*Psychological Medicine* (2016), **46**, 1069–1078. © Cambridge University Press 2015
doi:10.1017/S0033291715002627

ORIGINAL ARTICLE

# Adolescents and adults at clinical high-risk for psychosis: age-related differences in attenuated positive symptoms syndrome prevalence and entanglement with basic symptoms

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**Background.** The attenuated positive symptoms syndrome (APSS) is considered an at-risk indicator for psychosis. However, the characteristics and developmental aspects of the combined or enriched risk criteria of APSS and basic symptom (BS) criteria, including self-experienced cognitive disturbances (COGDIS) remain under-researched.

**Method.** Based on the Structured Interview of Prodromal Syndromes (SIPS), the prevalence of APSS in 13- to 35-year-old individuals seeking help in an early recognition program for schizophrenia and bipolar-spectrum disorders was examined. BS criteria and COGDIS were rated using the Schizophrenia Proneness Instrument for Adults/Children and Youth. Participants meeting APSS criteria were compared with participants meeting only BS criteria across multiple characteristics. Co-occurrence (APSS+/BS+, APSS+/COGDIS+) was compared across 13–17, 18–22 and 23–35 years age groups.

**Results.** Of 175 individuals (age = 20.6 ± 5.8, female = 38.3%), 94 (53.7%) met APSS criteria. Compared to BS, APSS status was associated with suicidality, higher illness severity, lower functioning, higher SIPS positive, negative, disorganized and general symptoms scores, depression scores and younger age (18.3 ± 5.0 *v.* 23.2 ± 5.6 years, $p < 0.0001$) with age-related differences in the prevalence of APSS (ranging from 80.3% in 13- to 17-year-olds to 33.3% in 23- to 35-year-olds (odds ratio 0.21, 95% confidence interval 0.11–0.37). Within APSS+ individuals, fewer adolescents fulfilled combined risk criteria of APSS+/BS+ or APSS+/COGDIS+ compared to the older age groups.

**Conclusions.** APSS status was associated with greater suicidality and illness/psychophathology severity in this help-seeking cohort, emphasizing the need for clinical care. The age-related differences in the prevalence of APSS and the increasing proportion of APSS+/COGDIS+ may point to a higher proportion of non-specific/transient, rather than risk-specific attenuated positive symptoms in adolescents.

*Received 11 July 2015; Revised 9 November 2015; Accepted 11 November 2015; First published online 16 December 2015*

**Key words:** Adolescents, at-risk for psychosis, attenuated positive symptoms, basic symptoms, cognitive disturbances, psychosis.

## Introduction

Since schizophrenia remains one of the most severe mental disorders, efforts at preventing the development of psychosis are crucial (Correll *et al.* 2010; Fusar-Poli *et al.* 2013). Based on prospective studies in clinical high-risk samples (Fusar-Poli *et al.* 2012; Schultze-Lutter *et al.* 2015), the Attenuated Psychosis Syndrome (APS) was included in DSM-5 as a condition for further study as well as an already codable condition under the 'Other specified psychosis disorder' category. However, data for the APS criteria, which define 'attenuated psychosis' as subthreshold delusions, hallucinations and

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disorganized speech/thought (APA, 2013), originate mostly from adult or age-mixed, help-seeking samples. This is problematic because developmental aspects may strongly influence experience and expression of attenuated positive symptoms during adolescence (Schimmelmann *et al*. 2013). Further studies in the general population and across different age groups have been demanded and first findings revealed a prevalence of the research-defined attenuated positive symptoms syndrome (APSS) as high as 7.7% in 11- to 13-year-old school-age children ($n = 212$) (Kelleher *et al.* 2012). Conversely, in a sample aged 16–40 years ($n = 1229$) (Schultze-Lutter *et al*. 2013) only 0.4% met APSS criteria. These data in the general population, albeit collected in different countries by different researchers, suggest the possibility of an age-related decline of the prevalence of APSS in the general population.

In psychiatrically ill adolescents, first studies showed a prevalence of APSS as high as 31.7% in mainly outpatients (Lindgren *et al.* 2014) without predicting the onset of psychoses 1 year later, and a prevalence of 23.6% in inpatients (Gerstenberg *et al.* 2015), further questioning the validity of current high-risk criteria in children and adolescents (Schimmelmann & Schultze-Lutter, 2012; Schimmelmann *et al*. 2013).

In help-seeking individuals at clinical high risk for psychosis, a recent meta-analysis further reported age-related effects regarding the transition to psychosis (Schultze-Lutter *et al.* 2015). Namely, lower transition rates occurred in samples of almost entirely minors compared to mixed samples and adults (Schultze-Lutter *et al.* 2015).

