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ORIGINAL ARTICLE

Baseline demographics, clinical features and predictors of conversion among 200 individuals in a longitudinal prospective psychosis-risk cohort

G. Brucato[1]*†, M. D. Masucci[1]†, L. Y. Arndt[1], S. Ben-David[1], T. Colibazzi[1], C. M. Corcoran[1], A. H. Crumbley[2], F. M. Crump[1], K. E. Gill[3], D. Kimhy[1], A. Lister[1], S. A. Schobel[4], L. H. Yang[5], J. A. Lieberman[1] and R. R. Girgis[1]

[1] *The Center of Prevention and Evaluation, New York State Psychiatric Institute, Columbia University Medical Center, New York, NY, USA*
[2] *City University of New York, New York, NY, USA*
[3] *Department of Psychology, The Catholic University of America, Washington, DC, USA*
[4] *F. Hoffman-LaRoche A.G., Basel, Switzerland*
[5] *Department of Social and Behavioral Sciences, College of Global Public Health, New York University, New York, NY, USA*

Background. DSM-5 proposes an Attenuated Psychosis Syndrome (APS) for further investigation, based upon the Attenuated Positive Symptom Syndrome (APSS) in the Structured Interview for Psychosis-Risk Syndromes (SIPS). SIPS Unusual Thought Content, Disorganized Communication and Total Disorganization scores predicted progression to psychosis in a 2015 NAPLS-2 Consortium report. We sought to independently replicate this in a large single-site high-risk cohort, and identify baseline demographic and clinical predictors beyond current APS/APSS criteria.

Method. We prospectively studied 200 participants meeting criteria for both the SIPS APSS and DSM-5 APS. SIPS scores, demographics, family history of psychosis, DSM Axis-I diagnoses, schizotypy, and social and role functioning were assessed at baseline, with follow-up every 3 months for 2 years.

Results. The conversion rate was 30% ($n = 60$), or 37.7% excluding participants who were followed under 2 years. This rate was stable across time. Conversion time averaged 7.97 months for 60% who developed schizophrenia and 15.68 for other psychoses. Mean conversion age was 20.3 for males and 23.5 for females. Attenuated odd ideas and thought disorder appear to be the positive symptoms which best predict psychosis in a logistic regression. Total negative symptom score, Asian/Pacific Islander and Black/African-American race were also predictive. As no Axis-I diagnosis or schizotypy predicted conversion, the APS is supported as a distinct syndrome. In addition, cannabis use disorder did not increase risk of conversion to psychosis.

Conclusions. NAPLS SIPS findings were replicated while controlling for clinical and demographic factors, strongly supporting the validity of the SIPS APSS and DSM-5 APS diagnosis.

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Key words: Attenuated psychosis, clinical high-risk for psychosis, first episode of psychosis, prodromal psychosis, schizotypy.

Introduction

Schizophrenia (SZ) and related psychoses are among the most severe and disabling of psychiatric disorders. Given the often progressive nature of these conditions, and evidence supporting the benefits of early detection and intervention in improving prognosis, research has focused on developing means of identifying individuals in the clinical high-risk (CHR) phase, characterized by attenuated positive symptoms, which typically antedates full-blown psychotic illness (Correll *et al.* 2010; Fusar-Poli *et al.* 2013). In North America, identification and progression of CHR individuals have chiefly been assessed using the Structured Interview for Psychosis-Risk Syndromes (SIPS, McGlashan *et al.* 2001; Miller *et al.* 2002; Rosen *et al.* 2002), which defines an Attenuated Positive Symptom Syndrome (APSS).

Evidence generated from this research led to the proposal of an Attenuated Psychosis Syndrome (APS) for the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, APA, 2013). The diagnosis is identical to the SIPS APSS, except that it requires that symptoms be sufficiently distressing and disabling to prompt help-seeking.

* Address for correspondence: G. Brucato, Ph.D., The Center of Prevention and Evaluation, New York State Psychiatric Institute, Columbia University Medical Center, 1051 Riverside Drive, Room 4818, New York, NY 10032, USA.
(Email: gb2428@columbia.edu)
† These authors contributed equally to this work.

Ultimately, it was not accepted as a formal diagnosis, but included in the appendix as a condition for further study, although it can be coded in the Other Specified SZ Spectrum and Psychotic Disorders category. While the syndrome's reliability and validity have been well-established, its readiness for clinical application remains uncertain (Woods *et al.* 2010; Tsuang *et al.* 2013). Specific issues include concerns that clinicians may not reliably identify APS based upon proposed criteria (Carpenter & Van Os, 2011); high false-positive rates (Haroun *et al.* 2006; Corcoran *et al.* 2010; Fusar-Poli *et al.* 2015); stigmatization (Drake & Lewis, 2010; Carpenter & Van Os, 2011; Yang *et al.* 2015); disagreement on the demarcation between attenuated and threshold psychosis (Fusar-Poli & Van Os, 2013); uncertainty about treatments (Stafford *et al.* 2013; Van der Gaag *et al.* 2013); high co-morbidity with other psychopathologies (Fusar-Poli *et al.* 2012; Guadiano & Zimmerman, 2013); and similarities with related categories, such as schizotypal personality disorder (SPD; Tsuang *et al.* 2013).

