



Autism-spectrum traits in First Episode Psychosis: Psychopathological and prognostic considerations from a 2-year follow-up study

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ABSTRACT

Introduction: There's a general lack of knowledge about autism attributes in early psychosis, although little initial evidence showed that having autistic features contributes to poorer recovery over time. The main aim of this examination was to compare sociodemographic and clinical variables between FEP patients with or without autistic characteristics treated within an “Early Intervention in Psychosis” (EIP) service both at entry and across 2 years of follow-up. We also examined the longitudinal course of autism severity levels in FEP to investigate whether they truly represented trait-like attributes.

Methods: FEP participants completed the AQ-spectrum Questionnaire (AQ), the Positive And Negative Syndrome Scale (PANSS), and the Global Assessment of Functioning (GAF) at baseline and over time. Inter-group comparisons were examined using Chi-Squared or Mann-Whitney test, Kaplan-Meier survival analysis, mixed-design ANOVA, and binary logistic regression. AQ score longitudinal stability was explored using Wilcoxon test for repeated measures and Spearman correlation coefficient.

Results: 132 subjects were recruited (28 [21.20 %] scored above the AQ cut-off score of ≥ 26). At presentation, they showed younger age and higher severity in psychopathology (especially negative symptoms). Across the follow-up, the AQ+ subsample had lower incidence rates of service disengagement, PANSS symptomatic remission, and GAF functional remission. AQ scores showed longitudinal stability over time.

Conclusions: The AQ represents a valid instrument to assess “trait-like” autistic features in FEP subjects. Specifically, it captures a distinct FEP subgroup characterized by more severe clinical presentation, poorer clinical and functional outcomes, and specific therapeutic needs.

1. Introduction

Autistic features are common outside Autism-Spectrum Disorders (ASD), especially in patients with psychosis (Huang et al., 2020). This virtually suggested the idea of their “trans-diagnostic” nature and the presence of bio-behavioral phenotypes beyond current nosographic categories, probably related to common neurodevelopmental vulnerability and overlapping biological pathways (Kalin, 2022; Guerrero et al., 2024). In particular, psychosis and ASD characteristics have historically been considered closely linked (Bleuler, 1911; Kanner, 1943) and often co-occur, although with heterogeneous prevalence rates at both the trait (9–60 %) and the diagnostic level (1–50 %) (Kincaid et al., 2017; De Crescenzo et al., 2019).

In this respect, within the multifaceted entity of psychosis (including First Episode Psychosis [FEP]), a distinct subgroup with autistic features has been recently defined (Jutla et al., 2022). Specifically, recent studies consistently showed that autistic traits in FEP were linked with greater cognitive and negative symptom burden. In detail, this “autistic phenotype” seems to be characterized by marked alterations in communication, social interaction, and processing emotions (Hajdúk et al., 2023), and was resulted to be associated with longer duration of illness, earlier age at onset, greater severity in psychopathology (especially negative and cognitive symptoms), poorer global functioning, and higher risk of suicide (Pina-Camacho et al., 2020; Abu-Akel et al., 2022; Nibbio et al., 2022). However, other authors showed that autistic traits in FEP not necessarily lead to worse outcomes. Indeed, Sunwoo et al.

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(2020) reported that individuals with a concurrent diagnosis of FEP and ASD were less likely to have comorbid substance use issues and were more likely to be engaged in employment or education at the time of discharge from services. Moreover, Abu-Akel et al. (2022) also found that the combined effect of autistic traits in FEP subjects identifies a group of patients with lower levels of functional impairment, suggesting a sort of compensation across mechanisms associated with autism and psychosis (Vaskinn and Abu-Akel, 2019; Dell'Osso et al., 2021). Finally, within the broader schizotypal personality disorder, some researchers observed that concurrent elevated levels of autistic and positive symptoms seem to be associated with improved sustained attention abilities (i.e., reduced omission errors) (Abu-Akel et al., 2020).

Given these mixed results on prognosis and clinical outcomes, research interest has recently focused on examining autism features in early psychosis, especially in young patients with FEP (Ferrara et al., 2023). This was also for the development of the PAUSS (“PANSS Autism Severity Score”) (Kästner et al., 2015), a quick psychopathological dimension score specifically calculated to measure autistic characteristics from 8 items of the “Positive And Negative Syndrome Scale” (PANSS) (Kay et al., 1987), which were selected to cover the main ASD domains as described in the DSM-5 criteria (APA, 2013). Specifically, it was reported that young FEP individuals highly scoring on the PAUSS showed poorer daily functioning, greater severity levels in psychopathology (especially in cognitive and negative symptoms), and lower education (Chisholm et al., 2019; Sunwoo et al., 2020; Davut et al., 2023; Jeong et al., 2024; Komatsu et al., 2025). However, while remaining popular, the PAUSS has been shown to have a poor long-term stability (Chisholm et al., 2023), suggesting that it may not capture enduring, autistic trait-like attributes, but represent a proxy for clinical severity in psychotic-state symptoms (Chisholm et al., 2023). This raised the suspicion that the PAUSS could not be a valid instrument to identify autistic features in patients with FEP and at the same time the need to use more *specific tools*, especially trait-focused instruments (such as the Autism-spectrum Questionnaire [AQ]) (Baron-Cohen et al., 2001). Indeed, to date, there is still a dearth of studies examining autism characteristics in early psychosis that adopted instruments specifically developed to detect them, especially in terms of traits and outcome analysis (Ribolsi et al., 2022). To the best of our knowledge, only two investigations explored autism characteristics in FEP patients using the AQ. Specifically, an interesting cross-sectional examination on 99 FEP individuals in the UK reported that higher levels of autistic features were correlated with poorer functioning, current psychotic symptoms, and quality of life at baseline (Chisholm et al., 2019). Additionally, a 1-year longitudinal research on 180 FEP from Singapore (Zheng et al., 2021) found that participants with more autistic features were more likely to be unemployed and to have a diagnosis of affective psychosis, psychotic disorder Not Otherwise Specified (NOS), or brief psychotic disorder. Moreover, although most patients showed improvement in their clinical outcomes after one year of follow-up, those with higher autistic characteristics improved less in general psychopathology.

