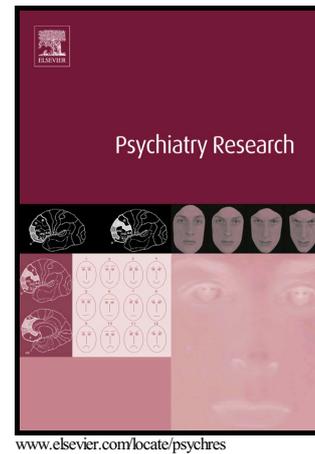# Author's Accepted Manuscript

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Psychiatry Research

www.elsevier.com/locate/psychres

Cite this article as: Julia Sevilla-Llewellyn-Jones, Gustavo Camino, Debra A. Russo, Michelle Painter, Angel L. Montejo, Susana Ochoa, Peter B. Jones and Jesus Perez, Clinically Significant Personality Traits in Individuals at High Risk of Developing Psychosis, *Psychiatry Research,* https://doi.org/10.1016/j.psychres.2018.01.027

Clinically Significant Personality Traits in Individuals at High Risk of Developing Psychosis

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Abstract

It is still unclear to what extent personality may influence the development of psychosis. We aimed to explore significant personality traits in individuals at high-risk (HR) for psychosis. Personalities of forty HR individuals and a matched sample of 40 HVs were evaluated with the Millon Multiaxial Inventory (MCMI-III). They were also assessed with the Positive and Negative Symptoms Scale (PANSS), Beck Depression and Anxiety Inventories (BDI-II and BAI), Global Assessment of Functioning (GAF) and Mini-International Neuropsychiatric Interview (MINI 6.0.0). Fisher's exact test was employed to compare frequency of traits. Mann-Whitney U test and logistic regression were used to establish relationships between traits and symptoms, and the effect of age, sex and symptoms on such traits. Most HR individuals (97.5%) had at least one significant trait; 75% had personality disorders, mainly depressive, borderline or schizotypal. Only histrionic and narcissistic traits were more prevalent in HVs. Negative symptoms were related to schizoid and paranoid traits. Depression was more severe with borderline traits. Most HR individuals (67.6%) had more than one DSM-IV Axis I diagnosis, mainly depressive/anxiety disorders. Transition rate was low (5%). Certain personality profiles may not be markers for conversions to psychosis but contribute to high morbidity in HR individuals.

Keywords: High-risk; Psychosis; Personality; Schizophrenia.

1. Introduction

The role of personality in the development of psychotic disorders still remains unclear. It has been argued that premorbid personality in psychosis may either have a pathoplastic effect, interacting with clinical symptoms at the onset of psychosis, or represent a vulnerability marker for such condition during neurodevelopmental processes in adolescence and young adulthood (Cuesta et al., 2002). Therefore, dysfunctional personality traits might emerge as manifestations of an evolving clinical picture that may end in full blown first-episode schizophrenia or other psychotic disorder (Heikkilä et al., 2004; Peralta et al., 1991).

In this context, the study of personality in individuals at high risk (HR) of developing psychosis seems relevant. Recent studies suggest that some clinically significant personality traits, such as borderline or schizotypal, despite being highly prevalent amongst HR individuals, have a very limited predictive value for conversions to psychotic disorders (Schultze-Lutter et al., 2012; Thompson et al., 2012). This finding raises the question as to what extent personality traits in HR individuals differ from non-HR populations and whether personality traits should not exclusively be investigated as predictors of conversion to psychosis but also as contributing factors to HR mental states.

In this study, we aimed to explore clinically significant personality traits in a group of help-seeking individuals at HR and compared them with a matched sample of healthy volunteers (HVs). We also analyzed the relationship of clinically significant personality traits with clinical symptoms, functioning and possible transitions to psychosis in HR individuals.

