Demographic and clinical characteristics of patients with borderline personality disorder: Real-world insights from a retrospective observational study

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Abstract

Background: Current treatment modalities demonstrate variable effectiveness across patients with borderline personality disorder (BPD). Here, we describe the presenting clinical characteristics of patients with BPD based on approximately 20 years of real-world data.

Methods: This retrospective, observational study was based on de-identified MindLinc electronic health records of individuals (aged ≥12 years with ≥1 diagnosis of BPD) receiving mental healthcare between 1999 and 2020 across 15 US states using the NeuroBlu database (vRel21R2). Demographic and clinical characteristics at first recorded BPD diagnosis (index date), baseline (index date ± 14 days), and in the 12 months prior to diagnosis were described. BPD symptoms were derived by natural language processing (NLP) of unstructured clinician-documented mental state examination (MSE) data.

Results: Across the 13,444 patients analysed at baseline (mean [SD] age 33 [12.8] years; 83.6% female; 97.5% with psychiatric comorbidities), the most frequent comorbid psychiatric conditions were major depressive disorder (45.7%), substance use disorder (34.6%) and post-traumatic stress disorder (29.2%). Emotional dysregulation (35.8%) and suicidal intent/ideation (31.3%) were the most frequent NLP-derived BPD symptoms. Emotional dysregulation was more common in older patients, whereas suicidal intent/ideation/attempt/self-injury were more prevalent in younger patients. Mean (SD) length of hospitalisation was 2.9 (4.2) days, with 46.5% of patients requiring ≥1 psychiatric hospitalisation. At diagnosis, 67.7% of patients were prescribed pharmacological treatment, including antidepressants (51.1%), second-generation antipsychotics (34.0%) and anticonvulsants (33.7%).

Conclusion: BPD symptoms varied according to patient characteristics, including age and gender. These insights may enable patient-specific treatment planning in the future and improve therapeutic outcomes.

Keywords: Borderline personality disorder, emotional dysregulation, patient characteristics, psychiatric comorbidities, real-world

Introduction

Borderline personality disorder (BPD) is a serious psychiatric disorder characterised by a pervasive pattern of emotional dysregulation and instability in relationships and identity (APA, 2013). Patients also often experience marked impulsivity, in addition to fear of abandonment, intense anger and suicidal thoughts/behaviours (APA, 2013). In the US, the estimated lifetime prevalence of BPD is 1.4–2.7% (APA, 2023). Typically, BPD manifests in adolescence with predominant symptoms of emotional dysregulation and impulsivity, and develops further in early adulthood with maladaptive interpersonal functioning and enduring functional impairment (Videler et al., 2019). Furthering the complex symptomatology of BPD among the patient population is the frequent presentation of comorbid mental health disorders, such as mood disorders (82.7%), anxiety disorders (84.8%), substance use disorders (SUD) (78.2%) and eating disorders (33.1%) (Barnow et al., 2007; Tomko et al., 2014).

Interestingly, gender-related differences have been observed in BPD, with diagnosis predominantly in females and gender-specific variation displayed in symptom expression and comorbidity (APA, 2013; Barnow et al., 2007; Grant et al., 2008; Herpertz et al., 2017; Johnson et al., 2003; Zlotnick et al., 2002). While females show an increased prevalence of comorbid mood disorders, eating disorders, and post-traumatic stress disorder (PTSD), males have a higher prevalence of comorbid SUD and antisocial personality disorder, along with symptoms related to aggression, anger and impulsivity (Barnow et al., 2007; Grant et al., 2008; Herpertz et al., 2017; Johnson et al., 2003; Zlotnick et al., 2002).

There are currently no approved pharmacological treatments for BPD. Instead, psychotherapy is considered the first-line treatment option, but is limited by significant costs, availability of specialist clinicians, and the need for high levels of patient commitment (Hastrup et al., 2019; McMain et al., 2022; Paris, 2015; Stoffers-Winterling et al., 2022). Despite this, pharmacological treatment is common in patients with BPD due to off-label use and the prescribing of medications for comorbid mental health conditions, such as selective serotonin reuptake inhibitors, mood stabilisers, second-generation antipsychotics and benzodiazepines (APA, 2023; Pascual et al., 2023; Stoffers-Winterling et al., 2022). However, evidence is inconsistent for the efficacy of these medications in reducing the severity of BPD (Gartlehner et al., 2021).

BPD is associated with substantial personal and economic burden on patients and their families. According to a Danish study, the total average annual costs for healthcare and lost productivity are 16-fold higher than for individuals without BPD (Hastrup et al., 2019). The burden of BPD is largely

attributable to its complex symptomatology, which creates diagnostic and therapeutic challenges. Accordingly, diagnosis of BPD requires comprehensive evaluation of patient history and presentation, and many diagnosable cases of BPD are missed in routine clinical practice (Tedesco et al., 2024; Zimmerman and Mattia, 1999).

The multifaceted nature of BPD in terms of its clinical characteristics, comorbidities, and potential subtypes contributes to individual variations in the effectiveness of pharmacological treatments. However, limited data from large observational studies are available that describe BPD symptoms and treatment responses. Through the use of real-world observational data, this study aimed to explore the characteristics, symptoms and treatment patterns of patients with BPD within a large US dataset. Here, we describe the clinical and demographic characteristics of US patients with BPD in the 12 months prior to, and at the time of, first diagnosis based on approximately 20 years of real-world observational data that include mental state examination (MSE) data. It was hypothesised that the study population would be typical of patients with BPD: female to male ratio of approximately 3:1, first presentation during early adulthood (APA, 2013) and frequent occurrence of comorbid psychiatric disorders, in particular anxiety disorder, major depressive disorder (MDD), PTSD and SUD (Shah and Zanarini, 2018). By gaining a deeper understanding of the clinical and demographic characteristics of patients at the time of diagnosis, both the design of clinical trials evaluating new treatments and patient care could be improved.

Methods

Data source

This retrospective, observational study utilised de-identified electronic health record (EHR) data from US mental healthcare providers operating the MindLinc EHR system contained within the NeuroBlu database (version Rel21R2) (Patel et al., 2022).