Given the paucity of evidence on autism attributes in early psychosis and their potential contribution to poorer recovery over time (Kyriakopoulos, 2019), the main *aim* of this investigation was to compare sociodemographic, clinical, and outcome variables between FEP individuals with or without autistic features at entry across 2 years of follow-up. An additional aim was to examine the longitudinal course of autism severity levels in the FEP total sample to discuss whether they represent trait-like attributes and remain stable over time, or whether they show longitudinal changes that may be associated with treatment response.

2. Methods

2.1. Setting

FEP participants were inpatients/outpatients consecutively recruited

within the “Parma-Early Psychosis” service (Pr-EP) between January 2019 and December 2022. The *Pr-EP* is a diffused EIP infrastructure implemented in all adult and adolescent centers of the Parma Department of Mental Health (Northern Italy) (Pelizza et al., 2024a).

For the specific aims of this research, *inclusion criteria* were: (a) age 16–35 years; (b) FEP within baseline DSM-5 diagnoses of schizophrenia, schizophreniform disorder, bipolar/major depressive disorder with psychotic features, brief psychotic disorder, delusional disorder, and psychotic disorder NOS (APA, 2013); and (c) a DUP (“Duration of Untreated Psychosis”) of <2 years. This DUP value was chosen because it is the usual time limit to provide effective interventions within the EIP paradigm (Malla, 2022). The DUP was defined as the time interval (in weeks) between the onset of full-blown psychotic symptoms and the first psychopharmacological treatment (Pelizza et al., 2025a) and was established using clinical information collected directly from patients (and/or family members) or reported in medical records.

Exclusion criteria were: (a) past psychotic disorder; (b) past exposure to antipsychotics (AP); (c) known intellectual disability (IQ < 70); and (d) medical/neurological illness with psychiatric symptoms. Past AP exposure (i.e., before the Pr-EP recruitment) was intended as a “functional equivalent” of past psychotic episode, according to the original criteria for psychosis threshold within the EIP paradigm (Mills et al., 2017). Additionally, a known IQ < 70 was established based on previous administration of the WAIS-IV (Wechsler Adult Intelligence Scale-IV) (Wechsler, 2008) or WISC-IV (Wechsler Intelligence Scale for Children-IV) (Wechsler, 2003).

This investigation was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments. Local relevant ethical approval was obtained (AVEN Ethics Committee: protocol n. 36.102/2019). All FEP patients and their parents (if minors) agreed to participate to the research and gave their written informed consent prior to their inclusion in the study.

2.2. Assessment

In this research, psychopathological assessment included the AQ, the PANSS, the GAF (“Global Assessment of Functioning” scale) (APA, 2013), and the HoNOS (“Health of the Nation Outcome Scale”) (Wing et al., 1999). These instruments were completed by trained Pr-EP team members both at baseline and every 12 months across the follow-up (Pelizza et al., 2022a). Supervision sessions and scoring workshops were regularly carried out to ensure inter-rater reliability (Pelizza et al., 2022b).

The AQ is a self-report questionnaire exploring autism-spectrum traits in subjects over the age of 16 (Bezemer et al., 2021). It is composed of 50 items scored using a 4-Likert rating scale (from 1 [“Definitely agree”] to 4 [“Definitely disagree”]). AQ total scores of ≥ 26 indicate the presence of autistic traits, while scores of ≥ 32 suggest a highly probable ASD diagnosis. ASD-trait individuals are unlikely to score below 26 (Ziermans et al., 2021). The AQ was validated in Italian clinical and nonclinical populations (Dell'Osso et al., 2017; Iannuzzo et al., 2022), and was previously used in FEP samples (Zheng et al., 2021).

The PANSS is commonly used to evaluate psychopathology in FEP subjects (Liechti et al., 2017). As indicated in the meta-analysis by Shafer and Dazzi (2019), we considered 5 main PANSS dimensions: “Disorganization”, “Negative Symptoms”, “Positive Symptoms”, “Affect” (“Depression/Anxiety”), and “Resistance/Excitement-Activity”. As symptomatic remission index at follow-ups, we used a score of ≤ 3 on all 8 PANSS items included in the criteria suggested by the “Remission in Schizophrenia Working Group” (Andreasen et al., 2005). In this research, we used the Italian version of the PANSS that showed good psychometric properties in patients with psychosis (Pancheri et al., 1995; Pelizza et al., 2025b).