2. Methods

2.1. Setting

CAMEO (http://www.cameo.nhs.uk) is an early intervention in psychosis service which offers management for people aged 18–35 years suffering from first-episode psychosis in Cambridgeshire, UK. Referrals are accepted from multiple sources including general practitioners, other mental health services, school and college counselors, relatives and self-referrals (Hui et al., 2013). CAMEO also accepts referrals of people at HR (Perez et al., 2015).

2.2. Sample

A consecutive cohort of 40 help-seeking individuals, aged 18-35, referred to CAMEO from February 2010 to September 2012 met criteria for HR, according to the Comprehensive Assessment of At Risk Mental States (CAARMS; Yung et al., 2005). Referrals came to our offices via a number of different routes including self-referral, carers and relatives, schools and colleges, but mainly Primary Care. All individuals identified as HR for psychosis living and detected in Cambridgeshire and Peterborough were offered a systematic follow-up in the context of a prospective, naturalistic study called PAATH: Prospective Analysis of At-risk-mental-states and Transitions into Psychosis. They were asked to attend interviews where they completed structured clinical assessments and questionnaires.

In our sample, all individuals fulfilled criteria for the attenuated psychotic symptoms group. Three individuals (12%) also qualified for the vulnerability traits group (individuals with a family history of psychosis in first degree relative OR schizotypal personality disorder PLUS a 30% drop in GAF score from premorbid level, sustained for a month, occurred within the past 12 months OR GAF score of 50% or

less for the past 12 months). Intake exclusion criteria included: [1] Acute intoxication or withdrawal associated with drug or alcohol abuse or any delirium, [2] confirmed intellectual disability (Wechsler Adult Intelligence Scale – tested IQ <70), or [3] prior total treatment with antipsychotics for more than one week.

During the same period (February 2010-September 2012), a random sample of 40 HVs was recruited by post, using the Postal Address File (PAF®) provided by Royal Mail, UK. To ensure that each HR and HV resided in the same geographical location, 50 corresponding postcodes, matching the first 4/5 characters and digits of each recruited HR participant (e.g. PE13 5; CB5 3), were randomly selected using **Microsoft SQL** Server, a relational **database** management system, in conjunction with the PAF database. Each of these 50 addresses was sent a recruitment flyer containing a brief outline of the study, inclusion criteria and contact details. If this failed to generate recruits, a consecutive sample of postcodes would be selected. This process was repeated until a match was recruited. An average of 70 flyers was sent to each postcode to recruit the 40 HVs. HVs interested in the study could only participate if they were aged 18-35, resided in the same geographical area as HR participants, and did not have previous contact with mental health services.

2.3. Ethical approval

Ethical approval was granted by the Cambridgeshire East Research Ethics Committee.

2.4. Measures

All participants were assessed with sociodemographic (age, gender and ethnicity) and clinical measures at the time of their referral to CAMEO. The

assessments were carried out by senior research clinicians trained in each of the measurement tools.

The personalities of HR individuals and HVs were assessed with the Millon Multiaxial Inventory, Version III (MCMI-III) (Millon et al., 1997). The MCMI-III is a 175-item true/false, self-report questionnaire that evaluates DSM-IV axis I and II psychopathology (fourteen personality traits/disorders and 10 clinical syndromes). The score for each personality trait ranges from 0 to 115. A score ≥75 suggests clinically significant personality trait; ≥85 indicates personality disorder. For the purpose of this study we employed personality scores (axis II), and considered personality traits that scored as clinically significant. Additionally, we grouped specific MCMI-III personality traits under the three DSM-IV clusters of personality disorders (A, B and C) (American Psychiatric Association (APA), 1996). The MCMI-III scores were calculated and evaluated by a senior clinical psychologist (GC), who was blind to the participants' identity, sociodemographic and clinical data, and to whether they were HR or HVs.

