSRS: 28). A recent large-scale study (29) indicated the C-SSRS evidenced strong psychometric properties. The 12-item World Health Organization Disability Assessment Schedule 2.0 (WHO-DAS 2.0: 30) is psychometrically sound measure of illness-related disability (31). The WHO-DAS 2.0 demonstrated excellent stability in the current sample ($\alpha = .91$). General well-being was monitored using the 5-item World Health Organization Well-Being Index (32: WHO, 1998). Review of this measure indicates adequate validity and sensitivity to change (33,34) with strong internal consistency in the current study ($\alpha = .91$). The Difficulties in Emotion Regulation Scale (35) served as an index of global affect regulation in the analyses of continuous symptom change. Total

scores are calculated as the sum of individual items (range: 36 to 180) with values below 75 interpreted as evidence of normative functioning. Research indicates strong psychometric properties in both non-clinical (35) and inpatient samples (36) with adequate internal consistency in the current sample (α = .94). All suicide attempts (SA) and NSSI were coded based on extant record of events as an ongoing internal safety and quality improvement project. Due to low prevalence rates, individual counts for SA and NSSI were summed over the course of hospitalization.

Data Analysis

Treatment Gains and Deterioration

Therapeutic gains, symptom deterioration, and adverse events (from intake to discharge) were quantified through several metrics for both cohorts. Confidence intervals for within-group change and corresponding effect sizes provided estimates for the magnitude of expected treatment response in those receiving care through this facility. Clinically significant change was operationalized as discharge scores falling closer to the mean of a functional sample relative to the original clinical population (37). Finally, indices of reliable change were calculated to detect symptom fluctuations (both improvement and deterioration at each assessment point) exceeding those attributable to measurement error alone (37). Reliable change is commonly employed as a metric of patient deterioration in the existing treatment literature (38,39).

Moderators of Continuous Recovery

Latent growth curve (LGC) models were used to evaluate moderators of the trajectory of PHQ-9 depression scores over the course of hospitalization. In this approach, patient-specific trajectories are aggregated to form a baseline model of overall recovery. Predictors of patient-specific change are incorporated in cases where growth parameters in the baseline model provide evidence of variability in the trajectory of recovery across individuals. A stepped approach was used for the current analyses (40). First, a series of baseline models were examined to identify plausible trajectories of recovery in the full

sample. Analyses specifying both linear and quadratic change were explored. Next, variance estimates from the best fit baseline model were examined to determine whether patient-specific trajectories of recovery varied meaningfully from those in the aggregate sample. Non-zero variance estimates suggest the potential for unique patterns of change associated with patient-specific factors (e.g., treatment response in BPD patients differs from that observed in reference patients). Assuming evidence of variability in latent growth parameters, patient-level factors were included to capture patterns of individual change. All predictors in the final model were grand-mean centered. Interaction terms were calculated as the product of centered component variables. Significant effects in the final solution reflect unique relations between patient factors and change in PHQ-9 depression, controlling for other variables in the model.

Analyses were conducted using MPlus 6.1 software with maximum likelihood (ML) estimation (41). A notable feature of ML is the ability to accommodate cases with partially missing values. For the current sample, missingness in bi-weekly scores was due primarily to differences in LOS across the 8-week treatment window (i.e., cases with longer hospital stay recorded a greater number of assessments than those with shorter hospitalizations). Given that (a) missing data at later assessments were a direct function of length of stay, and (b) length of stay was explicitly modeled in the larger analyses, data loss was assumed to meet standards for missing at random (MAR) and appropriate for ML estimation (42).

Model Fit. Model adequacy was evaluated using comparative fit index (CFI), Tucker-Lewis index (TLI), and root-mean-square of approximation (RMSEA) values. For these analyses, CFI and TLI > .90, and RMSEA < .08 were considered evidence of adequate fit (43-45). CFI and TLI > .95 and RMSEA < .06 were interpreted as indicative of close fit (45).

Results

Sample Characteristics

Patients presenting with a diagnosis of BPD evidenced greater symptom and functional impairment (see Table 1) at intake relative to reference patients (all $p \leq .001$), with between-group effects falling in the small-to-medium range. BPD patients continued to evidence incrementally greater impairment at discharge (all $p \leq .020$), although data indicate a consistent reduction in the discrepancy between BPD and reference sample functioning.

Pre- to Post-Treatment Gains

Similar trajectories of recovery were observed across BPD and reference groups (see Fig. 1) for all measures over the 8-week treatment window. Absolute change from intake to discharge was substantial in both samples (see Table 2). Reference patients demonstrated a .81 to 1.15 standard deviation improvement across all clinical outcomes. Lower limits of corresponding confidence intervals exceeded standard benchmarks for large effects (46) with the exception of change in suicidal ideation. Absolute change in patients with a diagnosis of BPD was more pronounced. Point estimates of effect and lower limits of corresponding confidence intervals indicated, at minimum, a full standard deviation improvement across all outcomes. Rates of clinically significant change were comparable across groups (see Table 3) based on non-clinical distributions for the PHQ-9 (47), GAD-7 (27), WHO-DAS 2.0 (48), and WHO-5 (49). Small to medium effects were noted in the occurrence of reliable change, however, with BPD patients demonstrating more frequent improvement in PHQ-9 ($p < .001$), GAD-7 ($p = .001$), WHO-5 ($p < .001$), and C-SSRS ($p = .058$) scores. Deterioration in symptoms over the course of hospitalization was rare, occurring in no more than 1.1% of BPD and reference patients on any outcome. There were no suicide attempts for either group. Prevalence of NSSI was low for both BPD (9 of 245: 3%) and reference (2 of 220: 1%) samples with no overall differences ($\chi^2=2.7$, p=.10).