The GAF is a scale frequently used to evaluate clinical and socio-occupational functioning in FEP individuals (Pelizza et al., 2022c). In

particular, according to Yang et al. (2022), we considered a GAF score of ≥ 60 at follow-ups as index of functional remission.

The HoNOS is an instrument commonly administered to assess mental health and social outcomes in FEP patients (Pelizza et al., 2024b). According to Morosini et al. (2003), 4 outcome domains were considered: “Impairment”, “Psychiatric Symptoms”, “Behavioral Problems”, and “Social Problems”. Moreover, in accordance with Kortrijk et al. (2012), we also considered HoNOS item 9, 10, and 11 scores of ≤ 2 at follow-ups as other index of functional remission.

Finally, a *clinical/sociodemographic chart* was filled out at baseline and at follow-ups. It also included information on DUP, new hospitalization, service disengagement (intended as complete lack of contact or untraceable for at least 3 months despite a need of treatment) (Pelizza et al., 2024c), new suicide attempt (defined as a potentially injurious, self-inflicted behavior without a fatal outcome for which there was [implicit or explicit] evidence of intent to die) (Pelizza et al., 2024d), current suicidal ideation (intended as a score of ≥ 2 on item 4 “Suicidality” of the Brief Psychiatric Rating Scale [BPRS], corresponding at least to occasional suicidal thinking without specific plans) (Pelizza et al., 2023), functional recovery (simply defined as return to work/school, in accordance with Silva and Restrepo (2019)), and Pr-EP psychosocial and pharmacological interventions (Pelizza et al., 2022d).

The DSM-5 diagnosis was identified at entry by two trained Pr-EP team professionals using the Structured Clinical Interview for DSM-5 mental disorders (SCID-5) (First et al., 2017).

2.3. Procedures

At baseline, FEP participants were divided into two subgroups based on AQ cut-off score of ≥ 26 (i.e., FEP/AQ+ vs FEP/AQ-). Between-group comparisons on sociodemographic, clinical, and treatment parameters were first examined. Moreover, along the follow-up, the two subsamples were compared in terms of specific clinical outcomes (e.g., service disengagement, new suicide attempt, new hospitalization) and stability of HoNOS, GAF, and PANSS scores. Between-group comparisons on treatment response were also analyzed.

Specifically, the Pr-EP is a 2-year comprehensive EIP intervention package that offers pharmacological therapy together with multi-component psychosocial interventions, combining individual cognitive-behavioral psychotherapy, psychoeducation for family members, and an early recovery-oriented case management (Pelizza et al., 2022e), according to the current EIP guidelines (Galletly et al., 2016; RER, 2024).

2.4. Statistical analysis

Data were analyzed using the Statistical Package for Social Science (SPSS) 29.0 for Windows (IBM, 2023). Significance level was set at 0.05 for all two-tailed analyses. Given the non-normality distributions of continuous parameters (Kolmogorov-Smirnov test's p values $< .05$), nonparametric tests were preferred (Habibzadeh, 2024). In between-group comparisons at baseline, Chi-square (X^2) test or Fisher exact test (where appropriate) for categorical variables and Mann-Whitney U test for continuous variables were carried out (du Prel et al., 2010). We also used the Bonferroni correction in order to correct for multiple testing (when applicable) (Armstrong, 2014).

As for time-to-event outcome parameters across the follow-up (e.g., service disengagement), Kaplan-Meier survival analysis was used, while for not time-to-event variables (e.g., current suicidal ideation) binary logistic regression analysis with AQ subgroups as independent parameter was preferred (Moscarelli, 2023). This was for better considering different time duration of individual follow-ups and patients who dropped-out before the end of our investigation (Jager et al., 2008). Finally, a mixed-design ANOVA was performed to explore between-group comparisons on longitudinal changes in GAF, PANSS, and HoNOS scores (Muhammad, 2023).

Additionally, the Wilcoxon test for repeated measures was used to examine the 1-year longitudinal stability of AQ scores, as well as Spearman correlation coefficient (Keller et al., 2016). This was to investigate whether AQ features represented enduring, “trait-like” attributes in FEP patients, or whether their longitudinal changes were affected by treatment response, thus indicating they were “state-like” symptoms.

3. Results

At baseline, 132 FEP subjects (87 [65.9 %] males; mean age = 22.61 \pm 5.81 years) were consecutively enrolled. Twenty-eight (21.2 %) participants scoring above the AQ cut-off score of ≥ 26 were included in the FEP/AQ+ subsample. Of them, 8 individuals also scored above the AQ cut off score of ≥ 32 . Sociodemographic and clinical features of FEP/AQ+ and FEP/AQ- subgroups are show in the Table 1.

3.1. Baseline comparisons

Compared to FEP/AQ-, FEP/AQ+ patients showed younger age at entry, a lower prevalence rate of baseline compulsory treatment with hospitalization (3.6 % VS 22.1 %), and higher severity levels in PANSS total score and PANSS “Negative Symptoms” factor subscore (Table 1).