HR individuals were also interviewed by senior trained psychiatrists working in CAMEO, using the Mini International Neuropsychiatric Interview (MINI), Version 6.0.0 (Sheehan et al., 1998), a brief structured diagnostic interview for DSM-IV Axis I psychiatric disorders. The study protocol did not routinely administer a MINI for HVs. However, if information elicited with the battery of questionnaires indicated any concerns about mental state, the protocol was to administer a MINI for verification.

The Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was also employed to capture the severity of psychotic symptoms in HR and HV participants, and possible associations with certain personality traits in the HR group. For the purpose of this study, we used Emsley´s five-factor model (2003) which considers

6

positive (6 items), negative (8 items), disorganized (7 items), excited (4 items), anxiety and depression (5 items) symptoms in a 7-point scale, with higher scores indicating greater severity of illness

The Beck Depression Inventory, Version II (BDI-II; Beck et al., 1996) Beck et al., 1987) and the Beck Anxiety Inventory (BAI; Beck et al., 1988) were used to assess depressive and anxiety symptoms in both groups. BDI-II and BAI are widely used self-report instruments to assess depressive and anxiety symptom severity in the past two week. Each of them consists of 21 items rated on a 4-point scale from absent (0), mild (1), moderate (2) to severe (3). Composite scores (range 0-63 points) were generated by summing up individual items. Scores obtained from both measures were also used to analyze possible associations with personality traits in HR individuals.

The Global Assessment of Functioning (GAF) is a commonly used functioning scale in psychiatric research (Hall, 1995). The GAF assesses global functioning in the past month. Both symptoms and disability dimensions were assessed using an impression score of 1 to 100, with 10 points separating each level (Endicott et al., 1976), and lower scores representing higher severity of symptoms and poorer level of functioning.

2.5. Statistical analysis

Sociodemographic, clinical and personality variables were described in terms of mean or frequency. Fisher's exact test was employed to compare frequency of clinically significant personality traits between both groups. Mann-Whitney U test was calculated to analyze the relationship of each clinically significant personality trait with clinical symptoms and functioning in the HR group. Finally, a logistic regression with Forward

Wald method was carried out in order to study the influence of sex, age and symptoms on personality traits. All analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22.0.

3. Results

3.1. Sociodemographic profile

Table 1 shows that there was no difference in age between HR individuals and HVs. Both groups had the same number of males and females. The main ethnicity for both groups was white.

[Table 1 about here]

3.2. Clinically significant personality traits

The presence of one or more clinically significant personality traits in our HR sample was very high (97.5%). The most common clinically significant personality traits in HR individuals were depressive (82.5%), borderline (67.5%) and masochistic (57.5%); followed by avoidant, dependent, negativistic and schizotypal in 50% of the sample. Most personality traits were significantly more frequent in the HR group than in HVs. Narcissistic and histrionic traits were more prevalent amongst HVs. Antisocial, sadistic and compulsive traits were similar in both groups (See Figure 1).

75% of the HR individuals met MCMI-III criteria (score ≥85) for at least one personality disorder, mostly depressive (56.7%), borderline (46.7%) and schizotypal

(36.7%); whereas only 32.5% of the HVs scored above the MCMI-III threshold for a

disorder, mainly compulsive (46.2%), histrionic (23.1%), and narcissistic (15.4%).

[Figure 1 about here]

3.3. DSM-IV Axis I Psychiatric Diagnoses

We obtained MINI DSM-IV Axis I diagnoses for 37 of the 40 HR individuals.

Twenty five (67.6%) had more than one DSM-IV Axis I psychiatric diagnosis, mainly

within the affective and anxiety diagnostic spectra. Primary diagnoses for this group

were ranked as follows: major depressive episode, current or recurrent (n=18; 48.7%) >

generalized anxiety disorder (n=7; 18.9%) > social phobia (n=6; 16.2%) > obsessive

compulsive disorder (n=2; 5.4%) > panic disorder (n=1; 2.7%). Three HR individuals

(8.1%) did not fulfill sufficient criteria for a DSM-IV Axis I diagnosis.

