



Rush, K., Fok, M. L. Y., Moran, P. A., Dorrington, S., Shetty, H., Stewart, R., & Chang, C. K. (2020). Risk of first general hospital admissions for self-harm among people with personality disorder: a retrospective cohort study. *Journal of Personality Disorders*. https://doi.org/10.1521/pedi_2020_34_489

Peer reviewed version

Link to published version (if available): 10.1521/pedi_2020_34_489

Link to publication record in Explore Bristol Research PDF-document

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Risk of first general hospital admissions for self-harm among people with personality disorder: a retrospective cohort study

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Conflict of interest: C-KC, HS, and RS have received research funding from Roche, Janssen, Lundbeck, and GSK.

Word count: 4,254; number of tables & figures: 3

Abstract

For personality disorder (PD), it is unknown whether additional psychiatric conditions increases their risk of self-harm. We thus performed a retrospective cohort study, using data from secondary mental healthcare in South London, linked to Hospital Episodes Statistics in England to identify self-harm admissions. Adults with diagnosed PD, followed up in a 6-year period, were involved (N=7,475). Cox regression was used to model the risk of self-harm admissions, with comorbid depression, substance use disorders (SUD), severe mental illness (SMI), anorexia nervosa (AN) and bulimia nervosa (BN) as primary exposures, with sociodemographics considered as confounders. In multivariable analyses, comorbid SUD (adjusted HR=1.66; 95%CI: 1.45, 1.90), depressive disorder (1.25; 1.09, 1.44), AN (1.63; 1.10, 2.39) and BN (1.65; 1.09, 2.51) were positively associated with increased risks of hospitalisation due to self-harm. However, negative association was found for comorbid SMI. The findings highlight the importance of assessing and treating comorbid psychiatric disorders in PD.

Introduction

Personality disorder (PD) is an enduring pattern of inner experience and behaviour that deviates markedly from the expectations of the individual's culture, is pervasive and inflexible, has an onset in adolescence or early adulthood, is stable over time, and leads to distress or impairment (World Health Organization, 1992). PD affects 3-10% of the general population (Coid, Yang, Tyrer, Roberts, & Ullrich, 2006; Samuels, 2011; Tyrer et al., 2010); the condition is prevalent among those attending primary care (Moran, Jenkins, Tylee, Blizard, & Mann, 2000) and up to half of people attending psychiatric outpatient clinics meet diagnostic criteria for PD (Beckwith, Moran, & Reilly, 2014; Zimmerman, Chelminski, & Young, 2008; Tyrer, Reed, & Crawford, 2015). The public health implications of PD have been increasingly appreciated over recent years: as a well characterised risk factor for subsequent suicide (Cooper et al., 2005) and associated increased all-cause mortality (Bergen, Hawton, Waters, Cooper, & Kapur, 2010), as well as associated with poorer health status (Fok et al., 2014; Moran et al., 2016), premature mortality (Bjorkenstam, Bjorkenstam, Holm, Gerdin, & Ekselius, 2015), and lower life expectancy (Fok et al., 2012). The economic cost of PD (including costs of mental health care and lost employment) in England was estimated at £7.9 billion in 2007 and projected to reach £12.29 billion by 2026, comparable to that of depression and anxiety disorders, and greater than schizophrenia and bipolar disorders, in terms of socioeconomic burdens (McCrone et al., 2008).

<u>Community studies have consistently found strong relationships between PD and other</u> mental disorders, such as anxiety and mood disorders (Skodol, Geier, Grant, & Hasin, 2014), <u>substance use disorder (Grant et al., 2015)</u>, psychosis (Davis, Compton, Wang, Levin, & <u>Blanco, 2013)</u>, and eating disorders (Samuels, 2011). Overall, Cluster B PDs have the <u>strongest relationship with Axis I disorders</u>, particularly substance use disorder and anxiety/mood disorders (Jackson, & Burgess, 2004; Coid et al., 2006; Lenzenweger, & Willett, 2007; Trull, Jahng, Tomko, Wood, & Sher, 2010). The presence of PD symptoms seems to worsen treatment outcomes of co-occurring Axis I disorders (Goddard, Wingrove, & Moran, 2015; Fan, & Hassell, 2008; Moran et al., 2003; Newton-Howes, Tyrer, & Johnson, 2006).

Self-harm, defined as <u>'the deliberate, self-inflicted destruction of body tissue without suicidal</u> <u>intent and for purposes not socially sanctioned' (American Psychiatric Association, 2013)</u>, is common in the general population (Fox et al., 2015) and is a marker of psychological distress. A systematic review of 50 studies from 24 countries concluded a 27.5% prevalence of PD among people presenting to hospital following self-harm (Hawton, Saunders, Topiwala, & Haw, 2013). Moreover, PD is a risk factor for repeated self-harm (Larkin, Di Blasi, & Arensman, 2014). For this population of patients therefore, an effective self-harm prevention strategy requires improved knowledge and understanding of the specific risk factors for self-harm in this vulnerable group.

Among people with BPD, having a history of traumatic experiences, and the presence of concurrent major depression have both been linked to an increase in the risk of suicidal behaviour (Soloff, Fabio, Kelly, Malone, & Mann, 2005; Zanarini, Laudate, Frankenburg, Reich, & Fitzmaurice, 2010). Meanwhile, we know little about the nature of vulnerability factors for self-harm among people with the full range of PD. In the current study, we set out to address this research gap: in particular to <u>investigate the role of comorbid psychiatric</u> disorders (including substance used disorder, SMI, depressive disorder, anorexia nervosa and <u>bulimia nervosa</u>) as vulnerability factors for the risk of self-harm among people diagnosed with PD.

<u>Method</u>

Setting and study design

A retrospective cohort study was performed using a sample obtained from the South London and Maudsley NHS Foundation Trust (SLaM), which provides secondary mental healthcare services for 1.36 million residents in a geographic catchment of four south London boroughs: Croydon, Lambeth, Lewisham and Southwark. The SLaM Biomedical Research Centre (BRC) Case Register collates de-identified copies of full electronic clinical records from SLaM, and renders them available for research through the Clinical Record Interactive Search (CRIS) platform, established in 2008 (Perera et al., 2016). Hospital Episodes Statistics (HES) data contain details of all admissions to National Health Service (NHS) hospitals in England. A linkage set up between CRIS and HES datasets was used to detect hospital admissions with a primary or secondary diagnosis of self-harm at discharge.

