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North American Prodrome Longitudinal Study (NAPLS 2): The Prodromal Symptoms

Jean Addington, PhD[1,*], **Lu Liu, MSc**[1], **Lisa Buchy, PhD**[1], **Kristin S. Cadenhead, MD**[2], **Tyrone D. Cannon, PhD**[3], **Barbara A. Cornblatt, PhD**[4], **Diana O. Perkins, MD**[5], **Larry J. Seidman, PhD**[6], **Ming T. Tsuang, MD**[2], **Elaine F. Walker, PhD**[7], **Scott W. Woods, MD**[8], **Carrie E. Bearden, PhD**[9], **Daniel H. Mathalon, MD**[10], and **Thomas H. McGlashan, PhD**[8]

[1]Department of Psychiatry, University of Calgary, Calgary, Alberta, Canada

[2]Department of Psychiatry, UCSD, La Jolla CA

[3]Department of Psychology, Yale University, New Haven CT

[4]Department of Psychiatry, Zucker Hillside Hospital, Long Island NY

[5]Department of Psychiatry, University of North Carolina, Chapel Hill NC

[6]Department of Psychiatry, Harvard Medical School at Beth Israel Deaconess Medical Center and Massachusetts General Hospital, Boston MA

[7]Departments of Psychology and Psychiatry, Emory University, Atlanta GA

[8]Department of Psychiatry, Yale University, New Haven CT

[9]Departments of Psychiatry and Biobehavioral Sciences and Psychology, UCLA, Los Angeles CA

[10]Department of Psychiatry, UCSF, and SFVA Medical Center, San Francisco CA

Abstract

In studies describing the long-term follow-up up of youth at clinical high risk (CHR) of psychosis, little attention has been given to details of specific prodromal symptoms. In this paper we describe the prodromal symptoms of 764 CHR participants recruited in the multi-site North American Prodrome Longitudinal Study (NAPLS). Symptoms were rated on the Scale of Prodromal Symptoms (SOPS) at baseline and 6, 12, 18 and 24 month follow-ups. Clinical outcome at the 2-year assessment was categorized as psychotic, prodromal progression, symptomatic or in remission. The majority of the CHR sample (93%) met criteria for the attenuated positive symptoms syndrome (APSS). Significant improvements in SOPS symptoms were observed overtime. Unusual thought content, disorganized communication and overall ratings on disorganized symptoms differentiated those who transitioned to psychosis from the other clinical outcome groups. Suspiciousness and total positive symptoms differentiated those in remission from the other clinical outcome groups.

[*] Corresponding Author: Dr Jean Addington, Mathison Centre for Mental Health Research and Education, University of Calgary, 3280 Hospital Drive NW, Calgary, Alberta T2N 4Z6 Canada. jmadding@ucalgary.ca.

Keywords

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INTRODUCTION

Interest in early detection and prevention of schizophrenia and other psychotic disorders has led to more than a decade of work studying young people who may be at risk of developing a psychotic illness. Several reviews and meta analyses have been published focusing on the development of the field (Fusar-Poli et al., 2012b), clinical studies (Addington and Heinssen, 2011), treatment outcome (Stafford et al., 2013) and conversion to psychosis (Fusar-Poli et al., 2012a). Identifying predictors and mechanisms of conversion to psychosis among such individuals ascertained to be in a clinical high risk (CHR) or prodromal clinical state are critical steps in the search for preventive strategies for psychosis. Achieving these aims requires sample sizes much larger than those typically available at a single research centre within a reasonable time period. The majority of the studies described in the reviews above were single site studies with small samples. However, three notably large samples have been described in the literature, namely the Personal Assessment and Crisis Evaluation (PACE) clinic in Melbourne Australia, the European Prediction of Psychosis Study (EPOS) and the North American Prodrome Longitudinal Study (NAPLS).