In adults and mixed samples, the additional detection of basic symptom (BS) criteria, particularly of a cluster of subtle cognitive disturbances (COGDIS), may help identify individuals at true risk for psychosis (Ruhrmann *et al.* 2010; Schultze-Lutter *et al.* 2014). Basic symptoms preceded, but also co-occurred with attenuated positive symptoms, and the presence of both, COGDIS and APSS, may increase predictive power for conversion to psychosis (Ruhrmann *et al.* 2010; Schultze-Lutter *et al.* 2014).

Taken together, data about the age-related distribution of APSS within one study population are sparse, and little is known about the combined prevalence of APSS and BS criteria across different age groups. Therefore, in the present study, a broad age range was chosen to allow the investigation of age-specific aspects of help-seeking individuals meeting APSS and/or BS criteria.

We aimed to analyze the age-specific distribution of APSS and BS criteria, especially COGDIS, as well as of their combination. Based on prior literature (Kelleher *et al.* 2012; Schultze-Lutter *et al.* 2013; Lindgren *et al.* 2014), we hypothesized that (1) APSS would be more frequent in adolescents than in adults, and (2) APSS with co-occurring BS criteria, a likely more specific risk constellation, would conversely be less frequent among youth with APSS than in adults with APSS.

## Material and method

### *Setting and participants*

As part of an on-going, longitudinal early recognition project for schizophrenia- and bipolar-spectrum disorders (http://www.zinep.ch), individuals were recruited in the Swiss region of Zurich, a 1.4 million people catchment area. The study was approved by the local ethics committee (E63/2009) and complies with the Declaration of Helsinki. Legal guardians of minors and adult participants were asked to give written informed consent, minors to provide written assent. The sample was accrued from April 2010 to July 2012. Potential participants had either learned about the study from a project website, flyers, newspaper advertisements, or were referred by general practitioners, counseling services, psychiatrists, or psychologists. Study design, inclusion, and exclusion criteria were previously described (Metzler *et al.* 2014; Theodoridou *et al.* 2014).

In brief, inclusion criteria for the initial sample were: individuals aged 13–35 years, sufficient German speaking ability, meeting at least one of the following at-risk criteria (1) a risk syndrome as defined by the Structured Interview of Prodromal Syndromes and the corresponding Scale for Prodromal Syndromes (SIPS/SOPS) (McGlashan *et al.* 2010), and/or (2) an at-risk state according to BS criteria [i.e. criteria for cognitive-perceptive symptoms (COPER) and/or cognitive disturbances (COGDIS)] as defined by the Schizophrenia Proneness Instrument (Schultze-Lutter, 2007; Schultze-Lutter & Koch, 2010) and/or (3) a potential risk for bipolar spectrum disorders, as defined by a score of either $\geqslant 14/32$ hypomanic symptoms as assessed with the Hypomania Checklist (Angst *et al.* 2005), or a score of $\geqslant 12$ on the Hamilton Depression Rating Scale (HAMD, Hamilton, 1960). Exclusion criteria were: (1) estimated premorbid IQ < 80, (2) meeting DSM-IV criteria for current substance dependence, any psychotic disorder confirmed by research diagnostic interviews, and/or a medical condition known to affect the brain, and for the present analysis (3) not fulfilling APSS or BS criteria.

Of 305 recruited participants, 52 (17.0%) withdrew their consent before full baseline assessments, 14 (4.6%) were excluded due to a confirmed diagnosis of schizophrenia or schizoaffective disorder, and 64 (21.0%) did not fulfill APSS and/or BS criteria (Fig. 1). The remaining 175 participants were grouped

