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Title – Sociodemographic and clinical characteristics of patients with borderline personality disorder enrolled for a first episode psychosis within a specialized “Early Intervention” service.

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ABSTRACT

Borderline Personality Disorder (BPD) is under-recognized in First Episode Psychosis (FEP). The aims of this investigation were: (a) to examine the prevalence of BPD in FEP patients enrolled within an Italian “Early Intervention in Psychosis” (EIP) service; (2) to compare sociodemographic, clinical and treatment characteristics at entry between FEP individuals with and without BPD; and (3) to compare their drop-out rates along a 2-year follow-up period. BPD was assessed using the Structured Clinical Interview for DSM-IV axis II personality disorders. All participants also completed the Positive And Negative Syndrome Scale (PANSS) and the Global Assessment of Functioning (GAF) scale. Forty-nine (9.6%) FEP participants showed a BPD diagnosis. FEP individuals with BPD were had a higher baseline prevalence of substance misuse, a lower baseline equivalent dose of antipsychotic medication, lower baseline levels of negative symptoms and higher baseline levels of anxious-depressive features. They also had a higher 2-year drop-out rate. In conclusion, BPD is present in 10% of FEP patients. This FEP subgroup has peculiar clinical challenges (e.g., high substance misuse at entry, high drop-out rate) and additional comorbidities (e.g., high levels of depressive symptoms at entry), which would require appropriate treatment guidelines.

Keywords – Borderline Personality Disorder, First Episode Psychosis, Early Psychosis, Early Intervention in Psychosis, Recruitment; Drop-out.

INTRODUCTION

Although the term “borderline state” historically defined patients with both neurotic and psychotic symptoms (De Panfilis et al., 2011), it was not until the fourth edition of the Diagnostic and Statistical Manual of mental disorders (DSM-IV) that psychotic features (in the form of transient, stress-related dissociative symptoms or paranoid ideation) were added as an additional diagnostic criterion for *Borderline Personality Disorder* (BPD) (APA, 1994). The DSM criteria for BPD categorical diagnosis have remained substantially unchanged also in the current fifth edition (APA, 2013). Moreover, in the alternative DSM-5 model of personality disorders, psychotic features are not presented as central characteristics of BPD, but the “psychoticism” trait (i.e., perceptual, and cognitive dysregulation) may be specified when appropriate (Terzi et al., 2017).

However, *psychotic symptoms* in BPD are relatively frequent, distressing and often challenging to treat (Schultz & Hong, 2017). Their prevalence range is quite wide (13-60%) (Frias, 2018) and clinical presentation is more heterogeneous than what current international nosography suggests. Specifically, it is not limited to the long-standing notion that psychotic features in BPD are transient, stress-dependent and confined to paranoia and dissociative symptoms (Cavelti et al., 2021). Indeed, *auditory verbal hallucinations* are the most frequent psychotic symptoms among individuals with BPD. In different adult samples, their prevalence ranged from 25% to 50% (Niemantsverdriet et al., 2017). Hallucinations in BPD are usually perceived as distressing, controlling, critical and malevolent (Gras et al., 2014), and are more frequently, but not exclusively, context-related (i.e., related to increased stress, interpersonal difficulties, memories of past traumatic experiences) (D’Agostino et al., 2019). Albeit having received less research attention, *delusions* in BPD showed a prevalence ranging from 15% to 30% (Pearse et al., 2014), with a predominance of paranoid themes (Schroeder et al., 2013). They are commonly non-bizarre, short-lived (i.e., lasting hours to days) and circumscribed to limited aspects of thought, but sometimes are

disconnected from shared reality, long-standing and persistent over time (Zanarini et al., 2013). In synthesis, although more generally increasing when the patient is under stress, psychotic symptoms in BPD are not always transient and strictly related to stressful events but may be prolonged even in the absence of ongoing stress (Adams & Sanders, 2011).

As adolescence and young adulthood are two sensitive life periods in which both psychotic symptoms and borderline personality features usually emerge for the first time (Sharp & Wall, 2018), research and clinical interest on BPD has recently involved patients with *First Episode Psychosis* (FEP). In this respect, knowledge on associations between BPD and threshold or subthreshold psychotic symptoms in young people with FEP or at clinical high risk of psychosis is still poor and limited to examine the co-occurrence of full-blown psychotic symptoms in adults with a previous diagnosis of BPD (and already under treatment for this disorder in mental healthcare services) (Archer et al., 2022). This may be also because at this early stage it is difficult to understand whether psychotic features are inherent to BPD or indicate an increased risk for developing psychosis (Catalan et al., 2016). However, this remains a topic requiring more attention, especially because psychotic symptoms in BPD are crucial psychopathological indicators of illness severity and poor outcome, already at the onset of BPD developmental trajectory (Slotema et al., 2018). Indeed, psychotic features in BPD are associated to a higher number of BPD criteria, more co-occurring mental disorders (e.g., mood disorders, substance use disorder, post-traumatic stress disorder), higher levels of psychopathology (e.g., more symptoms of anxiety and depression), a greater suicide risk, a higher number of hospital admission and a quicker re-admission to acute psychiatric inpatient care after discharge (Cavelti et al., 2021).

As BPD in young people with FEP is under-researched and often under-recognized, the *aims* of this investigation were:

(1) to examine the prevalence of BPD diagnosis in a sample of FEP patients recruited within an “Early Intervention in Psychosis” (EIP) program;

- (2) to compare sociodemographic data, clinical characteristics and acceptance of EIP intervention proposals at entry between FEP individuals with and without BPD; and
- (3) to compare baseline some outcome indicators (i.e., service disengagement condition, hospital admission, suicide attempt and self-harm behavior) between the two subgroups across a 2-year follow-up period.

To the best of our knowledge, this is the second study specifically examining BPD in FEP populations to be published in the literature to date.

MATERIALS AND METHODS

Setting and subjects

Participants were enrolled within the “Parma Early Psychosis” (*Pr-EP*) program between January 2013 and December 2021. The *Pr-EP* program is a specialized EIP protocol specifically implemented in all Child/Adolescent and Adult Mental Health Services (CAMHS and AMHS) of the Parma Department of Mental Health, in the Northern Italy (Leuci et al., 2020).

For the specific purposes of this investigation, *inclusion criteria* were: (1) specialist help-seeking request; (2) age 12-35 years; (3) FEP within one of the following DSM-IV-TR diagnoses (APA, 2000): schizophrenia, schizophreniform disorder, brief psychotic disorder, schizoaffective disorder, delusional disorder, affective (bipolar or major depressive) psychosis, or psychotic disorder not otherwise specified; and (4) a “Duration of Untreated Psychosis” (DUP) of < 2 years. This DUP duration was chosen because it is the usual time limit to provide specialized interventions within the EIP paradigm (Krebs et al., 2018).