Growth Models

Baseline linear and quadratic models were examined to determine the overall shape of change in depression severity. Loadings for growth parameters were weighted to reflect time (in weeks) since

admission. Growth parameters in baseline models were regressed onto LOS (mean centered) to account for variability in the duration of hospitalization. Bootstrapped standard errors were estimated using 500 redraws from the original sample.

The baseline model of linear change was poor (CFI = .829, TLI = .802, RMSEA = .133, $CI_{90\%}$ [.122, .155]). Subsequent estimation of quadratic change in PHQ-9 depression evidenced adequate fit (CFI = .968, TLI = .939, RMSEA = .074, $CI_{90\%}$ [.045, .104]). Parameters in this model identify a trajectory of rapid initial improvement with slowed but continuous recovery over time. Variance estimates indicated reliable differences between BPD and reference patients in PHQ-9 scores at admission (intercept: $p < .001$) but little evidence of differences in rate of initial change (slope; $p = .065$) or in the tapering of recovery over time (quadratic: $p = .168$).

Estimation of the full quadratic model offered further support for homogeneity of change (see Supplemental Table 4). Although inclusion of patient-specific factors produced notable improvements in overall model fit (CFI = .975, TLI = .994, RMSEA = .044, $CI_{90\%}$ [.023, .064]), moderating effects were limited to the prediction of initial depression (intercept). Alcohol/substance use disorders were associated with lower PHQ-9 scores at admission ($\beta = -.126$, $p = .011$) whereas initial depression was more severe among patients reporting a history of interpersonal trauma ($\beta = .114$, $p = .019$). BPD status failed to evidence independent relations with recovery parameters controlling for other variables in the model. An interactive effect of BPD diagnosis and initial affect dysregulation was noted, however, in the prediction of depression scores at admission ($\beta = -.128$, $p = .011$). Follow-up tests indicated elevated depression among BPD patients relative to reference patients only within the context of low dysregulation ($\beta = .191$, $p = .027$). Initial PHQ-9 scores were similar in BPD and reference patients reporting (see Figure 2) elevated emotional dysregulation ($\beta = -.088$, $p = .226$). Slope and quadratic parameters in the final model were unrelated to BPD status, trauma history, or DERS scores at admission ($p \geq .102$).

Discussion

Borderline personality disorder (BPD) is characterized by emotion dysregulation, impulsivity, self-injurious behavior, and suicidal behavior all of which contribute to the highest emergency and inpatient service utilization of any psychiatric disorder (4). The prevalence of BPD is estimated to range from 10 percent in outpatient clinics to between 15 and 25 percent in inpatient settings (2). High-quality randomized controlled trials have demonstrated the efficacy of outpatient treatment of patients with BPD (see Leichsenring et al, 2011 for a detailed review), such that there is an international consensus that the core, or primary, evidence-based treatment for BPD is psychotherapy, accompanied as needed by symptom-targeted, adjunctive pharmacotherapy. The broad acceptance of evidence-based outpatient therapy stands in stark contrast to the polarized debate regarding inpatient treatment. One reason for this state is the limited data on how patients respond to acute and extended inpatient admission.

Prior results for extended inpatient treatment are limited to a small number of trials that assessed pre-post functioning but provided no insight into potential deterioration during the course of treatment. Several open trials utilizing inpatient cognitive behavior therapy (CBT) and inpatient dialectical behavior therapy (DBT) indicated fewer episodes of non-suicidal self-injury (NSSI) and overdose attempts than a hospitalized treatment-as-usual (TAU) group (50,51). A multi-center clinical trial of 207 patients with personality disorders (77% were diagnosed with BPD) indicated a slight advantage of intensive inpatient treatment over outpatient, day hospital and group therapies at 18-month follow-up (52). Recent reports of hospital-based psychodynamic treatment for individuals with personality disorders (61% were diagnosed with BPD) demonstrated large effect size improvement in symptoms (ES= 1.06) between admission and discharge (53). The only published RCT of inpatient treatment for BPD (54) demonstrated superiority of inpatient treatment over outpatient TAU at termination and one-month post-termination. By comparison, brief (5-day) inpatient treatment was

ineffective in reducing symptoms and functional impairment at point-of discharge (55). This single study of brief inpatient treatment provides limited support for Paris' assertion (9) but is far from definitive. On balance, findings from treatment trials support the relative effectiveness of extended inpatient treatment for BPD; however, the pre-post nature of past trials leave open the question of potential deterioration and adverse events during the course of hospitalization. This was the primary focus of our study.

Contrary to the iatrogenic hypotheses, BPD patients evidenced minimal deterioration during hospitalization as well as large effect size improvement and reliable change scores equivalent to the reference sample. Suicide attempts were non-existent and NSSI rates were low for both groups. Furthermore, linear growth model trajectories indicated that BPD diagnosis did not impact change in depression severity during the course of treatment. An interactive effect of BPD diagnosis and baseline emotion dysregulation did emerge with respect to depression scores assessed at intake. Here, BPD diagnosis was associated with elevated levels of initial depression, but only within the context of low emotion dysregulation. Individuals presenting for treatment with high levels of baseline dysregulation evidenced similar depression scores, irrespective of BPD status.