Inclusion criteria

Our analysed cohort, extracted using CRIS, consisted of individuals meeting the following criteria: 1) Having a 10th version International Classification of Diseases (ICD-10) diagnosis of a PD (ICD-10 codes F60.0 to F61.0), dated from 1 January 2007 to 31 March 2013; 2) Aged 18 years old or above on the start date of the observation window (for those individuals whose PD diagnosis was given before the window), or on the date of PD diagnosis (for those whose PD diagnosis was given within the observation window). Diagnoses of mental disorders were extracted from CRIS, from either a specific field of structured ICD-10 codes, or from free-text fields elsewhere in the case record, using a bespoke natural language processing algorithm on Generalised Architecture for Text Engineering (GATE) software to extract diagnostic statements. <u>All CRIS diagnoses are clinical diagnoses made by clinicians</u> and entered into the electronic clinical records of service users as a routine part of their

<u>clinical care.</u> The face validity of PD diagnoses on the CRIS system has been previously examined against clinical rating of case records, and found to be <u>moderate</u> (kappa = 0.72, pvalue < 0.001) (Fok, Stewart, Hayes, & Moran, 2014; McHugh, 2012).

Comorbid psychiatric disorders

The following psychiatric disorders (diagnosed at any time before the end of the observation window) that are known to a) co-exist frequently with personality disorder, and b) that are of particular clinical importance in secondary mental health settings, were selected as the major exposures of interest:

- substance use disorders (ICD 10 codes F10–F19)
- schizophrenia (F20)
- schizoaffective disorder (F25)
- bipolar affective disorder (F31)
- depressive disorder (F32 or F33)
- anorexia nervosa (F50.0 or F50.1) and bulimia nervosa (F50.2 or F50.3).

For the analysis, schizophrenia, schizoaffective disorder and bipolar affective disorder were combined as one group - severe mental illness (SMI).

Outcome measure

The first general hospital admission with self-harm, after the diagnosis of PD and within the observation period (1 January 2007 to 31 March 2013), was obtained as the main outcome of interest for our analysis. Self-harm was defined in two ways based on the following primary or secondary discharge diagnoses associated with HES hospitalisation episodes: a broad definition of self-harm (ICD-10 codes X60-84) and a more specific subgroup of self-harm by self-poisoning (ICD-10 codes X60-69).

Definition of covariates

Data on age, gender, ethnicity, marital status, residing borough and neighbourhood socioeconomic status were retrieved from CRIS. Age in years was defined at the individual's first PD diagnosis date in the observation window or at 1 January 2007, if the PD diagnosis preceded the window. Ethnicity was classified into three categories: 'White' (including 'British', 'Any other white background' and 'Irish'); 'Black' (including 'African', 'Any other black background' and 'Caribbean'); and 'Others/Unknown/Mixed'. Marital status was classified into four categories: 'Married' (including 'cohabitation', 'married' and 'married/civil partnership'); 'Single'; 'Divorced/Separated' (including 'divorced/ civil partnership dissolved', 'separated', 'widowed' or 'widowed/ surviving civil partner'), and 'Others'. <u>Same sex couples were not represented in a distinct category; they were classed in the same way as other couples, i.e. as 'single', 'cohabitation', 'married/civil partnership', 'divorced/civil partnership dissolved', or 'widowed/surviving civil partner', according to their marital status. Borough was classified by the subject's designated primary care trust (PCT), and was based on their address of residence: Croydon, Lambeth, Lewisham and Southwark, with a fifth 'other' group for residents outside the SLaM catchment.</u>

The Index of Multiple Deprivation (IMD) score is an area-level measure of socioeconomic status, calculated at the level of lower super output area for residence (LSOA) - a UK address grouping construct which contains an average of 1,500 residents. The IMD score is derived from a range of area-level domains (including employment, income, education, health, barriers to housing and services, crime and the living environment), where each domain is given a specific weighting in the calculation of the index. For the analysis, deprivation score was assigned based on the individual's address of residence at the time of PD diagnosis or at the beginning of the observation window (for those whose PD diagnosis was made before the

window). The score is then transformed into national percentiles (from 1 to 100%), with higher scores indicating greater deprivation (lower socioeconomic status) and for our analyses, these were further classified by tertiles, with a fourth group for homeless status.

Statistical Analysis

Because of the cohort study design and the 'time-to-event' characteristic in our data for current analysis, survival analysis was adopted. Thus, we used Cox proportional hazards model to estimate the association of the exposure of interest with self-harm event in the follow-up period by hazard ratio (HR), which revealed the relative risk of self-harm in the presence of the diagnosis exposure categories listed above. The beginning of the follow-up period was defined as the start of the observation window (1 January 2007), if the diagnosis was given before the observation window, otherwise the beginning was taken on the date of first PD diagnosis occurring within the window. Censoring was defined as the end of the observation window (31 March 2013) or the date of death, whichever occurred first. Univariable analysis was performed to estimate crude or unadjusted HRs with 95% confidence intervals. Multivariable analysis was undertaken using psychiatric comorbidities as major exposure of interest to estimate the adjusted hazard ratios (aHRs), controlling for age, sex, ethnicity, borough, marital status and deprivation score as confounders. Further subgroup analyses by dividing the cohort into Borderline PD and non-Borderline PD subgroups on self-harm for outcome with psychiatric comorbidities as the major exposure of interest were also performed by univariable analysis and multivariable modelling. All statistical analyses were performed using Stata 12.1 (Stata Corporation: College Station, Texsas, USA, 2011) and the criteria of statistical significance (alpha level) was set at 0.05.

Ethical approval

CRIS is approved for secondary data analyses of its anonymised health records by the Oxfordshire Research Ethics Committee C (latest reference 18/SC/0372) and is stringently monitored by a specific patient-led governance structure.