Exclusion criteria were: (1) past full-blown psychotic episode within a DSM-IV-TR diagnosis of both affective and non-affective psychosis; (2) past exposure to antipsychotic medication or current antipsychotic intake for more than 2 months prior to the *Pr-EP* recruitment; (3) neurological disease or any other medical condition presenting with psychiatric symptoms; and (4) known intellectual

disability (i.e., intelligence quotient < 70). In the current study, we considered previous exposure to antipsychotic drug (i.e., in past illness episodes prior to the Pr-EP enrollment) as a functional equivalent of a past psychotic episode. This is in line with the psychosis threshold definition proposed by Yung and co-workers (2005) within the EIP paradigm (i.e., “...essentially that at which antipsychotic medication would probably be started in the common clinical practice”).

All individuals and their parents (if minors) gave their written informed consent prior to their inclusion in the research. Local ethical approvals were obtained for the study (AVEN protocol n. 36102/09.09.2019). This investigation was also conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Instruments and measures

The clinical assessment of this prospective research included the Positive And Negative Syndrome Scale (PANSS) (Kay et al., 1987) and the Global Assessment of Functioning (GAF) scale (APA, 2002). Such instruments were completed at baseline by trained Pr-EP team members. Regular scoring workshops and supervision sessions assured the inter-rater reliability of the scales (Leuci et al., 2022).

The *PANSS* is a widely used instrument to assess psychopathology in psychosis. As proposed by Shafer and Dazzi (2019) in their meta-analysis on the PANSS factor structure, we considered the following 4 main psychopathological domains: “Negative Symptoms”, “Positive Symptoms”, “Affect” (i.e., anxious-depressive), “Disorganization” and “Resistance/Activation”. In the current study, we used the Italian version of the PANSS, which showed good psychometric properties also in young FEP samples (Pelizza et al., 2021a).

The *GAF* is commonly used to assess clinical and socio-occupational functioning in individuals with psychotic disorders. In this investigation, we administered the Italian version of the GAF, which had good psychometric properties also in young FEP populations (Pelizza et al., 2020).

Finally, a *sociodemographic/clinical schedule* collecting information on gender, years of education, age, migrant status, ethnic group, marital status, housing condition, employment status, DUP, source of referral, previous hospitalization, past specialist contact, age at the first specialist contact, previous suicide attempt and self-harm, and current substance misuse (i.e, alcohol, cannabis, opioid, hallucinogens, cocaine and other stimulants) was also completed at baseline (Landi et al., 2021). Specifically, the *DUP* was defined as the time interval (in months) between the onset of full-blown psychotic symptoms and the first pharmacological treatment (Srihari et al., 2022). Moreover, we defined “*suicide attempt*” as a potentially injurious, self-inflicted behavior without a fatal outcome for which there was (explicit or implicit) evidence of intent to die (Silverman et al., 2007). It was differentiated from undetermined suicide-related and self-harm behaviors (i.e., acts of deliberate self-harm or intoxication with alcohol or drugs), which were referred to as “*self-harm behavior*” (Pelizza et al., 2022).

Procedures

The axis-I and axis-II diagnoses were formulated at baseline (“provisional” diagnosis) and reformulated after 12 months (“final” diagnosis) during the follow-up period. Within the Pr-EP program, this diagnostic procedure allowed us to better define the more temporally unstable diagnoses identified at entry (e.g., brief psychosis, substance-induced psychosis, schizophreniform disorder, or psychotic disorder NOS), as well as to confirm or not the more structured ones (e.g., affective psychosis, schizophrenia spectrum disorders) and to consequently focus on them our specialized therapeutic intervention. Specifically, each diagnosis was defined by at least two trained Pr-EP team members on each occasion in accordance with the DSM-IV-TR diagnostic criteria, using both the Structured Clinical Interview for DSM-IV-TR Axis I disorders (*SCID-I*) (First et al., 2002) and the Structured Clinical Interview for DSM-IV axis II personality disorders (*SCID-II*) (First et al., 1997). For each FEP participant who dropped out the Pr-EP program in the first year of

treatment, diagnosis was however reformulated at 12-month assessment time with the help of the treatment staff and by consulting clinical notes. Individuals with BPD as “final” primary psychiatric diagnosis were included in the *FEP/BPD subgroup*. The remaining subjects (i.e., who did not meet DSM-IV-TR criteria for BPD as “final” primary psychiatric diagnosis) were grouped in the FEP subgroup.

Based on their symptom severity, all participants were provided with a *2-year comprehensive intervention protocol* including psychopharmacological therapy and a multicomponent psychosocial treatment, combining psychoeducational sessions for family members, an intensive recovery-oriented case management and an individual psychotherapy inspired on cognitive-behavioral principles, as suggested by the current guidelines on the topic (Üçok, 2021). Low-dose atypical antipsychotic drug was used as first-line pharmacological therapy (Barnes et al., 2020). Mood stabilizers, benzodiazepines and serotonin selective reuptake inhibitors could also be used to treat anxiety, mood disorders and insomnia.

As for inter-group *comparisons*, baseline sociodemographic and clinical characteristics were examined, as well as baseline acceptance of Pr-EP intervention proposals (i.e., individual psychotherapy, family psychoeducation, case management, pharmacological prescriptions). Finally, we compared the two subgroups on four main outcome indicators across the 2-year follow-up period: i.e., service disengagement (i.e., “drop-out”) condition, new hospital admission, new suicide attempt, and new self-harm behavior. Specifically, as suggested by Robson and Greenwood (2022) in their meta-analysis on the strength of engagement in FEP patients, we defined “*service disengagement*” as “complete lack of contact or untraceable for at least 3 months despite a need of treatment, counted from the date of the last face-to-face meeting with the clinical staff”. This definition included FEP people who actively refused further contact with the treatment staff and were no longer traceable (Pelizza et al., 2023a), those who did not return phone calls or not attend

appointments for at least 3 months, and those who prematurely exit Pr-EP treatments against clinicians' advice (Pelizza et al., 2023b).

Statistical analysis

Data were analyzed using the Statistical Package for Social Science (SPSS) for Windows, version 15.0 (SPSS Inc., 2010). All tests were two-tailed, with a significance level set at 0.05. In between-group comparisons, qualitative measures were examined using the Mann-Whitney U test, while quantitative parameters were analyzed using the Chi-square (χ^2) test. A Kaplan-Meier survival analysis to compare outcome indicators between the two subgroups was also performed. This specifically ensured to consider the different time duration of individual follow-ups and participants who dropped-out before the end of the study (Jager et al., 2008). Specifically, in our survival analyses, informative censoring occurred when FEP participants were lost to follow-up due to service disengagement or to the occurrence of the specific outcome in question (Ranganathan & Pramesh, 2012).