Additionally, little is known about clinical and demographic factors beyond psychosis-risk criteria which might contribute to conversion risk (Fusar-Poli *et al.* 2012). Common co-morbid mental disorders, such as anxiety and depression, have not been shown to independently predict conversion (Fusar-Poli *et al.* 2014). One study (Waford *et al.* 2015) found that older CHR participants exhibited increased suspiciousness, females reported more perceptual disturbances, and higher education level was associated with more severe unusual thought content and less severe perceptual abnormalities. However, demographic variables did not predict psychosis. Barajas *et al.* (2015) found similar conversion rates across sexes. Anglin *et al.* (2016) identified no direct relationship between ethnicity and psychosis risk, but fewer symptoms in participants with stronger ethnic group affiliation.

In an effort to identify more definitive demographic and clinical predictors, CHR researchers have combated studies' generally low sample sizes (Woods *et al.* 2009; Van der Gaag *et al.* 2013), partly attributable to the rarity of CHR individuals [estimated prevalence in the general population as low as 0.3% (Schultze-Lutter *et al.* 2014)]; estimated incidence 1/10 000 (Addington *et al.* 2007) by employing multi-site or network approaches (Addington *et al.* 2007, 2012, 2015). The six-site European Prediction of Psychosis Study (EPOS) recruited 245 participants (Ruhrmann *et al.* 2010). The eight-site North American Prodrome Longitudinal Study (NAPLS-1; Addington *et al.* 2007) followed 370 participants for 2 years. A second phase, NAPLS-2, followed 764 participants for 2 years (Addington *et al.* 2015). Only a few large single-site samples have been collected, including, but not limited to, Melbourne, Australia's Personal Assessment and Crisis Evaluation (PACE) clinic (Nelson *et al.* 2013) and the Recognition and Prevention (RAP) program in Long Island, New York (Cornblatt *et al.* 2003). Of note, reliance upon multiple sites and the need for separate raters may contribute to the heterogeneity of participant characteristics, symptoms found to predict conversion, and site-by-site conversion rates. Thus, sufficiently powered single-site studies can meaningfully contribute to our knowledge regarding attenuated psychosis.

Declining conversion rates have also impeded progress (Yung *et al.* 2007; Simon *et al.* 2014). Hartmann *et al.* (2016) observed that, in the initial years of CHR research, 40% of individuals converted within 12–30 months (Miller *et al.* 2002; Yung *et al.* 2003; Mason *et al.* 2004; Cannon *et al.* 2008), but the global rate has gradually decreased to 15% within 12 months (Yung *et al.* 2006, 2007; Simon & Umbricht, 2010; Ziermans *et al.* 2011; Nelson *et al.* 2013; Simon *et al.* 2014), supported by an independent meta-analysis (Fusar-Poli *et al.* 2012). The authors hypothesized that more recent studies ascertain individuals with less severe symptoms, satisfying enrollment criteria, but rarely progressing. Consistent with this finding, NAPLS-1 (Addington *et al.* 2012) reported 35% conversions after 2 years, while NAPLS-2 (Addington *et al.* 2015) noted 15.2%, or 25.3% of 367 participants who either converted or completed 2-year follow-up.

Additionally, Addington *et al.* (2015) noted that little is known about the individual frequencies and relationships to conversion of the 19 symptoms assessed by the Scale of Prodromal Symptoms (SOPS) within the SIPS (Miller *et al.* 2003). They found that baseline ratings of Unusual Thought Content, Disorganized Communication and overall Disorganization symptom scores distinguished converters and non-converters. This critical finding, while thus far never fully independently replicated, is partially supported by DeVylder *et al.* (2014), who performed a trajectory analysis on a subset of the present cohort. Elevated SIPS/SOPS Disorganized Communication scores over time predicted conversion, but less so than baseline Disorganized Communication scores. Positive symptoms were the most common in NAPLS-2 (Addington *et al.* 2015), followed by Negative, Disorganization, and General symptoms. Previously, Velthorst *et al.* (2009) found that 18 converters showed more Social Anhedonia and Bizarre Thinking than 55 non-converters, although neither is part of the Positive symptom subset determining conversion. Piskulic *et al.* (2012) reported that 82% of 138 NAPLS-1 participants had at least one Negative symptom scored 4–6.

The Center of Prevention and Evaluation (COPE), located in the New York State Psychiatric Institute

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(NYSPI) at Columbia University Medical Center (CUMC) in New York City, has prospectively studied 200 CHR individuals, monitoring symptom progression over 2 years. All participants met criteria for the SIPS Attenuated Positive Symptom Syndrome (APSS), and additionally met DSM-5 APS criteria, as all were help-seeking. To address both the dearth of literature on specific SIPS/SOPS symptoms, and concerns surrounding the APS, we analyzed our cohort's baseline demographic and clinical characteristics to determine: (1) individual SIPS/SOPS symptoms most associated with progression to psychosis, with the *a priori* hypothesis that Unusual Thought Content and Disorganized Communication would best predict conversion, as in NAPLS-2 (Addington *et al.* 2015); (2) demographic and clinical features of predictive value beyond APSS and APS criteria; and (3) differences in time to conversion and conversion age between sexes and conversion diagnoses.

Method

Subjects

We recruited 200 help-seeking individuals from 2003 to 2015, all meeting criteria for the APSS and some additionally meeting for one of the other two syndromes defined by the SIPS (see below), as well as DSM-5 APS criteria. Recruitment sources are listed in online Supplement 1.

Following telephone screening, potential participants underwent in-person evaluations. Written informed consent was provided by those aged $\geqslant$18 years. Minors gave written assent, with written informed consent provided by a parent/legal guardian. Separate consents and assents were signed by eligible individuals electing to participate. The study was pre-approved by NYSPI's Institutional Review Board.