Results

A total of 7,475 eligible individuals were identified from the CRIS platform as the study cohort. <u>Of these, 5,546 subjects had been given PD diagnoses of one or more subtype, and 1,929 had been diagnosed with no information about subtype.</u> Table 1 shows the breakdown of specific personality disorders within the cohort. The most prevalent PD diagnosis was emotionally unstable PD (i.e. borderline) PD, which was present in 43% of the sample. Just under 1/5 of the sample met criteria for mixed/other personality disorder. Table 2 shows descriptive data on sociodemographic characteristics and comorbid psychiatric disorders in the sample. The mean age of study subjects was 37 years, over half of them were female and the majority (70%) were white and single (69%). The cohort was evenly spread across the four boroughs, with 26% from outside the catchment area. The commonest psychiatric comorbidity was depression (39%), followed by SMI (32%), substance use disorder (25%), anorexia nervosa (1.4%), and bulimia nervosa (1.2%).

In the observation period, there were 956 events of first hospitalisation due to self-harm (ICD-10 codes X60-84); 15% of women and 11% of men in the cohort had at least one admission due to self-harm. Younger age, female gender, and living outside the SLaM catchment area, were associated with an increased risk of first admission due to self-harm. In univariable analysis (Table 2, column 3), comorbidity of substance use disorder, anorexia, and bulimia were found to be associated with an elevated risk for first self-harm admissions, whilst comorbid depression was not a significant correlate and comorbid SMI was associated

with lower risk. After adjustment for sociodemographic variables (columns 4-5, Table <u>2</u>), PD subjects with substance use disorder (adjusted HR 1.66; 95% CI: 1.45, 1.91 <u>– representing an elevation of relative risk by 66%</u>), depressive disorder (1.25; 1.09, 1.43), anorexia nervosa (1.63; 1.10, 2.40) and bulimia nervosa (1.64; 1.08, 2.50) retained significantly increased risks of first hospitalisation due to self-harm; whilst comorbid SMI was associated with a significantly reduced risk (0.85; 0.74, 0.98).

Considering first admissions specifically due to self-poisoning (ICD 10 codes X60-69) as an outcome, similar findings were detected (Table <u>3</u>). In univariable analysis, comorbidities of substance use disorder, anorexia nervosa, and bulimia nervosa were associated with increased risk, comorbid depressive disorder was not a significant correlate and comorbid SMI was associated with reduced risk. After adjustment for confounders, comorbid substance use disorder (adjusted HR 1.71; 95% CI: 1.48, 1.98 <u>- representing an elevation of relative risk by 71%</u>), depressive disorder (1.27; 1.10, 1.46), anorexia nervosa (1.53; 1.01, 2.30) and bulimia nervosa (1.61; 1.04, 2.49) were associated with an elevated risk of hospitalisation due to self-poisoning, whilst comorbid SMI was associated with reduced risk (0.85; 0.73, 0.99 <u>-</u> representing a reduction of relative risk by 15%).

Some differences in demographics and comorbidities were found by comparing persons diagnosed with borderline PD with persons diagnosed with other (non-borderline) PD in the cohort (Supplementary Table 1). In summary, the BPD group were younger in age (mean 34 vs. 39 years) and had a greater female preponderance (72% vs. 42%); a larger proportion of the BPD group were of white ethnicity (73% vs. 67%), lived outside SLaM catchment area (27.3% vs. 24.8%), and fell within the lowest tertile for deprivation (i.e. higher socioeconomic status) (33% vs. 30%). In terms of comorbidities, the BPD group had higher prevalence of depression (43% vs. 36%), anorexia nervosa (2.4% vs. 0.6%) and bulimia nervosa (2.0% vs. 0.6%), lower prevalence of SMI (28% vs. 36%), and comparable prevalence of substance use disorder (26% vs. 24%), compared to the non-BPD group.

In the observation period, there were 547 events of first hospitalisation due to self-harm (ICD-10 codes X60-84) amongst the BPD group, and 409 events amongst the non-BPD group, yielding an adjusted HR of 1.65 (95% CI: 1.44, 1.89) for the diagnosis of BPD. As to the outcome of a narrower definition of self-harm (i.e. ICD-10 codes X60-69), a similar adjusted HR of 1.68 (95% CI: 1.45, 1.94) was estimated for BPD. Considering risk of first admission due to self-harm (Supplementary Table 2), younger age, and living outside the SLaM catchment area, were associated with an increased risk in both the BPD and non-BPD group; being female is associated with an increased risk only in the non-BPD group. Being homeless, and being of low socioeconomic status, were associated with increased risk in the non-BPD group and the BPD group respectively. In univariable analysis (Supplementary Table 2, columns 1 and 3), comorbidities of substance use, depression, and bulimia nervosa were associated with increased risk in the non-BPD group; in the BPD group substance use and anorexia nervosa were associated with increased risk, SMI was associated with reduced risk. After adjustment for confounders, non-BPD subjects with comorbid substance use disorder (adjusted HR 1.80; 95% CI 1.46, 2.22), depressive disorder (1.54; 1.26, 1.90) and bulimia nervosa (2.49; 1.17, 5.32) retained significantly increased risks of first hospitalisation due to self-harm. BPD subjects with comorbid substance use disorder (1.48; 1.23, 1.78) and anorexia nervosa (1.68; 1.10, 2.56) remained with significantly increased risk; and those with SMI (0.81; 0.67, 0.99) remained with significantly reduced risk.

In terms of risk of hospitalisation due to self-poisoning (Supplementary Table 3); similar findings were detected in the non-BPD group but different in the BPD group. In the observation period, there were 498 events of first hospitalisation due to self-harm (ICD-10 codes X60-84) amongst the BPD group, and 357 events amongst the non-BPD group. In univariable analysis, comorbidities of substance use disorder, depression, and bulimia nervosa were associated with increased risk in the non-BPD group; in the BPD group only substance use disorder was associated with increased risk. After adjustment for confounders, non-BPD subjects with comorbid substance use disorder (adjusted HR 1.77; 95% CI 1.41, 2.22), depression (1.54; 1.23, 1.92), and bulimia nervosa (2.86; 1.34, 6.11) retained significantly increased risks of first hospitalisation due to self-poisoning. BPD subjects with comorbid substance use disorder (1.58; 1.31, 1.92) also remained with significantly increased risk.