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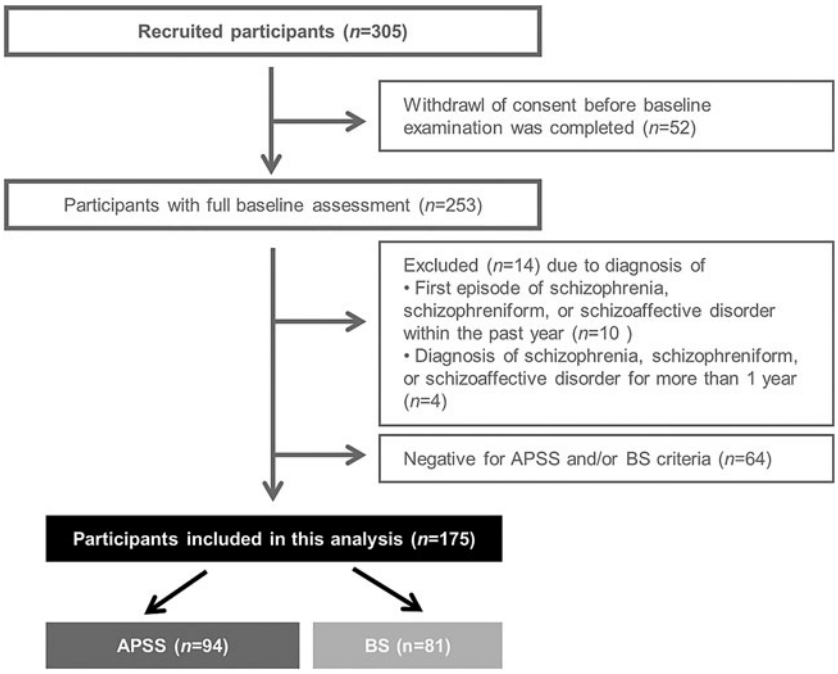


**Fig. 1.** Recruitment, analyzed sample and group composition. APSS, Attenuated positive symptoms syndrome; BS, basic symptom criteria.

into APSS *v.* BS and compared on demographic, diagnostic, symptom, and treatment variables.

### *Procedures*

Demographic, past psychiatric illness and treatment information was obtained from participants and, in case of minors, augmented by information from guardians. DSM-IV Axis I diagnoses were screened with the Mini International Neuropsychiatric Interview (MINI/MINI-KID; Lecrubier *et al.* 1997; Sheehan *et al.* 2010). The presence and severity of positive, negative, disorganized, and general symptoms, including attenuated levels, were assessed with the SIPS and rated using the companion SOPS (McGlashan *et al.* 2010). BS criteria were assessed with the Schizophrenia Proneness Instrument – Adult or Child and Youth version, and risk criteria for COGDIS and COPER were coded (Schultze-Lutter, 2007).

Severity of positive symptoms was assessed using the Positive and Negative Syndrome Scale (PANSS; Kay *et al.* 1987), depressive symptoms with the HAMD (Hamilton, 1960); frequency of lifetime hypomanic symptoms with the Hypomania Checklist, and anxiety with the Beck Anxiety Inventory (BAI; Beck *et al.* 1988). Lifetime suicidality was detected with the MINI/MINI-KID and current suicidality was defined by a score $\geqslant 2$ (0–4) on the HAMD suicidality question. Illness severity was rated using the Clinical Global Impressions – Severity scale (CGI-S; Guy, 1976). The Global Assessment of Functioning scale (GAF; Hall, 1995) was used to assess current and, highest functioning in the past year, and decline within the past year. IQ was estimated with a word recognition test for adults [Mehrfachwahl-Wortschatz-Intelligenztest (MWT-B; Lehrl *et al.* 1995)] or a test of receptive vocabulary for minors [Peabody Picture Vocabulary Test (PPVT; Dunn *et al.* 1965)]. All semi-structured interviews and cognitive testing were administered by experienced and extensively trained psychologists and psychiatrists.

### *Statistical analysis*

Descriptive statistics were provided for sociodemographic and clinical characteristics. To assess group differences, $\chi^2$ statistics for categorical variables (or Fisher's exact test whenever $\geqslant 1$ cell weights were $\leqslant 5$) were used. Continuous outcomes that were normally distributed were analyzed using *t* tests and analysis of variance. Continuous outcomes that were not normally distributed were analyzed using the non-parametric Mann–Whitney *U* test.

Moreover, ordinal logistic regressions using a proportional odds model were performed to examine the relationship between APSS status and the three age groups (1) adolescents (13–17 years, $n = 66$), (2) young adults (18–22 years, $n = 52$), and (3) adults (23–35 years, $n = 57$). Odds ratio (OR) estimates and their 95% confidence intervals (CIs) were reported. Finally,

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associations between APSS status and psychopathology were assessed. Group comparisons were performed using *t* tests for two-group comparisons (APSS *v.* BS). All analyses were conducted using STATA/SE 12 (Stata Statistical Software: Stata/SE v. 12.0 for Windows; Stata Corporation, USA); all tests were two-sided.

## Results

### *Age-related aspects of APSS and BS prevalences*

Of 175 non-psychotic individuals (age = 20.6 ± 5.8 years, age range = 13–35, female = 38.3%), 94 (53.7%) fulfilled APSS criteria (Table 1). Compared to BS criteria, APSS status was associated with younger age (23.2 ± 5.6 *v.* 18.3 ± 5.0, $p < 0.0001$).