Exclusion criteria included being outside the age range (<13 or >30); lack of proficiency in English; a current or lifetime DSM Axis-I psychotic disorder, including affective psychoses; a DSM disorder better accounting for the clinical presentation; IQ < 70; medical conditions affecting the central nervous system; marked risk of harm to self or others; unwillingness to participate in research; geographic distance; or current substance abuse or dependence. Use of antipsychotic medication was not exclusionary, provided clear evidence that positive symptoms of an attenuated, but never fully psychotic level were present at medication onset.

Clinical assessments

The SIPS (McGlashan *et al.* 2001; Miller *et al.* 2002; Rosen *et al.* 2002) involves a semi-structured interview which probes for past and current signs and symptoms of attenuated *v.* threshold psychotic states. The measure includes the SOPS (Miller *et al.* 1999; McGlashan *et al.* 2001; Hawkins *et al.* 2004), a checklist of symptoms of SPD taken from DSM-IV (APA, 1994), a questionnaire collecting family history of mental illness (Andreasen *et al.* 1977), and a modified version of the DSM-IV Global Assessment of Functioning scale (GAF; Hall, 1995). Participants were included in the study if they met the criteria for any of the SIPS-defined psychosis-risk syndromes (APSS, Genetic Risk and Deterioration (GRD), or Brief Intermittent Psychotic Syndrome (BIPS), detailed in online Supplement 1) without meeting the criteria for a full-blown psychotic illness.

Participants were seen for follow-up with the SIPS every 3 months for 2 years, or else whenever conversion was suspected. Post-conversion diagnoses were established by COPE psychologists and/or psychiatrists. SIPS administrators were certified and established scoring consensus.

At baseline, participants also completed either the Diagnostic Interview for Genetic Studies (DIGS, Nurnberger *et al.* 1994) or Structured Clinical Interview for DSM-IV Axis-I Disorders, Patient Edition (SCID-I/P, First *et al.* 2002). Those aged <16 completed the Kiddie Schedule for Affective Disorders and Schizophrenia, Present and Lifetime Version (K-SADS-PL, Kaufman *et al.* 1996).

Social (conflict and quality of interpersonal relationships) and role (performance in age-appropriate roles) functioning were also assessed at baseline and follow-up using the Global Functioning Scale: Social (GF: Social) and Global Functioning Scale: Role (GF: Role, Cornblatt *et al.* 2007).

Statistical analyses

Descriptive statistics, and mean differences in baseline demographic (age, gender, race, ethnicity, and education level) and clinical features (SIPS/SOPS individual and subsection total scores and COPS category; first-degree family history of psychosis; SPD; DSM diagnosis; antipsychotic use; and GF scores) between converters and non-converters were derived using SPSS v. 22 (IBM Corporation, 2013). Group differences were evaluated using one-way ANOVAs for continuous variables (e.g. SIPS scores) and, for categorical variables (e.g. diagnosis), Pearson χ^2 tests, or Fisher's exact test where warranted by low cell counts. Variables of interest identified through a comprehensive review of the literature were used to predict conversion in a binomial logistic regression, evaluating the impact of baseline clinical and demographic variables on conversion likelihood. Analyses revealed no group effects of missing data (see online Supplement 1).

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Results

Basic baseline demographics

Demographic data (see Table 1) indicate a racially diverse, predominantly male sample. Five (2.5%) participants were transgender. Of note, no sex differences in age were observed ($t_{198} = -1.861$, $p = 0.064$). Mean follow-up time was 12.65 months (S.D. = 12.21), with a range of 1 (where participants left the program prematurely) to 74 months (where medical records or contact with participant beyond the time of the program indicated the participant's conversion status).

Baseline clinical characteristics

Evaluating individual SIPS/SOPS symptoms (see Table 2), P1 (Unusual Thought Content/Delusional Ideas) had the highest mean score (3.56, S.D. = 1.11), closely followed by P2 (Suspiciousness/Persecutory Ideas; 3.33, S.D. = 1.26). P3 (Grandiose Ideas) showed the lowest mean (2.03, S.D. = 1.58). The Positive symptoms most frequently endorsed at baseline were P1 (87%) and P2 (82%). P4 (Perceptual Abnormalities/Hallucinations) and P5 (Disorganized Communication) were endorsed in 68% and 57.5% of the sample, respectively. P3 was the least endorsed (46.5%).

All participants met SIPS APSS criteria. While 53.5% met SPD criteria and 17.2% with known family histories reported first-degree relatives with past or current psychosis, only seven (3.5%) satisfied the GRD syndrome's prerequisite GAF decline. No participant met BIPS criteria.

In terms of DSM diagnoses, 78% and 47.8% of participants met criteria for one or more than one Axis-I disorder, respectively (see online Supplement 2 for specific diagnoses). The most common lifetime diagnoses were major depressive disorder (MDD, 40.1%), obsessive-compulsive disorder (OCD, 17.0%) and social phobia (SP, 13.1%). Past substance dependence or abuse were present in 8.8% and 9.9%, respectively, with cannabis being the substance most used (17.4%). (See Table 3 and online Supplement 3 for information regarding baseline medication use, family history of psychosis and GF scores.) Participants showed generally low average scores on both the GF: Social (mean = 5.48, S.D. = 1.73) and GF: Role (mean = 5.45, S.D. = 2.3).

Conversion outcomes

Table 4 displays conversion outcome data. Sixty (30%; 50 males, 10 females) participants progressed to psychosis. Excluding 41 non-converters who had not yet completed 2-year follow-ups, the rate becomes 60/159 (37.7%).