Discussion

Main Findings

In this cohort of secondary mental healthcare patients with a diagnosis of personality disorder, observed over a 6-year period, 13% had at least one general hospital admission due to self-harm (n=956), the vast majority of which were due to self-poisoning (n=855; 89.4%). BPD was associated with a higher risk of first hospitalisation due to self-harm, compared to non-BPD, no matter which definition of self-harm was adopted. Comorbid substance use disorder was independently associated with increased risk of hospitalisation for self-harm, in the PD cohort generally, and amongst both BPD and non-BPD subgroups; the association is also seen for risk of hospitalisation specifically for self-poisoning. Comorbid depression and comorbid bulimia nervosa were independently associated with increased risk of self-harm in the PD cohort generally and in the non-BPD subgroup, but not for the BPD subgroup.

<u>Comorbid anorexia nervosa was independently associated with increased risk of self-harm in</u> <u>the PD cohort generally and in the BPD subgroup but not in the non-BPD subgroup; this</u> <u>pattern was also found in self-harm specific to self-poisoning in the whole PD cohort, but not</u> <u>for self-poisoning in the BPD subgroup. Comorbid SMI had a protective effect on the risk of</u> <u>first self-harm admission, within the PD cohort generally and in the BPD-subgroup, but not</u> <u>the non-BPD subgroup; this pattern was also found for self-poisoning in the whole cohort but</u> <u>not for self-poisoning in the BPD subgroup.</u>

Comparison to previous research

To our knowledge, no prior research has focused on comorbid psychiatric disorders as risk factors for general hospital admissions for self-harm among individuals with personality disorders. Specifically, no other study has investigated comorbid SMI, anorexia nervosa and bulimia nervosa as risk factors for self-harm in PD. Our study provides new knowledge of comorbid psychiatric disorders as risk factors for self-harm across the whole range of PD. Previous studies looking at comorbid psychiatric conditions as predictors of self-harm or suicidality in PD have yielded mixed findings. In the Collaborative Longitudinal Study of Personality Disorders, which included four types of PD (schizotypal, borderline, avoidant and obsessive-compulsive PD), depressive disorder and substance use disorder were not predictive of repeated suicide attempts (Boisseau et al., 2013). Studies in BPD samples have found depressive disorder to be both predictive of self-harm and not predictive of self-harm; whilst substance use disorder appears to be not predictive of self-harm (Zanarini, Laudate, Frankenburg, Reich, & Fitzmaurice, 2010; Soloff, & Chiappetta, 2012; Soloff, & Fabio, 2008; Soloff et al., 2012; Links, Kolla, Guimond, & McMain, 2013). Our finding that both comorbid substance use disorder and comorbid depressive disorder increases risk of general hospital admission for self-harm is somewhat different to these studies.

To the best of our knowledge, no previous study has examined the effect of comorbid anorexia nervosa and bulimia nervosa on the risk of self-harm or suicidal behaviour in patients with PD. Among people with eating disorders, the presence of comorbid PD, especially Cluster BPD, is associated with higher suicidality (Milos, Spindler, Hepp, & Schnyder, 2004). The frequencies of both anorexia and bulimia in our study are considerably lower than those reported in other comparable studies, meaning that we have likely captured a subset of patients with more severe eating disorder and higher likelihood of attracting the diagnoses.

<u>A body of literature implicates</u> Axis I comorbidity as an important factor for longitudinal outcome in PD. In the Children in the Community Study (Cohen, Crawford, Johnson, & Kasen, 2005), co-occurring Axis I with PD in early adolescence increased the odds of PD persisting into adulthood; in extended follow-up, over 20 years, co-occurring Axis I and Axis II disorders consistently presented the highest risk, often approximating the sum of the axisassociated risk or even several times the risk of disorders in either axis alone (Crawford et al., 2008). This risk applies to long-term outcomes in functioning, and persistence of psychopathology. The authors posit that, as psychiatric disorders increase in number, they may overwhelm a person's capacity to cope with increased distress, thus leading to worse functioning and more persistent disorders over time. <u>In the present study, amongst our cohort of individuals with PD, the presence of comorbid psychiatric disorders (excepting comorbid SMI) may confer a greater severity and burden of psychopathology and dysfunction, which overwhelms the individual's capacity and resources, thus leading to greater risk of self-harm. The finding of lower risk with SMI, however, is inconsistent with this explanation (While et al., 2012).</u> Also, no prior study has investigated comorbid SMI as a risk factor for self-harm in PD, although psychosis has been linked to other negative outcomes in PD, such as risk of violence (Moran et al., 2003). <u>Our finding that comorbid SMI is associated with lower risks of self-harm may have a number of potential explanations, including</u> the possibility of residual confounding from protective factors which we failed to adjust for. These include the involvement of crisis teams, which may reduce the risk of suicide in some patients with SMI (While et al., 2012). Furthermore, people with SMI comorbid with PD use more secondary mental health services compared with the ones diagnosed with SMI or PD alone (Fok et al, 2014). This increased contact with mental health services (involving support, treatment and/or monitoring) may play a role in mitigating self-harm behaviour. Antipsychotic drugs - the mainstay of treatment for many patients with SMI – may also reduce the risk of self-harm (Hawton et al., 2015), but we were not able to adjust for these variables in analyses.

Strengths and Limitations

The main strengths of this study were the study design and large clinical cohort. The cohort of over 7,000 patients with PD was derived from a secondary mental health setting, which covered a full range of inpatient and community-based services, giving sufficient statistical power as well as good sociodemographic data for analysis. A range of comorbid psychiatric conditions could also be included for investigation, including some that had not been previously investigated for self-harm outcomes in people with PD. As for the outcome of interest, use of HES linkage data enabled a comprehensive capture of the first hospital admissions for self-harm in England. However, there are certain limitations of this study that should be noted. We relied on ICD-10 diagnoses as opposed to standardised assessments, but the use of routinely collected clinical data allowed us to obtain data on a very large sample size, thus optimising the precision of our findings. Moreover, our use of routine clinical

diagnoses in a very large population favours generalisability to real-world clinical practice. While this study provided a comprehensive sample of people who accessed secondary mental healthcare, many people with personality disorders are not seen in secondary mental health services and are either managed in a primary care setting, or do not seek or receive any treatment at all. Therefore, the results are potentially generalisable only to other secondary mental healthcare settings. For the fact of more than a quarter of our study cohort were from outside of SLaM service areas, the concern of selection bias may occur when introducing these individuals into the analytic sample as their problems may be more intractable and, thus, referred to national units in SLaM services for second opinions, advanced assessment or treatment. This issue has to be borne in mind for further interpretation of the results. In terms of the outcome, given that we only focussed on events which led to hospitalisation, our findings cannot be generalised to reflect the risk for all self-harm events among people with PD, as many self-harm events either do not come to professional attention, or are not severe enough to warrant hospital admission. Lastly, the specific treatment received from mental health services, including the provision of crisis support and antipsychotic medication, was not included in the analysis, and may represent residual confounding in the study.

