Frequency and Correlates of *DSM-5* Attenuated Psychosis Syndrome in a Sample of Adolescent Inpatients With Nonpsychotic Psychiatric Disorders

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ABSTRACT

Objectives: *DSM-5* conceptualized attenuated psychosis syndrome (APS) as self-contained rather than as a risk syndrome, including it under "Conditions for Further Study," but also as a codable/billable condition in the main section. Since many major mental disorders emerge during adolescence, we assessed the frequency and characteristics of APS in adolescent psychiatric inpatients.

Methods: Consecutively recruited adolescents hospitalized for nonpsychotic disorders (September 2009–May 2013) were divided into APS youth versus non-APS youth, based on the Structured Interview of Prodromal Syndromes (SIPS) and according to *DSM-5* criteria, and compared across multiple characteristics.

Results: Of 89 adolescents (mean ± SD age = 15.1 ± 1.6 years), 21 (23.6%) had APS. Compared to non-APS, APS was associated with more comorbid disorders (2.7 ± 1.0 vs 2.2 ± 1.3), major depressive disorder (61.9% vs 27.9%), oppositional defiant disorder/conduct disorder (52.4% vs 25.0%), and personality disorder traits (57.1% vs 7.4%, the only diagnostic category surviving Bonferroni correction). APS youth were more severely ill, having higher SIPS total positive, negative, and general symptoms; Brief Psychiatric Rating Scale total and positive scores; depression and global illness ratings; and lower Global Assessment of Functioning (GAF). Conversely, Young Mania Rating Scale scores, suicidal behavior, prescribed psychotropic medications, and mental disorder awareness were similar between APS and non-APS groups. In multivariable analysis, lowest GAF score in the past year (odds ratio [OR] = 51.15; 95% confidence interval [CI], 2.46–2,439.0) and social isolation (OR = 27.52; 95% CI, 3.36–313.87) were independently associated with APS ($r^2 = 0.302$, $P < .0001$). Although psychotic disorders were excluded, 65.2% (APS = 57.1%, non-APS = 67.7%, $P = .38$) received antipsychotics.

Conclusion: One in 4 nonpsychotic adolescent inpatients met *DSM-5* criteria for APS. APS youth were more impaired, showing a complex entanglement with a broad range of psychiatric symptoms and disorders, including depression, impulse-control, and, especially, emerging personality disorders.

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After considerable debate, the attenuated psychosis syndrome (APS) was added to Section III of *DSM-5*[1] to be considered for further study.[2,3] Additionally, APS is listed under "Other Specified Schizophrenia Spectrum and Other Psychotic Disorder" in Section II. APS criteria were originally derived from at-risk concepts developed in specialty research programs assessing mainly adult/mixed samples. Although newly emerging/worsening attenuated positive symptoms within 12 months predicted conversion to psychosis in up to 35% of patients over 3 years,[4] concern was raised that these findings were driven by specific sampling strategies that would not generalize to clinical settings. More importantly, most individuals did not convert to psychosis, despite being psychiatrically ill and functionally impaired, calling the label of "risk syndrome" into question.[5–7] Subsequently, the "risk" approach was abandoned in favor of a "syndrome" approach based on the presence of attenuated symptoms, rather than an undetermined outcome.[8]

Data about the prevalence and characteristics of APS in clinical care and especially in adolescents are sparse.[9] First findings in preselected at-risk adolescents confirmed lower transition rates compared to adults, suggesting that attenuated positive symptoms/APS may be less specific in adolescents or that longer follow-up may be needed to determine true at-risk status.[4,10,11] Conversely, the "at-risk for psychosis" classification has been associated with many co-occurring mental disorders and has predicted psychiatric hospitalization in adolescents.[11–13] Even in non–help-seeking, school-aged children, the research criteria determined "at-risk" status to be associated with more *DSM-IV* diagnoses and poorer functioning compared to controls.[14]

Critics of *DSM-5*'s inclusion of APS acknowledged that *DSM-IV* did not adequately address the attenuated/emerging psychosis syndrome, but pointed to the lack of data regarding reliability of assessments in routine practice, questioning clinical

Clinical Points

- Attenuated psychosis syndrome (APS), as listed under "Other Specified Schizophrenia Spectrum and Other Psychotic Disorder" in *DSM-5*, was present in 24% of psychiatrically hospitalized adolescents.
- In our sample of inpatients, APS was associated with emerging personality disorder traits and higher severity of illness.
- Outcomes of APS in youth are unclear, causing the clinical dilemma of when and how to intervene.

utility.[3,13,15–18] Thus, the need for specified research criteria for APS and its placement in Section III were stressed.[3] However, the fact that APS was simultaneously placed under the "Other Specified Schizophrenia Spectrum and Other Psychotic Disorder" category in Section II necessitates research in individuals and especially youth fulfilling APS criteria in clinical care.

Thus, we aimed to (1) determine the frequency of APS status in psychiatrically hospitalized adolescents with nonpsychotic disorders and (2) assess correlates of APS status. Based on prior data mainly in adults,[4,19] we hypothesized that compared to the non-APS group, adolescents with APS would have more comorbid *DSM-5* disorders and be more functionally impaired.

METHOD

Setting

From September 2009 through May 2013, we consecutively enrolled adolescents admitted to a 23-bed adolescent psychiatric unit in a semiurban, academic teaching facility with a catchment area of 3.5 million people, supplemented by few direct outpatient referrals. The protocol was approved by the Institutional Review Board of the North Shore-Long Island Jewish Health System. Written informed consent was obtained from legal guardians of minors who gave written assent.

This study was registered at ClinicalTrials.gov (NCT01383915).

Participants

Inclusion criteria for the current study were (1) age 12–17 years, (2) chart diagnosis of a nonpsychotic psychiatric disorder with subsequent confirmation of a nonpsychotic *DSM-IV* diagnosis per research interview and consensus conference, and (3) sufficient English speaking ability.

Exclusion criteria were (1) estimated premorbid IQ <70[20]; (2) *DSM-IV* criteria for autism spectrum disorders, current substance dependence; and (3) medical/neurologic condition known to affect the brain.