Average conversion time was 11.05 months (S.D. = 11.76, median = 5.5), with no difference between sexes. The majority (36, 60%) developed SZ or schizoaffective disorder (SAD). Notably, conversion time to SZ (mean = 7.97 months, S.D. = 9.89) was significantly briefer than to other psychoses (mean = 15.68 months, S.D. = 12.98; $F_{1,58} = 6.800$, $p = 0.012$). Mean conversion age was 20.83 years (S.D. = 3.97). The averages were 20.30 years (S.D. = 3.53) and 23.5 years (S.D. = 5.12) for males and females, respectively. While this difference was statistically significant ($t_{58} = -2.414$, $p = 0.019$), the distributions failed Levene's test ($F = 6.390$, $p = 0.014$), likely due to few female converters.

Demographic differences between converters and non-converters

There was no relationship between baseline age and conversion ($F_{1,197} = 0.003$, $p = 0.960$). Significantly more males (50/146, 34.2%) than females (10/54, 18.5%) converted to psychosis ($\chi^2_{1,200} = 4.644$, $p < 0.05$). Race was also significant ($\chi^2_{3,200} = 14.438$, $p = 0.004$) with fewer Caucasians (18/96, 18.75%) and more Asians/Pacific Islanders (9/15, 60.0%) converting than might be expected by chance. Group differences for other demographic factors were insignificant (see Table 1).

Clinical differences between converters and non-converters

Ten SIPS/SOPS indices distinguished converters from non-converters (see Table 2). Of the positive symptoms, group differences were found in P1 ($F_{1,198} = 13.235$, $p < 0.001$), P5 ($F_{1,198} = 7.835$, $p < 0.01$) and the sum of Positive symptoms ($F_{1,198} = 5.887$, $p < 0.05$), driven by P1 and P5.

N1 (Social Anhedonia: $F_{1,191} = 7.450$, $p < 0.01$) and N5 (Ideational Richness: $F_{1,191} = 6.008$, $p < 0.05$) were significantly related to conversion, along with the sum of Negative symptoms ($F_{1,191} = 7.700$, $p < 0.01$). In addition, group differences were also found in D1 (Odd Behavior or Appearance: $F_{1,191} = 6.291$, $p < 0.05$) and D3 (Trouble with Focus and Attention: $F_{1,191} = 6.647$, $p < 0.05$), the sum of Disorganization symptoms ($F_{1,191} = 4.653$, $p < 0.05$) and of General symptoms, G3 (Motor Disturbances; $F_{1,190} = 7.600$, $p < 0.01$).

Additionally, baseline GF: Social score significantly distinguished converters from non-converters ($F_{1,123} = 5.495$, $p < 0.05$). Group differences were insignificant for all other clinical variables.

Examining predictors of conversion

To examine which baseline demographic and clinical characteristics might facilitate or protect against conversion, conversion status was regressed on these characteristics using binomial logistic regression. Variables were

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Table 1. *Baseline demographic characteristics of COPE sample*

Variable	Total CHR participants ($n = 200$)	Converters ($n = 60$)	Non-converters ($n = 140$)	Test statistic
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	F
Age (years)	20.03 (3.85)	20.01 (3.74)	20.04 (3.92)	0.003
	Count (%)	Count (%)	Count (%)	χ^2
Sex				**4.644***
Male	146 (73.0%)	50 (83.3%)	96 (68.6%)	
Female	54 (27.0%)	10 (16.7%)	44 (31.4%)	
Race				**14.438****
Caucasian	96 (48.0%)	18 (30%)	78 (55.7%)	
Black/African American	44 (22.0%)	17 (28.3%)	27 (19.3%)	
Asian/Pacific Islander	15 (7.5%)	9 (15.0%)	6 (4.3%)	
More than one race	45 (22.5%)	16 (26.7%)	29 (20.7%)	
Ethnicity				0.325
Not Hispanic	139 (69.5%)	40 (66.7%)	99 (70.7%)	
Hispanic	61 (30.5%)	20 (33.3%)	41 (29.3%)	
Education level[a]				0.033
<High school	50 (25.4%)	15 (25.0%)	35 (25.5%)	
High school	40 (20.3%)	13 (21.7%)	27 (19.7%)	
Technical school	1 (0.5%)	0 (0.0%)	1 (0.7%)	
Some college	78 (39.6%)	23 (38.3%)	55 (40.1%)	
BA or BS	24 (12.2%)	7 (11.7%)	17 (12.4%)	
Graduate school	4 (2.0%)	2 (3.3%)	2 (1.5%)	

COPE, Center of Prevention and Evaluation; CHR, clinical high risk.

[a] $n = 197$.

*$p < 0.05$, **$p < 0.01$, comparisons between converters and non-converters.

included in the model with the aims of identifying positive symptoms more likely to predict psychosis; confirming and expanding upon NAPLS-2 findings (Addington *et al.* 2015); including baseline differences in demographic variables and SIPS/SOPS scores other than positive symptoms and; minimizing covariation of predictors; and maximizing analytic sample size. Specifically, we included race ['White' (reference group), 'Black/African-American', 'Asian/Pacific Islander,' 'more than one race']; sex ('male', 'female'); and ethnicity ('not Hispanic', 'Hispanic'); age; all SIPS/SOPS Positive symptoms; and totals of Negative, Disorganization and General symptoms. The latter subscale totals were used to limit the number of predictors, reducing the possibility of overfitting to the data. Although ANOVAs demonstrated lower baseline GF: Social scores among converters, GF scores were excluded from the regression to avoid sample size limitations.