Future research could aim to replicate our findings in various settings in the UK and other countries with other medical service systems, and to elucidate the potential mechanisms of differential outcomes among those with PD and comorbid psychiatric conditions. In particular, the finding of a reduced risk associated with SMI comorbidity warrants further investigation. Further analysis of the subtypes or clusters of PD with respect to comorbidity and self-harm risk would be helpful, as different subtypes of PD are more closely associated with certain psychiatric conditions.

Conclusion

Among patients with PD, Axis I comorbidities including substance use disorder, depression, anorexia nervosa, and bulimia nervosa are independently associated with increased risk of first hospital admissions for self-harm, whilst comorbid SMI may be associated with a reduction of such a risk. Our findings highlight the importance of assessing and considering comorbid psychiatric disorders as a risk factor among people with PD in clinical settings. Clinicians and service providers should be aware that comorbidity matters, as it has a bearing on treatment outcomes and service use. Early identification of psychiatric comorbidity may lead to better treatment and more personalised management of the individual. Subgroups of patients with PD and comorbid Axis 1 disorders could also be a target for specific interventions to reduce self-harm behaviours. Alertness to the increased vulnerability of those with comorbid psychiatric disorders, who have a higher risk of hospitalisation for self-harm, allows for the possibility of more effective or pre-emptive engagement on the clinician's part. Effective management of self-harm behaviours at an earlier stage of PD is an urgent and crucial part of tackling the early suicide and unnatural mortality of people with PD.

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<u>Table 1. Breakdown of specific personality disorder (PD) diagnosis within study cohort (N = 7,475)</u>

ICD-10 Specific Personality Disorders	Frequency (% of total cohort)
Paranoid PD	<u>249 (3.3)</u>
Schizoid PD	<u>108 (1.4)</u>
Dissocial PD	<u>371 (5.0)</u>
Emotionally Unstable PD	<u>3219 (43.1)</u>
Histrionic PD	<u>57 (0.8)</u>
Anankastic PD	<u>43 (0.6)</u>
Anxious (Avoidant) PD	<u>90 (1.2)</u>
Dependent PD	<u>150 (2.0)</u>
Mixed or Other	<u>1,334 (17.9)</u>

	Mean ± SD / Number	Number of first admissions for			p-value for adjusted
	of individuals (% of	intentional self-harm (%	Crude Hazard	Adjusted Hazard	hazard
Variables	total cohort)	in row)	Ratio (95% CI)	Ratio* (95% CI)	ratio
Age (years)	36.9 ± 13.3		0.98 (0.97, 0.98)		
Gender					
Female	4,100 (54.9)	596 (14.5)	Reference		
Male	3,374 (45.1)	359 (10.6)	0.68(0.60, 0.78)		
Unknown	1(0.01)	1 (100.0)			
Marital Status					
Married	736 (9.9)	82 (11.1)	Reference		
Single	5,166 (69.1)	668 (12.9)	1.15 (0.92, 1.45)		
Divorced/Separated	842 (11.3)	103 (12.2)	1.02 (0.77, 1.37)		
Other	731 (9.8)	103 (14.1)	1.10 (0.82, 1.47)		
Borough					
Croydon	1,440 (19.3)	194 (13.5)	Reference		
Southwark	1,525 (20.4)	97 (6.4)	0.44 (0.35, 0.56)		
Lewisham	1,223 (16.4)	144 (11.8)	0.84 (0.68, 1.05)		
Lambeth	1,354 (18.1)	110 (8.1)	0.59 (0.47, 0.75)		
Other	1,933 (25.9)	411 (21.3)	1.70 (1.44, 2.02)		
Ethnicity					
White	5,205 (69.6)	770 (14.8)	Reference		
Black	1,077 (14.4)	70 (6.5)	0.41 (0.32, 0.52)		
South Asian	103 (1.4)	<u>9 (8.7)</u>	0.54 (0.28, 1.04)		
East Asian	127 (1.7)	20 (15.80)	1.13 (0.73, 1.77)		
Mixed/Other/Unknown	<u>963 (12.9)</u>	<u>87 (9.0)</u>	0.59 (0.47, 0.73)		

Table <u>2</u>. Sociodemographic characteristics and psychiatric comorbidities in relation to the first general hospital admissions for intentional self-harm (ICD-10 codes X60-84) among people with personality disorder by Cox regression (N = 7,475)

Deprivation Score in tertiles					
1 st tertile (1.44-25.81 percentile)	2,328 (31.1)	312 (13.4)	Reference		
2 nd tertile (25.82-35.13 percentile)	2,336 (31.3)	275 (11.8)	0.86 (0.73, 1.01)		
3 rd (35.14-100 percentile)	2,333 (31.2)	285 (12.2)	0.88 (0.75, 1.04)		
Homeless	478 (6.4)	84 (17.6)	1.17 (0.92, 1.48)		
Comorbid psychiatric disorders					
Substance use disorder					
No	5,592 (74.8)	635 (11.4)	Reference	Reference	
Yes	1,883 (25.2)	321 (17.1)	1.51 (1.32, 1.72)	<u>1.66 (1.45, 1.91)</u>	< 0.01
SMI ^					
No	5,060 (67.7)	689 (13.6)	Reference	Reference	
Yes	2,415 (32.3)	267 (11.1)	0.75 (0.65, 0.86)	<u>0.85 (0.74, 0.98)</u>	0.03
Depressive disorder					
No	4,537 (60.7)	562 (12.4)	Reference	Reference	
Yes	2,938 (39.3)	394 (13.1)	1.06 (0.94, 1.21)	<u>1.25 (1.09, 1.43)</u>	< 0.01
Anorexia nervosa					
No	7,373 (98.6)	929 (12.6)	Reference	Reference	
Yes	102 (1.4)	27 (26.5)	2.42 (1.65, 3.55)	<u>1.63 (1.10, 2.40)</u>	0.01
Bulimia nervosa					
No	7,385 (98.8)	933 (12.6)	Reference	Reference	
Yes	90 (1.2)	23 (25.6)	2.25 (1.49, 3.40)	1.64 (1.08, 2.50)	0.02

