# Buprenorphine and Interpersonal Dysregulation in Borderline Personality Disorder

## A Mechanistic, Stratified Observational Pilot

## Background

Borderline Personality Disorder (BPD) is characterized by severe interpersonal instability, affective reactivity, and elevated suicide risk. While psychotherapy remains the cornerstone of treatment, there are currently no pharmacologic interventions approved specifically for BPD, and existing medications have limited impact on core interpersonal pathology.

Low-dose buprenorphine has demonstrated rapid clinical effects in adjacent domains, including reductions in severe suicidal ideation and benefit as an adjunct in treatment-resistant depression, particularly in opioid-naïve populations. In at least one randomized trial of ultra-low-dose buprenorphine for suicidality, participants with BPD features showed a notably strong response relative to placebo, though this signal was not pursued as a primary outcome.

Buprenorphine is most commonly prescribed for opioid use disorder (OUD), a population with substantial overlap with BPD. Emotional and interpersonal changes observed during OUD treatment are typically attributed to stabilization of substance use, complicating interpretation of whether buprenorphine may exert effects on underlying affective or interpersonal vulnerability.

Separately, buprenorphine is prescribed in non-addiction contexts, including chronic pain and, in select cases, severe suicidality or treatment-resistant depression. Case-level evidence, including a published report of buprenorphine/naloxone use in an opioid-naïve individual with BPD, suggests potential benefit beyond acute crisis suppression alone.

Despite these converging observations, buprenorphine’s effects have been studied primarily in the context of suicidality, depression, pain, or addiction. Its potential impact on interpersonal dysregulation, often considered a core and defining feature of BPD, has not been directly examined.

## Mechanistic Rationale

Attachment-related distress and sensitivity to interpersonal threat are closely linked to endogenous opioid signaling, particularly at the μ-opioid receptor. Traditional opioids activate both μ and κ receptors: while μ-opioid activation may attenuate attachment distress, κ-opioid activation is associated with dysphoria, dissociation, and stress-related negative affect.

Buprenorphine's pharmacologic profile, partial agonism at the μ-opioid receptor combined with κ-opioid antagonism, suggests a potential capacity to reduce attachment-related distress and interpersonal threat sensitivity while avoiding κ-mediated dysphoria. This profile may be particularly relevant to the interpersonal instability characteristic of BPD.

Importantly, the timing, magnitude, and dose required for these effects may be moderated by prior opioid exposure. Opioid-naïve individuals may experience effects at lower, steady doses, whereas opioid-exposed or opioid-tolerant individuals may require higher doses to achieve comparable μ-opioid engagement.

## Study Objective

To characterize changes in interpersonal dysregulation following initiation of buprenorphine and to examine whether the timing, magnitude, and dose associated with these changes are moderated by prior opioid exposure.

## Design

Prospective, observational, stratified cohort study of adults initiating buprenorphine as part of routine clinical care (e.g., opioid use disorder, chronic pain, or adjunctive treatment for severe suicidal ideation or treatment-resistant depression).

- No randomization or alteration of clinical care
- Buprenorphine prescribed independently of study participation
- Stratification by opioid exposure history and baseline interpersonal dysregulation

## Primary Outcome

Interpersonal dysregulation, assessed using a two-tier approach:

- **Early phase:** brief, repeated state-level self-report items capturing attachment threat sensitivity, perceived rejection or abandonment, interpersonal distress, and recovery following interpersonal stressors
- **Weekly:** a validated interpersonal functioning scale to assess broader patterns over time

## Secondary Outcomes

- **Affective instability:** Borderline Symptom List (BSL-23)
- **Suicidal ideation:** Beck Scale for Suicide Ideation or Columbia-Suicide Severity Rating Scale
- **Depression and anxiety symptoms:** brief validated self-report measures
- **Functioning / quality of life:** brief validated functional outcome measure

## Timing

- Baseline within 24 hours prior to initiation
- Early follow-up at 24 hours and 72 hours post-initiation
- Short-term follow-up at 1 week, 2 weeks, and 4 weeks
- Durability assessment at 8 or 12 weeks (feasibility-dependent)

Same-day post-dose assessments are exploratory and formulation-dependent; primary analyses emphasize 24-hour and later timepoints.

## Significance

This observational pilot addresses a clinically meaningful gap by examining interpersonal dysregulation as a primary outcome and prior opioid exposure as a moderating variable. By focusing on temporal dynamics and dose–response patterns rather than diagnostic-level efficacy, the study aims to clarify heterogeneous clinical observations and inform rational patient selection, risk stratification, and the design of future observational or controlled studies.