Procedures

Demographic, past psychiatric illness, and treatment information were obtained from the parent/guardian augmented by medical chart information. Diagnostic interviews were conducted separately in youth and parent/guardian. *DSM-5* diagnoses were based on a combination of the Structured Clinical Interview for *DSM-IV* Axis I Disorders, text revision (SCID-I),[21] Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-PL),[22] and Structured Interview for *DSM-IV* Personality (SIDP-IV).[23] For disorders for which criteria had changed between *DSM-IV* and *DSM-5*, we applied *DSM-5* criteria. Adolescents fulfilling personality disorder criteria except for the required age criterion[24,25] were considered to have personality disorder traits. Positive, negative, disorganized, and general symptoms, including subthreshold/attenuated levels, were assessed with the Structured Interview for Prodromal Syndromes (SIPS)[26]. As part of the SIPS, the Scale of Prodromal Symptoms (SOPS)[26] was used to determine whether participants met research criteria for attenuated positive symptoms syndrome (APSS). In this sample, all participants also met *DSM-5* criteria for APS as defined in Sections II and III (Table 1).

We also used the Brief Psychiatric Rating Scale (BPRS)[27] with the total, positive symptoms (6 items),[28] and withdrawal (3 items)[29] subscales; Montgomery-Asberg Depression Rating Scale (MADRS)[30]; Young Mania Rating Scale (YMRS)[31]; Clinical Global Impressions-Severity (CGI-S) scale[32]; Scale to Assess Unawareness of Mental Disorder (SUMD; using 3 general awareness items only: mental disorder, social consequences of mental disorder, and achieved effect of medication)[33]; Global Assessment of Functioning (GAF) scale[34]; and specific scales for role functioning (Global Functioning: Role [GF:R] scale)[35] and social functioning (Global Functioning: Social [GF:S] scale),[36] developed to characterize functioning in individuals considered at risk for psychosis. IQ was estimated with the Wide Range Achievement Test 3 (WRAT-3).[20]

All interviews and cognitive testing were administered by masters- or doctoral-level psychologists or medical doctors who were extensively trained on the interviews with ongoing supervision through consensus conferences.

Statistical Analysis

Of 112 youth with full baseline assessments, 23 patients were excluded (psychotic disorders: n = 20; autism spectrum disorders and/or psychotic symptoms due to a medical condition: n = 3) (Supplementary eFigure 1). Eighty-nine youth were divided into APS and non-APS groups and compared on demographic, illness, symptom, and treatment variables using χ^2 statistics or Fisher exact test for categorical and nonparametric Mann-Whitney *U* test for continuous variables. Additionally, we calculated Rosenthal[37] r ($z/\sqrt{N}$) as an effect size measure (0.1 = small, 0.3 = moderate, 0.5 = large). Negative effect sizes indicate that APS subjects have higher symptoms and lower functional ratings. We used the nonparametric Spearman rank correlation coefficient to analyze the relationship between SIPS symptom domains and measures of global, social, and role functioning across the entire sample. To identify variables independently related to group status, we conducted a backward elimination multivariate logistic regression analysis entering into the

Table 1. Research-Defined Attenuated Positive Symptoms Syndrome (APSS) vs *DSM-5*–Defined Attenuated Psychosis Syndrome (APS), Section III and Section II

Criterion	APSS Research Criteria According to the Structured Interview of Prodromal Syndromes	*DSM-5*, Section III APS	*DSM-5*, Section II 298.8 Other Specified Schizophrenia Spectrum and Other Psychotic Disorder
Severity	≥1 of the following attenuated positive symptoms rated as 3–5 on the Scale of Prodromal Symptoms: • unusual thought content/delusions (P1) ◦ suspiciousness (P2) ◦ grandiosity (P3) • perceptual abnormalities/hallucinations (P4) • disorganized communication (P5)	Criterion A: ≥1 of the following in attenuated form with intact reality testing: • delusions • hallucinations • disorganized speech	Examples of presentations that can be specified using this designation include APS. This syndrome is characterized by psychotic-like symptoms that are below a threshold for full psychosis (eg, the symptoms are less severe and more transient, and insight is relatively maintained)
Frequency	The symptoms occurred at an average frequency of at least 1 per week in the past month	Criterion B: Identical to APSS	Not specified
New onset and/or worsening	Any of the attenuated positive symptoms have begun within the past year or currently rate 1 or more scale points higher compared to 12 months ago	Criterion C: Identical to APSS	Not specified
Distress/disability	All patients meeting APSS were admitted to a psychiatric inpatient unit and suffered from marked functional impairment	Criterion D: Symptoms are sufficiently distressing and disabling to the individual to warrant clinical attention	Symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning
Rule out of other diagnosis	Symptoms were not better explained by any *DSM-IV* diagnosis, including substance-related disorder, based on all available information confirmed by a diagnostic consensus conference	Criterion E: Symptoms are not better explained by any *DSM-5* diagnosis, including substance-related disorder	Symptoms do not meet the full criteria for any of the disorders in the schizophrenia spectrum and other psychotic disorders diagnostic class
Lack of lifetime psychotic disorder	Patients with a lifetime diagnosis of a psychotic disorder, based on all available information confirmed by a diagnostic consensus conference, were excluded	Criterion F: Clinical criteria for any *DSM-5* psychotic disorder have never been met	Not specified

Abbreviation: P1–5 = positive symptoms.

initial model all variables that were different between the APS and non-APS groups at $P < .05$ (see Tables 2–4). We excluded from the initial model SIPS positive symptom items and BPRS total score (as positive symptoms were used to define the 2 groups), as well as total and highest SIPS scores (as we sought to identify specific symptom items correlating with APS status). The percent variance explained by the significant variables contained in the final multivariable logistic regression model was expressed as r^2. Data were analyzed using JMP 5.0.1, 1989–2003 (SAS Institute); all tests were 2-sided. To reduce the chance of type I error due to multiple testing, we used Bonferroni corrected P values, despite the exploratory nature of this study, dividing $P < .05$ by the number of tests within each domain, ie, demographic variables (Table 2); illness variables (Table 2); treatment variables (Table 2); prodromal psychopathology (Table 3); attenuated psychopathology (Table 3); and illness severity, functional level, illness insight, and suicidality (Table 4).