*Adjusted for age, sex, ethnicity, borough, marital status and deprivation score, separately for comorbid psychiatric disorders ^ Severe mental illness, including schizophrenia, bipolar disorder, and schizoaffective disorder

	Mean ± SD /	Number of first			p-value for
	Numbers of	admissions for			adjusted
	individuals (% of	intentional self-harm by	Crude Hazard	Adjusted Hazard	hazard
Variables	total cohort)	poisoning (% in row)	Ratio (95% CI)	Ratio* (95% CI)	ratio
Age (years)	36.9 ± 13.3		0.98 (0.97. 0.98)		
Gender					
Female	4,100 (54.9)	549 (13.4)	Reference		
Male	3,374 (45.1)	305 (9.0)	0.63 (0.54, 0.72)		
Unknown	1 (0.01)	1 (100.0)			
Marital Status					
Married	736 (9.9)	77 (10.5)	Reference		
Single	5,166 (69.1)	595 (11.5)	1.09 (0.86, 1.38)		
Divorced/Separated	842 (11.3)	92 (10.9)	0.97 (0.72, 1.32)		
Other	731 (9.8)	91 (12.5)	1.02 (0.76, 1.39)		
Borough					
Croydon	1,440 (19.3)	175 (12.2)	Reference		
Southwark	1,525 (20.4)	82 (5.4)	0.41 (0.32, 0.54)		
Lewisham	1,223 (16.4)	138 (11.3)	0.90 (0.72, 1.12)		
Lambeth	1,354 (18.1)	97 (7.2)	0.58 (0.45, 0.74)		
Other	1,933 (25.9)	363 (18.8)	1.65 (1.38, 1.98)		
Ethnicity					
White	5,205 (69.6)	685 (13.2)	Reference		
Black	1,077 (14.4)	65 (6.0)	0.43 (0.33, 0.55)		
South Asian	<u>103 (1.4)</u>	<u>8 (7.8)</u>	0.54 (0.27, 1.08)		
<u>East Asian</u>	<u>127 (1.7)</u>	<u>17 (13.4)</u>	<u>1.08 (0.67, 1.74)</u>		
Mixed/Other/Unknown	<u>963 (12.9)</u>	80 (8.3)	0.61(0.48, 0.77)		

Table 3. Sociodemographic characteristics and psychiatric comorbidities in relation to the first general hospital admissions due to self-harm by poisoning (ICD 10 codes X60-69) among people with personality disorder by Cox regression (N=7,475)

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Deprivation Score in tertiles					
1 st (1.44-25.81 percentile)	2,328 (31.1)	282 (12.1)	Reference		
2 nd (25.82-35.13 percentile)	2,336 (31.3)	240 (10.3)	0.83 (0.70, 0.99)		
3 rd (35.14-100 percentile)	2,333 (31.2)	256 (11.0)	0.88 (0.74, 1.04)		
Homeless	478 (6.4)	77 (16.1)	1.18 (0.92, 1.52)		
Comorbid psychiatric disorders					
Substance use disorder					
No	5,592 (74.8)	565 (10.1)	Reference	Reference	
Yes	1,883 (25.2)	290 (15.4)	1.53 (1.33, 1.76)	<u>1.71 (1.48, 1.98)</u>	<u><0.01</u>
SMI ^					
No	5,060 (67.7)	618 (12.2)	Reference	Reference	
Yes	2,415 (32.3)	237 (9.8)	0.74 (0.64, 0.86)	<u>0.85 (0.73, 0.99)</u>	<u>0.03</u>
Depressive disorder					
No	4,537 (60.7)	499 (11.0)	Reference	Reference	
Yes	2,938 (39.3)	356 (12.1)	1.08 (0.95, 1.24)	<u>1.27 (1.10, 1.46)</u>	<u><0.01</u>
Anorexia nervosa					
No	7,373 (98.6)	831 (11.3)	Reference	Reference	
Yes	102 (1.4)	24 (23.5)	2.37 (1.58, 3.56)	<u>1.53 (1.01, 2.30)</u>	<u>0.04</u>
Bulimia nervosa					
No	7,385 (98.8)	834 (11.3)	Reference	Reference	
Yes	90 (1.2)	21 (23.3)	2.28 (1.48, 3.52)	1.60 (1.04, 2.49)	0.03

*Adjusted for age, sex, ethnicity, borough, marital status and deprivation score, separately for comorbid psychiatric disorders ^ Severe mental illness, including schizophrenia, bipolar disorder, and schizoaffective disorder