3.2. Longitudinal comparisons

Compared to FEP/AQ-, FEP/AQ+ individuals had a lower incidence rate of service disengagement across the follow-up period (37.5 % VS 14.3 %) (Table 2) (see also Supplementary Materials [Fig. S1] for details on Kaplan-Meier survival functions). No between-group difference in terms of new hospitalization and new attempted suicide along the follow-up was found.

Furthermore, they showed lower incidence rates of PANSS symptomatic remission at T1 (1-year assessment time) (40.0 % VS 64.1 %) and GAF functional remission at T2 (2-year assessment time) (43.5 % VS 74.6 %) (Table 3).

Our mixed-design ANOVA results pointed out longitudinal improvements in all HoNOS, GAF, and PANSS scores within the FEP total group along the follow-up (Table 4). However, some statistically relevant “group” effects were also observed. Specifically, compared to FEP/AQ-, FEP/AQ+ subjects showed higher PANSS total scores and higher PANSS “Negative Symptoms” and “Disorganization” factor subscores over time (see Supplementary Materials [Fig. S2] for details on profile plots). Moreover, a statistically significant interaction (“time x group”) effect was found for GAF scores across the follow-up. In particular, compared to FEP/AQ-, FEP/AQ+ individuals had a worse longitudinal improvement in their global assessment of functioning.

Finally, no statistically significant difference in AQ total scores was observed in the FEP total group after 1 year of follow-up (Table 5). On the contrary, a statistically relevant positive correlation was found in the FEP total sample between AQ scores at baseline and at T1.

4. Discussion

Even today, research and clinical practice are characterized by a general lack of knowledge about the psychopathological relevance of autism features in early psychosis (Vita et al., 2020), especially in prognostic terms (Deste et al., 2019, 2021). Our study was developed to help fill this knowledge gap, specifically exploring AQ long-term stability and its relevant associations with several outcome parameters across a 2-year follow-up period. This was to better clarify the clinical meaning of autism characteristics in young patients at psychosis onset, especially if and how much they could influence the long-term outcomes of FEP individuals treated in EIP services.

values are reported. Statistically significant p values are in bold. Adjusted residuals are in square brackets.

^a Other ethnicity included Hispanic and other ethnic group.

^b Schizophrenia spectrum disorder included schizophrenia, schizophreniform disorder, and schizoaffective disorder.

4.1. Baseline findings

In the current examination, just over a *fifth* (21.2 %) of our FEP participants at presentation scored above the AQ cut-off of ≥ 26 , indicating the possible presence of autistic traits. Of them, 8 (about 6 %) subjects had an AQ score of ≥ 32 , suggesting a highly probable ASD diagnosis (Ziermans et al., 2021). Six of these eight individuals had a baseline DSM-5 diagnosis of schizophrenia spectrum disorder; the remaining two patients were affected by affective psychosis or psychosis NOS. These findings are substantially in line with those reported in previous studies, suggesting an average prevalence rate of AQ traits in FEP subjects equal to 28.2 % (Chisholm et al., 2019; Zheng et al., 2021) and prevalence rates of highly probable ASD diagnosis ranging from 3.5 % to 9.2 % (Davidson et al., 2014; Strålin and Hetta, 2019; Sunwoo et al., 2020; Treise et al., 2021; Kwok et al., 2024). These small discrepancies among investigations may be due to differences in diagnostic instruments used (e.g., AQ vs ADOS-2) and sample size. Moreover, AQ cut-offs were mainly standardized on ASD patients and the general population, lacking extensive testing and confirmation in clinical samples with other mental disorders, especially FEP (Lugnegård et al., 2015). In this respect, no significant difference in AQ scores was detected between adults with ASD and psychosis, potentially reducing the discriminating power of the instrument in the separation of psychotic disorders from autism (Fusar-Poli et al., 2020). Therefore, further research aiming to face these psychometric matters and to detect the

best AQ cut-offs to use in different clinical populations is needed, especially multicentric studies on large, clinically homogeneous samples.

Compared to FEP/AQ– at entry, FEP/AQ+ participants had *higher* severity levels in *psychopathology*, especially in *negative symptoms*. These findings partly confirm a more severe clinical presentation in this subgroup, as previously reported in another comparable, cross-sectional FEP study, although mostly due to greater PANSS “General psychopathology” subscale scores (Chisholm et al., 2019). However, in the present research, despite more serious clinical pictures, FEP/AQ+ individuals showed a *lower* prevalence rate of *baseline compulsory hospital admission* than FEP/AQ– ones. Together with our evidence of a *younger age* at presentation, the presence of autistic attributes in FEP patients appears to induce an earlier first contact with specialized EIP services, but without resorting to compulsory treatments. This can also be traced back to the great negative impact that negative symptoms have from a functional and subjective suffering point of view (Unrau et al., 2022), most frequently requiring active help-seeking behaviors (Pelizza et al., 2024e). Future studies exploring the subjective experience of negative features in FEP individuals may clarify some of these aspects (Butcher et al., 2020). In this regard, Chisholm et al. (2019) reported significant associations between baseline AQ scores and poorer daily functioning and quality of life. Moreover, Zheng et al. (2021) observed higher prevalence rate of unemployment in FEP/AQ+ subjects. Using the PAUSS, Davut et al. (2023) also found poor educational levels and worse social performance and cognitive functions in FEP patients with autistic attributes.