RESULTS

Over the course of this study, 509 FEP patients were enrolled (see Figure 1 for details). Forty-nine (9.6%) of them were included in the FEP/BPD subgroup. The remaining 460 subjects were grouped in the FEP subsample: their more common "final" primary psychiatric diagnosis were schizophrenia (n = 249; 54.1%), affective psychosis (n = 131; 28.3%) and schizotypal personality disorder (n = 29; 6.3%). The clinical and sociodemographic characteristics of the two subgroups are shown in the Table 1.

(Figure 1 and Table 1 here)

Sociodemographic data

Compared to FEP, FEP/BPD patients showed a greater percentage of employed subjects at presentation. No differences on other sociodemographic characteristics were found.

Clinical data

In comparison with FEP, FEP/BPD individuals showed a shorter DUP, a younger age at first (past) specialist contact, and higher baseline percentages of substance misuse and mental healthcare services other than CAMHS and AMHS as sources of referral (i.e., pathological addiction services, psychological counseling services for adolescents and/or young adults, school psychologists, private psychiatrists, and psychologists). Furthermore, they had a lower baseline equivalent dose of antipsychotic medication, a lower baseline PANSS “Negative Symptoms” factor score, and a higher baseline PANSS “Affect” factor score. Finally, as for baseline (“provisional”) DSM-IV-TR diagnosis, FEP/BPD subjects showed higher percentages of brief psychotic disorder and substance-induced disorder, as well as lower percentages of schizophrenia and affective psychosis. No differences in other clinical characteristics and baseline acceptance of Pr-EP intervention components were observed.

Outcome indicators

Three hundred and fifty-three (69.3%) FEP participants concluded the 2-year follow-up period and 72 passed the 1-year assessment time point without having yet reached the end of our observation period. Compared to FEP, FEP/BPD subjects had a higher 2-year service disengagement rate (Table 2 and Appendix 1). In this respect, our Kaplan-Meier survival analysis results showed a lower mean survival estimate in FEP/BPD participants in comparison with FEP individuals. No differences in terms of 2-year hospital admission, suicide attempt and self-harm behavior rates were observed (Tables 3-5 and Appendices 2-4).

(Tables 2-5 here)

DISCUSSION

First aim of this investigation was to examine the prevalence of BPD diagnosis in a sample of FEP patients recruited within an Italian specialized EIP program. Over the course of the study, approximately 10% of our FEP participants met DSM-IV-TR criteria for BPD as primary psychiatric diagnosis across the follow-up period. This finding was lower than that (18.4%) was recently reported in a cohort of 457 young FEP people enrolled within the “Early Psychosis Prevention and Intervention Centre” (EPPIC) at Orygen in Melbourne, Australia (Schandrin et al., 2022). This difference in prevalence could be attributed to different methods in the diagnostic assessment. In the EPPIC cohort, the authors determined the prevalence of a “borderline personality pathology” (i.e., categorical disorder + subthreshold features) co-occurring with FEP at baseline. On the contrary, we exclusively considered BPD categorical disorder as primary (and “definitive”) psychiatric diagnosis across the follow-up period. Indeed, in this investigation, all DSM-IV-TR axis I and II diagnoses were checked and re-formulated every 12 months, in a context of a more general research interest on longitudinal stability of the categorical diagnoses in FEP people. In our opinion, the term “FEP” was specifically coined to capture the onset of psychotic symptoms and includes different mental disorders with potentially various psychopathological trajectories (Kaleda & Tikhonov, 2022).

As for sociodemographic comparisons, FEP/BPD individuals exclusively showed a significantly higher baseline percentage of *employed* subjects. This finding suggests a better occupational functioning at entry compared to FEP patients without BPD diagnosis. In the EPPIC cohort, Schandrin et al. (2022) reported that people with FEP and co-occurring borderline personality pathology were more likely to be younger, female, and Australian-born. They also were less likely to have completed post-secondary education (Francey et al., 2018) and had more relevant interpersonal difficulties at presentation. In this respect, our FEP/BPD subgroup showed high

baseline percentages of singles (91.8%) and subjects still living with parents (71.4%). This condition of poor relational emancipation had no intra-group specificity and probably represents a general characteristic of the FEP condition (Poletti et al., 2021).

Compared to FEP, FEP/BPD subjects also showed a higher prevalence rate (57.1%) of *substance misuse* at entry. Similarly, in the EPPIC cohort, Schandrin et al. (2022) reported that FEP patients with borderline personality pathology were more likely to have alcohol (29.2%) and substance (20.8%) abuse disorders at presentation than individuals with FEP alone.

In the present study, FEP/BPD individuals had a higher baseline percentage of *mental healthcare services other* than CAMHS and AMHS as primary source of Pr-EP referral, a *shorter DUP* and a *younger age at first (past) specialist contact*. These findings overall suggest that psychological distress related to BPD clinical features (often evident before the onset of psychotic symptoms) could initially drive the help-seeking behavior of this specific subgroup of patients towards less specialist mental healthcare services and professionals (such as pathological addiction staffs, psychological counseling services for adolescents and young adults, school psychologists, private psychiatrists and psychologists). This could also contribute to both DUP reduction and younger age at first (past) specialist contact, especially involving the term of adolescence (Pelizza et al., 2021b). Indeed, it is known that people with BPD present more frequently to primary health care settings than do those with other mental health conditions (Poletti et al., 2023).

Although more typical of the FEP condition, FEP/BPD subjects showed severe levels of *previous psychopathology*. At presentation, they had moderately high prevalence rates of past hospitalization (28.6%), past self-harm behaviors (40.8%) and previous specialist contact (42.9%) (especially for conduct disorder [52.4%] and anxious-depressive disorders [19%]). This indirectly supports the evidence that psychotic symptoms characterize BPD patients with high illness severity (Martino et al., 2020). In this respect, in the EPPIC cohort, FEP individuals with borderline personality pathology were more likely to have severe problems with self-harm at baseline than patients with

FEP alone (Schandrin et al., 2022). They also were more likely to have had a psychiatric inpatient admission prior to the EPPIC referral (Francey et al., 2018).

As for clinical features, our FEP/BPD individuals showed significantly higher prevalence rates of *brief psychiatric disorder* (32.6%) and *substance-induced psychosis* (24.4%) as baseline DSM-IV-TR “provisional” diagnosis in comparison with FEP subjects, as well as significantly lower percentages of schizophrenia and affective psychosis. Differently, in the EPPIC cohort, young FEP patients with borderline personality pathology were more likely to have a diagnostic of psychotic disorder not otherwise specified at presentation (Schandrin et al., 2022).