Study design and setting

Data between 1999 and 2020 were assessed. The index date was defined as the first date of BPD diagnosis (International Classification of Diseases [ICD]-9: 301.83/ICD-10: F60.3) recorded in the database. Due to variations in the frequency and/or timing of patient visits, a 14-day window on either side of the index date (baseline period) was applied to capture demographic and clinical characteristics. Data were collected at the time of diagnosis and for the 12 months preceding diagnosis. EHR data were analysed from individuals receiving mental healthcare from outpatient, inpatient (including emergency room [ER] visit) and residential care facilities across 15 states in the

US. Data extracted from the EHR database comprised structured patient-level data, including demographic information (e.g. age) and quantitatively measured clinical variables (e.g. Clinical Global Impression – Severity [CGI-S] score) (Patel et al., 2022), and unstructured free text, including a semi structured 'status assessment' field in which clinicians could document features associated with a patient's MSE. The status assessment field allowed clinicians to choose predefined features from a list of options. However, because predefined features do not adequately capture the complexity and variability of MSE between different individuals, clinicians could also document features using the aforementioned unstructured free text. This unstructured free text was then transformed into structured, quantifiable data using natural language processing (NLP) (Mukherjee et al., 2020), including social stressor data that are not commonly available in real-world datasets.

The full details of the NLP pipeline extraction methods and accuracy statistics have been previously published (Mukherjee et al., 2020). The original 69 categories from the clinical status assessment in the MindLinc EHR are reclassified into 27 standardised categories by a subject matter expert (Mukherjee et al., 2020). Within each category, the most common sentences in the free text are subcategorised into factors (Mukherjee et al., 2020). An optimiser trains the NLP model in an iterative process to learn these classifications and predict new classifications which are validated by the subject matter expert (Mukherjee et al., 2020). For this study, the raw MSE data for each patient are "cleaned" and passed through the NLP model. This model identifies certain text strings which may reflect a particular MSE feature and extracts this information. The final output is a data table for each patient, which represents whether a given MSE feature is present or absent within their EHR. For the long short-term memory-based NLP model, Mukherjee et al. reported a median area under the receiver operating characteristics (AUROC) curve of approximately 0.9 for the 241 individual MSE features (or symptoms) in the NeuroBlu dataset (Mukherjee et al., 2020). The current study identified 18 of these MSE features as reflective of key symptoms of BPD (**Supplementary Table 1**).

Participants

Data were analysed for patients who met the prespecified inclusion criteria of at least one diagnosis of BPD (ICD-9: 301.83/ICD-10: F60.3) recorded between 2001 and 2020, and age ≥12 years at the time of first recorded diagnosis. The requirement for only one recorded diagnosis of BPD was based on the relative underdiagnosis of BPD in clinical practice, thus providing a larger and therefore better-powered sample size. No exclusion criteria were defined for this analysis.

Ethical considerations

This study was conducted in accordance with the 1964 Declaration of Helsinki and its subsequent amendments (October 2013). A waiver of HIPAA authorisation was obtained prior to study conduct and covers data originating from all sites represented. Approval was granted by the Western-Copernicus Group (WCG) Institutional Review Board (The Holmusk Real-World Evidence Parent Protocol; IRB registration number 1-1470336-1; Protocol ID HolmuskRWE_1.0).

Variables

The variables analysed were baseline demographic and clinical characteristics, including illness severity (CGI-S) and psychiatric comorbidities, and in the 12 months prior to diagnosis. Clinically relevant symptoms indicative of BPD, as derived by NLP of clinician-documented information in the MSE fields of clinical notes, were also assessed for the overall population and by age subgroup. Additional endpoints included psychiatric hospitalisation (days) in the 12 months before and after diagnosis (calculated by hospital inpatient episode end date minus hospital inpatient episode start date + 1 day), and pharmacological treatment for the 12 months prior to baseline and at baseline. For patients who did not receive pharmacological treatment at baseline, time to first treatment was analysed. For subgroup analysis, patients were categorised by age as 12–17 / 18–25 / 26–35 / 36–45 / 46–55 / 56–65 / >65 years.

Bias

Since data from real-world clinical practice are not recorded in a uniformly structured manner, the missing data may introduce a selection bias if certain types of patients are more likely to have missing data. In the case of mental healthcare, patients who are more unwell may have increased contact with mental healthcare services and therefore have more data recorded and are more likely to meet inclusion criteria for entry into the study cohort. Conversely, patients who are more unwell may disengage from services and therefore have more missing data. Potential sources of bias were addressed where feasible. Data interpretation was conducted with input from clinical experts with experience in EHR data analytics to identify where results could be biased by confounding or other artefactual findings. The term ‘gender’ was subject to the interpretation of the reporting clinician.

Statistical analysis

Data were reported as descriptive statistics from a cross-sectional analysis of baseline clinical and demographic variables, with continuous variables summarised by mean (standard deviation; SD) or median (interquartile range; IQR). Categorical and ordinal variables were summarised by frequency

and percentage. Between-group comparisons were performed to compare demographic and clinical characteristics between subgroups. Chi-square analysis or Mann-Whitney U tests were used to compare distributions between categorical subgroups. A significance level of 0.05 was used for all analyses.

Results

Participants

Of the 13,788 patients in the database with a diagnosis of BPD, 13,444 patients met the inclusion criteria for the study (**Supplementary Figure 1**).

Patient characteristics

Mean (SD) age at the index date was 33 (12.8) years, 83.6% of patients were female and the majority of patients (59.1%) were white (**Table 1**). Over half of patients were aged 18–35 years; 3591 (26.7%) in the 18–25-year category and 3654 (27.2%) in the 26–35-year category. BPD diagnosis was most commonly made in an outpatient setting (n=9650; 71.8%). The mean (SD) CGI-S score was 4.6 (1.1), with the majority of patients (n=9064; 67.4%) having CGI-S scores of 4–5, reflecting moderate to marked illness. Nearly all patients (97.5%) had ≥1 psychiatric comorbidity at baseline (index date ± 14 days). MDD was the most common comorbidity both in the 12 months prior to baseline (42.7%) and at baseline (45.7%) (**Table 2 and Supplementary Table 2**). Other common comorbidities included anxiety disorders, SUD and PTSD.