RESULTS

Prevalence and Demographic Characteristics of APS

Of 89 nonpsychotic adolescents (mean ± SD age 15.1 ± 1.6 years, 58.4% female, 49.4% white), 21 (23.6%) fulfilled APS criteria (Table 2). Age, sex, and IQ did not differ between APS and non-APS groups, but fewer white adolescents (38.1% vs 52.9%) and more "other" racial groups (28.6% vs 5.9%) fulfilled APS criteria ($P = .040$).

Diagnostic Characteristics

APS adolescents had significantly more *DSM-5* diagnoses (2.7 ± 1.0 vs 2.2 ± 1.3, $P = .041$) and more often had ≥3 diagnoses (57.1% vs 32.4%, $P = .041$) (Table 2).

In the total sample, the most frequent diagnoses included depressive disorders (58.4%), mainly major depressive disorder (MDD; 36.0%); disruptive behavior disorders (42.7%), mainly oppositional defiant disorder (ODD)/conduct disorder (CD) (31.5%); bipolar spectrum disorders (37.1%); and neurodevelopmental disorders (24.7%). APS status was significantly associated with MDD (61.9% vs 27.9%, $P = .0046$), ODD/CD (52.4% vs 25.0%, $P = .018$), and personality disorder traits (57.1% vs 7.4%, $P < .0001$), ie, borderline (42.9% vs 5.9%, $P < .0001$) and other personality disorder traits (19.1% vs 3.0%, $P < .027$) (Table 2).

Only personality disorder traits survived stringent correction for multiple comparisons among diagnoses.

Treatment Characteristics

In this naturalistic study, 97.8% were inpatients, and 94.4% received psychotropic drugs (mean = 1.7 ± 1.0) (Table 2). Most received atypical antipsychotics (65.2%), antidepressants (39.3%), or mood stabilizers (34.8%). Anxiolytics/tranquilizers (13.5%) and anti-ADHD medications (4.5%) were less common. APS and non-APS groups did not differ regarding psychotropic treatment variables (P values = .26–.90) (Table 2).

Table 2. Demographic, Illness, and Treatment Characteristics[a]

Characteristic	Total (N = 89)	APS (n = 21)	Non-APS (n = 68)	*P* Value
Demographic characteristics				
Age, mean ± SD, y	15.1 ± 1.6	15.0 ± 1.4	15.1 ± 1.6	.83
Sex, female, n (%)	52 (58.4)	11 (52.4)	41 (60.3)	.41
Race/ethnicity, n (%)				.040
African-American	25 (28.1)	5 (23.8)	20 (29.4)	
Hispanic	10 (11.2)	2 (9.5)	8 (11.8)	
White	44 (49.4)	8 (38.1)	36 (52.9)	
Other	10 (11.2)	6 (28.6)	4 (5.9)	
Estimated IQ,[b] mean ± SD	105.1 ± 16.7	106.9 ± 14.4	104.5 ± 17.4	.64
Lifetime consensus diagnoses, n (%)				
Number of *DSM-5* diagnoses, mean ± SD	2.3 ± 1.3	2.7 ± 1.0	2.2 ± 1.3	.041
Number of diagnoses ≥ 3, n (%)	34 (38.2)	12 (57.1)	22 (32.4)	.041
Depressive disorders[c]	52 (58.4)	14 (66.7)	38 (55.9)	.38
Major depressive disorder	32 (36.0)	13 (61.9)	19 (27.9)	.0046
Other specified depressive disorder	17 (19.1)	1 (4.8)	16 (23.5)	.056
Persistent depressive disorder	6 (6.7)	1 (4.8)	5 (7.4)	1.00
Disruptive, impulse-control, and conduct disorders	38 (42.7)	12 (57.1)	26 (38.2)	.13
Oppositional defiant and conduct disorder	28 (31.5)	11 (52.4)	17 (25.0)	.018
Other disruptive, impulse-control, and conduct disorder	10 (11.2)	1 (4.8)	9 (13.2)	.28
Bipolar disorders	33 (37.1)	10 (47.6)	23 (33.8)	.25
Other specified bipolar and related disorder	26 (29.2)	9 (42.9)	17 (25.0)	.12
Bipolar I or II disorder	7 (7.9)	1 (4.8)	6 (8.8)	.55
Neurodevelopmental disorders	22 (24.7)	4 (19.0)	18 (26.5)	.49
Attention-deficit/hyperactivity disorder	20 (22.5)	3 (14.3)	17 (25.0)	.30
Other specified attention-deficit/hyperactivity disorder	2 (2.2)	1 (4.8)	1 (1.5)	.42
Personality disorder traits[c]	17 (19.1)	12 (57.1)	5 (7.4)	**< .0001**
Borderline personality disorder traits	13 (14.6)	9 (42.9)	4 (5.9)	**< .0001**
Other personality disorder traits (narcissistic, schizotypal, avoidant)	6 (6.7)	4 (19.1)	2 (2.9)	.027
Anxiety disorders[c]	16 (18.0)	5 (23.8)	11 (16.2)	.43
Panic and/or agoraphobia	10 (11.2)	3 (14.3)	7 (10.3)	.69
Generalized anxiety disorder	8 (9.0)	1 (4.8)	6 (8.8)	1.00
Social anxiety disorder	6 (6.7)	2 (9.5)	4 (5.9)	.62
Specific phobia	2 (2.2)	0 (0.0)	2 (2.9)	1.00
Separation anxiety disorder	1 (1.1)	1 (4.8)	0 (0.0)	.24
Other specified anxiety disorder	1 (1.1)	0 (0.0)	1 (1.5)	1.00
Substance-related and addictive disorders[c]	13 (14.6)	3 (14.3)	10 (14.7)	1.00
Marijuana abuse	10 (11.2)	3 (14.3)	7 (10.3)	.69
Alcohol abuse	6 (6.7)	2 (9.5)	4 (5.9)	.62
Trauma- and stressor-related disorders	8 (9.0)	2 (9.5)	6 (8.8)	.92
Posttraumatic stress disorder	4 (4.5)	2 (9.5)	2 (2.9)	.24
Adjustment disorder	4 (4.5)	0 (0.0)	4 (5.9)	.57
Other diagnostic categories	7 (7.9)	2 (9.5)	5 (7.4)	.75
Obsessive-compulsive and related disorder	4 (4.5)	1 (4.8)	3 (4.4)	.95
Eating disorder	3 (3.4)	1 (4.8)	2 (2.9)	.56
Treatment characteristics at time of the interview				
Inpatients, n (%)	87 (97.8)	21 (100)	66 (97.1)	.43
Days of psychiatric hospitalization, mean ± SD	14.8 ± 14.9	12.8 ± 7.2	15.4 ± 16.5	.67
Receiving any psychotropic drug medication, n (%)	84 (94.4)	19 (90.5)	65 (95.6)	.59
Number of psychotropic medications, mean ± SD	1.7 ± 1.0	1.6 ± 0.9	1.8 ± 0.97	.52
Specific psychotropic medications, n (%)				
Antipsychotics[d]	58 (65.2)	12 (57.1)	46 (67.7)	.38
Antidepressants[e]	35 (39.3)	8 (38.1)	27 (39.7)	.90
Mood stabilizers[f]	31 (34.8)	7 (33.3)	24 (35.3)	.87
Anxiolytics/tranquilizer[g]	12 (13.5)	3 (14.3)	9 (13.2)	1.00
Anti-ADHD medications[h]	4 (4.5)	0 (0.0)	4 (5.9)	.26