Furthermore, compared to FEP, FEP/BPD participants had *higher levels of anxious-depressive symptoms* at presentation, as well as *lower severity levels of negative symptoms*. No inter-group difference in terms of disorganization, positive symptoms and socio-occupational functioning were found. In this regard, Schandrin et al. (2022) reported that FEP people with borderline personality pathology experienced more severe depressive symptoms and hallucinations (but less severe delusions, bizarre behavior and thought disorders) than patients with FEP alone. The gap in positive symptom severity between the two studies may also be due to differences in FEP control group composition. However, in this investigation, delusions were the most frequent psychotic symptoms experienced in the FEP/BPD subgroup (nearly 87.7%), followed by conceptual disorganization (53.1%) and hallucinations (51%). These results are only partially in line with what has been reported in the current literature, indicating that auditory verbal hallucinations are the most common psychotic symptoms experienced in BPD (Niemantsverdriet et al., 2017; Pelizza et al., 2023c; Biancalani et al., 2023).

As for specialized Pr-EP intervention components, FEP/BPD individuals showed a *lower equivalent dose of antipsychotic medication* at entry in comparison with FEP patients. No inter-group differences in terms of other pharmacological prescriptions and baseline acceptance of Pr-EP psychosocial intervention proposals were also found. In the EPPIC cohort, no statistically

significant difference in antipsychotic dose prescribed at baseline was found between FEP people with borderline personality pathology and those with FEP alone, as well as differences in terms of psychoeducation about illness, family psychoeducation and type of psychosocial therapy received (Francey et al., 2018). FEP subjects with borderline personality pathology were only more likely to be on antidepressant.

However, although without intra-group specificity, our FEP/BPD participants overall showed *good acceptance of EIP intervention components* (both pharmacological and psychosocial) at entry.

Indeed, about 78% of them had a low-dose antipsychotic prescription (especially olanzapine [39.4%] and risperidone [36.8%]), which is warmly recommended in FEP (Keating et al., 2021).

Moreover, 83% of our FEP/BPD individuals accepted to receive individual psychotherapy, 77% accepted case management proposal and 67% accepted to receive family psychoeducation.

Differently, in the EPPIC cohort, FEP subjects with borderline personality pathology showed poorer access to treatment for FEP than the FEP alone subgroup (Francey et al., 2018). Specifically, they accessed more agencies in their pathway to care (as previously reported also in this paper) and experienced longer delay between their first contact with the EPPIC and commencement of treatment.

Finally, as for outcome indicators, compared to FEP, FEP/BPD patients showed a significantly *higher 2-year service disengagement rate* (i.e., 30.5% vs 16.1%). No inter-group difference in terms of 2-year hospitalization, self-harm behavior and suicide attempt rates was observed. However, our FEP/BPD subjects had a moderately low incidence of hospitalization, suicide attempt and self-harm behavior across the follow-up (15.4%, 13.8% and 17.2% respectively). Differently, in the EPPIC cohort, FEP people with borderline personality pathology were over 10 times more likely to have moderate to severe problems with self-harm at discharge compared to young individuals with FEP alone (Schandrin et al., 2022).

As the results of this research showed higher service disengagement rates in FEP patients with BPD, it is crucial to implement treatment strategies to decrease their service disengagement. In particular, it is important an early identification of BPD features in FEP subjects as soon as possible (i.e., already at the recruitment time within EIP programs) because of their potential role as indicators of poor treatment engagement. Moreover, it may be useful to strengthen and maintain treatment motivation in FEP/BPD patients and their family members, also increasing specific psychoeducational meetings. Finally, it is crucial that individual (“person-tailored”) therapeutic-rehabilitation plans of FEP/BPD individuals define specific and realistic short-term treatment goals, more easily and quickly achievable within few months.

Limitations

A first methodological weakness of this investigation is related to the relatively small sample size ($n = 49$) of the FEP/BPD subgroup. Future studies on larger FEP samples meeting BPD diagnostic criteria are thus needed. Moreover, we examined FEP patients in a “real-world” care setting, primarily aimed at delivering specialized EIP treatments within community mental health services. Thus, our results should be preferentially compared to similar clinical samples.

Another limitation is associated with the diagnostic assessment procedure. In this research, the DSM-IV-TR diagnoses were formulated both at baseline (“provisional” diagnoses) and after 12 months of follow-up period (“final diagnosis”). Only the FEP individuals with BPD as primary psychiatric diagnosis across the 1-year follow-up period were then included in the FEP/BPD subgroup. Therefore, our findings should be compared exclusively to similar FEPBPD samples (i.e., selected with similar assessment procedures). Indeed, difficulties in result comparison could arise using other evaluation methods to categorize FEP patients with or without BPD (such as BPD screening instruments administered without a structured interview able to differentiate the categorical disorder from subthreshold features).

Third, another concern included the use of DSM-5 BPD diagnosis in adolescence. In this respect, some authors suggested that BPD in adolescents (especially under the age of 18) can be a harmful, invalid construct that is unnecessary for effective treatments and evaluation of alternatives (Hartley et al., 2022). However, in this research, there were only 4 minors in the FEP/BPD subgroup (all aged 17 years at entry and with a “final” diagnosis of BPD reformulated after 1 years of follow-up). Fourth, the current study was designed within a specialized EIP program not specifically focused on detecting BPD in FEP. Specifically, BPD psychopathology was not longitudinally assessed. Thus, future research longitudinally exploring BPD symptoms with more specific assessment instruments (such as the “Borderline Personality Disorder Checklist”) (Arntz & Dreessen, 1995) are needed. This is of primary importance since investigations exploring BPD in FEP populations are still scarce and the presence of psychotic symptoms in BPD patients is a clinical indicator of illness severity, frequently associated with poor outcomes and suicide risk (Cavelti et al., 2021). Moreover, it is also important to consider that our results were based on statistically different subgroups in terms of DUP. A larger DUP can have consequences in terms of differences in diagnoses. Indeed, a significantly different DUP could explain (at least in part) our diagnostic differences. It’s thus obvious to have more brief psychotic disorders in participants with a lower DUP and more chronic psychosis in those patients with a higher DUP. This could influence the inference that the diagnostic between-group difference can be solely explained by the presence of a BDP diagnosis. Furthermore, this inter-group difference in DUP may also raise questions about the proportion of negative symptoms (because there were more diagnoses of schizophrenia in the FEP subgroup), the employment rate, and the quantity of treatment. Finally, a weakness possibly affecting interpretation of our findings is that no adjustment was made for multiple comparisons, due to the exploratory nature of the study.

Conclusions

BPD as categorical disorder is present in 10% of FEP people enrolled within our specialized EIP service. This is a FEP subgroup with peculiar clinical challenges (e.g., high prevalence of current substance misuse, high service disengagement rate), additional comorbidities (e.g., high severity levels of depressive symptoms at entry) and high clinical risk (indeed, psychotic symptoms in BPD are important psychopathological indicators of illness severity and poor outcome). As knowledge on BPD in FEP is still poor and BPD is often under-recognized in FEP populations, future studies establishing appropriate treatment guidelines for this complex patient group are needed.