In this examination, no baseline inter-group differences in terms of other clinical and sociodemographic characteristics were observed. Zheng et al. (2021), on the other hand, reported higher prevalence rates in affective psychosis, brief psychosis, and psychosis NOS in FEP/AQ+

Table 2

Kaplan-Meier survival analysis results: comparisons on 2-year time-to-event outcome incidence rates among the two FEP subgroups.

FEP subgroup	Number of events	1-Cumulative proportion surviving at the time		Mean (in months) for 2-year <i>service disengagement</i> incidence rate			
		Estimate	SE	Estimate	SE	95 % CI	
						Lower bound	Upper bound
FEP/AQ–	39	0.3750	0.0470	19.038	0.6570	17.750	20.327
FEP/AQ+	4	.143	.066	21.893	.9850	19.962	23.823
(Overall)	43	–	–	19.644	.568	18.532	20.756
Log Rank (Mantel-Cox)				X ²	df	p	
				4.472	1	.034	

FEP subgroup	Number of events	1-Cumulative proportion surviving at the time		Mean (in months) for 2-year new hospitalization rate			
		Estimate	SE	Estimate	SE	95 % CI	
						Lower bound	Upper bound
FEP/AQ–	23	0.2680	0.0490	21.155	0.5160	20.143	22.166
FEP/AQ+	7	.286	.092	21.198	.9320	19.371	23.025
(Overall)	30	–	–	21.147	.453	20.259	22.035
Log Rank (Mantel-Cox)				X ²	df	p	
				0.010	1	.920	

FEP subgroup	Number of events	1-cumulative proportion surviving at the time		Mean (in months) for 2-year new suicide attempt incidence rate			
		Estimate	SE	Estimate	SE	95 % CI	
						Lower bound	Upper bound
FEP/AQ–	5	0.0620	0.0270	23.419	0.2550	22.920	23.919
FEP/AQ+	1	.042	.041	23.708	.2860	23.149	24.268
(Overall)	6	–	–	23.476	.211	23.062	23.890
Log Rank (Mantel-Cox)				X ²	df	p	
				0.179	1	.672	

Note. FEP = First Episode Psychosis; AQ = Autism-spectrum Quotient; FEP/AQ+ = FEP patients with AQ score of ≥ 26 ; FEP/AQ– = FEP patients with AQ score of < 26 ; SE = Standard Error; 95 % CI = 95 % Confidence Intervals; Log Rank = Logarithm Rank Test; X² = Chi-Square test; df = degrees of freedom; p = statistical value. Significant statistical p values are in bold.

Table 3
Binary logistic regression analysis results for 2-year not time-to-event outcome variables in the two FEP subgroups.

Dependent variable (n = 117)	FEP/AQ– (n = 92)	FEP/AQ+ (n = 25)	Statistic test				
			B (SE)	HR	95 % CI		p
					Lower	Higher	
1-Year current suicidal ideation	14 (15.2 %)	5 (20.0 %)	–0.311 (0.578)	0.7180	0.2310	2.230	.567
1-Year functional recovery	49 (53.3 %)	12 (48.0 %)	0.211 (0.452)	.810	.3340	1.963	.641
1-Year GAF functional remission	56 (60.9 %)	11 (44.0 %)	.683 (0.456)	1.980	.8100	4.840	.134
1-Year HoNOS functional remission	67 (72.8 %)	16 (64.0 %)	.410 (0.478)	1.507	.591	3.847	.391
1-Year PANSS symptomatic remission	59 (64.1 %)	10 (40.0 %)	.986 (0.463)	2.682	1.083	6.639	.033

Dependent variable (n = 90)	FEP/AQ– (n = 67)	FEP/AQ+ (n = 23)	Statistic test				
			B (SE)	HR	95 % CI		p
					Lower	Higher	
2-Year current suicidal ideation	7 (10.4 %)	3 (13.0 %)	–0.251 (0.737)	0.7780	0.1840	3.296	.733
2-Year functional recovery	48 (71.6 %)	13 (56.5 %)	0.664 (0.500)	.515	.193	1.372	.184
2-Year GAF functional remission	50 (74.6 %)	10 (43.5 %)	1.341 (0.506)	3.824	1.4190	10.302	.008
2-Year HoNOS functional remission	56 (83.6 %)	17 (73.9 %)	.586 (0.578)	1.797	.5790	5.580	.311
2-Year PANSS symptomatic remission	50 (74.6 %)	13 (56.5 %)	.816 (0.506)	2.262	.840	6.096	.106

Note. FEP = First Episode Psychosis; AQ = Autism-spectrum Quotient; FEP/AQ+ = FEP patients with AQ score of ≥ 26 ; FEP/AQ– = FEP patients with AQ score of < 26 ; GAF = Global Assessment of Functioning; HoNOS = Health of the Nation Outcome Scale; PANSS = Positive And Negative Syndrome Scale; B = regression coefficient, SE = Standard Error; HR = Hazard Ratio; 95 % CI = 95 % confidence intervals for HR; p = statistical significance. Significant statistical p values are in bold. Cumulative incidence rates are reported.