The results of growth modeling highlight the impact of the initial severity of emotion dysregulation on baseline depression severity, as well as differential end-point functioning. As can be seen in Figure 2, BPD and reference inpatients with high levels of emotion dysregulation manifested differential depression severity from those with lower emotion dysregulation. Emotion dysregulation, as we have argued elsewhere (56), may represent a cross-cutting dimension of psychopathology that exerts significant influence on baseline symptom expression and treatment response, regardless of primary diagnosis. In this vein, the NIMH RDoC initiative (57) with its emphasis on underlying cross-cutting dimensions of psychopathology may provide a better model for understanding patients at risk for attenuated treatment response.

Finally, the large effect size improvements for BPD inpatients across symptom and functional domains were surprising. While beyond the scope of the study design to explore mechanisms of change, there are several treatment features at the study institution worth noting. First, BPD inpatients were in a contained and secure environment in which self-defeating and self-destructive behaviors (such as alcohol and drug abuse) were minimized, and medication adherence for both groups was approximately 99% for all standing psychotropic orders. The volume of therapeutic encounters (an average of 59 hours of active programming per week) is far beyond community-level treatment as usual and may be a significant factor in treatment response. Finally, the mentalization-based treatment may have been particularly well-suited for the BPD sample.

The large sample of BPD inpatients (n = 245) with research confirmed diagnoses, systematic assessment of treatment response, and well-matched reference sample are strengths of the current study. Nonetheless, several limitations are noteworthy. The sample does not include outpatient controls and is comprised of individuals with severe mental illness with relatively high levels of PD traits. It is clear from the literature that outpatient treatment can be effective for many patients with BPD. However, for patients with BPD who have complex illnesses that have not responded to outpatient treatment, intensive extended inpatient treatment can be highly beneficial. Finally, it is important to note that our study did not assess post-discharge functioning, which is a significant limitation--data are currently being collected on post-discharge patients.

The expected differences between reference and BPD groups did not emerge perhaps in part because confounds of age, gender, history of prior psychiatric hospitalization, co-occurring psychiatric disorders, and length of hospitalization were controlled through the PSM procedure. It seems plausible that prior observations of iatrogenic effects for BPD inpatients were due to comorbid conditions or a lack of structured, evidence-based treatment. With over 250 variations within the BPD diagnosis (57), it has long been established that two individuals diagnosed with BPD can manifest extremely different

levels of psychopathology and treatment response—in that light, experts advocating against extended hospitalization of BPD patients may base such global assertions on particularly salient memories of adverse outcomes among a limited set of BPD inpatients (a case of Berkson's bias). Third, some extended inpatient settings may induce iatrogenic effects such as those noted by Paris (9). Inpatient settings with a lack of clear structure and expectation inevitably lack systematic delivery of contemporary evidence-based treatments for BPD and thus may create invalidating environments that may be particularly prone to iatrogenic effects (8).

References

1. Fowler JC, Oldham, JM: Co-Occurring disorders and treatment complexity. Focus 2013; 11: 123-128.

2. Leichsenring F, Leibing E, Kruse J, New AS, Leweke F: Borderline personality disorder. Lancet 2011; 377(9759):74-84.

3. McMain S, Alberta PE: Advances in psychotherapy of personality disorders: a research update. Curr Psych Rep 2007; 46-52.

4. Bender DS, Skodol AE, Pagano ME, Dyck IR, Grilo CM, Shea MT, Sanislow CA, Zanarini MC, Yen S, McGlashan TH, Gunderson JG. Prospective assessment of treatment use by patients with personality disorders. Psychiatric Services. 2006;57(2):254-7.

5. Dawson D, MacMillan HL: Relationship Management of the Borderline Patient: From Understanding to Treatment. New York: Brunner/ Mazel; 1993.

6. Livesley WJ: The Practical Management of Personality Disorder. New York: Guilford Press; 2003.

7. Paris J, 2004. Is hospitalization useful for suicidal patients with borderline personality disorder?: J Pers Dis; 1;18(3: Special issue):240-247.

8. Swenson CR, Sanderson C, Dulit RA, Linehan MM: The application of dialectical behavior therapy for patients with borderline personality disorder on inpatient units. Psych Quar. 2001 Dec 1;72(4):307-24.

9. Paris J. Stepped Care for Borderline Personality Disorder, Academic Press, London, 2017.

10. American Psychiatric Association. Practice guideline for the treatment of patients with borderline personality disorder. American Psychiatric Pub; 2001.

11. Borderline personality disorder: Treatment and management. NICE clinical guideline 78 (2009). https://www.nice.org.uk/guidance/cg78. 2014.

12. Clinical Practice Guideline for the Management of Borderline Personality Disorder. Australian Government National Health and Medical Research Council. 2012. https://www.nhmrc.gov.au/guidelines/publications/mh25. 2014.

13. Newton-Howes G, Tyrer P, Johnson T: Personality disorder and outcomes of depression: meta-analysis of published studies. British Journal of Psychiatry 2006; 188, 13-20.