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DECLARATION OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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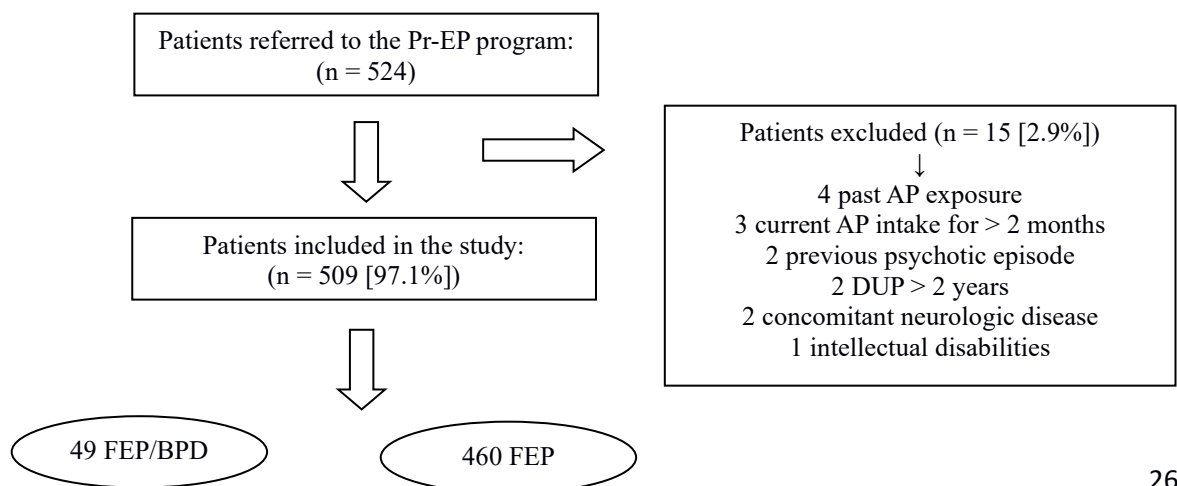
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Figure 1 - Flowchart of referrals to the Pr-EP program (January 2013 to December 2021).



Note – Pr-EP = Parma Early Psychosis, AP = Antipsychotic medication, DUP = Duration of Untreated Psychosis, BPD = Borderline Personality Disorder; FEP = participants with First Episode Psychosis and without BPD; FEP/BPD = FEP participants with BPD.

Table 1 – Sociodemographic, clinical and treatment characteristics of the two FEP subgroups (n = 509).

Variable	FEP/BPD (n = 49)	FEP (n = 460)	X ² /z	p
Gender (male)	33 (66.7%)	289 (62.8%)	0.389	0.533
Age at entry (in years)	24.39 ± 6.43	25.95 ± 6.42	-1.601	0.109
Education (in years)	11.96 ± 2.98	11.39 ± 2.86	-1.182	0.237
Ethnic group (white Caucasian)	42 (85.7%)	384 (83.5%)	0.162	0.687
Migrant status	11 (22.4%)	123 (26.7%)	0.420	0.517
<i>Marital status</i>				
Single	45 (91.8%)	402 (87.4%)	0.818	0.366
Married/partnership	3 (6.1%)	49 (10.7%)	0.991	0.457
Separated/divorced	1 (2.0%)	9 (2.0%)	0.002	0.999

<i>Housing condition</i>				
Alone	5 (10.2%)	37 (8.0%)	0.273	0.584
Living with partners	8 (16.3%)	101 (22.0%)	0.834	0.361
Living with parents	35 (71.4%)	303 (65.9%)	0.613	0.434
Living in residential facility	1 (2.0%)	17 (3.7%)	0.355	0.999
Homeless	0 (0.0%)	2 (0.4%)	0.214	0.999
<i>Occupation</i>				
Unemployed	21 (42.9%)	248 (53.9%)	2.172	0.141
Employed	17 (37.4%)	101 (22.0%)	4.034	0.045
Student	11 (22.4%)	111 (24.1%)	0.069	0.793
DUP (in months)	6.15 ± 6.44	9.73 ± 9.69	-2.505	0.012
<i>Source of referral</i>				
Primary care	14 (28.6%)	156 (33.9%)	0.568	0.451
Other mental health services	13 (26.5%)	68 (14.8%)	4.567	0.033
Emergency room	10 (20.4%)	138 (30.0%)	1.976	0.160
Family members	6 (12.2%)	48 (10.4%)	0.153	0.696
Self-referral	5 (10.2%)	33 (7.2%)	0.232	0.463
School/social services	1 (2.0%)	17 (3.7%)	0.036	0.999
Past hospitalization	14 (28.6%)	130 (30.0%)	0.553	0.713
Past specialist contact	21 (42.9%)	190 (41.3%)	0.044	0.843
Age at first (past) specialist contact	17.80 ± 6.69	21.62 ± 7.13	-2.249	0.025
Past suicide attempt	8 (16.3%)	45 (9.8%)	2.033	0.154
Past self-harm behavior	20 (40.8%)	189 (41.1%)	0.001	0.971
Substance misuse (at entry)	28 (57.1%)	156 (33.9%)	10.353	0.001
<i>Baseline primary DSM-IV-TR diagnosis</i>				
Brief psychotic disorder	16 (32.6%)	44 (9.6%)	22.701	0.0001
Substance-induced psychosis	12 (24.4%)	8 (1.8%)	60.719	0.0001
Schizophreniform disorder	10 (20.4%)	71 (15.4%)	0.819	0.366
Psychotic disorder not otherwise specified	9 (18.4%)	62 (13.5%)	0.882	0.348
Schizophrenia	1 (2.0%)	165 (35.9%)	23.059	0.0001
Affective psychosis	1 (2.0%)	73 (15.9%)	6.816	0.009
Delusional disorder	0 (0.0%)	18 (3.9%)	1.988	0.241
Schizoaffective disorder	0 (0.0%)	12 (2.6%)	1.309	0.617
Schizotypal personality disorder	0 (0.0%)	7 (1.5%)	0.756	0.999
Baseline PANSS “Positive” factor	18.00 ± 4.66	16.38 ± 6.21	-1.574	0.116
Baseline PANSS “Negative” factor	21.19 ± 7.98	25.19 ± 9.70	-2.185	0.029
Baseline PANSS “Disorganization” factor	19.12 ± 8.32	21.21 ± 7.97	-1.552	0.121
Baseline PANSS “Affect” factor	17.96 ± 5.05	15.70 ± 5.60	-2.033	0.048
Baseline PANSS “Resistance” factor	8.27 ± 3.48	9.65 ± 4.80	-1.159	0.246
Baseline PANSS total score	87.96 ± 19.61	91.29 ± 24.69	-0.937	0.349
Baseline GAF score	44.72 ± 12.33	44.84 ± 9.94	-0.147	0.883
Baseline Antipsychotic prescription	38 (77.6%)	391 (85.0%)	1.855	0.173
Baseline Antidepressant prescription	6 (12.2%)	89 (19.3%)	1.472	0.225
Baseline Mood Stabilizer prescription	4 (8.2%)	69 (15.0%)	1.685	0.194