The work from the PACE clinic (Nelson et al., 2013) describes the long term follow-up of 416 young people at CHR of psychosis that have been treated at the PACE clinic and/or participated in one of their studies between 1993 and 2006. EPOS is a prediction study of 245 individuals meeting criteria for being at CHR of psychosis who were recruited from six early detection outpatient centers in Germany, Finland, the Netherlands and England (Ruhrmann et al., 2010). NAPLS is a consortium of eight programs focusing on the psychosis prodrome in North America. The sites are located at Emory University, Harvard University, University of Calgary in Canada, University of California at Los Angeles, University of California at San Diego, University of North Carolina at Chapel Hill, Yale University, and Zucker Hillside Hospital. In the first phase of the NAPLS project (NAPLS 1), these sites collaborated to combine previously collected datasets and produced a series of analyses on predictors of psychosis in a sample of 291 CHR participants followed longitudinally (Addington et al., 2007). Results of these analyses indicated that risk for the onset of psychosis in this population was 35% after 2 ½ years of follow-up, with a decelerating rate of conversion over this period. The NAPLS 1 data set was used to derive a psychosis prediction algorithm with high positive predictive power (~80%), but only modest sensitivity (~40%) (Cannon et al., 2008). The published prediction algorithm included genetic risk (having a first degree relative with a psychotic disorder and functional decline), more severe unusual thought content, and greater social impairment.

This first project from the NAPLS group resulted in a six year prospective study “Predictors and Mechanisms of Conversion to Psychosis”, funded by NIMH in 2008, and described as NAPLS 2 that included all eight NAPLS sites. The sample size of NAPLS 2 is anticipated to be sufficient to address fundamental questions about the neurobiological correlates of the

development of psychosis. The project has recruited a sample of 764 CHR participants and 280 healthy controls, making it the largest study of individuals at CHR of psychosis to date. The overall methodology of NAPLS 2 and a description of the ascertainment and demographics has been described in detail elsewhere (Addington et al., 2012). Assessment areas for NAPLS 2 include psychopathology, early risk factors, social functioning, social cognition, neuropsychology, treatment monitoring, neuroimaging, electrophysiology, stress and hormones and genomics (Addington et al., 2012). Interestingly, despite the fact that individuals at CHR of psychosis are identified on the basis of clinical symptoms, i.e. the five attenuated positive symptoms from the Scale of Prodromal Symptoms (SOPS), little has been published about these prodromal symptoms, particularly individual symptoms. Thus, the focus of this paper will be on the prodromal symptoms.

Several studies have reported on the severity of attenuated psychotic symptoms. The EPOS study (Ruhrmann et al., 2010) reported that at baseline, the SOPS negative symptoms were rated with the greatest severity, followed by SOPS positive, general and disorganization symptoms, a finding supported elsewhere (Comparelli et al., 2014;Fulford et al., 2014;Lee et al., 2014;Velthorst et al., 2009). Findings from NAPLS 1 (Piskulic et al., 2012) indicated that for 138 participants at CHR of psychosis, 82% presented with moderate severity (i.e. score of 4 on the SOPS) or greater on at least one negative symptom. Moreover, after 12 months, these symptoms remained in the above moderate severity range for 54% of the sample. Another study from NAPLS 1 (Alderman et al., 2014) reported that amongst Latino CHR participants, positive symptoms were rated with the highest severity and that unusual thought content was particularly prevalent. Amongst negative symptoms, social anhedonia was the most common. Trouble with focus and attention was the most common disorganized symptom while dysphoric mood was the most common general symptom.

In terms of change over time, a Japanese study (Morita et al., 2014) reported similar severity of positive and negative symptoms at baseline in a CHR sample but that after one year, 48% of the sample showed little improvement in either positive or negative symptoms. In contrast, findings from NAPLS 1 suggest that those at CHR of psychosis who did not transition to psychosis over a 2.5 year period showed significant improvement in SOPS positive and negative symptoms between baseline and one year later (Addington et al., 2011). Lee and colleagues (Lee et al., 2014) reported that CHR participants who achieved remission of positive symptoms at two years had lower SOPS positive symptom scores at baseline, compared to CHR non-remitted individuals, and that SOPS positive symptom score was a significant predictor of longer time to remission. Examination of the severity of specific attenuated psychotic symptoms is rare. One study (Simon et al., 2009) reported that full remission of SOPS subclinical hallucinations occurred in 54% of CHR participants and either full or partial remission occurred in 68% of these individuals after one year in the study.