Table 5 displays regression results and model fit information. The model accounts for significantly more variance than a constant-only model ($\chi^2 = 44.505$, $p < 0.001$, df = 14). P1, P5 and total Negative symptoms significantly predicted conversion. Accounting for the variance produced by all other variables, CHR individuals are 2.32 (S.E. = 0.244, $p = 0.001$), 1.482 (S.E. = 0.167, $p = 0.019$) and 1.075 (S.E. = 0.036, $p = 0.041$) times as likely to convert for every one-point increase in baseline P1, P5, and total Negative symptom score, respectively. Additionally, race significantly predicted conversion, where 'Black/African-American' and 'Asian/Pacific Islander' participants were, respectively, 2.638 (S.E. = 0.470, $p = 0.039$) and 4.590 (S.E. = 0.679, $p = 0.025$) times as likely to convert as 'Caucasian' participants.

Adding baseline diagnosis (collapsed into any lifetime anxiety disorder, depressive disorder, bipolar disorder, past substance/alcohol use disorder, eating disorder, and any other disorder); SPD; family history of psychosis; and medication status ['none' (reference group), 'neuroleptics', 'antidepressants', 'both'] to the model did not affect the significance of these SIPS factors, or yield additional significant predictors. However, 'Black/African-American' race was no longer significant ($p = 0.081$), while the significance of 'Asian/Pacific Islander' race remained [odds ratio (OR) 5.739, S.E. = 0.732, $p = 0.017$]. Notably, this model reduced the analytic sample from 193 (with 60 converters) to 168 (54 converters).

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Table 2. *SIPS scores for COPE sample (n = 200)*

Variable	COPE CHR participants (*n* = 200)	NAPLS sample[a] (*n* = 764)	COPE converters (*n* = 60)	COPE Non-converters (*n* = 140)	Test statistic
SIPS scores					
Positive symptoms	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	*F*
P1 Unusual Thought Content/ Delusional Ideas	3.56 (1.11)	3.34 (1.33)	3.98 (1.04)	3.37 (1.10)	**13.325*****
P2 Suspiciousness/Persecutory Ideas	3.33 (1.26)	2.76 (1.51)	3.43 (1.29)	3.29 (1.24)	0.575
P3 Grandiose Ideas	2.03 (1.58)	1.00 (1.30)	2.12 (1.65)	2.00 (1.55)	0.226
P4 Perceptual Abnormalities/ Hallucinations	2.75 (1.46)	3.07 (1.50)	2.83 (1.55)	2.71 (1.42)	0.311
P5 Disorganized Communication	2.72 (1.33)	1.75 (1.47)	3.12 (1.31)	2.55 (1.31)	**7.835****
Total P score	14.36 (4.12)	–	15.43 (3.93)	13.91 (4.13)	**5.887***
Negative symptoms[b]					
N1 Social Anhedonia	3.5 (1.55)	2.36 (1.74)	3.95 (1.52)	3.30 (1.53)	**7.450****
N2 Avolition	3.25 (1.64)	2.54 (1.62)	3.47 (1.65)	3.16 (1.63)	1.463
N3 Expression of Emotion	2.08 (1.74)	1.36 (1.52)	2.43 (1.84)	1.92 (1.67)	3.684
N4 Experience of Emotions and Self	2.36 (1.81)	1.75 (1.68)	2.53 (1.72)	2.28 (1.85)	0.819
N5 Ideational Richness	1.84 (1.43)	1.16 (1.31)	2.22 (1.60)	1.68 (1.32)	**6.008***
N6 Occupational Functioning	3.68 (1.68)	2.84 (2.01)	4.03 (1.60)	3.53 (1.70)	3.794
Total N score	16.7 (6.61)	–	18.63 (7.02)	15.83 (6.25)	**7.700****
Disorganized symptoms[b]					
D1 Odd Behavior or Appearance	2.52 (1.37)	0.84 (1.20)	2.88 (1.40)	2.35 (1.33)	**6.291***
D2 Bizarre Thinking	2.46 (1.48)	0.91 (1.20)	2.58 (1.61)	2.41 (1.43)	0.585
D3 Trouble with Focus and Attention	3.09 (1.20)	2.64 (1.28)	3.42 (1.25)	2.94 (1.16)	**6.647***
D4 Impairment in Personal Hygiene	1.59 (1.66)	0.76 (1.21)	1.67 (1.64)	1.55 (1.67)	0.207
Total D score	9.66 (3.87)	–	10.55 (4.11)	9.26 (3.70)	**4.653***
General symptoms					
G1[c] Sleep Disturbance	2.58 (1.71)	2.32 (1.56)	2.68 (1.80)	2.54 (1.68)	0.257
G2[c] Dysphoric Mood	3.1 (1.51)	3.34 (1.61)	2.81 (1.57)	3.23 (1.47)	3.064
G3[c] Motor Disturbances	1.91 (1.57)	0.83 (1.06)	2.37 (1.73)	1.71 (1.45)	**7.600****
G4[c] Impaired Tolerance to Normal Stress	3.77 (1.86)	2.70 (1.88)	3.78 (1.90)	3.77 (1.85)	0.002
Total G score[b]	11.36 (4.24)	–	11.62 (3.94)	11.24 (4.37)	0.324
Family history of psychosis[c]	Count (%)		Count (%)	Count (%)	χ^2
Psychosis	33 (17.2%)	–	9 (15.3%)	24 (18.0%)	0.224
Unspecified Positive Symptoms	6 (3.1%)	–	2 (3.4%)	4 (3.0%)	0.018

SIPS, Structured Interview for Psychosis-Risk Syndromes; COPE, Center of Prevention and Evaluation; CHR, clinical high risk; NAPLS, North American Prodrome Longitudinal Study.