14. Clapp JD, Grubaugh QL, Allen JG, Mahoney J, Oldham JM, Fowler JC, Ellis T, Elhai JD, & Frueh BC: Modeling Depression Symptom Trajectory Over Time among Psychiatric Inpatients: A Latent Growth Curve Approach. J Clin Psych 2013; 72: 492-499

15. Fowler JC**,** Madan A, Allen JG, Ellis T, Mahoney J, Frueh BC, Oldham JM: Improvements in health related quality of life among seriously mentally ill individuals receiving inpatient treatment at a specialty hospital. J Clin Psych 2015; *76*(5), 471-478.

16. Fowler JC, Clapp JD, Madan A, Allen JG, Frueh BC, Oldham JM. An open effectiveness trial of a multimodal inpatient treatment for depression and anxiety among adults with serious mental illness. Psychiatry. 2017;80(1):42-54.

17. Madan A, Clapp J, Osborne P, Walker C, Frueh BC, Allen J, Oldham JM, Fowler JC: Improvements in somatic complaints among individuals with serious mental illness receiving treatment in a psychiatric hospital. Psychosom Med 2016; 78: 271-280.

18. Allen JG, Fonagy P: Mentalizing in psychotherapy. In RE Hales, SC Yudofsky, & LW Roberts (Eds) The American Psychiatric Publishing Textbook of Psychiatry, DSM-5 Edition. Washington, DC: American Psychiatric Publishing, 2014, pp. 1095-1118.

19. Allen JG, Frueh BC, Ellis TE, Latini D, Mahoney JS, Oldham JM, Sharp C, Wallin L: Integrating outcomes assessment and research into clinical care in inpatient adult psychiatric treatment. Bull Menn Clin 2009; 73:259-295.

20. Austin, PC: An introduction to propensity square methods for reducing the effects of confounding in observational studies. Mult Behav Res 2011; 46(3), 399-424.

21. Rosenbaum PR, Rubin DB: The central role of the propensity score in observations studies for causal effects. Biometrika 1983; 70(1), 41-55.

22. Elhai JD, Miller ME, Ford JD, Biehn TL, Palmieri PA, Frueh BC: Posttraumatic stress disorder in *DSM-5*: Estimates of prevalence and symptom structure in a nonclinical sample of college students. J Anx Dis 2012; 26, 58–64.

23. Allen JG, Madan A, Fowler JC: Reliability and validity of the Stressful Life Events Screening Questionnaire among inpatients with severe neuropsychiatric illness. Bulletin of the Menninger Clinic 2015; 79, 187-202.

24. First MB, Gibbon M, Spitzer RL, Williams JBW, Benjamin LS: Structured clinical interview for DSM-IV axis II personality disorders, (SCID-II). Washington, DC: American Psychiatric Press. 1997.

25. First MB, Spitzer RL, Gibbon M, Williams JBW: Structured clinical interview for DSM-IV-TR axis I disorders, research version, patient edition. (SCID-I/P). New York: Biometrics Research, New York State Psychiatric Institute. 2002.

26. Kroenke K, Spitzer RL: The PHQ-9: a new depression diagnostic and severity measure. Psych Ann 2002; 9: 1-7.

27. Löwe B, Decker O, Müller S, Brähler E, Schellberg D, Herzog W, Herzberg PY: Validation and standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the general population. Med Care 2008; 46.3: 266-274.

28. Posner K, Brown GK, Stanley B, Brent DA, Yershova KV, Oquendo MA, Currier GW, Melvin GA, Greenhill L, Shen S, Mann JJ: The Columbia-Suicide Severity Rating Scale: initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry 2011; 168(12): 1266-1277.

29. Madan A, Frueh BC, Allen JG, Ellis T, Rufino KA, Oldham JM,Fowler JC: Psychometric re-evaluation of the Columbia Suicide Severity Rating Scale (C-SSRS): Findings from 2016 Jul 27;77(7):867-73m a prospective, inpatient cohort of severely mentally ill individuals. J Clin Psych 2016;77(7):867-73.

30. World Health Organization: World Health Organization Disability Assessment Schedule 2.0., 2014. (Access September 8, 2015, at http://www.who.int/classifications/icf/whodasii/en/)

31. Ustun TB, Kostanjsek N, Chatterji S, Rehm J: Measuring Health and Disability: Manual for WHO Disability Assessment Schedule (WHODAS 2.0). World Health Organization, Geneva. 2010

32. World Health Organization (WHO): Wellbeing Measures in Primary Health Care: The DepCare Project. WHO, Regional Office for Europe, Copenhagen. 1998

33. Topp CW, Østergaard SD, Søndergaard S, Bech P: The WHO-5 Well-Being Index: a systematic review of the literature. Psych and Psychosom 2015; 84(3):167-76.

34. Newnham EA, Hooke GR, Page AC: Monitoring treatment response and outcomes using the World Health Organization's Wellbeing Index in psychiatric care. J Aff Dis 2010; 30;122(1):133-8.

35. Gratz KL, Roemer L: Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the difficulties in emotion regulation scale. J Psychopath Beh Asses 2004; 26(1): 41-54.

36. Fowler JC, Charak R, Elhai JD, Allen JG, Frueh BC, Oldham, JM: Construct validity and factor structure of the Difficulties in Emotion Regulation Scale among adults with severe mental illness. J. Psychiatr. Res. 2014; *58*, 175-180.