There are even less data on the frequency of individual SOPS symptoms as well as the timing of the onset of these attenuated psychotic symptoms in CHR individuals. A retrospective study in patients with a first-episode of psychosis reported that attenuated psychotic symptoms occurred on average 3.9 years before admission to a hospital for a psychotic episode (Schultze-Lutter et al., 2010). A recent prospective study (Woodberry et

al., 2014) reported that in a sample of 39 people at CHR for psychosis, for 23% the onset of SOPS unusual thought content, suspiciousness or perceptual abnormalities occurred in childhood, for 38.5% in adolescence, and for 38.5% in adulthood.

The aim of this paper is to (i) describe the extent of prodromal symptoms in the large NAPLS2 study, (ii) examine the change over time of these symptoms and (iii) determine the role of these early symptoms in terms of later clinical follow-up.

METHODS

Participants

NAPLS participants were help-seeking and were referred from health care providers, educators, or social service agencies, or they self-referred in response to intensive community education efforts. These initiatives included grand rounds, educational talks, mailings, postings, websites and internet hits, and public service announcements. Each of the eight sites developed extensive referral sources in their area, and routinely contacts them personally, with mail outs, and through educational efforts. Potential participants underwent a telephone screen. Those who screened positive were invited to an in-person eligibility and consent evaluation.

The CHR sample met the Criteria of Prodromal Syndromes (COPS) which is based on the Structured Interview for Prodromal Syndromes (SIPS)(McGlashan et al., 2010). The COPS has three possible prodromal syndromes - attenuated positive symptom syndrome (APSS), genetic risk and deterioration (GRD) and/or brief intermittent psychotic syndrome (BIPS). APSS requires the presence of at least one attenuated positive psychotic symptom (unusual thought content, suspiciousness, grandiose ideas, perceptual abnormalities, or disorganized communication) of insufficient severity to meet diagnostic criteria for a psychotic disorder. The attenuated psychotic symptom(s) has to have begun or worsened in the past year. The GRD requires having a combination of both functional decline (at least a 30% drop in Global Assessment of Function score over the last month as compared to 12 months ago) and genetic risk; genetic risk refers to having either schizotypal personality disorder or a first-degree relative with a schizophrenia spectrum disorder. The BIPS state requires the presence of any one or more threshold positive psychotic symptoms (unusual thought content, suspiciousness, grandiosity, perceptual abnormalities, and disorganized communication) that are too brief to meet diagnostic criteria for psychosis. The APSS criteria used in NAPLS 2 is similar to the more recent addition to DSM-V the Attenuated Psychosis Syndrome (APS) which is characterized by psychotic-like symptoms that are below threshold for full psychosis (Tsuang et al., 2013). Criteria are similar except that APS requires that they are sufficiently distressing and disabling to the individual to lead them to seek help. However, the very nature of recruitment for NAPLS 2 means the participants are help-seeking.

After a comprehensive assessment that included administering the Structured Clinical Interview for DSM-IV (SCID) (First et al., 1995) and the SIPS, vignettes were developed for each CHR participant for the purpose of obtaining a consensus diagnosis. The attenuated psychotic symptoms rated on the Scale of Prodromal Symptoms (SOPS) are described at

length and include both recent and longstanding symptoms. The vignettes are written so that raters from all other sites can review the information under each symptom category and provide a reliable rating. Once approved at the site level, the vignette is presented on a conference call for a consensus decision on the symptom ratings as well as the diagnosis. The NAPLS-2 consensus call, chaired by JA, was held once a week and was attended by members of each of the eight sites. Submitted vignettes are individually reviewed and a consensus must be reached on each symptom rating, diagnosis and ultimate admission into the study. It was often challenging making differentiations with respect to some of the exclusion criteria listed below, but the calls were used to discuss issues such as the impact of substance abuse and use of antipsychotics.