Current suicidal ideation = BPRS item 4 score of ≥ 2 ; Functional recovery = return to work/school; GAF functional remission = GAF score of ≥ 60 ; HoNOS functional remission = HoNOS item 9, 10, and 11 scores of ≤ 2 ; PANSS symptomatic remission = PANSS item P1, P2, P3, N1, N4, N6, G5, G9 scores of ≤ 3 .

patients.

4.2. Longitudinal findings

As for *outcome* parameters, our FEP/AQ+ participants showed *lower* incidence rates of PANSS *symptomatic remission* at 1 year and GAF *functional remission* at 2 years compared to FEP/AQ– ones. These findings support and longitudinally extend the evidence reported in the 1-year longitudinal study by Zheng et al. (2021) in Singapore. In this respect, the baseline FEP/AQ+ subgroup appears to be a clinically relevant predictor of symptomatic and functional non-remission over time. Therefore, implementing screening and diagnostic protocol to detect autistic features in EIP services may help identify specific treatment needs that differed from FEP/AQ– patients, improving their prognosis and long-term outcomes.

However, in the present investigation, we interestingly found a lower 2-year incidence rate of *service disengagement* in FEP/AQ+ participants compared to the FEP/AQ– subgroup. This suggests the tendency of Pr-EP team members to provide stronger and more temporally stable retention in care to FEP/AQ+ individuals. This clinical practice does not seem to be related to baseline between-group differences in DSM-5 diagnosis, insight, cooperativeness, and hostility. Conversely, it may be due to the staff perception of greater severity in psychopathology, especially in negative symptoms, and its need of more enduring care programs (Drake et al., 2020).

In this respect, in agreement and longitudinal extension of the results reported in the 1-year follow-up research by Zheng et al. (2021), we observed statistically significant *group effects* in longitudinal improvements of GAF and PANSS scores. Specifically, compared to FEP/AQ–, our FEP/AQ+ subjects had poorer outcomes across the follow-up in terms of daily *functioning* and *psychopathological severity*, especially in *negative symptoms* and *disorganization* dimensions (i.e., they had higher PANSS scores and lower GAF scores). Additionally, FEP/AQ+ participants showed a significant interaction (“time x group”) effect in terms of functioning (i.e., they had poorer improvements in GAF scores over time). This could be due to a poorer treatment response in FEP/AQ+ participants within the Pr-EP program, confirming their specific treatment needs compared to FEP/AQ– ones.

Finally, after 1 year of follow-up, no statistically relevant change in AQ total scores was found in the FEP total group. Together with the significant positive correlation found between AQ scores at baseline and at 1 year, this finding supports the *long-term stability* of AQ levels (Keller et al., 2016) and their most likely clinical link with enduring autistic traits rather than state-like symptoms. This was also confirmed by our k statistic results (see Supplementary Materials [Table S1] for details), supporting a near perfect agreement in the proportion of observed concordance of FEP patients with AQ score of ≥ 26 at presentation after one year of follow-up ($k = 0.852$) (Sim and Wright, 2005). Therefore, unlike the PAUSS that more probably represents a proxy for psychotic symptoms' severity (especially negative and disorganized features) (Chisholm et al., 2023), the AQ seems to more reliably assess autistic trait-like attributes in FEP patients, also detecting a distinct subgroup with more severe psychopathology and poorer outcomes. The administration of the PAUSS in FEP individuals should be avoided because it probably does not truly capture autistic features.

4.3. Limitations

Some major limitations should also be acknowledged. First, the study results are generalizable only to young populations with FEP. No comparisons with patients affected by prolonged psychosis or of different age groups should not be permitted. Indeed, discrepancies in samples can lead to differences in interpretations of findings among studies. Moreover, our research should not also be compared to FEP investigations using different assessment tools for autism features.

Further relevant limitations are related to the absence of a control group (including individuals with a diagnosed ASD and psychiatric patients with mental disorder outside psychosis) and the relatively small sample size, especially in terms of FEP/AQ+ subjects. Future examinations on larger FEP/AQ+ samples are thus needed.

Third, AQ cut-offs were actually standardized on ASD individuals and the general population. Extensive testing and confirmation in FEP samples are lacking (Poon et al., 2020). In this respect, ROC analysis on AQ by Chisholm et al. (2019) showed that lower cut-offs are needed in FEP patients to better prevent symptom severity, quality of life, and functioning. Furthermore, our FEP population included different

Table 4
Mixed-design ANOVA results: psychopathological and outcome parameters across the 2-year follow-up period in the two FEP subgroups.