Regarding HVs, information obtained from our battery of assessments did not

suggest concerns that warranted further evaluation with the MINI for any of them.

3.4. Clinical Symptoms

The mean scores for the PANSS five-factor model in the HR group were 12.79

(SD = 3.31) for positive, 13.94 (SD = 5.56) for negative, 9.66 (SD = 2.81) for

disorganised, 5.68 (SD = 1.74) for excited and 14.39 (SD= 4.64) for anxiety/depressive

symptoms. These scores indicated a "mildly ill" group according to the PANSS (Leucht et al., 2005). These symptoms were significantly lower in HVs (p=0.000).

With regards to anxiety and depressive symptoms, the mean scores for BAI and BDI-II in the HR group were 27.58 (SD=12.46) and 29.47 (SD=13.40), respectively. Both scores were significantly higher than those of the HV group (p=0.000). These values indicated severe anxiety (Beck et al., 1988) and moderate depression (Beck et al., 1996). The GAF for the HR group was 46.57 (SD=7.89), significantly lower than in HVs (85.68(SD=5.95)) (See Table 1).

3.5. Relationship of clinically significant personality traits with clinical symptoms and functioning in HR individuals

We studied the relationship between specific clinically significant personality traits, functioning and symptoms of psychosis, anxiety and depression in HR individuals.

PANSS negative symptoms were more common in HR individuals with clinically significant schizoid, avoidant and paranoid personality traits (p=0.033, p=0.003 and p=0.020, respectively). Conversely, HR individuals with antisocial traits scored lower in the PANSS negative dimension (p=0.016). Symptoms of the PANSS excited factor were more prevalent in HR people with antisocial (p= 0.037) and borderline (p= 0.017) personality traits. HR individuals with histrionic clinical personality traits suffered from less PANSS positive symptoms (p= 0.041).

BDI-II scores were significantly higher in HR people with borderline (p=0.030) and paranoid (p=0.040) personality traits. With regards to the BAI, only the HR subgroup with depressive personality traits exhibited more anxiety symptoms

(p=0.003). No specific personality traits in HR individuals were associated with the level of functioning as determined by the GAF scale.

3.6. Effect of sex, age and clinical symptoms on clinically significant personality traits

We carried out an analysis to check the possible influence of sociodemographic variables, such as age and sex, and clinical symptoms on specific clinically significant personality traits. Table 2 exclusively shows the clinically significant personality traits that could have been influenced by the aforementioned variables in our sample. The PANSS negative symptoms explained 24.4% and 20.5% of the variance of avoidant and paranoid traits, respectively. PANSS negative and excited symptoms explained 44.6% of the variance of antisocial personality trait. Sex (female) and anxiety explained 74.5% of the variance of depressive trait. Additionally, PANSS excited symptoms explained 24.1% of the borderline personality trait, 18.6% of DSM cluster B and 17.8 % of cluster C personality traits. PANSS negative and positive symptoms explained 43.4% of the cluster A traits.

[Table 2 about here]

3.7. Transitions from HR to First Episode Psychosis

After at least three years of follow-up for each HR individual in our sample, only 2 (5%) made a transition into FEP. None of the HR individuals from this cohort received antipsychotics. The clinically significant personality traits in these two individuals were: schizoid, avoidant, depressive, dependent, masochistic, schizotypal for both of them.

No HV developed either a psychotic disorder or a HR mental state over a two-year follow-up.

4. Discussion

To the best of our knowledge this is the first study that explores clinically significant personality traits in help-seeking individuals at HR of developing psychosis and compares them with those of HVs matched for age, sex and geographical residency.