Cross-site reliability in the ratings of the SOPS was conducted on an annual basis using a new videotape each year. Ratings from all raters at all sites were compared to “gold standard” ratings on the SOPS. Intraclass correlations, over four years, for the total SOPS scores ranged from 0.82 to 0.93 and for the attenuated positive symptom score from the SOPS ranged from 0.92 to 0.96. There were minimal differences across the individual sites. All intraclass correlations were in the excellent range.

Inclusion and exclusion criteria

Individuals at CHR had to be between 12 and 35 years old and meet diagnostic criteria for a prodromal syndrome as per the COPS criteria (McGlashan et al., 2010), or if under 19, meet criteria for schizotypal personality disorder (SPD). Participants were excluded if they met criteria for current or lifetime Axis I psychotic disorder, including affective psychoses, IQ < 70, or had a past history of a central nervous system disorder, substance dependence in the past 6 months, or if the diagnostic prodromal symptoms were clearly caused by an Axis I disorder. Other non-psychotic DSM-IV disorders were not exclusionary (e.g., substance abuse disorder, major depression, anxiety disorders, Axis II disorders), as long as the disorder did not account for the individual's prodromal symptoms. Use of antipsychotics was not an exclusion provided there was clear evidence that prodromal (but not psychotic) symptoms were present when the medication was started. Control subjects could not meet criteria for any prodromal syndrome, any current or past psychotic disorder or a Cluster A personality disorder diagnosis, and could not have a family history (in first-degree relatives) of any psychotic disorder or any other disorder involving psychotic symptoms. They could not be currently using psychotropic medication.

Measures

The SCID (First et al., 1998) was used to rule out the presence of psychosis. The SIPS and the SOPS were used to assess COPS criteria and severity of attenuated positive symptoms and negative symptoms.

The SOPS is a 19-item scale designed to measure the severity of prodromal symptoms. The SOPS contains four subscales for Positive, Negative, Disorganization and General Symptoms. The five positive symptoms are P1-unusual thought content/delusional ideas, P2-suspiciousness/persecutory ideas, P3-grandiose ideas, P4-perceptual abnormalities, P5-disorganized communication. The six negative symptoms are N1-social anhedonia, N2-

avolition, N3-expression of emotion, N4-experience of emotion and self, N5-ideational richness, N6-occupational functioning. The four disorganization symptoms are D1-odd behavior or appearance, D2-bizarre thinking, D3- trouble with focus and attention, D4-impairment in personal hygiene. The four general symptoms are G1-sleep disturbance, G2-dysphoric mood, G3-motor disturbances, G4-impaired tolerance to normal stress. Positive symptoms are rated from 0 (absent) to 6 (severe/psychotic). Negative, disorganized and general symptoms are rated from 0 (absent) to 6 (extreme).

Clinical outcome at each follow-up assessment was determined in the following way: (i) remission (remission from all syndromes which means scores of 2 or less on all five positive symptoms on the SOPS scale, or for those who have only GRD, “in remission” will require GAF to have returned to 90% of previous best GAF.); (ii) symptomatic (not currently meeting criteria for a prodromal risk syndrome but having ratings of 3-5 on any one of the five positive symptoms on the SOPS, or with the no change in the GAF); (iii) prodromal progression (currently meeting criteria for one of the at risk syndromes; APSS, GRD, BIPS) and (iv) psychotic (currently meeting criteria for a psychotic disorder or evidencing scores of 6 on one or more positive symptoms of the SOPS).