37. Jacobson NS, Truax P: Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psych 1991; 59(1):12.

38. Foa EB, Zoellner LA, Feeny NC, Hembree EA, Alvarez-Conrad, J: Does imaginal exposure exacerbate PTSD symptoms? J Consul Clin Psychol 2002; 70(4), 1022.

39. Clapp JD, Kemp JJ, Cox KS, Tuerk P: Patterns of change in response to Prolonged Exposure: Implications for treatment outcome. Depression and Anxiety 2016*; 33,* 807-815.

40. Bollen KA, Curran PJ: Latent Curve Models: A Structural Equation Perspective. Hoboken, NJ: John Wiley & Sons 2006

41. Muthén LK, Muthén BO: Mplus User's Guide (6th ed.) Los Angeles, CA: Muthén & Muthén 1998-2010

42. Arbuckle JL: Full information estimation in the presence of incomplete data. In G. A. Marcoulides, & R. E. Schumacker (Eds.), Advanced structural equation modeling: Issues and techniques. Mahwah, NJ: Lawrence Erlbaum Associates, Inc. 1996.

43. Kline RB: Principals and practice of structural equation modeling (2nd ed). Guilford Press, New York. 2005

44. Bentler PM: Comparative fit indexes in structural models. Psychol Bul. 1990; 107(2):238-246.

45. Browne MW, Cudeck R: Alternative ways of assessing model fit. In: Bollen KA, Long JS, eds. Testing structural equation models. Sage Publications, Newbury Park, CA, 1993; 136-162.

46. Cohen J: *Statistical power analysis for the behavioral sciences (*2nd ed*.)*. Hillsdale, NJ: Lawrence Erlbaum Associates, Inc. 1988

47. Löwe B, Unützer J, Callahan CM, Perkins AJ, Kroenke K: Monitoring depression treatment outcomes with the patient health questionnaire-9. Med Care 2004*;* 42(12), 1194-1201.

48. Andrews G, Kemp A, Sunderland M, Von Korff M, Ustun TB, 2009. Normative data for the 12 item WHO Disability Assessment Schedule 2.0. PloS One; *4*(12): e8343.

49. Sibai AM, Chaaya M, Tohme RA, Mahfoud Z, Al-Amin H, 2009. Validation of the Arabic version of the 5-item WHO Well Being Index in elderly population. Int J Geriatr Psych; 24(1), 106-107.

50. Barley WD, Buie SE, Peterson EW, Hollingsworth AS, Griva M, HIckerson SC, Lawson JE, Bailey BJ: Development of an inpatient cognitive-behavioral treatment program for borderline personality disorder. J Personal Disord. 1993; 7:232–40.

51. Bohus M, Haaf B, Stiglmayr C, Pohl U, Bohme R, Linehan M: Evaluation of inpatient dialectical-behavioral therapy for borderline personality disorder—a prospective study. Behav Res Ther. 2000; 38:875–887.

52. Bartak A, Andrea H, Spreeuwenberg MD, Ziegler UM, Dekker J, Rossum BV, Hamers EF, Scholte W, Aerts J, Busschbach JJ, Verheul R, Stijnen T, Emmelkamp PM: Effectiveness of outpatient, day hospital, and inpatient psychotherapeutic treatment for patients with cluster B personality disorders. Psychother Psychosom 2011; 80: 28-38.

53. Lowyck B, Luyten P, Vermote R, Verhaest Y, Vansteelandt K. Self-critical perfectionism, dependency, and symptomatic distress in patients with personality disorder during hospitalization-based psychodynamic treatment: A parallel process growth modeling approach. Personality Disorders: Theory, Research, and Treatment. 2017;8(3):268.

54. Bohus M, Haaf B, Simms T, Limberger MF, Schmahl C, Unckel C, Lieb K, Linehan MM: Effectiveness of inpatient dialectical behavioral therapy for borderline personality disorder: a controlled trial. Behav Res Ther 2004; 42:487–99.

55. Berrino A, Ohlendorf P, Duriaux S, Burnand Y, Lorillard S, Andreoli A: Crisis intervention at the general hospital: an appropriate treatment choice for acutely suicidal borderline patients. Psych Res 2011; 186: 287-292.

56. Fowler JC, Clapp JD, Madan A, Allen JG, Oldham JM, Frueh BC. Emotion dysregulation as a cross-cutting target for inpatient psychiatric intervention. J. Affective Dis 2016; 206:224-31.

57. Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P: Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. Am J Psych 2010; 1;167(7):748-51.

58. Oldham JM: Guideline watch: Practice guideline for the treatment of patients with borderline personality disorder. Focus 2005; 3.3:396-400.