[a]Significance level for demographic variables: $P < .007$; significance level for illness variables: $P < .002$; significance level for treatment variables: $P < .006$; bolded *P* values below significance level.
[b]Data available for 80 patients.
[c]The total number of patients in the main diagnostic category can be smaller than the sum of the individual diagnoses due to comorbidity.
[d]Antipsychotics: aripiprazole, molindone, quetiapine, risperidone, ziprasidone.
[e]Antidepressants: amitriptyline, bupropion, citalopram, duloxetine, fluoxetine, paroxetine, sertraline, venlafaxine.
[f]Mood stabilizers: lamotrigine, lithium, valproic acid.
[g]Anxiolytics/tranquilizers: clonazepam, lorazepam.
[h]Anti-ADHD medications: atomoxetine, lisdexamfetamine, methylphenidate, modafinil.
Abbreviation: APS = attenuated psychosis syndrome (according to *DSM-5* Sections II and III).

Table 3. Severity of Symptoms and Symptom Domains[a]

Characteristic	Total (N = 89), Median (IQR 25, 75)	APS (n = 21), Median (IQR 25, 75)	Non-APS (n = 68), Median (IQR 25, 75)	*P* Value	Effect Size, Rosenthal *r*[b]
Structured Interview of Prodromal Syndromes					
Positive symptoms					
Total positive symptom score	3.0 (0.0, 6.0)	9.0 (6.0, 11.0)	2.0 (0.0, 4.0)	**< .0001**	**−0.64**
Highest positive symptom score	2.0 (0.0, 3.0)	4.0 (3.0, 4.0)	2.0 (0.0, 2.0)	**< .0001**	**−0.66**
P1 Unusual thought content	0.0 (0.0, 2.0)	2.0 (0.0, 3.0)	0.0 (0.0, 1.0)	**.0003**	**−0.38**
P2 Suspiciousness	0.0 (0.0, 2.0)	3.0 (1.0, 3.0)	0.0 (0.0, 1.0)	**< .0001**	**−0.52**
P3 Grandiosity	0.0 (0.0, 2.0)	0.0 (0.0, 2.5)	0.0 (0.0, 1.0)	.14	−0.15
P4 Perceptual abnormalities/ hallucinations	0.0 (0.0, 2.0)	3.0 (1.5, 4.0)	0.0 (0.0, 0.0)	**< .0001**	**−0.60**
P5 Disorganized communication	0.0 (0.0, 0.5)	0.0 (0.0, 2.5)	0.0 (0.0, 0.0)	**.001**	**−0.33**
Negative symptoms					
Total negative symptom score[c]	6.0 (2.0, 12.0)	11.0 (7.5, 14.5)	4.5 (1.8, 10.0)	**.0011**	**−0.35**
Highest negative symptom score[d]	3.0 (2.0, 4.0)	4.0 (3.0, 5.0)	3.0 (1.0, 4.0)	.0042	**−0.30**
N1 Social anhedonia[d]	0.0 (0.0, 2.0)	2.0 (0.0, 5.0)	0.0 (0.0, 1.0)	**.0001**	**−0.41**
N2 Avolition[d]	1.5 (0.0, 3.0)	3.0 (2.0, 4.0)	1.0 (0.0, 3.0)	.0068	−0.29
N3 Expression of emotions[d]	0.0 (0.0, 1.0)	0.0 (0.0, 2.5)	0.0 (0.0, 1.0)	.071	−0.19
N4 Experience of emotions and self[c]	0.0 (0.0, 1.0)	1.0 (0.0, 3.5)	0.0 (0.0, 0.0)	**.0008**	**−0.36**
N5 Ideational richness[d]	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	.63	−0.05
N6 Occupational functioning[c]	2.0 (0.0, 4.0)	3.0 (0.5, 4.0)	2.0 (0.0, 3.3)	.17	−0.15
Disorganized Symptoms					
Total disorganized symptom score[c]	2.0 (0.0, 5.0)	3.0 (1.0, 6.0)	2.0 (0.0, 4.3)	.072	−0.19
Highest disorganized symptom score[c]	2.0 (0.0, 3.0)	3.0 (1.0, 4.0)	2.0 (0.0, 3.0)	.14	−0.16
D1 Odd behavior or appearance[d]	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	0.0 (0.0, 0.0)	**.0009**	**−0.35**
D2 Bizarre thinking[d]	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	.39	−0.09
D3 Trouble with focus and attention[d]	2.0 (0.0, 3.0)	3.0 (0.5, 3.0)	1.0 (0.0, 3.0)	.033	−0.23
D4 Impairment in personal hygiene[c]	0.0 (0.0, 1.0)	0.0 (0.0, 1.5)	0.0 (0.0, 0.0)	.31	−0.11
General symptoms					
Total general symptom score[d]	9.0 (6.0, 11.0)	12.0 (8.5, 15.0)	8.0 (5.0, 11.0)	**.0004**	**−0.37**
Highest general symptom score[d]	5.0 (4.0, 6.0)	6.0 (4.5, 6.0)	4.0 (4.0, 5.0)	.0080	−0.28
G1 Sleep disturbance[d]	3.0 (0.0, 4.0)	3.0 (3.0, 4.0)	2.0 (0.0, 3.0)	.017	−0.25
G2 Dysphoric mood[d]	3.3 (1.0, 5.0)	6.0 (4.0, 6.0)	4.0 (3.0, 5.0)	.011	−0.27
G3 Motor disturbance[c]	0.0 (0.0, 0.0)	0.0 (0.0, 2.0)	0.0 (0.0, 0.0)	**.0013**	**−0.34**
G4 Impaired stress tolerance[c]	2.0 (0.0, 3.0)	3.0 (1.0, 5.0)	1.0 (0.0, 3.0)	.013	−0.27
Additional Psychopathology Scales					
Psychosis					
BPRS total[e]	33.0 (27, 37)	39.5 (31.8, 42.8)	32.0 (26.0, 35.0)	**.0017**	**−0.34**
BPRS positive symptoms[f]	7.0 (6.0, 8.0)	9.0 (8.0, 10.0)	7.0 (6.0, 8.0)	**< .0001**	**−0.52**
BPRS withdrawal[g]	4.0 (3.0, 5.5)	5.0 (3.0, 6.0)	3.0 (3.0, 5.0)	.054	−0.21
Depression					
MADRS sum score[h]	24.0 (13.0, 33.0)	34.0 (22.5, 40.0)	21.0 (10.5, 29.5)	**.0014**	**−0.35**
Mania					
YMRS past month[i]	11.0 (4.0, 22.0)	11.0 (6.0, 21.0)	11.0 (4.0, 33.0)	.61	−0.06