Transition to psychosis was determined by meeting the Presence of Psychotic Symptoms (POPS) (Miller et al, 2003) criteria. Transition criteria is that at least one of the five SOPS positive symptoms reached a psychotic level of intensity (rated 6) for a frequency of ≥ 1 hour per day for 4 days per week during the past month or that symptoms seriously impacted functioning (e.g., severely disorganised or dangerous to self or others).

Statistical Analysis

Chi-square and t-tests were used to compare groups on demographics. One-way ANOVAs were used to compare the different clinical outcome groups on prodromal symptoms. To accommodate missing data and account for intra-participant correlation over time, the generalized linear mixed model for repeated measures was used for the whole CHR sample to examine changes over time (baseline, 6 months, 12 months, 18 months and 24 months) for the five positive symptoms, the six negative symptoms and the total sub-scores for positive, negative, disorganized and general symptoms on the SOPS for those at CHR.

RESULTS

Sample Characteristics

The sample consisted of 280 individuals in the control group (141 males and 139 females) and 764 in the CHR group (436 males and 328 females). The controls (HC) were significantly older than the CHR group (19.7 versus 18.5 years), and had significantly more years of education (12.7 years versus 11.3 years). The groups did not differ in ethnicity, with the majority being white (CHR 62.6%, HC 59.6%) or marital status with the majority being single (95%) or living at home (CHR 75.9%, HC 63.2%) or enrolled as a student (CHR 82.3%, HC 81.1%). Significantly more of the controls were working (46.1% vs 25%). These details are presented in Table 1. In addition the majority of all participants were born in the

USA or Canada. Eighty percent of CHR and 93% of control participants had English as their first language. Spanish was the first language of 50% of the non-English speaking group.

Of the total CHR sample, 93 (12.2%) transitioned to a psychotic disorder, 151 (19.8%) did not have any follow-up, 87 (11.4%) had only the 6-month follow-up, 103 (13.4%) were only followed to 12 months, 56 (7.3%) to 18 months and 274 (36.9%) completed a two year follow-up. Ninety-three of 764 cases converted to psychosis, with a mean ± SD time to conversion of 288.3 ± 287.1 days since the baseline evaluation. However eight of the cases converted after the final 24 month follow-up.

Clinical presentation

The majority of the CHR sample (92.0%) met criteria for the attenuated positive symptoms syndrome, either alone (83.9%) or in combination. A small proportion met other criteria. This information is presented in Table 2.

The mean age at the presentation of the first attenuated psychotic symptom was 16.3 years, (SD=4.60, median =15.5 years). These data were available for 674 CHR participants in the sample. The mean length of time since the appearance of the first positive symptom was 792.7 days (SD = 950.5, median=365.5 days, range=16 days to 19 years).

The means and standard deviations of all 19 SOPS symptoms are presented in Table 3. The most common positive symptoms were unusual thought content and perceptual abnormalities. For negative symptoms this ranged from 56.4% endorsing poor functioning to 19.4% endorsing decreased ideational richness. Apart from “trouble with focus and attention” disorganization symptoms were infrequently endorsed. With the exception of impaired tolerance to normal stress, approximately 50% endorsed each of the general symptoms. See Table 3.

Change in symptoms over time

Results of the mixed-effect models demonstrated that overall, there were significant improvements in all 19 SOPS symptoms at each follow-up time point compared with baseline. Although most of the clinical improvement occurred in the first 6 months, there was still significant continued improvement occurring between 6 and 12 months for P1, P4, positive total, N1, negative total and D2 symptoms and between 12 and 18 months for P1, P2, P4, P5, positive total, N4, N5, D2, D3 symptoms. There were continued improvements from 12 to 18 or 12 to 24 months for all positive symptoms except P3, N1, N3, N5, N6, D2 and D3. However, there were no significant improvements in any SOPS symptoms between 18 and 24 months.

Clinical Outcome

Since 52% of the sample was not available at the 2-year outcome, we examined clinical outcome in two ways. First, for the 48% that either completed two years or converted and secondly as a last observation carried forward (LOCF). These numbers are presented in Table 4.