Variable	Time effect				Group effect				Interaction effect (time x group)			
	df	F	p	η ²	df	F	p	η ²	df	F	p	η ²
PANSS Positive symptoms	1.6	63.679	.001	0.4200	1	1.357	.247	0.0150	1.6	0.9380	.376	0.0110
PANSS Negative symptoms	1.6	23.279	.001	.2090	1	4.979	.028	.0540	1.6	.0910	.875	.0010
PANSS Disorganization	1.5	43.691	.001	.3340	1	6.2750	.014	.0670	1.5	.2580	.707	.0030
PANSS Affect	1.6	32.949	.001	.2720	1	.169	.682	.0020	1.6	.3970	.632	.0040
PANSS Resistance/Excitement	1.4	12.538	.001	.1250	1	2.625	1.09	.0290	1.4	.1080	.824	.0010
PANSS Total score	1.6	55.826	.001	.3910	1	5.539	.023	.0580	1.6	.313	.689	.0040
GAF score	1.7	109.383	.001	.5540	1	1.4740	.228	.0160	1.7	5.3980	.008	.0580
HoNOS Behavioral problems	1.5	57.188	.001	.3940	1	.9000	.345	.0100	1.5	.0620	.899	.0010
HoNOS Impairment	1.4	20.282	.001	.1890	1	.0280	.868	.0010	1.4	.147	.789	.0020
HoNOS Psychiatric symptoms	1.9	103.186	.001	.5400	1	.0480	.827	.0010	1.9	1.681	.191	.0190
HoNOS Social problems	1.4	30.358	.001	.2560	1	.1960	.659	.0020	1.4	3.103	.064	.0340
HoNOS total score	1.6	86.884	.001	.500	1	.214	.645	.002	1.6	1.559	.217	.018

Variable	EMM (SE)	
	FEP/AQ-	FEP/AQ+
T0 PANSS Positive symptoms	18.209 (0.764)	18.522 (1.305)
T1 PANSS Positive symptoms	10.418 (0.729)	12.739 (1.244)
T2 PANSS Positive symptoms	10.239 (0.614)	11.478 (1.048)
T0 PANSS Negative symptoms	20.000 (0.965)	23.870 (1.648)
T1 PANSS Negative symptoms	15.388 (0.933)	18.870 (1.593)
T2 PANSS Negative symptoms	14.522 (0.959)	17.609 (1.673)
T0 PANSS Disorganization	18.561 (0.867)	21.870 (1.469)
T1 PANSS Disorganization	13.697 (0.794)	17.652 (1.345)
T2 PANSS Disorganization	13.136 (0.706)	16.217 (1.196)
T0 PANSS Affect	15.910 (0.635)	15.913 (1.083)
T1 PANSS Affect	11.821 (0.623)	12.000 (1.064)
T2 PANSS Affect	10.746 (0.591)	11.783 (1.008)
T0 PANSS Resistance/Excitement	8.403 (0.523)	9.391 (0.893)
T1 PANSS Resistance/Excitement	6.388 (0.403)	7.783 (0.689)
T2 PANSS Resistance/Excitement	6.328 (0.417)	7.522 (0.712)
T0 PANSS Total score	84.788 (2.907)	93.565 (4.924)
T1 PANSS Total score	59.318 (3.011)	72.478 (5.101)
T2 PANSS Total score	56.364 (2.867)	67.652 (4.857)
T0 GAF score	41.567 (1.020)	44.174 (1.742)
T1 GAF score	60.343 (1.399)	56.217 (2.389)
T2 GAF score	64.731 (1.430)	58.870 (2.440)
T0 HoNOS Behavioral problems	3.313 (0.254)	3.652 (0.434)
T1 HoNOS Behavioral problems	1.284 (0.204)	1.696 (0.349)
T2 HoNOS Behavioral problems	1.015 (0.211)	1.261 (0.361)
T0 HoNOS Impairment	2.333 (0.221)	2.304 (0.374)
T1 HoNOS Impairment	1.288 (0.173)	1.304 (0.294)
T2 HoNOS Impairment	1.182 (0.178)	1.348 (0.301)
T0 HoNOS Psychiatric symptoms	11.955 (0.351)	11.130 (0.599)
T1 HoNOS Psychiatric symptoms	5.851 (0.497)	6.217 (0.849)
T2 HoNOS Psychiatric symptoms	4.761 (0.442)	5.652 (0.754)
T0 HoNOS Social problems	6.672 (0.399)	6.000 (0.680)
T1 HoNOS Social problems	4.045 (0.393)	4.522 (0.671)
T2 HoNOS Social problems	3.134 (0.401)	4.217 (0.684)
T0 HoNOS total score	24.303 (0.899)	23.087 (1.523)
T1 HoNOS total score	12.561 (1.073)	13.739 (1.818)
T2 HoNOS total score	10.197 (1.060)	12.478 (1.796)

Note. As all Mauchly's tests of sphericity are statistically significant ($p < 0.05$), Greenhouse–Geisser corrected degrees of freedom to assess the significance of the corresponding F value are used. Statistically significant p values are in bold. Statistical trends in p value ($p < 0.01$) are underlined. ANOVA = analysis of variance; AQ = Autism-spectrum Quotient; FEP/AQ+ = FEP patients with AQ score of ≥ 26 ; FEP/AQ- = FEP patients with AQ score of < 26 ; PANSS = Positive And Negative Syndrome Scale; df = degrees of freedom; F = F statistic value; GAF = Global Assessment of Functioning; HoNOS = Health of the Nation Outcome Scale; p = statistical significance; η² = partial eta squared; EMM = Estimated Marginal Mean; SE = Standard Error; T0 = baseline assessment; T1 = 1-year assessment time; T2 = 2-year assessment time. Bonferroni's corrected p values are reported. Statistically significant p values are in bold.