Table 1. Background characteristics for borderline personality disorder and matched reference patients with effect sizes for between-group comparisons[a]

	Reference	Borderline	ES
N	220	245	
Sex (% female)*	62.7	62.4	*.00*
Age*	32.7 (13.5)	28.5 (11.0)	*.34*
Prior Hospitalization (%)*	62.7	71.8	*.10*
LOA (weeks)*	5.9 (2.0)	5.7 (2.0)	*.10*
Race (% minority)	11.8	11.4	*.01*
Education (%)			*.14*
- High school or less	12.7	14.7	
- Some College/A.S./Tech	39.1	50.2	
- Bachelor's	55.0	20.8	
- Post-graduate	18.2	14.3	
Married (%)	21.4	15.5	*.07*
DERS	99.4 (28.3)	122.5 (20.4)	*.95*
ETOH/Substance Dx (%)	49.1	75.5	*.27*
Trauma History (%)	53.2	73.1	*.21*
PHQ-9			
- Intake	18.31 (5.52)	14.93 (7.49)	*.51*
- Discharge	7.82 (6.32)	5.96 (5.89)	*.30*
GAD-7			
- Intake	14.83 (5.10)	11.69 (6.11)	*.56*
- Discharge	7.27 (5.65)	5.23 (4.77)	*.39*
WHODAS			
- Intake	19.79 (8.97)	15.61 (9.15)	*.46*
- Discharge	8.51 (7.67)	6.40 (6.70)	*.29*
WHO-5			
- Intake	6.12 (4.09)	7.91 (5.78)	*.36*
- Discharge	13.77 (5.36)	15.11 (5.77)	*.24*
C-SSRS (severity past mo)			
- Intake	11.62 (6.86)	8.02 (7.97)	*.49*
- Discharge	2.87 (5.43)	1.76 (4.65)	*.22*

Note: LOA = Length of Admission; DERS = Difficulties in Emotion Regulation Scale; PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder 7-Item Scale; WHODAS = WHO Disability Assessment Schedule 2.0; WHO-5 = WHO Well-Being Index; C-SSRS = Columbia Suicide Severity Rating Scale – Ideation severity over the previous month

* Indicates characteristics included in the propensity score matching (PSM) procedure

[a] Effects sizes (ES) are given as ϕ (small = .10, medium = .30, large = .50) and *g* (small = .20, medium = .50, large = .80) for categorical and continuous variables, respectively

Table 2. Change scores (*M*, *SD*), effect sizes, and interval estimates for improvements in borderline personality disorder and matched reference groups from intake to discharge

	Δ	**95% CI**	***t***	***d*[a]**	**95% CI**
PHQ-9					
- Reference	8.20 (7.11)	[7.23, 9.16]	16.713	1.15	[0.98, 1.33]
- Borderline	10.16 (7.09)	[9.26, 11.06]	22.25	1.43	[1.25, 1.61]
GAD-7					
- Reference	6.43 (6.12)	[5.53, 7.33]	14.10	1.05	[0.87, 1.23]
- Borderline	7.62 (6.43)	[6.76, 8.47]	17.53	1.18	[1.01, 1.36]
WHODAS					
- Reference	9.17 (8.36)	[8.05, 10.29]	16.12	1.10	[0.93, 1.27]
- Borderline	11.36 (9.74)	[10.13, 12.58]	18.26	1.17	[1.00, 1.33]
WHO-5					
- Reference	7.41 (6.48)	[6.46, 8.36]	15.39	1.14	[0.96, 1.33]
- Borderline	7.79 (5.48)	[7.06, 8.52]	21.04	1.42	[1.23, 1.61]
C-SSRS (severity past mo)					
- Reference	6.05 (7.48)	[5.04, 7.05]	11.87	0.81	[0.65, 0.96]
- Borderline	8.65 (7.24)	[7.73, 9.57]	18.54	1.19	[1.03, 1.36]

Note: PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder 7-Item Scale; WHODAS = WHO Disability Assessment Schedule 2.0; WHO-5 = WHO Well-Being Index; C-SSRS = Columbia Suicide Severity Rating Scale – Ideation severity over the previous month

[a] Effects sizes for within-subject tests (small = .20, medium = .50, large = .80) standardized using the standard deviation of change from intake to discharge to permit calculation of corresponding interval estimates.

Table 3. Patient percentages and between-group effects for clinically significant change,[a] reliable change, and symptom exacerbation

	Reference	Borderline	ϕ[b]
PHQ-9			
- Clinically Sig Change	62.9	63.5	.006
- Reliable Change	40.0	70.5	.307
- Exacerbation	0.4	0.0	-
GAD-7			
- Clinically Sig Change	67.6	63.5	.043
- Reliable Change	43.8	58.9	.151
- Exacerbation	0.9	0.9	-
WHO-DAS			
- Clinically Sig Change	69.4	62.9	.069
- Reliable Change	51.4	59.2	.078
- Exacerbation	0.9	1.1	-
WHO-5			
- Clinically Sig Change	78.1	79.6	.018
- Reliable Change	57.1	75.4	.194
- Exacerbation	0.9	1.1	-
C-SSRS (severity past mo)			
- Reliable Change (w/pre-ideation)	59.8	70.0	.108
- Exacerbation	0.0	0.4	-

Note: PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder 7-Item Scale; WHODAS = WHO Disability Assessment Schedule 2.0; WHO-5 = WHO Well-Being Index; C-SSRS = Columbia Suicide Severity Rating Scale – Ideation severity over the previous month; reliable change in severity of suicidal ideation restricted to the subset of reference (25.0%) and borderline (40.4%) patients acknowledging ideation at intake

[a] Criteria for clinically significant change in reference patients were scores at or below 6.0, 6.0, and 7.0 on the PHQ-9, GAD-7, and WHO-DAS, and 11.0 or above for the WHO-5; criteria for PBD patients were scores at or below 8.0, 7.0, and 9.0 on the PHQ-9, GAD-7, and WHO-DAS, and 10.0 or above for the WHO-5; clinically significant change for C-SSRS was not calculated given the absence of non-clinical scores for this measure