In ordinal regression models, compared to BS criteria, APSS status was negatively associated with age, with prevalences ranging from 80.3% in adolescents to 33.3% in adults (OR 0.21, 95% CI 0.11–0.37, $p < 0.001$).

Within APSS+ individuals, fewer adolescents fulfilled combined risk criteria of APSS+/BS+ 75.5% compared to the older age groups (APSS+/BS+ in young adults 95.5%, in adults 94.7%) (Table 2, Fig. 2).

Similarly, fewer adolescents fulfilled combined risk criteria of APSS+/COGDIS+ (52.8% *v.* 72.7% in young adults, and 78.9% in adults) (Table 2, Fig. 2). Accordingly, significantly more adolescents meet APSS+/BS− (24.5% *v.* 4.6% in young adults and 5.3% in adults) or APSS+/COGDIS− (47.2% *v.* 27.3% in young adults and 21.1% in adults) criteria (Table 2, Fig. 2). All differences were significant comparing adolescents to young adults ($p < 0.0001$–$0.003$), whereas no differences between the two adult groups were found.

### *APSS* v. *BS: diagnostic and treatment characteristics, illness severity, functioning and suicidality*

APSS status was associated with a higher frequency of obsessive compulsive disorder (8.6% *v.* 20.2%, $p = 0.035$) and post-traumatic stress disorder (12.8% *v.* 1.2%, $p = 0.003$) (Table 1). In the adolescent subgroup, conduct disorder was more frequent in the BS group (38.5% *v.* 9.4%, $p = 0.020$) (Supplementary Table S2).

Treatment characteristics did not differ between the groups. However, APSS status was associated with higher CGI-Severity, poorer current GAF, and lifetime suicidality (Table 1). Additionally, a decline of ⩾30% was more frequent in APSS compared to BS (42.4% *v.* 23.5%, $p = 0.015$) groups. In contrast, current suicidality did not differ between the groups (Table 1).

### *Psychopathology in APSS* v. *BS groups*

In addition to the group-defining SIPS positive scores, the SIPS negative, disorganized and general symptom total scores were significantly higher in the APSS than BS group. Similarly, the PANSS positive, negative and general and depressive sum scores were significantly higher in the APSS *v.* BS group ($p < 0.0001$–$0.015$), whereas anxiety sum scores did not differ significantly (Table 3).

## Discussion

Assessing the age-specific distribution of APSS and BS we found that (1) APSS status was associated with younger age and an age-related differences in prevalences of APSS, ranging from 80.3% in 13- to 17-year-old adolescents to 33.3% in 23- to 35-year-olds, and (2) in adolescents compared with adults, the proportion of co-occurring APSS and BS or the COGDIS risk criterion alone was lowest, whereas the proportion of APSS without BS or COGDIS was highest.

Comparing our overall APSS prevalence of 53.7% to previous studies, our specific sampling strategy, which involved including also participants reporting BS and/or hypomanic symptoms, requires consideration. In clinical high-risk groups of 'The European Prediction of Psychosis Study' (Klosterkötter *et al.* 2005) and the 'North American Prodrome Longitudinal Study' (NAPLS; Addington *et al.* 2007) the prevalence of APSS was 81.6%, and 94.3%, respectively, but decreased to 50.4% in NAPLS when considering all help-seeking individuals. Therefore, the APSS prevalence in our sample is intermediate between high prevalences in at-risk samples ascertained in early recognition centers and lower prevalences of 31.7% (Lindgren *et al.* 2014) in unselected adolescent psychiatric outpatients, or 28.3% (Gaudiano & Zimmerman, 2013) in unselected adult psychiatric outpatients.

Finding significantly more frequent APSS status in adolescents than adults, we assessed the co-occurrence of APSS+/BS+ or APSS+/COGDIS+, both proposed as more specific risk constellations for psychosis (Ruhrmann *et al.* 2010; Schultze-Lutter *et al.* 2014). Interestingly, our results showed that the ratio of APSS+/COGDIS+ to APSS+/COGDIS− was almost 1:1 (52.8% *v.* 47.2%) in adolescents, whereas in both adult groups, the proportion rose to approximately 3:1 pointing to possibly more non-specific/transient attenuated positive symptoms in adolescents. While we cannot draw further conclusions from our cross-sectional data, this hypothesis is supported by first naturalistic longitudinal studies focusing explicitly on help-seeking adolescents (12–18 years). These studies yielded transition rates of only 7.1–15.6% (Ziermans