psychiatric diagnoses. This diagnostic heterogeneity could affect the longitudinal stability of AQ scores. Additionally, it should also be considered that enduring association between AQ attributes and negative symptoms may be due to the clinical similarity and the consequent overlap between the two psychopathological constructs (Deste et al., 2019). However, although these AQ cut-offs were mainly standardized on ASD subjects and the general population, we used them to compare our results with those reported in previous studies in FEP samples

(Chisholm et al., 2019; Zheng et al., 2021), as well as to effectively identify a subgroup of patients with potentially autistic features (similarly to what happens in for ASD individuals and the general population). In this sense, we preferred to use this statistical approach rather than to the one based on the continuous scale for the AQ.

Fourth, a relevant limitation was also related to heavily imbalanced sample sizes (i.e., FEP/AQ+ VS FEP/AQ- subgroup). This may reduce statistical power of our analyses (i.e., smaller sample sizes generally

Table 5

Longitudinal comparisons on AQ total scores in the FEP total group after 1 year of follow-up.

Variable	T0 (n = 132)	T1 (n = 117)	z (p)	ρ (p)
AQ scores	21.26 ± 6.14	20.40 ± 5.61	−1.642 (.100)	0.686 (.001)

Note. AQ = Autism-spectrum Quotient; FEP = First Episode Psychosis; FEP/AQ+ = FEP patients with AQ score of ≥ 26 ; T0 = baseline assessment time; T1 = 1-year assessment time; T2 = 2-year assessment time; p = statistical significance. Mean ± standard deviation, Wilcoxon test (z) and Spearman correlation coefficient (ρ) values are reported. Statistically significant p values are in bold.

result in reduced power) meaning it can be more difficult to detect statistically significant inter-group differences (Dong et al., 2017). Moreover, it should be considered that this samples' imbalance may introduce bias in interpreting our results, especially in order to avoid overgeneralizing findings (Han et al., 2012). For these reasons, we also selected nonparametric tests, which do not consider the potential heterogeneity of variance between the two subgroups (Zhou et al., 2022). As for ANOVA, we choose the options to adjust for unequal variances and sample sizes (Klich et al., 2018).

Fifth, a further issue concerned the specificity of measurement of negative symptoms and autistic traits, due to their potential psychopathological overlap. In this investigation, we used psychometric instruments specifically developed to assess psychotic symptoms (i.e., the PANSS) or autistic traits (i.e., the AQ), but which are unable to explicitly distinguish one from the other (e.g., social deficits). New assessment tools specifically developed to differentiate them and capture the uniqueness of each symptom clusters are therefore needed, especially those capable of capturing their state or trait characteristics.

Finally, another weakness is that our FEP subjects were enrolled within only one EIP service and were taking antipsychotic medications that may affect the longitudinal course of AQ scores. Future multicenter investigations are therefore needed.

5. Conclusion

The results of this investigation suggested that the AQ appears to reliably assess trait-like attributes in FEP individuals. However, to be adequately determined, future studies comparing this screening tool with gold standard instruments for autistic features are needed.

Moreover, AQ scores appear to detect a distinct subgroup of FEP patients (approximately 20 %) characterized by more severe clinical presentation (particularly greater severity of negative symptoms), younger age at presentation, a worse baseline functioning, and poorer psychopathological and functional outcomes over a 2-year follow-up period. As these findings overall matched up the traditional description of deficit syndrome (Carpenter Jr., 1994) quite accurately, they raise an interesting clinical question: are we just calling a different name to this old psychopathological concept? Although no difference was observed between groups in terms of DSM-5 diagnoses (including schizophrenia spectrum disorder) in our research, future perspective investigations on larger FEP/AQ+ populations are needed to explore this potential clinical overlap. EIP services should be prepared to adequately address the therapeutic needs of FEP subjects with higher autism traits, which may be overshadowed by prodromal symptoms and left undetected. Careful autism assessment and screening is therefore highly recommended, especially to implement personalized care pathway. However, although there are currently no validated instruments for the diagnosis of ASD in psychiatric population, the AQ should not replace an accurate clinical judgment and the administration of more appropriate tools evaluating ASD diagnosis.

CRedit authorship contribution statement

Lorenzo Pelizza: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Emanuela Leuci:** Writing – review & editing, Data curation. **Emanuela Quattrone:** Writing – review & editing, Data curation. **Derna Palmisano:** Writing – review & editing, Data curation. **Simona Pupo:** Writing – review & editing, Writing – original draft, Methodology, Data curation. **Giuseppina Paulillo:** Writing – review & editing. **Clara Pellegrini:** Writing – review & editing, Data curation. **Pietro Pellegrini:** Writing – review & editing. **Marco Menchetti:** Writing – review & editing.

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Declaration of competing interest

The authors have nothing to declare.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.schres.2025.07.014>.

Data availability

The data that support the findings of this research are not publicly available due to privacy and/or ethical restrictions. However, the data are available on reasonable request from the corresponding author.

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