[b] Small: $\phi = .10$, Medium: $\phi = .30$, Large: $\phi = .50$

Supplemental Table 1. Parameter estimates for latent growth model of change in PHQ-9 depression

	Intercept (B_0 = 16.864, p < .001)			Slope (B_1 = -3.321, p < .001)			Quadratic (B_2 = .265, p < .001)		
	β	**b**	***se***	**β**	**b**	***se***	**β**	**b**	***se***
LOS	-.020	**-.016**	*.039*	.402	**.058**	*.025*	-.414	**-.007**	*.004*
BPD[b]	.051	.057	*.065*	.005	.002	*.036*	.010	.000	*.005*
SUD[b]	-.126	**-.144**	*.057*	.018	.007	*.037*	-.062	-.003	*.005*
Trauma[b]	.114	**-.131**	*.056*	-.052	-.002	*.033*	.062	-.003	*.005*
DERS[c]	.601	**.247**	*.023*	-.148	-.011	*.014*	.005	.000	*.002*
BPD x SUD	.010	.002	*.011*	.038	.003	*.007*	-.031	.000	*.001*
BPD x Trauma	-.011	-.003	*.012*	.040	.003	*.007*	-.060	-.001	*.001*
BPD x DERS	-.128	**-.011**	*.004*	.131	.002	*.003*	-.117	.000	*.000*

Note: PHQ-9 = Patient Health Questionnaire; LOS = length of admission; BPD = borderline personality disorder (0 = no, 1 = yes); SUD = substance/alcohol use disorder (0 = no, 1 = yes); Trauma = history of interpersonal trauma (0 = no, 1 = yes); DERS = Difficulties in Emotion Regulation Scale.

[a] Bolded figures $p \leq .05$; Bolded/underlined figures $p \leq .01$

[b] Dichotomous indicators for borderline personality diagnosis, alcohol/substance use diagnosis, and history of interpersonal trauma were rescaled by multiplication of a constant (x10) to optimize analysis of the covariance matrix

[c] LOA and DERS scores were rescaled by division of constant (/2)to optimize analysis of the covariance matrix