	Mean ± SD / Numbers of individuals (% in columns)		
	Non-Borderline Personality Disorder	Borderline Personality Disorder	
<u>Variables</u>	<u>(n=4,256)</u>	<u>(n=3,219)</u>	<u>^p-value</u>
Age (years)	39.4 ± 13.9	33.5 ± 11.7	<u><0.01</u>
Gender			
Female	<u>1,789 (42.0)</u>	2.311 (71.8)	<0.01
Male	2,644 (58.0)	908 (28.2)	<u><0.01</u>
<u>Unknown</u>	1 (0.01)	0(0.0)	
Marital Status			
Married	<u>418 (9.8)</u>	<u>318 (9.9)</u>	
Single	<u>2,898 (68.1)</u>	<u>2,268 (70.5)</u>	<u>0.07</u>
Divorced/Separated	<u>510 (12.0)</u>	<u>332 (10.3)</u>	
Other	<u>430 (10.1)</u>	<u>301 (9.4)</u>	
<u>Borough</u>			
Croydon	<u>752 (17.7)</u>	<u>688 (21.4)</u>	
Southwark	<u>908 (21.3)</u>	<u>617 (19.2)</u>	<0.01
Lewisham	<u>678 (15.9)</u>	<u>545 (16.9)</u>	<u>~0.01</u>
Lambeth	<u>864 (20.3)</u>	<u>490 (15.2)</u>	
Other	<u>1,054 (24.8)</u>	<u>879 (27.3)</u>	
<u>Ethnicity</u>			
White	<u>2,842 (66.8)</u>	<u>2,363 (73.4)</u>	
<u>Black</u>	<u>723 (17.0)</u>	<u>354 (11.0)</u>	< 0.01
South Asian	<u>64 (1.5)</u>	<u>39 (1.2)</u>	-0.01
<u>East Asian</u>	<u>72 (1.7)</u>	<u>55 (1.7)</u>	
Mixed/Other/Unknown	<u>555 (13.0)</u>	<u>408 (12.7)</u>	
Deprivation Score in tertiles			
1^{st} (1.44-25.81 percentile)	<u>1,255 (29.5)</u>	<u>1,073 (33.3)</u>	
<u>2nd (25.82-35.13 percentile)</u>	<u>1,364 (32.1)</u>	<u>972 (30.2)</u>	<u><0.01</u>
<u>3rd (35.14-100 percentile)</u>	<u>1,310 (30.8)</u>	<u>1,023 (31.8)</u>	
Homeless	<u>327 (7.7)</u>	<u>151 (4.7)</u>	

Supplementary Table 1. Comparisons of demographics and comorbidities between groups of borderline PD and non-borderline PD

<u>Comorbid</u>	psychiatric	disorders
Substance	usa disardar	

Substance use disorder			0.05
No	<u>3,220 (75.7)</u>	<u>2,372 (73.7)</u>	0.05
Yes	<u>1,036 (24.3)</u>	<u>847 (26.3)</u>	
<u>SMI &</u>			
No	<u>2,739 (64.4)</u>	<u>2,321 (72.1)</u>	<u><0.01</u>
Yes	<u>1,517 (35.6)</u>	<u>898 (27.9)</u>	
Depressive disorder			
No	<u>2,707 (63.6)</u>	<u>1,830 (56.9)</u>	<u><0.01</u>
Yes	1,549 (36.4)	<u>1,389 (43.1)</u>	
Anorexia nervosa			
No	<u>4,203 (99.4)</u>	<u>3,143 (97.6)</u>	<u><0.01</u>
Yes	<u>26 (0.6)</u>	76 (2.4)	
Bulimia nervosa			
No	4,230 (99.4)	<u>3,155 (98.0)</u>	<u><0.01</u>
Yes	26 (0.6)	<u>64 (2.0)</u>	
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^ Independent t-tests for continuous variables and Chi-square tests for categorical variables & Severe mental illness, including schizophrenia, bipolar disorder, and schizoaffective disorder

Supplementary Table 2. Effects of sociodemographic characteristics and psychiatric comorbidities in relation to the first general hospital admissions for intentional self-harm (ICD-10 codes X60-84) among people with personality disorder by Cox regression, stratified by diagnosis with borderline PD and with other (non-borderline) PD (N=7,475)

	Non-Borderline Persona	ulity Disorder (n=4,256)	Borderline Personality	Disorder (n=3,219)
Variables	<u>Crude Hazard Ratio</u> (95% CI)	<u>Adjusted Hazard</u> <u>Ratio* (95% CI)</u>	<u>Crude Hazard Ratio</u> (95% CI)	<u>Adjusted Hazard</u> Ratio* (95% CI)
<u>Age (years)</u>	0.98 (0.97. 0.98)	<u></u>	0.98 (0.98. 0.99)	
Gender				
Female	Reference		Reference	
Male	<u>0.69 (0.57, 0.84)</u>	—	<u>0.97 (0.80, 1.16)</u>	—
<u>Unknown</u>				
<u>Marital Status</u>				
Married	<u>Reference</u>		<u>Reference</u>	
Single	<u>1.11 (0.78, 1.56)</u>	<u></u>	<u>1.18 (0.87, 1.61)</u>	<u></u>
Divorced/Separated	<u>1.01 (0.65, 1.56)</u>		<u>1.07 (0.73, 1.58)</u>	
Other	<u>1.15 (0.75, 1.77)</u>		<u>1.07 (0.72, 1.59)</u>	
<u>Borough</u>				
<u>Croydon</u>	<u>Reference</u>		<u>Reference</u>	
Southwark	<u>0.52 (0.36, 0.74)</u>		0.42 (0.30, 0.58)	
Lewisham	<u>1.04 (0.76, 1.45)</u>		0.73 (0.55, 0.98)	<u> </u>
Lambeth	<u>0.78 (0.56, 1.08)</u>		<u>0.51 (0.36, 0.71)</u>	
Other	<u>1.45 (1.10, 1.92)</u>		<u>2.03 (1.64, 2.52)</u>	
<u>Ethnicity</u>				
White	<u>Reference</u>		<u>Reference</u>	
Black	0.38 (0.26, 0.54)		0.51 (0.37, 0.72)	
South Asian	0.50 (0.19, 1.35)	<u></u>	0.63 (0.26, 1.52)	<u> </u>
<u>East Asian</u>	<u>0.86 (0.41, 1.82)</u>		<u>1.47 (0.85, 2.55)</u>	
Mixed/Other/Unknown	<u>0.73 (0.53, 0.99)</u>		<u>0.49 (0.36, 0.68)</u>	