Emotional dysregulation (characterised by symptom labels identified by NLP: affect - aggressive, affect - irritable/angry, affect - labile, affect - intense, mood - irritable/angry, mood - labile) was the most frequently reported symptom of BPD at baseline (35.8% of patients, n=4370), followed by suicidal intent/ideation (31.3%, n=3819) (**Table 3**). Suicidal attempt/self-injury was reported in 14.0% of patients (n=1706) and impulsivity in 0.3% of patients (n=42). A high proportion of all 13,444 patients had a history of negative family (50.7%) and social (26.7%) stressors. Negative family stress was mainly attributed to physical (13.7%), sexual (10.8%) and emotional (7.1%) abuse or isolation (12.5%) and separation (13.6%). In addition, there was a high occurrence of poverty (21.1%), unemployment (18.6%) and victims of crime (17.0%) among patients with a BPD diagnosis.

BPD symptoms by age group

When BPD symptoms at baseline were analysed by age, emotional dysregulation was more pronounced in patients aged ≥46 years (39.0–39.9%) than those aged 12–45 years (34.0–36.0%), with significant differences across all age categories ($p<0.05$) (**Table 3**). Significant differences

between age group categories were also found in irritable/angry and labile affect and irritable/angry mood (all $p<0.05$). A greater proportion of patients with suicidal intent/ideation was observed among the 12–25 year age group (33.9–37.6%) compared with those aged ≥26 years (28.6–30.2%), with a similar trend being observed for suicidal attempt/self-injury (17.4–18.5% for the 12–25 year group and 7.1–13.3% for those aged ≥26 years); the differences across age categories for both these parameters were statistically significant ($p<0.05$). Patients aged 56–65 years had the lowest tendency for suicidal intent/ideation (28.6%), whereas patients aged >65 years had the lowest tendency for suicidal attempt/self-injury (7.1%).

Hospitalisation

Approximately half of patients (46.5%) had been hospitalised at least once in the 12 months prior to diagnosis (**Table 4)**. In patients with ≥1 psychiatric hospitalisation in the 12 months prior to diagnosis, mean (SD) length of stay was 2.9 (4.2) days. An increase in hospitalisations was observed in the 12 months following diagnosis; among patients with ≥1 psychiatric hospitalisation, the proportion with >3 psychiatric hospitalisations increased from 3.6% at baseline to 11.5% at 12 months post diagnosis.

Treatment patterns

Figure 1 shows pharmacological treatment during the baseline period categorised under prespecified treatment groups. In the overall population, 9101 (67.7%) patients were prescribed pharmacological treatment during the baseline period. For the 4343 (32.3%) patients with no pharmacological treatment during baseline, mean (SD) time to first treatment was 211 (439) days (median [IQR] 57 [149] days). In both the 12 months prior to and including baseline and at baseline alone, the most common medication classes prescribed were antidepressants, second-generation antipsychotics and anticonvulsants (**Figure 1**). The proportion of patients that received treatment in the 12 months prior to and including baseline (79.5%) was higher than at baseline alone (67.7%).

Discussion

This retrospective, observational study analysed the demographic and clinical characteristics of a large cohort of patients with BPD in the US to better understand the disorder and gain real-world insights that may help inform future study designs and improve patient care.

At 33 years, the mean age of patients at baseline (index date ± 14 days) is slightly older than reports in the wider literature, where BPD symptoms have been described to develop throughout adolescence and typically “peak” during late adolescence or early adulthood. This suggests that

there may be a long interval between onset and diagnosis of BPD (Bohus et al., 2021; Videler et al., 2019). While 18.9% of patients in the dataset were diagnosed after age 45, it is unclear if these were first-time diagnoses. It should also be considered that younger individuals with BPD may be underrepresented in the study population. Although diagnostic criteria for BPD are consistent across age groups, current clinical guidelines, such as those from the National Institute for Health and Care Excellence, recommend caution in formally diagnosing individuals age <18 years due to its stigma and limited temporal stability (Garland and Miller, 2020). Given that the data assessed in this study span 20 years, earlier BPD diagnoses may not have been captured, including initial diagnoses in other healthcare settings where EHR data were not captured. Nonetheless, the finding does align with the update from ICD-10 to ICD-11 which implies that personality disorders are not necessarily stable after adolescence and may onset later in life (Bach and First, 2018; Jo et al., 2023). This has led to the description of late-onset personality disorders which may be triggered by a significant life event such as illness, the death of a spouse or transition to a nursing home (Rosowsky et al., 2019).

Previous studies have shown personality disorders, particularly BPD, to have low diagnostic stability compared with other psychiatric disorders (Baca-Garcia et al., 2007; d'Huart et al., 2023). This exemplifies limitations of the categorical model of personality disorders, which has persisted in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) and in the ICD until the ICD-11, which introduced a dimensional classification model (d'Huart et al., 2023; Garland and Miller, 2020). BPD, like many DSM-5 disorders, is diagnosed using a polythetic approach. This means that while multiple diagnostic criteria are listed, not all are required for a diagnosis. Specifically, a diagnosis of BPD requires the presence of 5 out of 9 possible criteria, resulting in 151 different potential ways to make the diagnosis (APA, 2013). Consequently, the high degree of variability in the clinical presentation of BPD, as seen in other DSM-5 disorders, may lead to diagnostic variability among clinicians and create barriers to diagnosis and treatment.