Baseline Benzodiazepine prescription	17 (34.7%)	157 (34.1%)	0.006	0.937
Baseline equivalent dose of Risperidone (mg/day)	2.35 ± 2.56	2.92 ± 2.63	-2.069	0.039
Baseline equivalent dose of Lorazepam (mg/day)	0.08 ± 1.58	0.94 ± 1.74	-0.357	0.721
Baseline Individual Psychotherapy acceptance	41 (83.7%)	368 (80.0%)	0.379	0.538
Baseline Family Psychoeducation acceptance	33 (67.3%)	301 (65.4%)	0.072	0.789
Baseline Case Management acceptance	38 (77.6%)	378 (82.2%)	0.634	0.426

Note. FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder; DUP = Duration of Untreated Psychosis; DSM-IV-TR = Diagnostic and Statistical Manual of mental disorders, IV edition, Text Revised; PANSS = Positive And Negative Syndrome Scale; GAF = Global Assessment of Functioning. Frequencies (percentages), mean ± standard deviation, Chi-squared test (X^2) and Mann-Whitney U test (z) values are reported. Statistically significant p values are in bold.

Table 2 – Kaplan-Meier survival analysis results: comparison on 2-year service disengagement condition between the two FEP subgroups (n = 509).

Time intervals (in months)	FEP/BPD (n = 49)				FEP (n = 460)			
	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)
	Estimate	SE			Estimate	SE		
0-12	0.929	0.040	3	17	0.933	0.012	30	55
12-24	0.695	0.078	11	49	0.839	0.018	67	460

FEP subgroup	Mean (in months)			
	Estimate	SE	95% CI	
			Lower bound	Upper bound
FEP/BPD	20.946	0.880	19.221	22.671
FEP	22.116	0.238	21.651	22.582
Overall	22.028	0.228	21.581	22.475

	X ²	df	p
Log Rank (Mantel-Cox)	3.849	1	0.048

Note. FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder; SE = Standard Error; 95% CI = 95% Confidence Intervals; Log Rank = Logarithm Rank Test; X² = Chi-Square test; df = degrees of freedom; p = statistical value. Statistically significant p values are in bold.

Table 3 – Kaplan-Meier survival analysis results: comparison on 2-year new hospitalization between the two FEP subgroups (n = 509).

Time intervals (in months)	FEP/BPD (n = 49)				FEP (n = 460)			
	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)
	Estimate	SE			Estimate	SE		
0-12	0.846	0.058	6	12	0.781	0.020	91	126
12-24	0.846	0.058	6	49	0.719	0.023	111	460

FEP subgroup	Mean (in months)			
	Estimate	SE	95% CI	
			Lower bound	Upper bound
FEP	22.154	0.693	20.886	21.845
FEP/BPD	21.366	0.245	20.795	23.513
Overall	21.433	0.232	20.979	21.888

	X ²	df	p
Log Rank (Mantel-Cox)	1.982	1	0.159

Note. FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder; SE = Standard Error; 95% CI = 95% Confidence Intervals; Log Rank = Logarithm Rank Test; X² = Chi-Square test; df = degrees of freedom; p = statistical value.

Table 4 – Kaplan-Meier survival analysis results: comparison on 2-year new suicide attempt rate between the two FEP subgroups (n = 509).

Time intervals (in months)	FEP/BPD (n = 49)				FEP (n = 460)			
	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)
	Estimate	SE			Estimate	SE		
0-12	0.949	0.035	2	9	0.954	0.010	19	55
12-24	0.862	0.066	4	49	0.948	0.011	21	460

FEP subgroup	Mean (in months)			
	Estimate	SE	95% CI	
			Lower bound	Upper bound
FEP	23.451	0.126	23.203	23.698
FEP/BPD	23.385	0.489	22.425	24.344
Overall	23.445	0.121	23.208	23.682

	X ²	df	p
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Log Rank (Mantel-Cox)	2.071	1	0.150
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Note. FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder; SE = Standard Error; 95% CI = 95% Confidence Intervals; Log Rank = Logarithm Rank Test; X^2 = Chi-Square test; df = degrees of freedom; p = statistical value.

Table 5 – Kaplan-Meier survival analysis results: comparison on 2-year new self-harm behavior rate between the two FEP subgroups (n = 509).

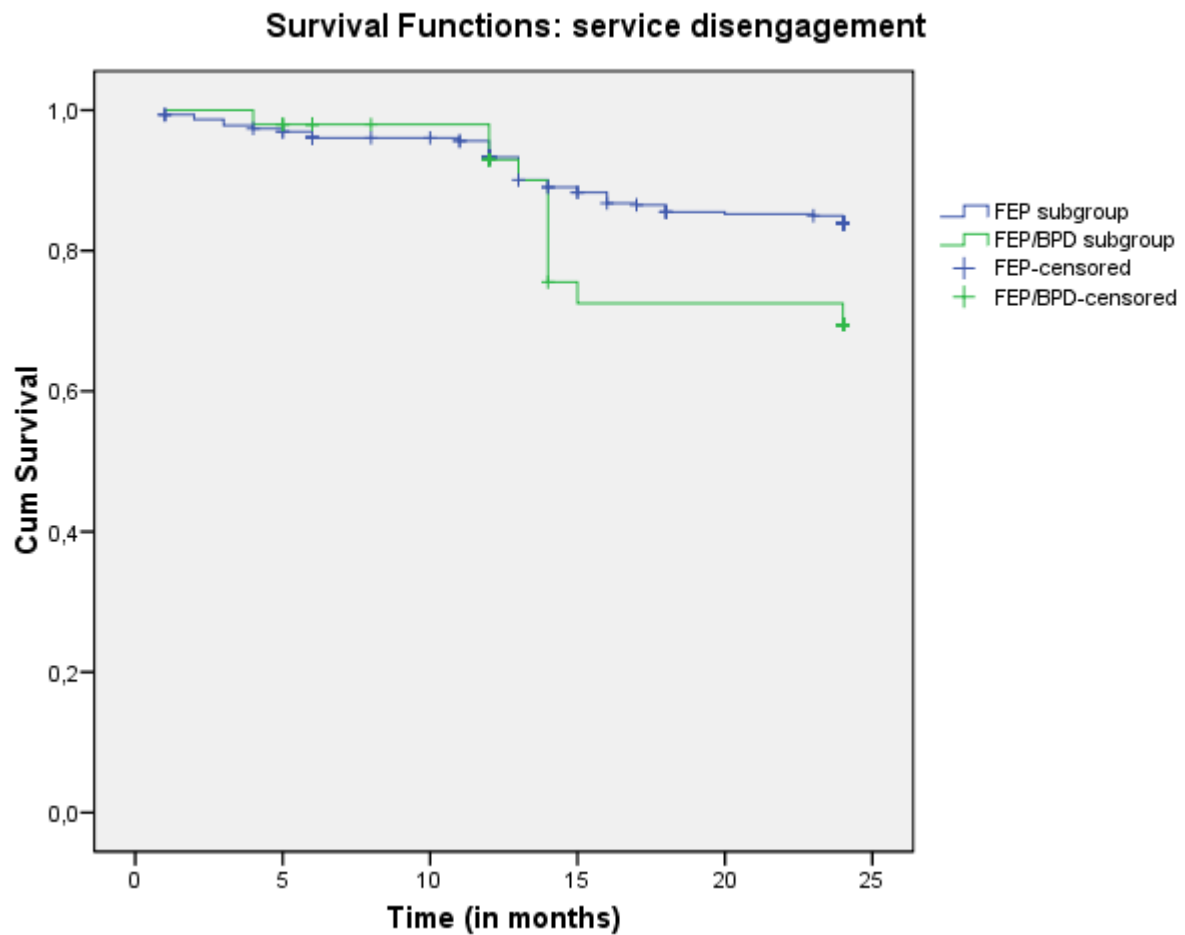
Time intervals (in months)	FEP/BPD (n = 49)				FEP (n = 460)			
	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)	Cumulative Proportion Surviving at the Time		Cumulative events (n)	Censored (n)
	Estimate	SE			Estimate	SE		
0-12	0.872	0.054	5	12	0.851	0.017	62	100
12-24	0.872	0.054	5	49	0.836	0.018	67	460