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**Table 1.** *Baseline demographics, treatment, diagnostic, and functional characteristics*

| | Total ($n = 175$) | APSS ($n = 94$) | BS ($n = 81$) | $p$ value |
|---|---|---|---|---|
| Demographics | | | | |
| Sex, female, *n* (%) | 67 (38.3) | 34 (36.2) | 33 (40.7) | 0.64 |
| Estimated IQ[a] (MWTB/PPVT) | 102.8 ± 12.4 | 102.1 ± 13.4 | 103.5 ± 11.2 | 0.47 |
| Age, mean ± S.D. | 20.6 ± 5.8 | 18.3 ± 5.0 | 23.2 ± 5.6 | **<0.0001** |
| Diagnoses, *n* (%) | | | | |
| Anxiety disorders[b] | 93 (53.1) | 50 (53.2) | 43 (53.1) | 1.00 |
| Social phobia | 37 (21.1) | 15 (16.0) | 22 (27.2) | 0.094 |
| Panic disorder | 36 (20.6) | 19 (20.2) | 17 (21.0) | 1.00 |
| General anxiety disorder | 29 (16.6) | 11 (11.7) | 18 (22.2) | 0.069 |
| Agoraphobia | 21 (12.0) | 12 (12.8) | 9 (11.1) | 0.82 |
| Obsessive-compulsive disorder | 26 (14.9) | 19 (20.2) | 7 (8.6) | **0.035** |
| Depressive disorders | 112 (64.0) | 63 (67.0) | 49 (60.5) | 0.43 |
| Major depressive disorder | 94 (53.7) | 54 (57.5) | 40 (49.4) | 0.29 |
| Dysthymic disorder | 18 (10.3) | 9 (9.6) | 9 (11.1) | 0.81 |
| Bipolar spectrum disorder | 52 (29.7) | 30 (31.9) | 22 (27.2) | 0.51 |
| Substance use disorders[b] | 26 (14.9) | 12 (12.8) | 14 (17.3) | 0.52 |
| Other drug abuse | 17 (9.7) | 9 (9.6) | 8 (9.9) | 1.00 |
| Alcohol abuse | 11 (6.3) | 5 (5.3) | 6 (7.4) | 0.76 |
| Trauma- and stressor-related disorders, PTSD | 13 (7.4) | 12 (12.8) | 1 (1.2) | **0.003** |
| Eating disorders | 6 (3.4) | 3 (3.2) | 3 (3.7) | 1.00 |
| Anorexia nervosa | 3 (1.7) | 2 (2.1) | 1 (1.2) | 1.00 |
| Bulimia nervosa | 3 (1.7) | 1 (1.1) | 2 (2.5) | 0.60 |
| Total number of diagnoses | | | | |
| 0–2 | 92 (52.6) | 48 (51.1) | 44 (54.3) | 0.76 |
| ⩾3 | 83 (47.4) | 46 (48.9) | 37 (45.7) | |
| Mean number of diagnoses ± S.D. | 2.6 ± 1.6 | 2.7 ± 1.6 | 2.4 ± 1.6 | 0.26 |
| Treatment characteristics | | | | |
| Participants receiving any psychotropic drug, *n* (%) | 65 (37.1) | 35 (37.2) | 30 (37.0) | 1.00 |
| Antipsychotics | 34 (19.4) | 22 (23.4) | 12 (14.8) | 0.18 |
| Chlorpromazine-equivalent[c], mean ± S.D. | 32.6 ± 118.0 | 47.6 ± 152.9 | 15.1 ± 50.2 | 0.12 |
| Antidepressants | 40 (22.9) | 17 (18.1) | 23 (28.4) | 0.15 |
| Other psychotropic drugs (methylphenidate, antiepileptics) | 5 (2.9) | 4 (4.3) | 1 (1.2) | 0.38 |
| Severity of illness | | | | |
| Severity of illness, CGI scale[d], mean ± S.D. | 4.1 ± 0.9 | 4.4 ± 0.8 | 3.7 ± 1.0 | **<0.0001** |
| Level of functioning | | | | |
| Current functional level, GAF scale[e], mean ± S.D. | 54.9 ± 13.8 | 51.5 ± 11.9 | 58.9 ± 14.9 | **0.001** |
| Highest GAF of past year[f] mean ± S.D. | 72.7 ± 13.4 | 72.5 ± 12.7 | 72.9 ± 14.4 | 0.80 |
| >30% of GAF decline within the past year[d], *n* (%) | 58 (33.1) | 39 (42.4) | 19 (23.5) | **0.015** |
| Suicidality | | | | |
| Lifetime suicidality (MINI), *n* (%) | 87 (49.7) | 54 (57.5) | 33 (40.7) | **0.034** |
| Current suicidality (HAMD)[g], *n* (%) | 46 (26.3) | 30 (32.6) | 16 (19.8) | 0.084 |