[a] Data from total sample of Addington *et al.* (2015).

[b] $n = 193$.

[c] $n = 192$.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, comparisons between converters and non-converters.

Additional sensitivity checks were run in which the potentially important factors of medication status, education level, SPD diagnosis, and past substance abuse were added individually and separately to the model. When either education level, past substance abuse or SPD was added, all beta weights remained within ±0.2 of their original values, and there were no changes to significant findings. Adding medication status alone to the model pushed 'Black/African-American' race slightly above the significance threshold ($p = 0.054$), but all beta weights remained within ±0.2 of their original values and P1, P5, Total N, and 'Asian/Pacific Islander' race remained significant.

Another concern may be that baseline total SIPS score as a measure of severity of global psychopathology, may predict psychosis over and above the Positive subscale or any individual symptom. Total SIPS score was significantly higher among converters (mean = 56.23, S.D. = 12.89) than non-converters (mean = 50.17, S.D. = 13.67; $t_{191} = 2.9$, $p = 0.004$). However, an additional regression containing only demographic characteristics, P1, and Total SIPS score excluding P1

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Table 3. *Additional baseline clinical characteristics: medication status, family history of psychosis, and GF scores for COPE Sample (n = 200)*

Variable	CHR participants (*n* = 200)	Converters (*n* = 60)	Non-converters (*n* = 140)	Test statistic
	Count (%)	Count (%)	Count (%)	χ^2
Medication status				2.739
None	144 (72%)	45 (75%)	99 (70.7%)	
Antipsychotics	11 (5.5%)	5 (8.3%)	6 (4.3%)	
Antidepressants	25 (12.5%)	6 (10.0%)	19 (13.6%)	
Both	20 (10%)	4 (6.7%)	16 (11.4%)	
Family history of psychosis[a]				
Psychosis	33 (17.2%)	9 (15.3%)	24 (18.0%)	0.224
Unspecified positive symptoms	6 (3.1%)	2 (3.4%)	4 (3.0%)	0.018
	CHR participants (*n* = 125)	Converters (*n* = 36)	Non-converters (*n* = 89)	Test statistic
GF scores	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	*F*
GF: Social	5.48 (1.73)	4.91 (1.79)	5.70 (1.67)	**5.495***
GF: Role	5.45 (2.30)[b]	5.02 (2.41)	5.63 (2.23)[c]	1.800

GF, Global Functioning; COPE, Center of Prevention and Evaluation; CHR, clinical high-risk.
[a] *n* = 192.
[b] *n* = 124.
[c] *n* = 88.
*$p < 0.05$, comparisons between converters and non-converters.

Table 4. *Conversion outcomes for COPE sample (n = 60)*

Variable	Total	Male (*n* = 50)	Female (*n* = 10)	Test statistic
	Mean (S.D.)	Mean (S.D.)	Mean (S.D.)	*F*
Age at conversion (years)	20.83 (3.98)	20.30 (3.53)	23.5 (5.13)	5.83
Time to conversion (months)	11.05 (11.76)	10.12 (11.46)	15.7 (12.73)	1.906
	Count (%)	Count (%)	Count (%)	χ^2
Conversion diagnosis				
Schizophrenia	34 (56.7%)	32 (64.0%)	2 (20.0%)	**6.57***
Undifferentiated	29 (48.3%)	27 (54.0%)	2 (20.0%)	
Disorganized	4 (6.7%)	4 (8.0%)	0 (0.0%)	
Paranoid	1 (1.7%)	1 (2.0%)	0 (0.0%)	
Schizoaffective	2 (3.3%)	1 (2.0%)	1 (10.0%)	1.655
Depressive type	1 (1.7%)	0 (0%)	1 (10.0%)	
Bipolar type	1 (1.7%)	1 (2.0%)	0 (0%)	
MDD with psychotic features	7 (11.7%)	5 (10.0%)	2 (20.0%)	0.809
Bipolar with psychotic features	4 (6.7%)	2 (4.0%)	2 (20.0%)	3.429
Delusional disorder – persecutory type	2 (3.3%)	0 (0%)	2 (20.0%)	**10.345***
Psychosis not otherwise specified	11 (18.3%)	10 (20.0%)	1 (10.0%)	0.557

COPE, Center of Prevention and Evaluation; MDD, Major depressive disorder.
*Two-sided Fisher's $p < 0.05$, comparisons between male and female converters.

found that baseline P1 (OR 1.832, S.E. = 0.210, $p = 0.004$) predicted conversion over and above Total SIPS (OR 1.021, S.E. = 0.210, $p = 0.142$). Furthermore, a regression containing demographic characteristics and total P, N, D, and G scores revealed total P score as significant (OR 1.121, S.E. = 0.051, $p = 0.025$), with only total N approaching significance (OR 1.061, S.E. = 0.049, $p = 0.068$). Importantly, total P yielded an odds ratio far below P1 separately, demonstrating specifically the utility of P1 in predicting conversion to psychosis.