[a]Significance level for attenuated variables: $P < .002$; significance level for syndromal variables: $P < .01$; bolded *P* values below significance level; bolded effect sizes ≥ 0.30 (at least moderate).
[b]Negative effect sizes indicate worse outcome in the APS group, ie, higher symptom ratings or lower functional scores.
[c]n = 87. [d]n = 88. [e]n = 83. [f]n = 86. [g]n = 85. [h]n = 81. [i]n = 84.
Abbreviations: APS = attenuated psychosis syndrome (according to *DSM-5* Sections II and III), BPRS = Brief Psychiatric Rating Scale, D1–4 = disorganized symptoms, G1–4 = general symptoms, IQR = interquartile range, MADRS = Montgomery-Asberg Depression Rating Scale, N1–6 = negative symptoms, P1–5 = positive symptoms, YMRS = Young Mania Rating Scale.

SIPS Symptoms and Domains

Total (attenuated) positive ($r = -0.64$), negative ($r = -0.35$), and general symptom ($r = -0.37$) scores were significantly higher in the APS than in the non-APS group. Conversely, total disorganized symptoms were not significantly different across groups. The group-defining SIPS/SOPS attenuated positive symptoms were significantly higher in the APS group except for grandiosity ($P = .14$) (*P* values = .003 to < .0001; $r = -0.33$ to -0.60) (Table 3). Two of the 6 negative symptom items (social anhedonia: $P = .0001$, $r = -0.41$ and decreased experience of emotions/self: $P = .0008$, $r = -0.36$), 1 disorganized (odd behavior or appearance: $P = .0009$, $r = -0.35$), and 1 general symptom item (motor disturbance: $P = .0013$, $r = -0.34$) were significantly higher in the APS group (Table 3). The BPRS total ($P = .0017$; $r = -0.34$) and positive ($P < .0001$; $r = -0.52$) scores were significantly higher in APS subjects (Table 3). Finally, MADRS scores ($P = .0014$; $r = -0.35$) were higher in APS subjects, without differences in the YMRS (Table 3).

Clinical and Functional Correlates of APS Status

Compared to the status of non-APS adolescents, APS status was associated with significantly worse CGI-S scores ($P = .0008$; $r = 0.36$) (Table 4). Moreover, APS status was associated with lower GAF scores at time of the interview ($r = -0.30$) and lowest GAF ($r = -0.40$) during the past year, whereas highest GAF during the past year did not survive Bonferroni correction. There were no differences in current role and social functioning (Table 4).

APS and non-APS adolescents did not differ regarding awareness of mental disorder or social consequences, suicidal

Table 4. Illness Severity, Functional Level, Illness Insight, and Suicidality[a]

Characteristic	Total (N = 89)	APS (n = 21)	Non-APS (n = 68)	*P* Value	Effect Size, Rosenthal *r*[b]
Illness severity (CGI-S), median (IQR 25, 75)					
Overall severity of illness[c]	4.0 (4.0, 5.0)	5.0 (4.3, 5.8)	4.0 (3.0, 5.0)	**.0008**	**0.36**
Functional level, median (IQR 25, 75)					
GAF					
Current[d]	35.0 (20.0, 48.0)	21.0 (20.0, 36.5)	40.0 (21.5, 49.8)	**.0050**	**−0.30**
Highest of past year[e]	56.5 (50.0, 68.0)	51.0 (42.0, 58.0)	60.0 (50.5, 68.0)	.020	−0.26
Lowest of past year[f]	29.0 (20.0, 48.0)	20.0 (10.0, 24.0)	38.0 (20.0, 50.5)	**.0006**	**−0.40**
% decline[e]	33.5 (16.0, 59.5)	41.0 (29.0, 61.0)	30.0 (15.0, 57.5)	.083	0.19
Current role functioning (GF:R)[g]	6.0 (5.0, 7.0)	6.0 (5.0, 7.3)	6.0 (5.0, 7.0)	.45	0.08
Current social functioning (GF:S)[g]	6.5 (5.0, 8.0)	6.0 (5.0, 7.0)	7.0 (5.0, 8.0)	.077	−0.20
SUMD, median (IQR 25, 75)					
Awareness of mental disorder[h]	1.0 (1.0, 3.0)	1.0 (1.0, 2.0)	1.0 (1.0, 3.0)	.61	
Awareness of the social consequences[i]	1.0 (1.0, 3.0)	1.0 (1.0, 1.0)	1.0 (1.0, 3.0)	.16	
Suicidality, n (%)					
Suicidal ideation/behavior					
Lifetime[c]	64 (74.4)	14 (77.8)	50 (73.5)	.71	
Present[c]	56 (65.1)	11 (61.1)	45 (66.1)	.69	
Suicide attempts					
Lifetime[c]	34 (39.5)	7 (38.9)	27 (39.7)	.95	
Present[c]	16 (18.6)	2 (11.1)	14 (20.6)	.51	