We found that the prevalence of clinically significant personality traits was very high amongst HR individuals. Almost all of them had at least one clinically significant personality trait. Previous studies found that approximately half of their HR samples suffered from personality disorders (Rosen et al., 2006; Schultze-Lutter et al., 2012). Our analysis revealed that three in four of our HR sample suffered some type of personality disorder, mainly depressive, borderline or schizotypal. Although this proportion is higher than in other HR samples previously reported, the difference may well be explained by the higher number of personality traits that the MCMI-III contemplates in comparison to other scales, such as the "Selbstbeurteilung nach der Aachener Merkmalsliste für Persönlichkeitsstörungen" (SAMPS; Woschnik and Herpertz, 1994) employed by Schultze-Lutter et al. (2012) or structured interviews, such as the Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV; Zanarini et al., 1987), used in Rosen et al.'s study (2006).

Most personality traits were significantly more prevalent in HR individuals than in HVs. Histrionic and narcissistic traits were more frequent in HVs. The most common clinically significant personality traits in the HR sample were depressive, borderline and masochistic. The high prevalence of depressive personality may be congruent with the high anxious and depressive morbidity of our HR sample. In fact, several studies

suggest that the majority of help-seeking individuals at HR present with co-morbid anxiety and/or depression (Addington and Heinssen, 2012; Hui et al., 2013; Velthorst et al., 2009; Wigman et al., 2012). In our study, we found a strong association between depressive personality traits and anxiety levels, and between borderline and paranoid traits and depressive symptoms. Thus, certain personality profiles may play a part in the co-morbidity of HR with depression/anxiety (Friborg et al., 2013; Hirschfeld, 1999). The significant number of HR individuals with masochistic personality traits might partly be explained by the high prevalence of traumatic events during childhood and adolescents in our cohort; data reported elsewhere (Russo et al., 2015). Indeed, it has been argued that those people who suffered significant traumatic events at early ages may seek reduction of the emotional tension associated with them by reenacting them, getting involved in dangerous situations, such as psychological or physical sadomasochistic relationships (Center for Substance Abuse Treatment (US), 2014).

Our secondary analysis of possible relationships between clinical symptoms and personality traits in HR suggested that schizoid, paranoid and avoidant traits were related to negative psychotic symptomatology. Whilst the association between schizoid manifestations and negative symptoms is well reported (Cannon et al., 1990; Cuesta et al., 2002; Sevilla-Llewellyn-Jones et al., 2017), studies exploring this relationship with paranoid and avoidant personalities are scarce. Nevertheless, considering that these three personality profiles may share certain behavioral and psychological patterns, such as social detachment (Craig, 2005), the link with negative symptoms could partly lie on social and emotional withdrawal. On the other hand, borderline and antisocial traits were more related with excitation as measured by the PANSS. Interestingly, HR individuals with clinically significant histrionic traits seemed to present with less intense positive psychotic symptoms than those at HR without these traits. Indeed,

previous studies on recent onset psychosis described the same finding, attributing it to more proactive (less isolative) social behaviors and seek for help (Sevilla-Llewellyn-Jones et al., 2017; Wickett et al., 2006).

The low transition rate in our HR sample precluded the possibility of testing the predictive power of personality traits. However, other studies have also suggested that clinically significant personality traits identified in our HR individuals may not be significant markers for the development of psychotic disorders. In fact, Thompson et al. (2012) demonstrated that the presence of borderline personality disorder (highly prevalent in our sample) in individuals at HR did not increase the likelihood of a conversion to a psychotic disorder. Furthermore, a recent study on patients with recent onset psychotic disorders, whose personalities were also explored with the MCMI-III, only detected a low proportion of borderline and masochistic personality traits among them (Sevilla-Llewellyn-Jones et al., 2017). This adds credence to the argument of the lack of diagnostic specificity and high heterogeneity of populations considered as HR, according to current measurement tools broadly based on descriptive psychopathology. Notably, functioning in our HR sample was severely impaired, but this did not seem to be directly associated with any personality trait. Nonetheless, as specified above, certain clinically significant personality traits may act as contributing factors for a variety of clinical symptoms, which, as a whole, may represent a significant burden to these people's lives.