However, the patient population in this study generally reflects what is seen in the existing literature, suggesting that the dataset captures a representative sample of patients with BPD. Consistent with previous studies, we found that most patients with BPD were female, received a diagnosis in early adulthood, presented with a moderate illness severity, had a high level of psychiatric comorbidity and were frequently prescribed pharmacological treatments. The predominance of female patients in this study can be attributed to several factors including a diagnostic bias amongst clinicians (Adler et al., 1990; Özel et al., 2024), the likelihood of females to seek treatment for mental disorders, or the diagnostic criteria employed (O'Brien et al., 2005; Smith et al., 2018; Tedstone-Doherty and Kartalova-O'Doherty, 2010). Indeed, the DSM-5 criteria contain

more items based on internalising symptoms than externalising symptoms, and females are more likely to present internalising symptoms (e.g., emotional instability), whereas males are more likely to present externalising symptoms (e.g., aggressiveness) (APA, 2013) (Qian et al., 2022). Males are also less likely than females to seek help and are unlikely to fully disclose all the symptoms they are experiencing (Courtenay, 2000), often due to socialisation and fear of stigma.

The general conceptualisation of BPD as a diagnostic entity is a common point of contention in research, owing to its debated reliability and validity. Existing research has highlighted disparities between the diagnostic rating of personality disorders by general practitioners (GPs) and standardised assessment in research, with GPs more likely to diagnose personality disorders for individuals perceived as less compliant or stressful to manage (Moran et al., 2001). This diagnostic bias has been suggested to extend beyond individual behaviour to personal identities, with sexual or gender minorities disproportionately overrepresented in the BPD patient population due to the overpathologising of these individuals with psychiatric disorders (Denning et al., 2022).

BPD was most commonly diagnosed in an outpatient setting in the dataset analysed, which contrasts with previous reports that have shown higher prevalence in an inpatient setting (Tomko et al., 2014). Over two-thirds of patients (67.4%) had moderate to marked illness at baseline, as defined by CGI-S scores of 4–5. Almost all patients in the present study had ≥1 psychiatric comorbidity, most commonly MDD, which agrees with the high rates of comorbid mood disorders (82.7%) that have been previously observed in patients with BPD (Tomko et al., 2014). The proportion of patients with anxiety disorders was lower than that seen in other studies (e.g., 27.6% of patients in this study vs 84.8% of patients in others) (Tomko et al., 2014). This discrepancy may be due to different categorisations of groups of disorders (e.g. anxiety disorder vs generalised anxiety disorder), or because BPD symptoms overlap with other psychiatric conditions, making it difficult to distinguish distinct disorders and identify comorbidities. Alternatively, due to the time-consuming nature of diagnostic interviews, it is possible that clinicians did not conduct extensive investigations at the time of BPD diagnosis, particularly when patients were experiencing a high degree of illness severity. Additionally, variation in the frequency of observed comorbidities may reflect differences in the timing of psychiatric comorbidity recording (lifetime vs at diagnosis) (Chapman et al., 2023).

In patients with MSE-derived symptoms indicative of BPD at baseline, the most frequently reported symptom was emotional dysregulation (35.8%; characterised by aggression, anger, irritability, intensity, lability), followed by suicidal intent/ideation (31.3%) and suicidal attempt/self-injury (14.0%). Impulsivity was notably low (0.3%). However, one possible explanation for this is that suicidal symptoms are a high priority for treatment, thus assessment of other symptoms, such as

impulsivity, may have been overshadowed and less likely documented by clinicians during the MSE. Further, since the MSE provides a description of the current clinical presentation of the patient, symptoms such as impulsivity that need to be observed over a longer clinical history may not have been captured. Future studies assessing impulsivity in EHR data may consider other locations within the clinical record, such as the subjective, assessment and plan portions of clinical notes.

Results of subgroup analysis indicated variation in BPD symptoms according to age. For example, emotional dysregulation was more common in older age groups: 39.7% in patients aged >65 years and 39.9% in those aged 56–65 years, compared with 34.0% in those aged 26–35 years. However, these findings contrast with observations in a smaller cross-sectional analysis of 93 patients, in which similar levels of emotional dysregulation were reported in younger and older patients ($p>0.05$) on various indicators of emotional dysregulation, including avoidance of abandonment, unstable relationship, identity disturbances and impulsiveness, among others (Martino et al., 2020). Another study, which examined 1477 patients aged 15–82, showed a decline in emotional turmoil with increasing age, although the rate and pattern of decline across patients was asymmetrical (Gutiérrez et al., 2012). The increase in emotional dysregulation symptoms (aggression, anger, irritability, intensity, lability) with age observed in our analysis could represent effect modification between BPD and other comorbidities. This potential interplay is supported by previous studies, which have proposed BPD as a clinical manifestation of the psychopathology underpinning other mental health conditions, such as MDD (Eaton et al., 2011; Gunderson et al., 2004). Alternatively, our observation of frequent emotional dysregulation in older patients with BPD may be attributable to greater symptom persistence across the treatment journey relative to symptoms such as impulsivity, as demonstrated in a 6-year longitudinal study (Zanarini et al., 2003). Younger patients with BPD have been shown to have a high risk of suicide (Paris, 2019; Pompili et al., 2005), while older patients were less likely to report suicidal/self-harm behaviour (Martino et al., 2020). These previous results align with our findings, where suicidal intent/ideation was most common in 12–17-year-olds and least common in 55–65-year-olds. Similarly, suicidal attempt/self-injury was highest in 12–17-year-olds and lowest in patients >65 years old. Overall, these data highlight the need for an age-reflective management strategy for this high-risk population.

In the 12 months prior to diagnosis, 6251 patients had at least one psychiatric hospital stay, with a mean duration of 2.9 days. This length of stay contrasts with other research reporting an average of 16.5 days (Paruk and Janse van Rensburg, 2016) in a small study of young females. The short length of stay identified in the current study may be indicative of a high rate of ER visits experienced by patients with BPD. Our results also showed that the number of hospital visits per patient increased

over the analysis period, suggesting that the burden of BPD on healthcare systems may increase over time.

Interestingly, the patients that received pharmacological treatment generally had more BPD symptoms at baseline than those without treatment. This might reflect clinician prescribing decisions, whereby more BPD symptoms reflect a worse illness severity and increased risk to life. With this in mind, the perceived risk to life may have been elevated in the group receiving pharmacological treatment as these patients were more likely to have had symptoms of suicidality attempt and self-harm. The high illness severity, poor functioning and high symptom burden reinforces the need for novel therapeutic compounds.