FEP subgroup	Mean (in months)			
	Estimate	SE	95% CI	
			Lower bound	Upper bound
FEP	22.209	0.211	21.795	22.624
FEP/BPD	22.462	0.642	21.202	23.721
Overall	22.231	0.201	21.837	22.625

	X^2	df	p
Log Rank (Mantel-Cox)	0.236	1	0.627

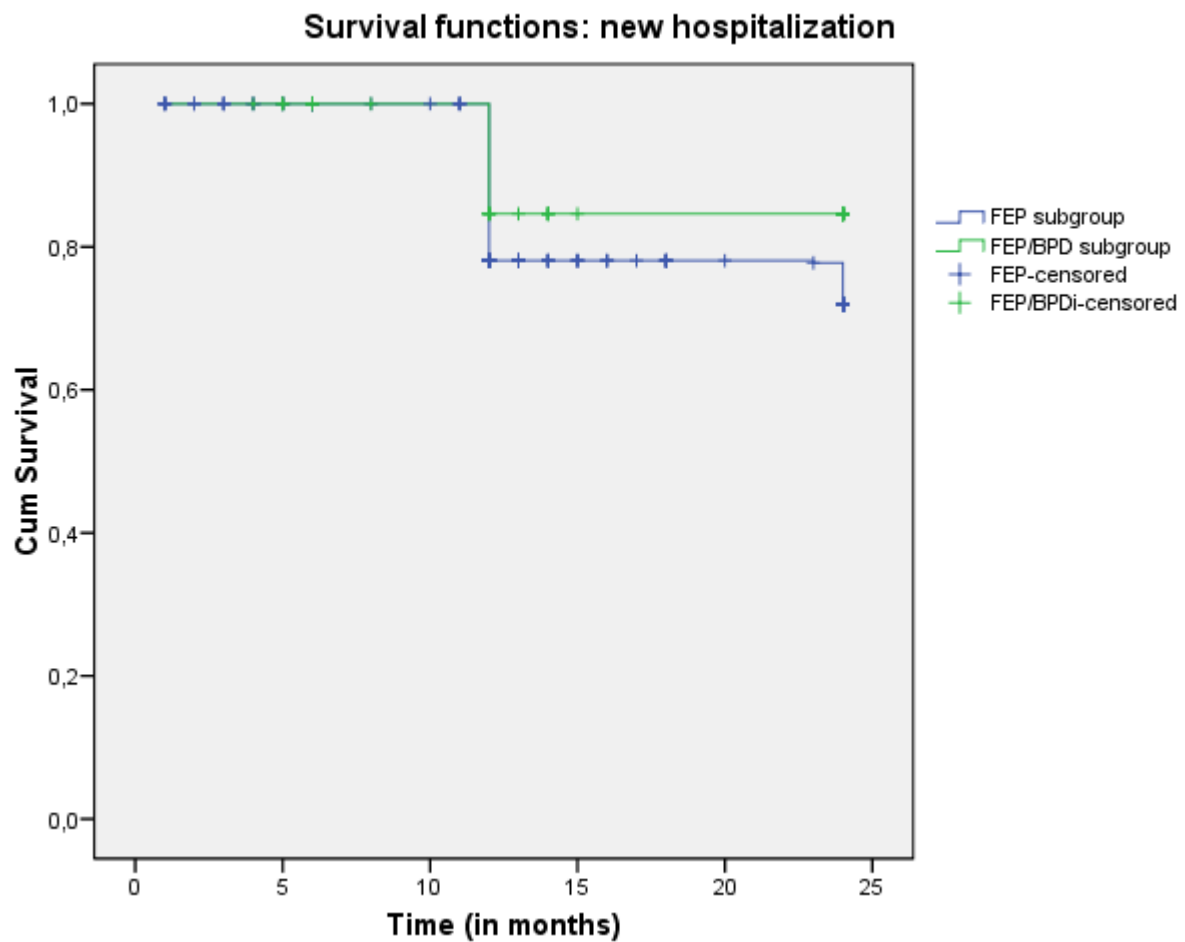
Note. FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder; SE = Standard Error; 95% CI = 95% Confidence Intervals; Log Rank = Logarithm Rank Test; X^2 = Chi-Square test; df = degrees of freedom; p = statistical value.

Appendix 1 – Kaplan-Meier survival analysis curve: comparison on 2-year service disengagement condition between the two FEP subgroups (n = 509).