[a]Significance level for illness severity: $P < .05$; significance level for functional level: $P < .008$; significance level for illness insight: $P < .03$; significance level for suicidality: $P < .01$; bolded *P* values below significance level; bolded effect sizes ≥ 0.30 (at least moderate).
[b]Negative effect sizes indicate worse outcome in the APS group, ie, higher symptom ratings or lower functional scores.
[c]n = 86. [d]n = 85. [e]n = 80. [f]n = 73. [g]n = 78. [h]n = 70. [i]n = 69 patients.
Abbreviations: APS = attenuated psychosis syndrome (according to *DSM-5* Sections II and III), CGI-S = Clinical Global Impressions-Severity scale, GAF = Global Assessment of Functioning scale, GF:R = Global Functioning: Role scale, GF:S = Global Functioning: Social scale, IQR = interquartile range, SUMD = Scale to Assess Unawareness of Mental Disorder.

Table 5. Correlation Between Symptom Domains of the Structured Interview of Prodromal Syndromes and Measures of Functioning in the Entire Sample of Adolescent Inpatients (Nonparametric Spearman Correlation Coefficient)[a]

	Current GAF		Current Role Functioning (GF:R)		Current Social Functioning (GF:S)	
Variable	Spearman ρ	*P* Value	Spearman ρ	*P* Value	Spearman ρ	*P* Value
Total positive symptom score	**−0.38**	**.0003**	−0.034	.77	**−0.25**	**.028**
Total negative symptom score	**−0.26**	**.015**	**−0.25**	**.025**	**−0.38**	**.0007**
Total disorganized symptom score	−0.20	.073	−0.15	.21	−0.18	.12
Total general symptom score	**−0.45**	**<.0001**	−0.20	.082	**−0.38**	**.0006**

[a]Bolded *P* values < .05; negative Spearman ρ indicates an inverse relationship, ie, higher symptoms being associated with lower levels of functioning.
Abbreviation: GAF = Global Assessment of Functioning, GF:R = Global Functioning: Role scale, GF:S = Global Functioning: Social scale.

ideation/behavior, and suicidal attempts (*P* values = .16–.95) (Table 4).

Correlations Between SIPS Domains and Functional Measures

Poorer current global functioning and social functioning were associated with more severe SIPS total positive, negative, and general symptoms (Spearman ρ = −0.25 to −0.45; *P* = .015 to < .0001) (Table 5). Conversely, current poor role functioning was significantly associated only with more severe total negative symptoms (Spearman ρ = −0.25; *P* = .025).

Multivariable Regression Analysis

Only greater "social isolation" scores (*P* = .0034, odds ratio [OR] = 27.52; 95% confidence interval [CI], 3.36–313.87) and a lower score on the item "lowest GAF score in the past year" (*P* = .020, OR = 51.15; 95% CI, 2.46–2,439.0) were independently significantly associated with APS status ($r^2 = 0.302$, $P < .0001$).

DISCUSSION

In this study, nonpsychotic adolescent psychiatric inpatients were examined regarding the frequency and correlates of *DSM-5* APS. The prevalence of 24% meeting criteria for *DSM-5* APS and research criteria for APSS in our acutely hospitalized adolescent sample approximates APSS prevalences of 29%–35% in adolescent samples of mainly outpatients.[12,38,39] Prevalence data of *DSM-5*–defined APS in the general adolescent population are sparse, but 7.7% of 11- to 13-year-old school-aged children (n = 212) fulfilled

research-defined APSS criteria, with 89% of them reporting being distressed by their symptoms (ie, Criterion D, required for APS in *DSM-5*, Section III),[14] whereas only 0.3% of 16- to 40-year-olds (n = 1,229) met *DSM-5* Section III APS criteria.[40] These data suggest an age-related decline in APS prevalence in the general population similar to the substantial decline of the prevalence of psychotic-like symptoms from childhood through adolescence assessed with different self-reports or semistructured interviews.[41–43] Therefore, late adolescence may represent the period when the age-related decline of *DSM-5* APS prevalence and the age-related increase of the true risk for progression of attenuated positive symptoms to full-fledged psychosis converge. However, due to the lack of reliable biological and clinical risk indicators, it is currently not possible to distinguish adolescents fulfilling APS criteria who are at true risk for psychosis from those with nonspecific symptoms who are not at risk. Further risk stratification is needed. One clinical example is the combined use of attenuated positive symptoms, which are detected by clinicians or informants, together with so-called basic symptoms, which are subtle, self-experienced, and subclinical disturbances in cognition and perception.[44] In a previous meta-analysis of clinical high-risk studies in adults, combining APS criteria with basic symptom criteria increased the prediction of ultimate conversion to psychosis[4] and may therefore be a promising approach.[45–47]