In the absence of an approved pharmacological treatment for BPD, off-label prescribing remains a common practice despite limited evidence of treatment efficacy of the medications typically prescribed (Stoffers-Winterling et al., 2022) (Gartlehner et al., 2021). Over two-thirds (67.7%) of patients in our study were receiving pharmacological treatments. Although this prescribing pattern may be partially attributable to the management of comorbidities, a recent 10-year analysis in Sweden highlighted persistent polypharmacy in individuals with personality disorders, including those without co-occurring psychiatric comorbidities (Di Leone et al., 2025). Further complicating the understanding of real-world prescribing practices in BPD is the variable definition of polypharmacy in existing literature (Masnoon et al., 2017). This demonstrates a clear lack of consensus and emphasises the need for a standardised definition for polypharmacy to comprehensively examine its prevalence and clinical implications for the BPD population.

When examining medication classes in the present study, antidepressants, second-generation antipsychotics and anticonvulsants were the most commonly recorded treatment around the time of diagnosis. Our findings are similar to those from a small study where psychotropic drug use in 87 patients with BPD was analysed over a 4-year period (Timäus et al., 2019). The study found that antidepressants (50.6%), antipsychotics (34.5%) and hypnotics (29.9%) were the most frequently prescribed drug classes. This could be explained by differences in the drug classifications; Timaus et al. classified diazepam and lorazepam as hypnotics (Timäus et al., 2019), whereas they were classed as anticonvulsants in the present study; furthermore, the patients exhibited different comorbidities in these studies, which could have impacted the results.

This study has several strengths and weaknesses. A major strength was that the analyses were conducted on a large cohort of patients (n= 13,444) from 15 states across the US and are representative of patients receiving mental healthcare in the US. However, as this study uses EHR

data from real-world clinical practice, data were not recorded in a uniformly structured manner, thus selection bias may have been introduced. EHR data are subject to limitations stemming from clinician input, meaning that diagnoses may not always be accurate, could reflect a patient in remission, or fail to capture diagnoses that are established in healthcare settings not covered by NeuroBlu data. Furthermore, the clinical history for patients prior to entering the EHR was not available. Therefore, patients may have received healthcare interventions in other clinical services, which may have impacted the recorded age of diagnosis, symptom presentation recorded during the MSE, or the frequency and duration of hospitalisation. Additionally, it should be noted that while the database provided information on prescribed medication class, the indication for which it was prescribed was not known. Data on the use of non-pharmacological treatments and adherence were also not available. Potential diagnostic bias should also be acknowledged. The database used in this study was slightly skewed towards a population with greater disease severity, as the available data originated from specialty psychiatry sites rather than general practitioners at the time of the study. Although limitations related to the risk of bias are present in all real-world studies, the present study benefited from a large sample size representative of real-world clinical practice. Subsequently, the study design helped to mitigate risks related to data completion and quality by enabling sensitivity analyses/stratification to evaluate noise/bias/confounding within the dataset. However, it should be noted that the study did not adjust for potential confounders.

There are also limitations inherent to the use of NLP models to obtain clinical information from the MSE documented in free text records. Such models are not necessarily 100% accurate and may include false positive or negative examples, whereas clinical measurements would have been more reliable if these were available. Although the NLP approach (Mukherjee et al., 2020) has restricted generalisability for impulsivity symptoms due to limited training examples, the present study used only patient data that were used in the NLP development. A further limitation of the approach concerns the use of word2vec embeddings, which can present issues when handling out-of-vocabulary words. Despite these limitations, the overall accuracy of the NLP model is considered acceptable (median AUROC ranging from 1.0 to 0.71) (Berrar, 2019; Hosmer Jr et al., 2013). Although the AUROC interval (1.0 to 0.71) appears broad, it represents the performance across several different symptom categories (27 in total). In view of this, while the generalisability of the results for smaller groups with smaller sample sizes may be limited, the other groups included a sufficient number of samples to report AUROC values with confidence. Therefore, the AUROC values reported for these groups are less likely to be overfitted. Finally, the exploration of symptoms within the MSE is only 1 source within the clinical notes where clinicians will document symptoms. As highlighted by Mukherjee et al., the reliance on unstructured MSE text produces a frequent number of unique

descriptors in certain categories, hindering the iterative training and validation of the NLP model (Mukherjee et al., 2020). Future studies might explore NLP approaches to the subjective portion of the clinical notes, or the assessment and plan fields, which may contain richer descriptions of symptoms than the MSE.

Conclusions

This real-world, observational study of patients with BPD found that the majority were female, had disease severity indicative of moderate to marked illness and a high level of psychiatric comorbidity. Patients were also commonly prescribed pharmacological treatments and half required at least one psychiatric hospitalisation, highlighting the dual burden of BPD on patients and healthcare systems. BPD symptoms were variable by patient age group, with emotional dysregulation being more frequent in older age groups, and suicidal intent/ideation/attempt/self-injury more frequent in younger age groups. Therefore, continuing research into the clinical manifestations of BPD by age may allow for future therapies to be more tailored to patients' needs and characteristics and help to alleviate the overall burden of BPD.

Glossary

AUROC, Area Under Receiver Operating Characteristic Curve

BPD, borderline personality disorder

CGI-S, Clinical Global Impression – Severity

DSM-5, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

EHR, electronic health records

ER, emergency room

ICD, International Classification of Diseases

MDD, major depressive disorder

MSE, mental state examination

NLP, natural language processing

PTSD, posttraumatic stress disorder

SUD, substance use disorder

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CRediT authorship contribution statement

All authors are responsible for the work described in this article and meet International Committee of Medical Journal Editors (ICMJE) authorship criteria. CW: Conceptualization, methodology, project administration, supervision, visualization, writing - review and editing. SSR: Conceptualization, funding acquisition, supervision, writing - review and editing. JBD: Conceptualization, investigation, project administration, resources, supervision, writing - review and editing. EOCP: Investigation, methodology, project administration, visualization, writing - original draft, writing - review and editing. JY: Formal analysis, methodology. KG: Methodology, visualization, writing – review and editing. BC: Data curation, formal analysis. MO: Investigation, writing - original draft, writing - review and editing. RP: Conceptualization, investigation, methodology, supervision, writing - review and editing. All authors drafted the work, or reviewed it critically for important intellectual content, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

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Declaration of competing interest

CW, SSR and **JBD** are employees of Boehringer Ingelheim.