Notwithstanding the strengths of our study, conducted in young adults, where personality is more developed than in adolescents (Roberts et al., 2006) , our results must be interpreted in light of the following limitations. First, personality was measured with a self-report questionnaire (MCMI-III) and not corroborated by structured interviews, such as the SCID-II. However, the MCMI-III is a validated instrument that

includes validity scales to ensure accurate detection of DSM personality traits and/or disorders (Strack and Millon, 2007). In addition, confidential self-report usually produces more truthful responses (Paulhus and Vazire, 2010). Second, the MCMI-III has not been officially validated in HVs. Previous studied have already employed it with HVs (Cohen et al., 2005; López Pantoja et al., 2012; Manchikanti et al., 2002; Prosser et al., 2008) and found that some traits, such as compulsive, histrionic or narcissistic, are relatively common in non-clinical samples (Craig, 2005), as we also elicited in our HV sample. Third, arguably, longer follow-ups might have detected more conversions to psychotic disorders in our HR sample, which could have allowed meaningful personality comparisons with non-converters. However, at the time of this report, all HR individuals were followed for three years or more, with no clear indication of further transitions in the short-term. Fourth, it should be acknowledged that personality may be influenced by cultural contexts (Sansone and Sansone, 2011); thus, this may affect the generalisability of our findings. Finally, given the clinical heterogeneity amongst individuals at HR, a larger sample, with more conversions, might have also provided a better idea of personality profiles that may contribute to the development of frank psychotic disorders. To date, on the basis of our results and findings from other accepted studies (Schultze-Lutter et al., 2012; Thompson et al., 2012), personality traits in those at HR offer a low predictive value for that purpose. Nonetheless, our work supports the importance of exploring clinically significant personality traits in this population as they seem to have an influence on psychiatric morbidity, perpetuating these mental states, and, ultimately, affecting functioning. Psychological interventions focusing on underlying personality traits may provide another avenue to achieve symptom and functional recovery in people suffering from HR mental states.

15

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Table 1. Comparison of sociodemographic and clinical variables between High Risk (HR) individuals and Healthy Volunteers (HVs).