The higher number of comorbid disorders, reported previously in school-aged children of the general population,[14] and the increased frequency of MDD as well as ODD/CD in the APS group of our severely affected adolescent sample support the association between APS and other mental disorders. Previous studies in adolescents and adults at-risk reported more internalizing disorders, ie, depression and anxiety.[13,17,48–50] In our sample, mood and anxiety disorders were frequent, but only MDD was significantly associated with *DSM-5* APS. Likewise, in the North American Prodrome Longitudinal Study,[17] lifetime MDD rates were higher among at-risk patients than help-seeking subjects without risk criteria. Since MDD has also been described in early stages of schizophrenia spectrum disorders,[19] conclusions have to be drawn with caution. Although impulse-control disorders are common in adolescents,[51] they seem to be less frequent in help-seeking individuals in research centers focusing on patients at risk for psychosis.[13,17,49,50] Interestingly, 21% of non–help-seeking children with APSS[14] and 38% of unselected adult outpatients with APS-like symptoms[52] also met criteria for an impulse-control disorder. A recent study focused on adolescents with severe behavioral problems (N = 53) and showed that 13% met APSS, but that this condition predicted hospital treatment for mood and conduct disorders rather than conversion to psychosis during 5 years.[53]

In a predominantly adult sample enrolled in high-risk psychosis clinics[17,54] and in a general adult psychiatric outpatient sample,[52] 44% to 46% of individuals meeting risk criteria also met personality disorder criteria. The high co-occurrence of APSS/APS-like symptoms with personality disorders (which survived stringent Bonferroni correction for multiple testing across all different diagnostic categories) corresponds with our finding that APS status was associated with personality disorder traits. In patients with borderline personality disorder, psychosis-like symptoms are often intermittent and may not predict psychotic disorder development.[55] However, our data suggest that attenuated psychotic symptoms are not only related to internalizing and externalizing disorders but may also emerge, stabilize, or progress within the first manifestation of personality disorders during adolescence. Therefore, in this age-group, to decide prospectively whether the Criterion E is met, ie, attenuated psychotic symptoms are not better explained by any other *DSM-5* diagnosis, is challenging.

In addition to diagnostic differences, *DSM-5* APS status was associated with significantly higher severity of negative and general SIPS symptoms in our sample. Effect sizes for these differences were moderate to large. Results from additional rating scales support the hypothesis that APS in adolescents is associated with a broad range of syndromal and subsyndromal symptomatology, including depressive symptoms, but neither hypomanic nor manic symptoms. However, since depression can be a precursor of nonaffective psychotic disorders as well as bipolar disorder, careful follow-up is required.

In multivariable analyses, only lower GAF scores in the preceding year and greater social isolation independently differentiated APS from non-APS subjects, explaining 30.2% of the variance. Social isolation has repeatedly been shown to be a precursor to schizophrenia[56–59] and the most common presenting symptom in adolescents enrolled in a high-risk program.[60] "Decreased need for social contacts" was 1 of the symptoms differentiating best between an adolescent at-risk and a clinical control group.[47] Hence, new-onset social isolation associated with decreased functioning should prompt psychiatric evaluation in adolescents.

Lower GAF and CGI scores in our *DSM-5*–defined APS group underscore that APS status is associated with marked impairment, consistent with data in adult psychiatric outpatients[52] and non–help-seeking children aged 11–13 years.[14] Notably, prospective studies indicated that within at-risk subjects lower functioning predicted persistence or aggravation of attenuated positive symptoms.[61,62] In our generally impaired inpatient sample, social and role functioning did not significantly differ in APS and non-APS youth. While in the entire sample, social functioning was significantly associated with total, positive, and negative SIPS scores, indicating a pervasive relationship with multiple symptom domains, role functioning was significantly associated only with negative symptomatology. In at-risk samples, especially poor social functioning predicted onset of psychosis, whereas data for role functioning were less consistent.[62–65]

We did not observe an association between suicidality and APS status in contrast to earlier reports of APS-like symptoms in adults.[52] In our study, suicidality was obtained using chart information and might be incomplete. Moreover, our inpatient sample is quite likely enriched for suicidality,

which was high in both groups, for reasons unrelated to APS status. Nevertheless, since psychosis is a risk factor for suicidality and more severe suicidal behavior,[66] adolescents with APS need to be carefully monitored. Of note, SUMD scores were similar across APS and non-APS adolescents. However, this lack of difference is most likely due to the fact that we assessed only general awareness and not awareness of specific symptoms.

Finally, an alarmingly high percentage of nonpsychotic adolescent inpatients (65.2%) in our sample received atypical antipsychotics at the time of the interview. There was no group difference and no significant correlation between antipsychotic prescribing and the severity of attenuated psychotic symptoms assessed with the SIPS or BPRS (data not shown). Since clinical decision-making was independent of research assessments, it is unclear to what degree clinicians were aware of the APS status. Still, these results provide first evidence that in clinical care APS status itself does not seem to account for more frequent use of antipsychotics, at least among a psychiatric inpatient sample with a high rate of utilization of antipsychotics that are being prescribed for many nonpsychotic conditions, despite worrisome adverse effects.[67–69]

Limitations

Limitations of this study include currently still insufficient prospective data from this sample, restricting us to cross-sectional analyses. Distress and disability are required, but not further operationalized for APS in Section II or III of *DSM-5*. In adults, distress seemed to be more related to associated depression or anxiety than to psychotic-like experiences.[70] Since we did not implement additional questions to link the level of experienced distress to specific symptoms or symptom domains and psychiatric admission in adolescents is also influenced by concerns of parents, teachers, and general practitioners, it remains unclear to what extent the distress was explicitly caused by experienced attenuated positive symptoms or the multiple comorbid diagnoses. Adding an alternative criterion, which required a combination of reported attenuated psychotic symptoms and a 30% decline of global functioning during the past year, we found that 73.7% met both criteria (decline not available for 2 patients). Therefore, in our sample the prevalence would diminish from 24% to approximately 16% ($\Delta = 34\%$), whereas this approach caused a reduction from 7.7% to 0.3% ($\Delta = 96\%$) in the school-going children not treated for mental diseases.[14] Further, patients were treated naturalistically and received several psychotropic medications, including antipsychotics. While this could have affected the results, the naturalistic design and inclusion of consecutive admissions to an inpatient unit serving a diverse urban and semiurban catchment area of 3.5 million people increase the generalizability of the results.