For the group that reached two years, the smallest subgroup comprised those who continued to meet prodromal progression. For the group using the LOCF, the subgroups were quite even with the psychotic subgroup being the smallest.

Using the LOCF, the clinical outcome groups varied on the following baseline symptoms: P1-unusual thought content ($F=8.89$, $p<0.001$), P2-suspiciousness ($F=11.67$, $p<0.001$), P5-disorganization ($F=6.31$, $p<0.001$), N2-avolition ($F=2.85$, $p<0.05$), positive symptom total score ($F=12.77$, $p<0.001$), and disorganization total score ($F=6.96$, $p<0.001$). There were no differences for P3 (grandiosity) , P4 (perceptual abnormalities), or any of the negative symptoms with the exception of N2 (anhedonia). When restricting the analyses to include only the subgroup with clinical outcome data at two years, ANOVA results demonstrated that with the exception of N2, the groups differed on the same baseline symptoms: P1 ($F=9.97$, $p<0.001$), P2 ($F=6.47$, $p<0.001$), P5 ($F=5.57$, $p<0.01$), positive total ($F=9.38$, $p<0.001$), and disorganization total ($F=5.40$, $p<0.01$). However, post hoc examinations revealed that the intergroup differences were not always the same. These are presented in Table 5.

DISCUSSION

The current study presents symptom data on the largest sample of adolescents and adults at CHR of psychosis to date. In terms of demographics, CHR subjects vary little from healthy controls, being on average younger by one year, which may account for the one year difference in years of education, and more likely to be living at home.

More than 92% of the CHR sample met criteria for attenuated psychotic symptom syndrome (APSS). Although 10% did present with genetic risk and deterioration (GRD), less than 5% met only this criterion, as those who met for GRD typically also present with APSS. Furthermore, the Brief Intermittent Psychotic symptom criterion (BIPS) rarely occurred on its own (n=6 cases, 0.8%). More frequently, we saw individuals who presented with APSS but reported an occurrence of BIPS in the past three months, although that too was infrequent (n=14 cases, 1.9%).

Next, we examined all prodromal symptoms individually. Our data support the few previous studies that suggest that the most common symptoms at baseline are positive in that 92% have at least one positive symptom, followed by negative and then disorganization and general. Eighty-two percent of the sample had at least one negative symptom and 44% had three or more negative symptoms. The most frequently endorsed positive symptoms were unusual thought content and perceptual abnormalities, followed by suspiciousness. Disorganized communication was infrequent and grandiosity endorsed even less often. Avolition and poor occupational functioning were the most common negative symptoms. None of the other symptoms were endorsed as much as unusual thought content and perceptual abnormalities, although dysphoric mood was endorsed by 68% of the sample.

Two earlier studies have reported symptom improvement over time (Lee et al., 2014;Addington et al., 2011). We observed that there were significant improvements in all 19 SOPS symptoms at each follow-up time point compared to baseline. Although most of

the clinical improvement occurred in the first six months, there was still significant continued improvement occurring between 6 and 12 months for unusual thought content, perceptual abnormalities, anhedonia, bizarre thinking, and overall positive symptoms and negative symptoms. Several symptoms continued to improve between 12 and 18 months, although none improved between 18 and 24 months. Although this is only the third sample reporting this kind of improvement it is possible that this may be the natural course over at least the first two years. Addington et al (2011) in the NAPLS 1 sample, also considered social functioning, and suggested that approximately one third may develop a psychotic illness, one third may improve and one third may continue to have fluctuating attenuated psychotic symptoms and poorer functioning. At this stage it is unclear as to the impact of treatments on such division of CHR samples, although the NAPLS 2 project will in the near future be able to address many questions related to the impact of treatment on the outcome of CHR individuals.