APSS, Attenuated positive symptoms syndrome; BS, basic symptom criteria; MWTB, Multiple Choice Vocabulary Intelligence Test (Mehrfachwahl-Wortschatz-Intelligenztest); PPVT, Peabody Picture Vocabulary Test; PTSD, post-traumatic stress disorder; CGI, Clinical Global Impression; GAF, Global Assessment of Functioning; MINI, Mini International Neuropsychiatric Interview; HAMD, Hamilton Depression Scale;

Bolded $p$ values <0.05, data available for [a]166, [c]173, [d]170, [e]167, [f]168 and [g]172 participants; [b]the total number of participants in each main diagnostic category can be smaller than the sum of the individual diagnoses due to co-morbidity.

*et al.* 2011; Welsh & Tiffin, 2014) at 24 months, which are much lower than the 2-year transition rate of 29% in mainly adult samples (Fusar-Poli *et al.* 2012). Notably, the clinical high-risk state in an unselected adolescent sample with first mental health contact was not predictive for transition to psychosis at 1 year, but for psychiatric hospitalization within a follow-up of up to 8.9 years (Lindgren *et al.* 2014). Our data may also indicate that the risk-orientated approach of combining APSS with COGDIS may account

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**Table 2.** *Age-group specific distribution of attenuated positive symptoms syndrome (APSS) and basic symptom criteria (BS)*

| Prevalence in relation to | Adolescents ($n = 66$, 13–17 years) | | Young adults ($n = 52$, 18–22 years) | | Adults ($n = 57$, 23–35 years) | | Total sample ($n = 175$, 13–35 years) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Participants in this age-group, *n* (%) | Frequency of APSS (%) | Participants in this age-group, *n* (%) | Frequency of APSS (%) | Participants in this age-group, *n* (%) | Frequency of APSS (%) | Participants in this sample, *n* (%) | Frequency of APSS (%) | *p* value adolescents *v.* young adults | *p* value young adults *v.* adults |
| APSS | 53 (80.3) | (100) | 22 (42.3) | (100) | 19 (33.3) | (100) | 94 (53.7) | (100) | **<0.0001** | 0.43 |
| APSS+/BS+ | 40 (60.6) | (75.5) | 21 (40.4) | (95.5) | 18 (31.6) | (94.7) | 79 (45.1) | (84.1) | **0.001** | 0.42 |
| APSS+/BS− | 13 (19.7) | (24.5) | 1 (1.9) | (4.6) | 1 (1.8) | (5.3) | 15 (8.6) | (16.0) | **<0.0001** | 1.000 |
| APSS +/COGDIS+ | 28 (42.4) | (52.8) | 16 (30.8) | (72.7) | 15 (26.3) | (78.9) | 59 (33.7) | (62.8) | **0.003** | 0.52 |
| APSS +/COGDIS− | 25 (37.9) | (47.2) | 6 (11.5) | (27.3) | 4 (7.0) | (21.1) | 35 (20.0) | (37.2) | **<0.0001** | 0.50 |

COGDIS, Cognitive disturbances.
Bolded *p* values <0.05.

better for developmental characteristics during adolescence since in our sample the overall prevalence decreased from 80.3% (APSS) to 42.4% (APSS +/COGDIS+). Although the two adult groups still showed lower prevalences of APSS+/COGDIS+, the age-related difference was less pronounced than for the other risk profiles. However, to confirm the greater specificity for true psychosis risk of APSS+/COGDIS+ in adolescents, longitudinal studies in youth are required.

Partly, the high frequency of APSS+/COGDIS− may be related to psychiatric co-morbidities that often emerge during adolescence, complicating diagnostic and treatment approaches of patients with attenuated positive symptoms (Welsh & Tiffin, 2012). Furthermore, in adolescents, it may be particularly difficult to differentiate obsessions and post-traumatic stress-related aberrations in thinking and perceptions from APSS. In this context the utility of the DSM-5 APS diagnosis within the psychosis spectrum may be questioned, especially for 13- to 17-year-olds (Yang *et al.* 2010; Arango, 2011). Subsequently, concerns have been raised about premature labeling, stigma and potentially harming treatment strategies, such as an increased use of antipsychotics in young, treatment-naive individuals reporting attenuated positive symptoms (Corcoran *et al.* 2010; Arango, 2011; Yung *et al.* 2012; Fusar-Poli *et al.* 2013).