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Appendix A: Supplementary data

Data sharing statement

To ensure independent interpretation of observational study results and enable authors to fulfil their role and obligations under the ICMJE criteria, Boehringer Ingelheim grants all external authors access to observational study data pertinent to the development of the publication. In adherence with the Boehringer Ingelheim Policy on Transparency and Publication of Clinical Study Data, scientific and medical researchers can request access to clinical study data when it becomes available on Vivli - Center for Global Clinical Research Data, and earliest after publication of the primary manuscript in a peer-reviewed journal, regulatory activities are complete, and other criteria are met. Please visit Medical & Clinical Trials | Clinical Research | MyStudyWindow for further information. The data supporting this study originate with Holmusk Technologies, Inc. These de-identified data may be made available upon request and are subject to license agreement with Holmusk. Interested parties should contact publications@holmusk.com to determine licensing terms.

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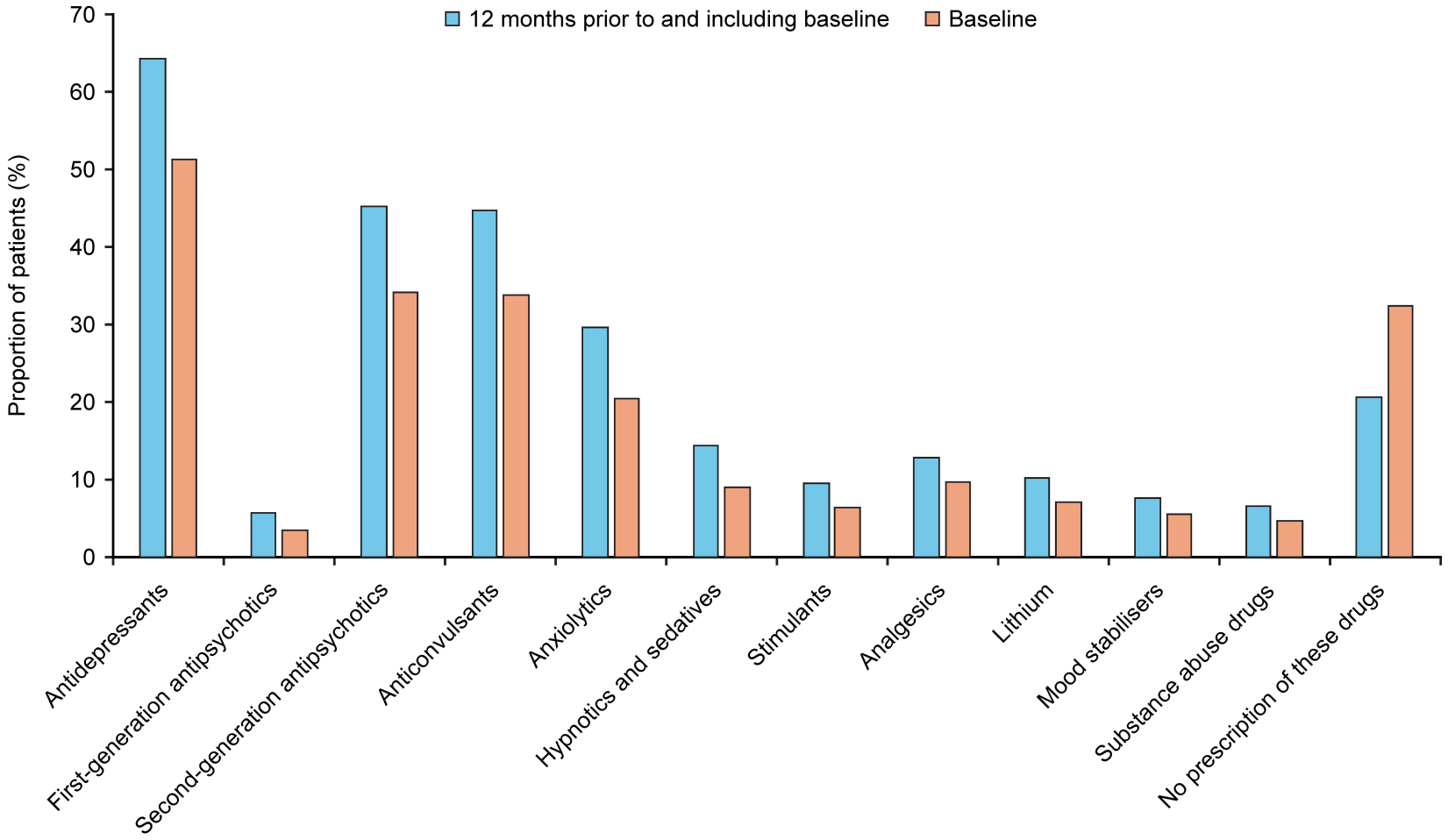
Figures

Figure 1. Pharmacological treatment based on prespecified treatment groups in the 12 months prior to and including baseline, and at baseline



Tables

Table 1. Demographics and clinical characteristics at baseline

	Study population (N=13,444)
Age at baseline, years	
Mean (SD)	33 (12.8)
Median (IQR)	31 (23–42)
Age category at baseline, years, n (%)	
12–17	1084 (8.1)
18–25	3591 (26.7)
26–35	3654 (27.2)
36–45	2573 (19.1)
46–55	1789 (13.3)
56–65	617 (4.6)
>65	136 (1.0)
Gender	
Female	11,241 (83.6)
Male	2180 (16.2)
Unknown	23 (0.2)
Race, n (%)	
White	7940 (59.1)
Black or African American	1394 (10.4)
Other[a]	795 (5.9)
Unknown	3315 (24.7)
Ethnicity, n (%)	
Hispanic or Latino	1412 (10.5)
Not Hispanic or Latino	5402 (40.2)
Unknown	6630 (49.3)
Clinical setting at diagnosis, n (%)[b]	
Outpatient	9650 (71.8)
Inpatient	3011 (22.4)
Emergency room	2163 (16.1)
CGI-S mean score (SD)[c]	4.6 (1.1)
CGI-S category, n (%)[c]	
1–3	1543 (11.5)
4–5	9064 (67.4)
6–7	2101 (15.6)
Not recorded	736 (5.5)

[a]Other includes Asian, Native American Indian, and Pacific Islander.