CONCLUSIONS AND FUTURE DIRECTIONS

Our data point to a relatively high prevalence and complex entanglement of *DSM-5* APS status with a broad range of mental symptoms and disorders, including depression, impulse-control disorders, and emerging personality disorders, in mentally ill adolescents. Consistent with previous findings in at-risk samples, *DSM-5* APS status was associated with increased severity of symptoms, suggesting the need for "staged" and age-adapted treatment approaches.[71,72] However, in adolescents admitted for major psychiatric disorders, such staged approaches may be complicated, because complex medical histories and frequent comorbidities require therapeutic attention, and as in the clinical care of symptomatic and impaired youth antipsychotics have, unfortunately, become a common clinical treatment, irrespective of APS status, at least in the United States. Clearly, large and long-term, prospective studies of representative clinical samples are needed to assess the frequency, associated characteristics, and long-term outcomes of *DSM-5* APS status and to monitor the evolution of APS from childhood to adulthood.

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Drug names: aripiprazole (Abilify), atomoxetine (Strattera and others), bupropion (Wellbutrin and others), citalopram (Celexa and others), clonazepam (Klonopin and others), duloxetine (Cymbalta), fluoxetine (Prozac and others), lamotrigine (Lamictal and others), lorazepam (Ativan and others), lisdexamfetamine (Vyvanse), methylphenidate (Ritalin and others), modafinil (Provigil and others), paroxetine (Paxil, Pexeva, and others), quetiapine (Seroquel and others), risperidone (Risperdal and others), sertraline (Zoloft and others), valproic acid (Depakene and others), ziprasidone (Geodon and others).

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Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Childhood and Adolescent Mental Health section. Please contact Karen D. Wagner, MD, PhD, at kwagner@psychiatrist.com.

Supplementary material follows this article.

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Supplementary Material

Article Title: Frequency and Correlates of DSM-5 Attenuated Psychosis Syndrome in a Sample of Adolescent Inpatients With Nonpsychotic Psychiatric Disorders

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List of Supplementary Material for the article

1. **eFigure 1** Patient Flowchart

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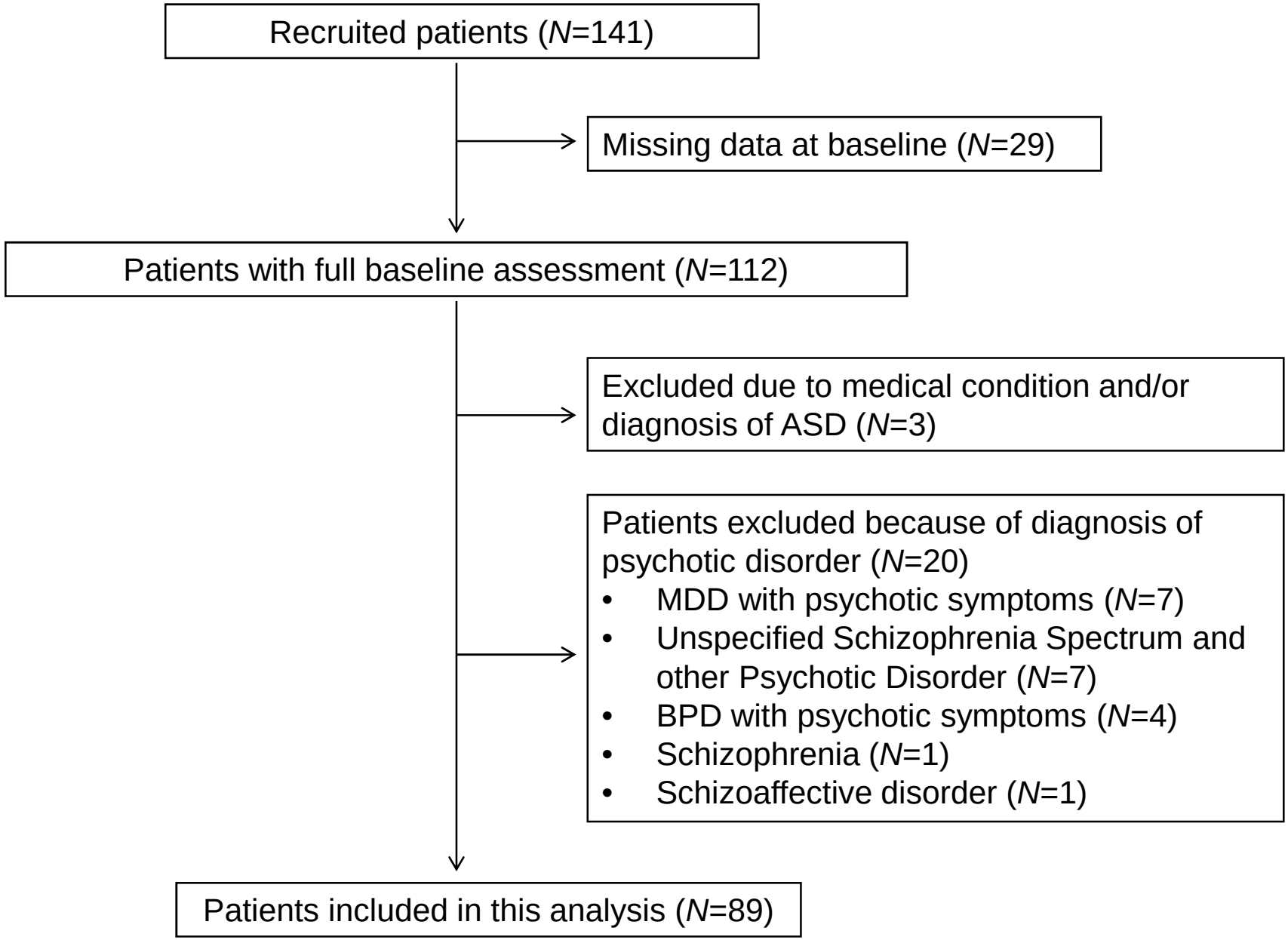
Supplementary eFigure 1: *Patient Flow*



ASD=autism spectrum disorder; MDD=major depressive disorder; BPD=bipolar disorder.