Our frequency of 19.4% of patients receiving antipsychotics at study entry corresponds to the rates reported in the NAPLS 1 (24.3%) and 2 (17.6%) studies (Woods *et al.* 2013). Interestingly, treatment characteristics, explicitly antipsychotic medication use and chlorpromazine equivalents did not differ between APSS and BS groups. Clinical decision-making was independent of research assessment, but even though APSS status was associated with a higher degree of symptomatology and overall impairment compared to BS, use and dosage of antipsychotics was similar in both groups. Likewise, in a sample of non-psychotic adolescent inpatients, there was no significant association between antipsychotic medication and severity of attenuated psychotic symptoms and no difference between antipsychotic prescription in APSS and non-APSS youth (Gerstenberg *et al.* 2015). Thus, it remains to be shown if awareness of APSS or the APS diagnosis itself may result in more frequent antipsychotic prescribing to youth or adults fulfilling these criteria.

Irrespective of age, APSS status was associated with suicidality and more clinical impairment, pointing to the close link between APSS and clinical need. Moreover, this finding raises at least the possibility that one reason for lower APSS status in adulthood, assessed cross-sectionally, could be a result of

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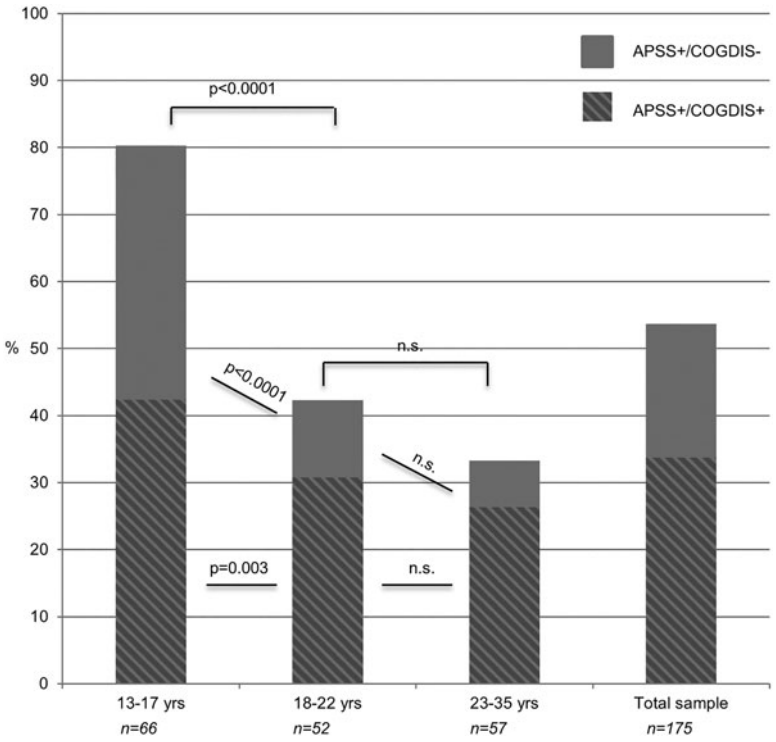


**Fig. 2.** Age-group specific distribution of the risk criteria attenuated positive symptoms syndrome (APSS) and cognitive disturbances (COGDIS). Each column represents the group-specific proportional prevalence of APSS: in adolescents, young adults, adults, and in the total sample. Within APSS+ individuals, the prevalence of the combined risk criteria APSS+/COGDIS+ is represented at the bottom, striped part of the column. To assess group differences, $\chi^2$ statistics for categorical variables were used; significant $p$ values between adolescents (13–17 years) and young adults (18–22 years), N.S., non-significant $p$ values between the two adult groups.

completed suicide in youth, requiring further study. For example, in a longitudinal study of general population adolescents, the risk for suicide attempt was associated with attenuated and/or frank psychotic symptoms. Within 1 year, 34% of the adolescents reported at least one suicide attempt compared to 13% of participants with psychopathology without psychotic symptoms, and 4% in the general population (Kelleher *et al.* 2013). The association of APSS with more clinical and/or functional impairment was also shown in selected at-risk populations, inpatients, outpatients and the general population (Addington & Heinssen, 2012; Kelleher *et al.* 2012; Lindgren *et al.* 2014; Schultze-Lutter *et al.* 2013; Gerstenberg *et al.* 2015). We acknowledge several limitations of this study. Although we recruited a large sample of 13- to 35-year-old individuals with a broad range of symptomatology, sample sizes in the age subgroubs were modest, the naturalistic design allowed for psychotropic medication treatment. The cross-sectional data limit further conclusions, especially concerning the predictive value of APSS with or without BS across the different age groups. Furthermore, since help-seeking behavior in adolescents is also influenced by caretakers, social services and/or general practitioners, we cannot exclude that the sample of adolescents may have differed regarding psychopathology from adults. However, our total sample consisted of self-referrals, out-, and inpatients screened for at-risk criteria. Comparing our APSS prevalence of 80.3% in adolescents to 31.7% APSS in an unselected sample of adolescent psychiatric patients (Lindgren *et al.* 2014), the frequency in our enriched sample still seems reasonable. In conclusion, the possibly transient character of attenuated positive symptoms, especially during adolescence, when APSS might occur in the context of various emerging mental diseases, is underlined by the age-specific differences of the prevalence of APSS in our sample and the proportional decrease of APSS+/COGDIS− in adults. More prospective studies in different age groups and large and clearly defined or generalizable samples followed long enough are required. Such studies might clarify the predictive value of APSS with and without other risk indicators, shed further light on the impact of APSS on suicidality and clinical impairment, and pave the way to identify the individual relevance of APSS and start targeted treatment.