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Table 5. *Results of binary logistic regression predicting conversion for COPE sample (n = 193)*

Variable		*B*	OR (S.E.)	95% CI	*p*
Sex		−0.781	0.458 (0.454)	0.188–1.115	0.085
Age		0.021	1.021 (0.049)	0.928–1.123	0.674
Hispanic ethnicity		0.041	1.041 (0.443)	0.437–2.483	0.927
Race					
Caucasian (Reference)		–	–	–	0.037
Black/African American*		0.970	2.638 (0.47)	1.05–6.627	0.039
Asian/Pacific Islander*		1.524	4.590 (0.679)	1.213–17.37	0.025
Multiple Races		0.987	2.682 (0.518)	0.972–7.40	0.057
SIPS scores					
P1**		0.842	2.320 (0.244)	1.437–3.746	0.001
P2		−0.018	0.983 (0.151)	0.731–1.321	0.907
P3		−0.082	0.921 (0.128)	0.717–1.185	0.523
P4		−0.095	0.909 (0.136)	0.696–1.187	0.484
P5*		0.393	1.482 (0.167)	1.068–2.056	0.019
Total N score*		0.073	1.075 (0.036)	1.003–1.153	0.041
Total D score		−0.037	0.964 (0.065)	0.849–1.095	0.571
Total G score		−0.064	0.938 (0.051)	0.849–1.036	0.204
Constant		−4.771	0.008 (1.564)	–	0.002
Model summary		−2 log likelihood		Cox & Snell R^2	Nagelkerke R^2
		194.839		0.206	0.289
		χ^2		df	*p*
Hosmer and Lemeshow test		9.812		8	0.278
Classification table		Constant-only model			Predictive model
		No	Yes	%	No	Yes	%
Converted	No	133	0	100%	120	13	90.2%
	Yes	60	0	0%	35	25	41.7%
Overall percentage				68.9%			75.1%
	Area	S.E.		*p*		95% CI	
AUROC	0.787	0.036		<0.001		0.716–0.857	

COPE, Center of Prevention and Evaluation; OR, Odds ratio; CI, confidence interval; SIPS, Structured Interview for Psychosis-Risk Syndromes; AUROC, Area Under ROC Curve.

Discussion

This large single-site longitudinal prospective psychosis-risk study examined the baseline demographic and clinical characteristics of 200 CHR individuals, to determine how these related to conversion to psychosis over 2 years of follow-up. We replicated findings from NAPLS-2 (2015) that the SIPS/SOPS Unusual Thought Content and Disorganized Communication subscales, measures of attenuated odd delusions and thought disorder, best predicted psychosis (Addington *et al.* 2015). We additionally found total Negative symptoms, and both African-American and Asian/Pacific Islander race to be predictive, although only the latter racial group survived multiple regression models. Converters and non-converters were further distinguished by five SIPS/SOPS subscales beyond Positive symptoms, male sex and GF: Social scores. As no Axis-I diagnosis or schizotypy predicted conversion, the APS diagnosis proposed in DSM-5 (APA, 2013) is supported as a distinct syndrome.

Our cohort's mean age (20.03, S.D. = 3.85) was slightly higher than that in NAPLS-2 (18.45, S.D. = 4.23; Addington *et al.* 2015). However, our age range was 13–30, while NAPLS-2 recruited participants aged 12–35. Regardless, both groups' data are in accord with the APS onset in mid- to late adolescence which the DSM-5 describes (APA, 2013). The DSM also notes a 'slight preponderance' of male APS cases. Our cohort was disproportionately male (73%), while the NAPLS-2 cohort was more evenly distributed (57.1%). Our 2.5% transgender rate is comparable to the 3% estimated rate in the general American

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population (Gates, 2011). Caucasian participants constituted the largest racial group in our cohort (48%) and NAPLS-2 (62.6%). NAPLS-2 participants reported, on average, 11.28 years of education (S.D. = 2.82). We categorically rated this variable, finding that 45.7% of participants completed high school or less and 53.3% completed some or all of college. Our cohort's somewhat higher education level may reflect that 13% of participants were recruited at college and university counseling centers.

Of note, nearly twice the number of males (34.2%) as females (18.5%) converted, although sex did not significantly predict conversion. Literature regarding sex differences in conversion rates among CHR individuals has been equivocal. Lemos-Giráldez *et al.* (2009) found 22.5% and 23.8% conversion rates for at-risk males and females, respectively, over 3 years. Ziermans *et al.* (2011) showed that more males than females developed psychosis across 2 years. In the NAPLS-2, there were no differences in transition rates (24.5% males, 26.5% females; Walder *et al.* 2013). Our finding appears more consistent with the literature on sex differences in the distribution of SZ and other psychoses (Ochoa *et al.* 2012), whereby males are more affected. It also supports a continuum from attenuated to threshold psychotic illness, whereby the same gender-related factors observed in full-blown illness might be expected in the prodromal phase (Van Os *et al.* 2009).

We find little support for our finding that 60% of Asian/Pacific Islander participants converted. In fact, a study (Cohen & Marino, 2013) of 16 423 members of the general population showed higher lifetime rates of psychotic symptoms for African-Americans (15.3%) and Latinos (13.6%) than Caucasians (9.7%) and Asians (9.6%). The literature suggests Asian-Americans tend to underutilize mental health services (Abe-Kim *et al.* 2007; Li *et al.* 2013) and harbor unfavorable attitudes toward help-seeking (Sue, 1994; Compton *et al.* 2004; Shea & Yeh, 2008; Masuda & Boone, 2011) so that they may seek treatment only after attenuated symptoms have progressed toward psychosis. However, one-way ANOVAs revealed no differences in conversion time ($F_{1,58} = 0.122$, $p = 0.728$) or total baseline Positive symptoms ($F_{1,198} = 0.051$, $p = 0.822$) between Asian/Pacific Islanders and other racial groups in our cohort.