Deprivation Score in tertiles				
<u>1st (1.44-25.81 percentile)</u>	<u>Reference</u>		<u>Reference</u>	
2 nd (25.82-35.13 percentile)	1.02 (0.79, 1.32)	<u></u>	0.81 (0.66, 1.00)	<u></u>
<u>3rd (35.14-100 percentile)</u>	<u>1.17 (0.91, 1.51)</u>		0.74 (0.60, 0.91)	
<u>Homeless</u>	<u>1.42 (1.00, 2.01)</u>		<u>1.23 (0.88, 1.73)</u>	
<u>Comorbid psychiatric disorders</u>				
Substance use disorder				
No	Reference	Reference	Reference	Reference
Yes	1.68 (1.37, 2.06)	1.80 (1.46, 2.22)	<u>1.34 (1.12, 1.60)</u>	1.48 (1.23, 1.78)
<u>SMI ^</u>				
<u>No</u>	Reference	Reference	Reference	Reference
Yes	0.82 (0.67, 1.01)	<u>0.97 (0.78, 1.19)</u>	<u>0.76 (0.63, 0.93)</u>	0.81 (0.67, 0.99)
Depressive disorder				
No	Reference	Reference	Reference	Reference
Yes	<u>1.37 (1.13, 1.67)</u>	<u>1.54 (1.26, 1.90)</u>	0.80 (0.67, 0.95)	1.01 (0.84, 1.21)
Anorexia nervosa				
<u>No</u>	Reference	Reference	Reference	Reference
Yes	<u>1.74 (0.65, 4.65)</u>	<u>1.10 (0.41, 2.98)</u>	<u>2.02 (1.33, 3.07)</u>	<u>1.68 (1.10, 2.56)</u>
Bulimia nervosa				
No	Reference	Reference	Reference	Reference
Yes	<u>3.27 (1.54, 6.90)</u>	<u>2.49 (1.17, 5.32)</u>	<u>1.55 (0.94, 2.55)</u>	<u>1.43 (0.86, 2.36)</u>
*Adjusted for age, sex, ethnicity, boro	ugh, marital status and depr	ivation score, separately for	comorbid psychiatric disor	ders

^ Severe mental illness, including schizophrenia, bipolar disorder, and schizoaffective disorder

Supplementary Table 3. Effects of sociodemographic characteristics and psychiatric comorbidities in relation to the first general hospital admissions for to self-harm by poisoning (ICD 10 codes X60-69) among people with personality disorder by Cox regression, stratified by if ever being diagnosed borderline personality disorder (N=7,475)

	Non-Borderline Person	ality Disorder (n=4,256)	Borderline Personality Disorder (n=3,219)	
Variables	<u>Crude Hazard Ratio</u> (95% CI)	<u>Adjusted Hazard</u> Ratio* (95% CI)	<u>Crude Hazard Ratio</u> (95% CI)	<u>Adjusted Hazard</u> Ratio* (95% CI <u>)</u>
Age (years)	<u>0.98 (0.97. 0.99)</u>	=	0.98 (0.98. 0.99)	=
Gender				
Female	Reference		Reference	
Male	0.62 (0.50, 0.76)	=	0.92 (0.76, 1.12)	<u></u>
Unknown				
Marital Status				
Married	<u>Reference</u>		Reference	
Single	<u>1.03 (0.72, 1.49)</u>	<u></u>	<u>1.12 (0.82, 1.53)</u>	
Divorced/Separated	0.98 (0.62, 1.56)		0.99 (0.66, 1.48)	
Other	<u>1.13 (0.72, 1.77)</u>		0.95 (0.63, 1.43)	
<u>Borough</u>				
<u>Croydon</u>	<u>Reference</u>		<u>Reference</u>	
<u>Southwark</u>	0.50 (0.33, 0.74)		0.39 (0.28, 0.56)	
<u>Lewisham</u>	<u>1.11 (0.78, 1.57)</u>	<u></u>	0.79 (0.59, 1.07)	<u></u>
<u>Lambeth</u>	<u>0.77 (0.54, 1.11)</u>		0.51 (0.36, 0.73)	
Other	<u>1.52 (1.13, 2.06)</u>		<u>1.87 (1.49, 2.35)</u>	
<u>Ethnicity</u>				
White	<u>Reference</u>		<u>Reference</u>	
Black	0.38 (0.26, 0.56)		0.56 (0.40, 0.78)	
Southern Asian	0.44 (0.14, 1.36)	=	0.70 (0.29, 1.69)	==
<u>East Asian</u>	0.84 (0.38, 1.90)		<u>1.37 (0.75, 2.49)</u>	
Others/Unknown/Mixed	0.75 (0.54, 1.04)		0.52 (0.38, 0.72)	

Deprivation Score in tertiles					
1 st (1.44-25.81 percentile)	<u>Reference</u>		<u>Reference</u>		
2 nd (25.82-35.13 percentile)	0.94 (0.71, 1.25)		0.82 (0.66, 1.01)	<u></u>	
3 rd (35.14-100 percentile)	1.21 (0.92, 1.58)		0.72 (0.58, 0.90)		
Homeless	1.59 (1.11, 2.28)		1.13 (0.78, 1.63)		
Comorbid psychiatric disorders					
Substance use disorder					
<u>No</u>	<u>Reference</u>	<u>Reference</u>	<u>Reference</u>	Reference	
Yes	<u>1.61 (1.30, 2.01)</u>	1.77 (1.41, 2.22)	1.42 (1.18, 1.71)	<u>1.58 (1.31, 1.92)</u>	
<u>SMI ^</u>					
<u>No</u>	<u>Reference</u>	<u>Reference</u>	<u>Reference</u>	Reference	
Yes	<u>0.77 (0.62, 0.97)</u>	0.92 (0.73, 1.16)	<u>0.80 (0.65, 0.98)</u>	0.86 (0.70, 1.05)	
Depressive disorder					
<u>No</u>	<u>Reference</u>	Reference	<u>Reference</u>	Reference	
Yes	<u>1.37 (1.11, 1.68)</u>	1.54 (1.23, 1.92)	0.83 (0.70, 0.99)	<u>1.04 (0.86, 1.26)</u>	
Anorexia nervosa					
No	<u>Reference</u>	<u>Reference</u>	<u>Reference</u>	<u>Reference</u>	
Yes	<u>2.01 (0.75, 5.38)</u>	<u>1.23 (0.45, 3.31)</u>	<u>1.88 (1.20, 2.95)</u>	<u>1.52 (0.96, 2.39)</u>	
Bulimia nervosa					
No	<u>Reference</u>	Reference	<u>Reference</u>	Reference	
Yes	<u>3.80 (1.80, 9.04)</u>	<u>2.86 (1.34, 6.11)</u>	<u>1.47 (0.86, 2.50)</u>	<u>1.29 (0.76, 2.22)</u>	
Adjusted for age, sex, ethnicity, borough, marital status and deprivation score, separately for comorbid psychiatric disorders					

^ Severe mental illness, including schizophrenia, bipolar disorder, and schizoaffective disorder