https://doi.org/10.1017/S0033291715002627 Published online by Cambridge University Press

**Table 3.** *Severity of symptom domains assessed with the Structured Interview of Prodromal Syndromes (SIPS) and additional psychopathology scales*

| | Total sample ($n = 175$) | APSS ($n = 94$) | BS ($n = 81$) | $p$ value |
|---|---|---|---|---|
| SIPS, symptom domains, mean ± S.D. | | | | |
| Total positive symptoms score | 8.1 ± 4.6 | 11.0 ± 3.5 | 4.6 ± 3.2 | **<0.0001** |
| Total negative symptoms score | 12.1 ± 6.1 | 13.5 ± 6.0 | 10.6 ± 5.9 | **0.002** |
| Total disorganized symptoms score | 4.6 ± 3.0 | 5.9 ± 3.1 | 3.0 ± 2.1 | **<0.0001** |
| Total general symptom score | 8.2 ± 3.7 | 8.8 ± 3.8 | 7.4 ± 3.5 | **0.015** |
| Additional psychopathology scales | | | | |
| Psychosis, mean ± S.D. | | | | |
| PANSS positive sum score[a] | 13.0 ± 4.4 | 15.3 ± 4.0 | 10.4 ± 3.2 | **<0.0001** |
| PANSS negative sum score[a] | 14.4 ± 5.9 | 16.4 ± 6.1 | 12.0 ± 4.7 | **<0.0001** |
| PANSS general sum score[a] | 31.6 ± 8.1 | 35.0 ± 7.5 | 27.7 ± 7.0 | **<0.0001** |
| Depression, mean ± S.D. | | | | |
| HAMD-17 sum score[b] | 15.3 ± 7.5 | 16.6 ± 7.9 | 13.8 ± 6.7 | **0.019** |
| Anxiety, mean ± S.D. | | | | |
| Beck Anxiety Inventory[c] | 19.1 ± 11.4 | 19.4 ± 11.4 | 18.7 ± 11.4 | 0.72 |

APSS, Attenuated positive symptoms syndrome; BS, basic symptom criteria; PANSS, Positive and Negative Syndrome Scale; HAMD, Hamilton Depression Scale.

Bolded $p$ values <0.05.

## Supplementary material

For supplementary material accompanying this paper visit http://dx.doi.org/10.1017/S0033291715002627.


## Acknowledgements

This work was supported by the Zürich Impulse Program for the Sustainable Development of Mental Health Services (http://www.zinep.ch). Beyond funding, this foundation had no further role in the experimental design; collection, analysis, and interpretation of data; the writing of this report; or the decision to submit this paper for publication.


## Declaration of Interest

Dr Correll has been a consultant and/or advisor to or has received honoraria from: Actavia, AbbVie, Alkermes, Bristol-Myers Squibb, Eli Lilly, Genentech, Gerson Lehrman Group, IntraCellular Therapies, Janssen/J&J, Lundbeck, MedAvante, Medscape, Otsuka, Pfizer, ProPhase, Reviva, Roche, Sunovion, Supernus, and Takeda. He has received grant support from BMS, Otsuka, and Takeda. Dr Walitza has received lecture honoraria from AstraZeneca, Eli Lilly, and Janssen Cilag in the last five years. Dr Rössler has served as a consultant or received honoraria from Eli Lilly Suisse, Janssen-Cilag, Interpharma, FOMF, Med-Update, SVA Sozialversicherungsanstalt Schweiz, I3G, and IVP Networks during the last 5 years.

Drs Gerstenberg, Theodoridou, Franscini, Wotruba, Metzler, Müller, Dvorsky, Heekeren and Ms. Traber-Walker have no conflicts of interest to report.

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