Our current conversion rate of 30%, or 37.7% excluding participants enrolled under two years, is comparable to the higher rates Hartmann *et al.* (2016) associated with earlier CHR studies, and has remained stable from 2003 to 2015. To determine if our high conversion rate was a function of more converters in the first half of the sample, we divided the sample into two epochs, separately analyzing the 56 participants ascertained from 2003 to 2008 and 86 from 2009 to 2013, and excluding 58 who did not reach the 2-year point. Seventeen out of 56 (30.36%) in the earlier group converted at an average of 17.78 months (S.D. = 15.46) and 26/86 (30.236%) in the later group converted at an average of 11.04 months (S.D. = 10.16). While our conversion rate is stable over time, the reduction in mean time to conversion between epochs does suggest some differences between individuals enrolled more recently compared to those enrolled a less recently.

Consistent with the APS features defined in DSM-5 (APA, 2013), most conversions (60%) in our cohort were to SZ, with 11 (18.33%) to psychotic affective disorders. The description also reflects collective knowledge from multiple investigations that genetic risk, poorer social functioning and Positive symptoms consistently predict conversion, with algorithms combining these factors yielding positive predictive power above 80% (Gee & Cannon, 2011). In contrast, we find no support for family history of psychosis as a risk factor ($\chi^2_{1,192} = 0.224$, $p = 0.636$). In terms of functioning, means for both the GF: Social (mean = 5.48, S.D. = 1.73) and GF: Role (mean = 5.45, S.D. = 2.3) were generally low in our cohort, suggesting impairments across multiple domains, although only GF: Social was related to psychosis ($F_{1,123} = 5.495$, $p < 0.05$), consistent with Cornblatt *et al.* (2012).

Our finding that neither baseline DSM Axis-I diagnosis nor SPD predicted conversion helps address concerns about the APS' high co-morbidity with other disorders (Fusar-Poli *et al.* 2012; Guadiano & Zimmerman, 2013) and its similarities with related conditions. Interestingly, 19/60 converters (31.67%) met criteria for MDD at baseline, but a majority of these (10/19; 52.63%) developed SZ, as opposed to psychotic MDD or bipolar disorder. Among the eight converters (13.33%) initially meeting OCD criteria, virtually all (7/8, 87.5%) developed SZ. In each case, the central obsession was implausible in nature and accompanied by the insight which characterizes both OCD and APS, highlighting the challenging differential between these diagnoses.

In examining the SIPS, we adopted NAPLS-2's approach of separately analyzing the SOPS symptoms, in terms of frequency and association with conversion (Addington *et al.* 2015). We independently replicated their key findings that P1 is the Positive symptom most associated with conversion, closely followed by P5. In both cohorts, P3 was less common, and P2 and P4 were frequently endorsed, but did not predict psychosis. In NAPLS-2, P5 was an uncommon symptom, whereas we found it in 57.5% of participants. Unlike NAPLS-2, we found that total Positive symptoms, N1, N5, total Negative symptoms, D1, D3, and G3 also distinguished converters from non-converters.

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In both cohorts, Positive symptoms were the most common, followed by Negative, Disorganization, and General. All COPE participants endorsed one positive symptom or more, similar to the 92% rate in NAPLS-2. In COPE, 91.09% had at least one Negative symptom and 71% had $\geqslant 3$; in NAPLS-2, the rates were 82% and 44%, respectively. In both groups, N2 and N6 were the most common. G2 was endorsed by 66.67% of our sample, while NAPLS-2 reported 68%.

The uniformity of SIPS/SOPS findings across NAPLS-2 and our cohort is quite striking. They suggest that attenuated odd delusions (P1) and thought disorder (P5) may predict psychosis, while attenuated suspiciousness (P2) and perceptual abnormalities (P4) may be commonly endorsed by CHR individuals, irrespective of conversion. Notably, while an ANOVA replicated the NAPLS-2 total Disorganization score result, this did not survive a binomial logistic regression. Also of note, even after accounting for baseline clinical and demographic characteristics, we found that total Negative symptoms predicts conversion, although it is solely Positive symptoms which presently define transition to psychosis in the SIPS.

While these results provide an important replication of the predictive capacity of specific symptom criteria, demographic and symptom-based measures remain inadequate to meet the requirements for diagnostic and treatment applications in standard clinical practice. Some recent studies (Cannon *et al.* 2016; Carrion *et al.* 2016) have proposed combining current CHR criteria with specific demographic factors, as well as various neurocognitive, psychosocial and/or biometric assessments, to develop algorithms with improved predictive power. Importantly, they observed that positive symptoms, primarily a combination of P1 and P2 from the SIPS, drove the predictive power of the calculator, as opposed to any other measure, similar to the findings from the current study. Those proposed thus far are clinically limited, in that they require data from psychological instruments not routinely available or employed in clinical practice. The factors beyond CHR criteria we have identified, which are readily elicited from patients by way of simple inquiry, might well be incorporated into future algorithms, if replicated by other research.

An additional limitation of our study is that 41 (20.5%) participants have not yet completed the 2-year follow-up. As all were help-seeking, and the sample was predominantly male, our findings may not be generalizable to the wider population. Furthermore, we were not able to analyze our entire sample's functional status in relation to conversion potential, as the GF scales were not published until the fourth year of the COPE study. Finally, there remains an ongoing debate about the benefits of identifying CHR as a 'unitary class' and transition to psychosis as a 'binary' variable. While the data presented herein, taken together with consistent data from numerous other sites, support the CHR diagnosis and treating transition to psychosis as a binary variable, further study is needed to determine the ideal nosological structure for individuals at risk for psychosis.

Supplementary material

The supplementary material for this article can be found at https://doi.org/10.1017/S0033291717000319.

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