[b]Patients could have ≥1 recorded clinical setting if ≥1 was recorded within 14 days of baseline.

[c]1–3, normal to mildly ill; 4–5, moderately to markedly ill; 6–7, severely to most ill.

CGI-S, Clinical Global Impression – Severity; IQR, interquartile range; SD, standard deviation.

Table 2. Psychiatric comorbidities experienced by ≥5% patients in the 12 months prior to baseline and at baseline

Psychiatric comorbidity[a], n (%)	**12 months prior to baseline (N=4860)**	**At baseline (N=13,033)**
Major depressive disorder	2075 (42.7)	5960 (45.7)
Other psychiatric disorders	1901 (39.1)	4214 (32.3)
Anxiety disorders	1484 (30.5)	3602 (27.6)
SUD	1449 (29.8)	4514 (34.6)
PTSD	1245 (25.6)	3804 (29.2)
Other bipolar disorders	1071 (22.0)	3179 (24.4)
Other mood disorders	958 (19.7)	2318 (17.8)
Bipolar 1 disorder	859 (17.7)	2451 (18.8)
Attention deficit hyperactivity disorder	371 (7.6)	849 (6.5)
Schizoaffective disorder	307 (6.3)	816 (6.3)
Eating-related disorders	208 (4.3)	663 (5.1)
No psychiatric comorbidities	486 (10.0)	332 (2.5)

[a]Comorbidities reported are not mutually exclusive.

SUD, substance use disorder; PTSD, posttraumatic stress disorder.

Table 3. Symptoms indicative of BPD at baseline in all ages and stratified by age group[a]

BPD symptom, n (%)	All (N=12,205)	Age group, years							p-value[b]
		12–17 (n=1048)	18–25 (n=3291)	26–35 (n=3280)	36–45 (n=2297)	46–55 (n=1617)	56–65 (n=546)	>65 (n=126)	
Impulsivity	42 (0.3)	4 (0.4)	10 (0.3)	15 (0.5)	9 (0.4)	4 (0.2)	0	0	0.63
Impulse control – limited/some Issues	13 (0.1)	3 (0.3)	1 (0.0)	5 (0.2)	2 (0.1)	2 (0.1)	0	0	0.37
Impulse control – poor/serious issues	33 (0.3)	2 (0.2)	9 (0.3)	11 (0.3)	9 (0.4)	2 (0.1)	0	0	0.53
Emotional dysregulation	4370 (35.8)	377 (36.0)	1157 (35.2)	1115 (34.0)	823 (35.8)	630 (39.0)	218 (39.9)	50 (39.7)	<0.05
Affect – Aggressive	698 (5.7)	58 (5.5)	208 (6.3)	174 (5.3)	122 (5.3)	92 (5.7)	35 (6.4)	9 (7.1)	0.55
Affect – Irritable/angry	1367 (11.2)	141 (13.5)	350 (10.6)	337 (10.3)	240 (10.4)	211 (13.0)	72 (13.2)	16 (12.7)	<0.05
Affect – Labile	1578 (12.9)	105 (10.0)	413 (12.5)	403 (12.3)	300 (13.1)	246 (15.2)	92 (16.8)	19 (15.1)	<0.05
Affect – Intense	360 (2.9)	31 (3.0)	89 (2.7)	88 (2.7)	74 (3.2)	55 (3.4)	22 (4.0)	1 (0.8)	0.28
Mood – Irritable, angry	2607 (21.4)	233 (22.2)	686 (20.9)	656 (20.0)	485 (21.1)	391 (24.2)	119 (21.8)	37 (29.4)	<0.05
Mood – Labile	386 (3.2)	42 (4.0)	98 (3.0)	107 (3.3)	62 (2.7)	52 (3.2)	22 (4.0)	3 (2.4)	0.41
Suicidal intent/ideation	3819 (31.3)	394 (37.6)	1117 (33.9)	982 (29.9)	666 (29.0)	466 (28.8)	156 (28.6)	38 (30.2)	<0.05
Mood – Suicidal	72 (0.6)	11 (1.0)	15 (0.5)	18 (0.5)	16 (0.7)	10 (0.6)	2 (0.4)	0	0.36
Suicidality – Suicidal ideation	3479 (28.5)	340 (32.4)	1,017 (30.9)	898 (27.4)	613 (26.7)	435 (26.9)	140 (25.6)	36 (28.6)	<0.05
Suicidality – Suicidal with intent	612 (5.0)	73 (7.0)	187 (5.7)	148 (4.5)	101 (4.4)	77 (4.8)	20 (3.7)	6 (4.8)	<0.05