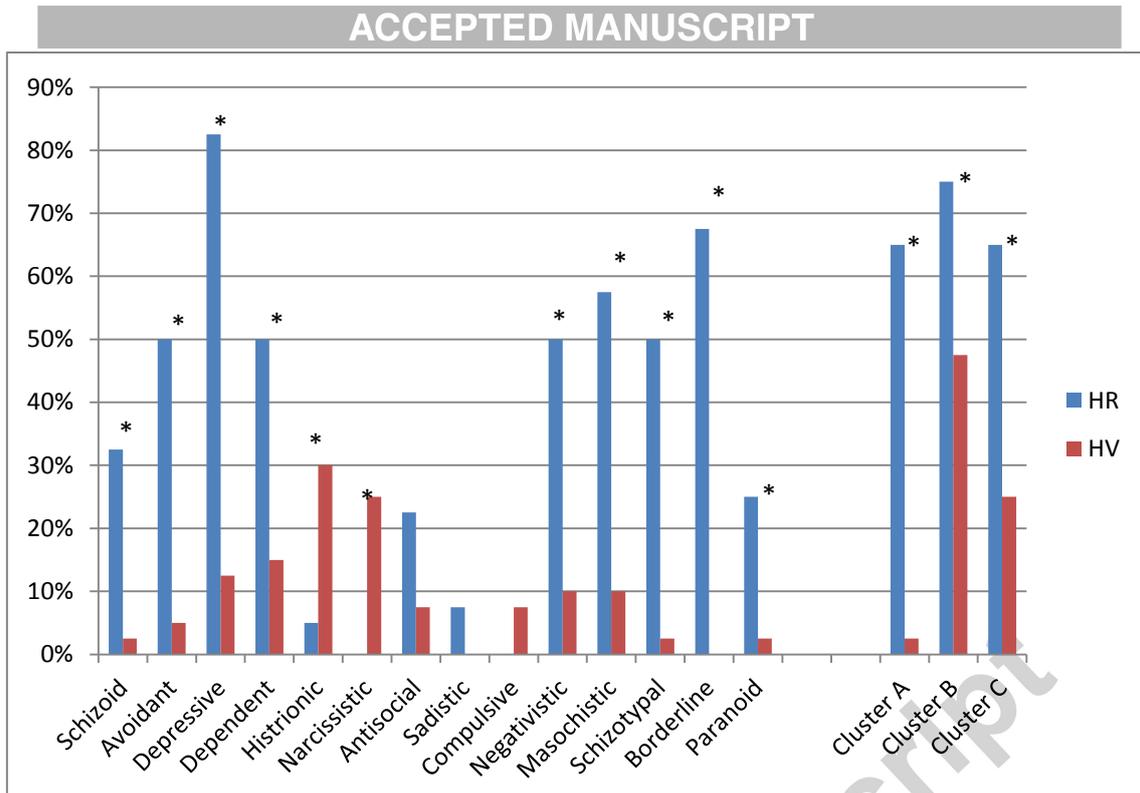|	HR	HV	*p*
Age mean (SD)	21.65 (2.64)	23 (4.79)	0.122[†]
Gender n (%)			1[‡]
Male	19 (47.5)	19 (47.5)	
Female	21 (52.5)	21 (52.5)	
Ethnicity n (%)			0.603[‡]
White	39 (97.5)	38 (95)	
Asian	1 (2.5)	1 (2.5)	
Back	0 (0)	1 (2.5)	
PANSS mean (SD)			
Positive	12.79 (3.68)	6.15 (0.43)	0.000[†]
Negative	13.95 (5.56)	8.18 (0.50)	0.000[†]
Disorganized	9.66 (2.81)	7.60 (0.74)	0.000[†]
Excited	5.68 (1.74)	4.08 (0.35)	0.000[†]
Anxiety/Depression	14.39 (4.64)	5.15 (0.58)	0.000[†]
BDI-II mean (SD)	29.47 (13.40)	6.45 (6.70)	0.000[†]
BAI mean (SD)	27.58 (12.46)	8.95 (8.65)	0.000[†]
GAF mean (SD)	46.57 (7.89)	85.68 (5.95)	0.000[†]

[†]T- Student, [‡]Chi^2 test

22

Table 2. Effect of sex, age and symptoms on clinically significant personality traits.

Personality traits	Sex (Female)			PANSS Positive			PANSS Negative			PANSS Excited			BAI		
	B (ET)	OR	$p^\dagger$	B (ET)	OR	$p^\dagger$	B (ET)	OR	$p^\dagger$	B (ET)	OR	$p^\dagger$	B (ET)	OR	$p^\dagger$
Avoidant							0.19 (0.08)	1.21	0.01						
Depresssive	5.99 (3.06)	401.37	0.05										0.41 (0.17)	1.50	0.01
Antisocial							-0.35 (0.18)	0.70	0.05	0.69 (0.29)	2.00	0.01			
Borderline										0.63 (0.27)	1.89	0.02			
Paranoid							0.16 (0.07)	1.17	0.02						
DSM Cluster A				0.32 (0.15)	1.38	0.03	0.24 (0.11)	1.28	0.03						
DSM Cluster B										0.59 (0.30)	1.80	0.04			
DSM Cluster C										0.52 (0.25)	1.69	0.04			

$\dagger$Logistic regression with Forward Wald method. The table only includes effects that were significant.

*p≤0.05 (Fisher's exact test)

Figure 1. Frequency of clinically significant personality traits in HR individuals and

HVs.

Highlights

Three in four individuals at high risk (HR) for psychosis had personality disorders.

The most frequent traits in HR were depressive, borderline and masochistic.

Borderline and paranoid traits were associated with depression in HR individuals.