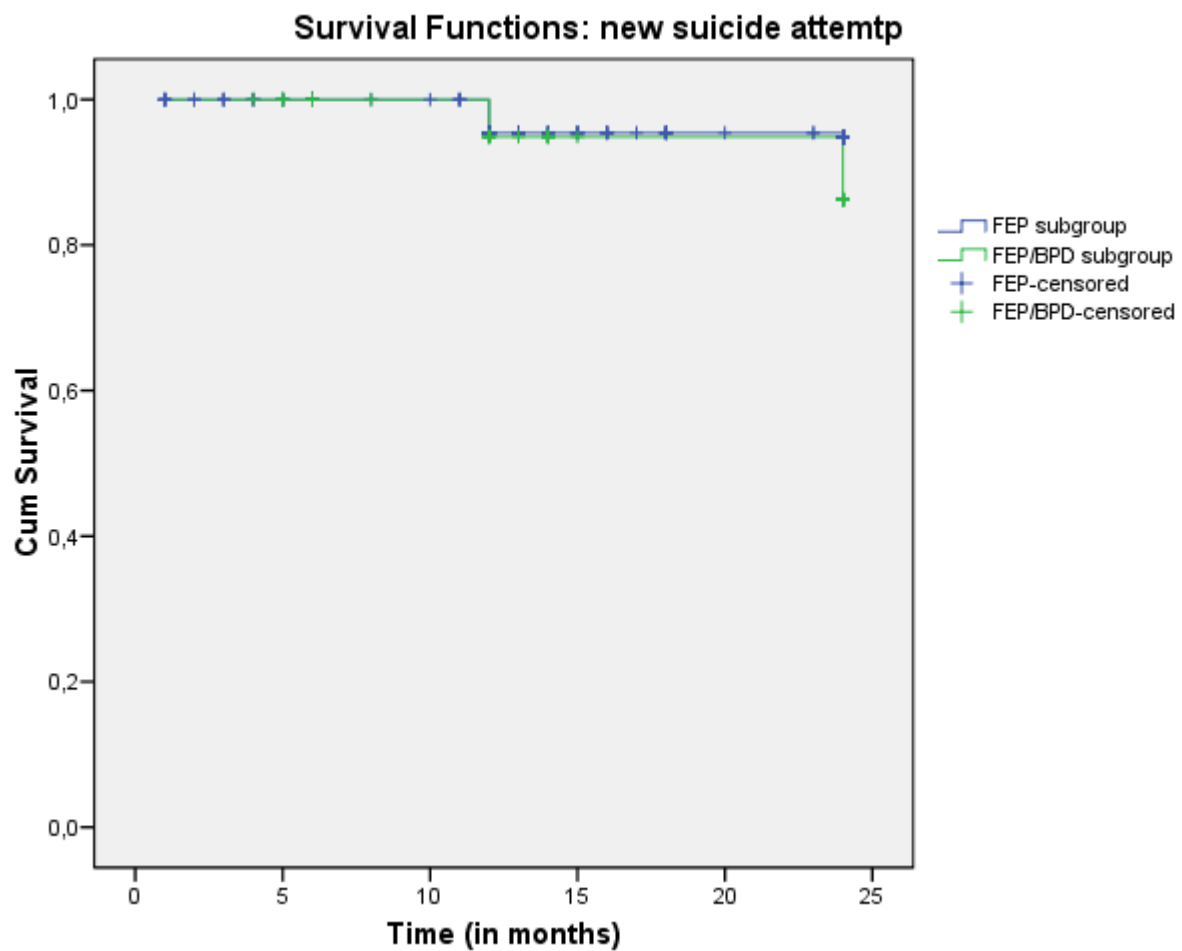
Note - FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder.

Appendix 2 – Kaplan-Meier survival analysis curve: comparison on 2-year new hospitalization condition between the two FEP subgroups (n = 509).



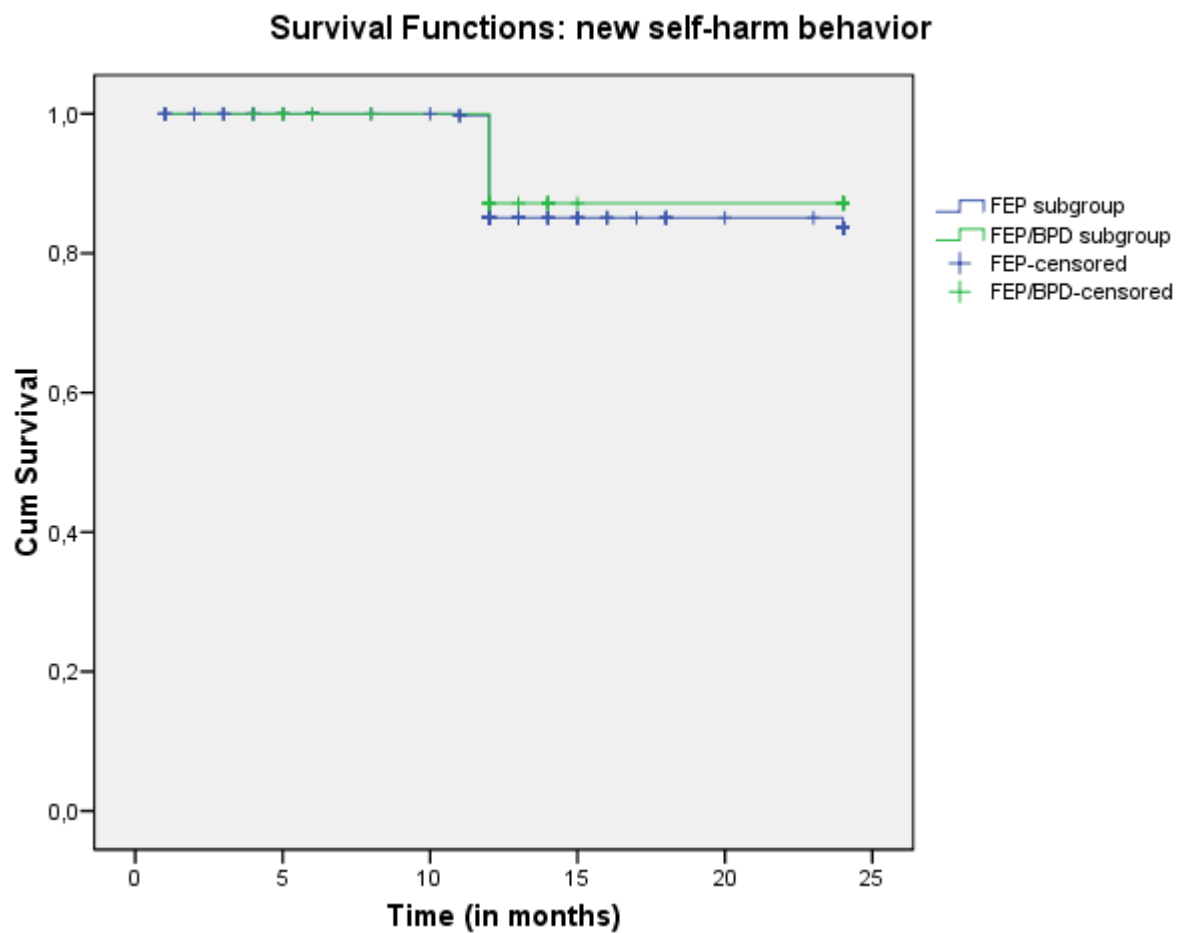
Note - FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder.

Appendix 3 – Kaplan-Meier survival analysis results: comparison on 2-year new suicide attempt rate between the two FEP subgroups (n = 509).



Note - FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder.

Appendix 4 – Kaplan-Meier survival analysis results: comparison on 2-year new self-harm behavior rate between the two FEP subgroups (n = 509).



Note - FEP = First Episode Psychosis; FEP/BPD = FEP patients with Borderline Personality Disorder; FEP = FEP patients without Borderline Personality Disorder.