Suicidality – Suicidal with plan	906 (7.4)	112 (10.7)	255 (7.7)	237 (7.2)	152 (6.6)	107 (6.6)	38 (7.0)	5 (4.0)	<0.05
Suicidality – History of ideation	46 (0.4)	8 (0.8)	13 (0.4)	11 (0.3)	6 (0.3)	4 (0.2)	4 (0.7)	0	0.22
Suicidality – Suicidal ideation with means	182 (1.5)	10 (1.0)	52 (1.6)	47 (1.4)	32 (1.4)	24 (1.5)	14 (2.6)	3 (2.4)	0.28
Suicidal attempt/self-injury	1706 (14.0)	194 (18.5)	574 (17.4)	408 (12.4)	305 (13.3)	171 (10.6)	45 (8.2)	9 (7.1)	<0.05
Suicidality – Suicide attempt	119 (1.0)	6 (0.6)	38 (1.2)	33 (1.0)	24 (1.0)	14 (0.9)	3 (0.5)	1 (0.8)	0.64
Suicidality – History of attempt	1258 (10.3)	114 (10.9)	396 (12.0)	312 (9.5)	246 (10.7)	146 (9.0)	38 (7.0)	6 (4.8)	<0.05
Suicidality – Self-injurious	528 (4.3)	110 (10.5)	216 (6.6)	105 (3.2)	62 (2.7)	27 (1.7)	6 (1.1)	2 (1.6)	<0.05
Suicidality – History of self-injury	1 (0.0)	1 (0.1)	0	0	0	0	0	0	0.10
Patients with MSE data and no BPD symptoms	5412 (44.3)	402 (38.4)	1421 (43.2)	1498 (45.7)	1059 (46.1)	732 (45.3)	243 (44.5)	57 (45.2)	<0.05

[a]Data shown for patients with at least one symptom indicative of BPD documented in the mental state examination at baseline using natural language processing.
[b]p-value represents difference in distribution of a specific BPD symptom across all age groups.
BPD, borderline personality disorder; MSE, mental state examination.

Table 4. Psychiatric hospitalisations in the 12 months prior to BPD diagnosis

Hospitalisation details	12 months prior to BPD diagnosis[b] (N=6251)	At baseline (N=5174)	12 months post diagnosis (N=7780)
Number of psychiatric hospitalisations[a] per patient, n (%)			
1	3177 (50.8)	3016 (58.3)	4262 (54.8)
2	1903 (30.4)	1654 (32.0)	1949 (25.1)
3	521 (8.3)	318 (6.1)	674 (8.6)
>3	650 (10.4)	186 (3.6)	895 (11.5)
Average length of stay for each psychiatric hospitalisation (days)			
Mean (SD)	2.9 (4.2)	3.2 (3.9)	2.8 (5.2)
Median (IQR)	1 (2.5)	1 (3.0)	1 (2.0)

[a]Psychiatric hospitalisations includes both inpatient and emergency room visits.

[b]Patients with ≥1 recorded psychiatric hospitalisation in the 12 months prior to baseline were included.

BPD, borderline personality disorder; IQR, interquartile range; SD, standard deviation.

Supplementary material

Supplementary Table 1. MSE Features by BPD symptom category and individual symptoms

Symptom Category	MSE Feature (BPD symptom)
Impulsivity	Impulse control - limited / some issues
	Impulse control - poor / serious issues
Emotional dysregulation	Affect - aggressive
	Affect - irritable / angry
	Affect - liable
	Affect - intense
	Mood - irritable / angry
	Mood - liable
Suicidal intent or ideation	Mood - suicidal
	Suicidality - suicidal ideation
	Suicidality - suicidal with intent
	Suicidality - suicidal with plan
	Suicidality - history of ideation
	Suicidality - suicidal ideation with means
Suicide attempt or self-injury	Suicidality - suicide attempt
	Suicidality - history of suicide attempt
	Suicidality - self-injurious
	Suicidality - history of self-injury

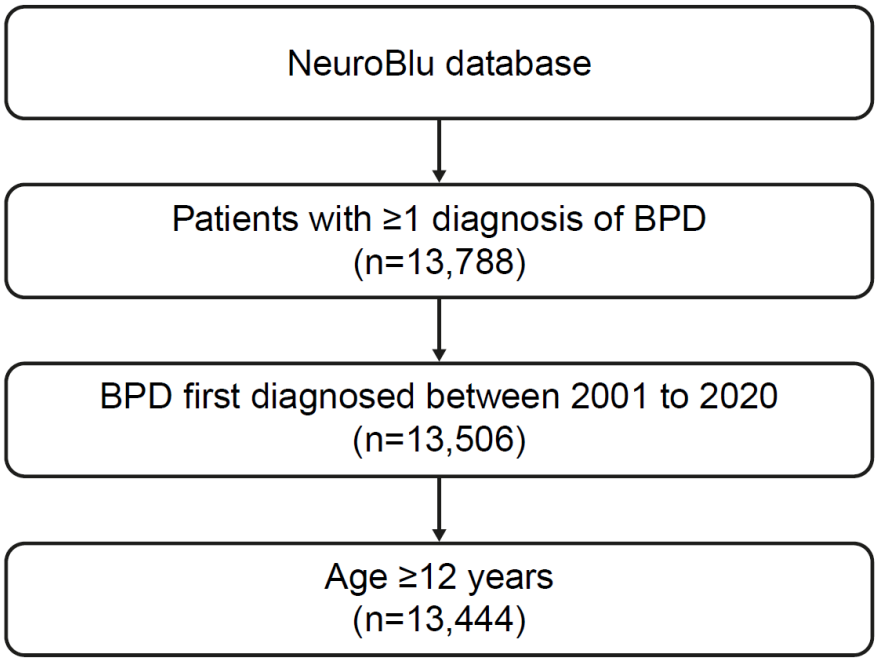
BPD, borderline personality disorder; MSE, mental state examination.

Supplementary Table 2. Psychiatric comorbidities experienced by <5% patients in the 12 months prior to baseline and at baseline

Psychiatric comorbidity[a], n (%)	**12 months prior to baseline (N=4860)**	**At baseline (N=13,033)**
Obsessive compulsive disorders	193 (4.0)	513 (3.9)
Schizophrenia	93 (1.9)	199 (1.5)
Antisocial personality disorders	43 (0.9)	295 (2.3)
Paranoid, schizoid, schizotypal personality disorders	34 (0.7)	79 (0.6)
Delusional disorders	20 (0.4)	27 (0.2)
Schizophreniform disorders	4 (0.1)	11 (0.1)

[a]Comorbidities reported are not mutually exclusive.

Supplementary Figure 1. Patient flow chart



BPD, borderline personality disorder.