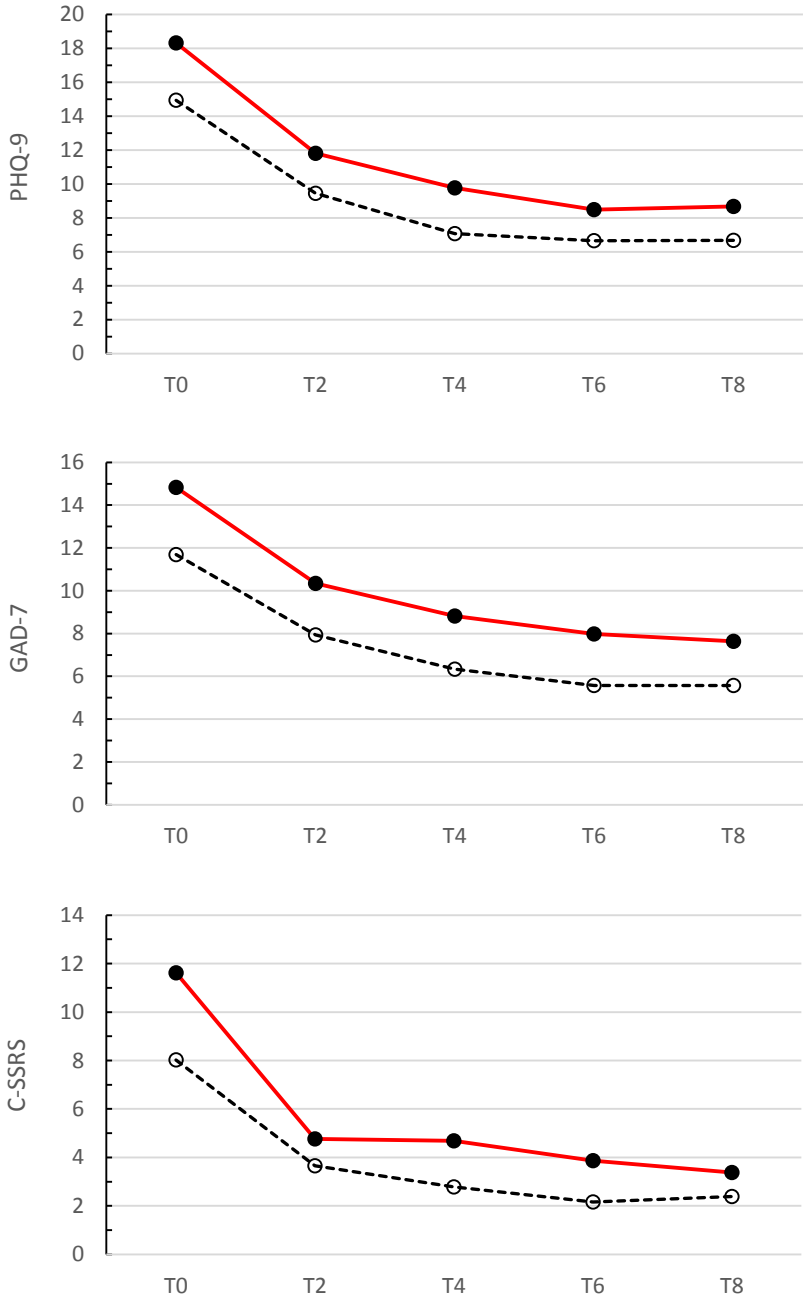


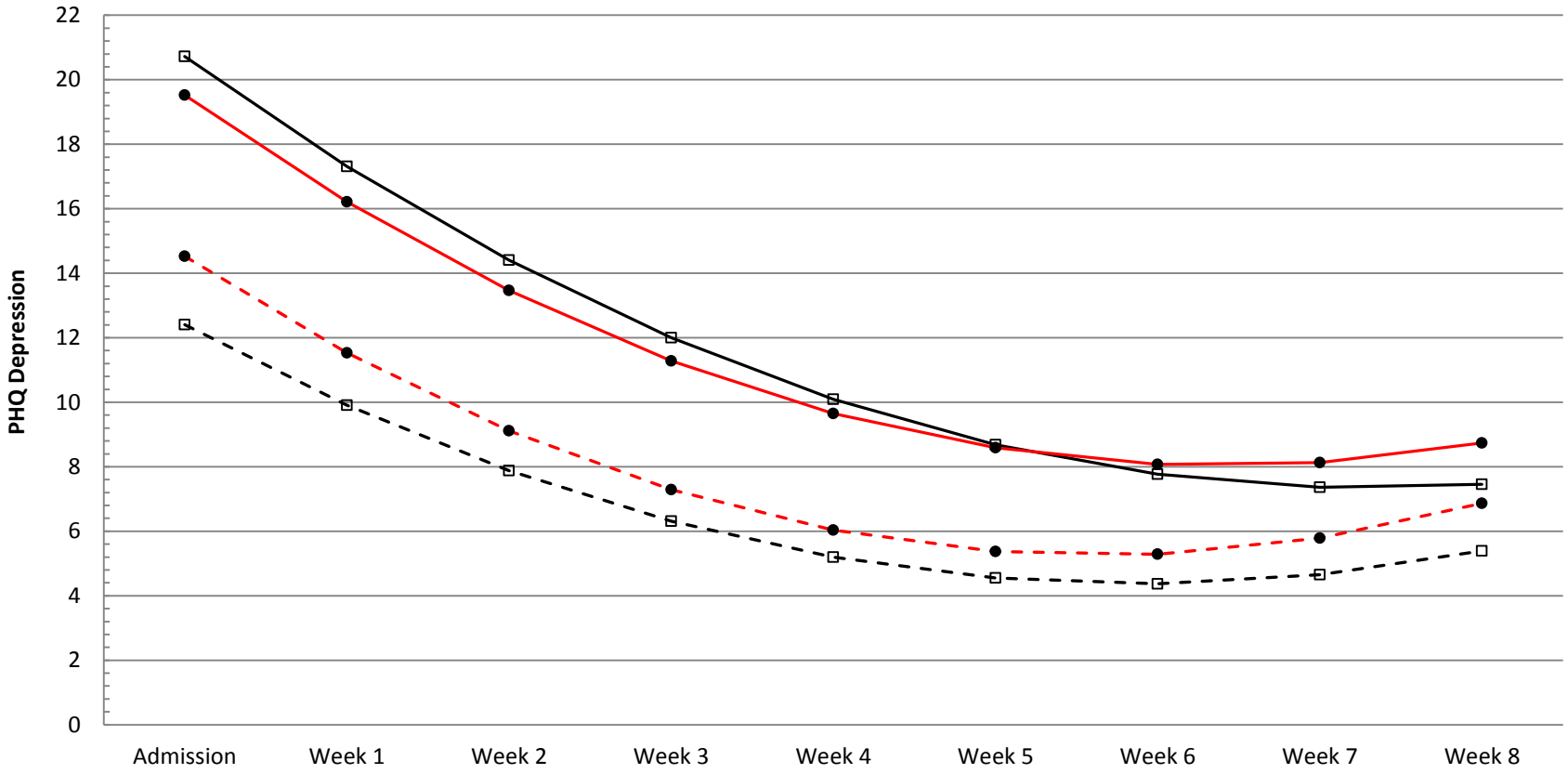
Figure 1. Observed scores for reference and borderline personality disorder patients.

Borderline

Reference

Note: PHQ-9 = Patient Health Questionnaire; GAD-7 = Generalized Anxiety Disorder 7-Item Scale; WHODAS = WHO Disability Assessment Schedule 2.0; WHO-5 = WHO Well-Being Index; C-SSRS = Columbia Suicide Severity Rating Scale – Ideation severity over the previous month

Figure 2. Interaction of emotion regulation and borderline diagnosis on the intercept of expected recovery trajectory



□ - - - - - - □ Reference-Low DERS (-1 *SD*) = 12.405-2.725(*week*) + .231($week^2$)

□ ——— □ Reference-High DERS (+1 *SD*)= 20.721-3.658(*week*) + .250($week^2$)

● - - - - - - ● Borderline-Low DERS (-1 *SD*) = 14.525-3.286(*week*) + .291($week^2$)

● ——— ● Borderline -High DERS (+1 *SD*) = 19.525-3.588(*week*) + .280($week^2$)