We were also interested in when these early symptoms began. As other SOPS symptoms are very difficult to date we focused only on the five positive symptoms. The average age of the CHR sample was 18.6 years and they reported that they were on average 16 years old when they were aware of the first attenuated psychotic symptom, suggesting an average of >2 years between first experiencing attenuated psychotic symptoms and seeking help. However, this gap actually ranged from 16 days to 19 years. Thus, for some, at their baseline assessment these attenuated psychotic symptoms are a new occurrence but for others they have been present for much of their lives. The implication is that these individuals who have had attenuated psychotic symptoms for many years, often since they were very young, are not presenting until either the symptoms worsen, or they begin to impact their functioning or they have a new attenuated psychotic symptom appearing. There is, therefore, the possibility that some of these CHR individuals could be identified even sooner. This may be particularly important for CHR with a long duration of symptoms as this has been shown to be one predictor of transition to psychosis in the PACE high risk sample (Nelson et al., 2013).

In studies of CHR, the outcome that receives the most attention is whether individuals make the transition to psychosis. However, in NAPLS 2 we have considered whether individuals are in remission from the attenuated psychotic symptoms or continue to present with attenuated psychotic symptoms albeit at the same or reduced severity as baseline. We also considered those who continue to meet criteria for at least one of the three prodromal syndromes. Since the COPS criteria require a worsening, this group is likely to have experienced an increase in symptoms over time, although not to the extent that they are of psychotic intensity or may have had a remission and then a re-occurrence of symptoms. To make the most of our data we examined outcome for those who had completed two years of follow-up but also examined outcome using the last outcome rating conducted. What was interesting was that although the majority of the baseline prodromal symptoms were unrelated to later outcome some symptoms differentiated the transition group from the other three groups, e.g., unusual thought content, disorganized communication and overall ratings on the disorganized symptoms whereas other symptoms differentiated those in remission from the other three groups, e.g., suspiciousness and total positive symptoms. This suggests that the presence of certain symptoms may be typical of at risk groups regardless of whether

they continue to have symptoms or even make the transition to psychosis; whereas others may be predictive of a later psychosis. Interestingly perceptual abnormalities, which was one of the most frequently endorsed symptoms at baseline, did not relate at all to later outcome.

One limitation of the examination of outcome is that almost 52% of the sample did not complete 2 years. Typically it is difficult to keep young people in studies for long periods of time, particularly in a study such as NAPLS 2 where in addition to clinical assessments participants were also involved in assessments for biological markers; i.e. imaging, EEG, blood draws and neurocognition. Dropping out was at times a functioning of individuals moving away or changing schools and sites being unable to recontact people. Since most of the young people are help-seeking and troubled by the onset of attenuated psychotic symptoms, it is not unusual for them to no longer be interested in help once their symptoms disappear.

In summary, our results suggest that APSS is by far the most common syndrome among those meeting CHR COPS criteria. Positive followed by negative symptoms are the most common, in particular, unusual thought content, perceptual abnormalities and suspiciousness. However on average all prodromal symptoms rated on the SOPS improve over time. For outcome groups based on clinical follow-up there are essentially three groups: those who make the transition to psychosis, those who have a remission of attenuated psychotic symptoms and those who continue to have attenuated psychotic symptoms, some of whom also continue to meet prodromal criteria. Further work with this large NAPLS sample will examine both clinical and biological predictors of psychosis. The importance of these attenuated positive symptoms will be considered in prediction models. However, these results suggest that more in depth study not just of those who convert but also of those who present with attenuated psychotic symptoms and who have a complete remission of these symptoms often within six months and of those who continue to experience at time fluctuating subthreshold symptoms who may not go on to develop a psychotic illness, is required. A greater understanding of those who remit may help our understanding of psychosis and improve our identification of those who are at real risk of developing a psychotic illness. For those who continue to experience attenuated psychotic symptoms, further attention to interventions that may help such individuals have improved quality of life would be the next step.

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Table 1

Differences in Demographic Characteristics between Clinical High Risk and Healthy Control Participants

Variable	Controls *n* = 280	Prodromal *n* = 764	Test Statistic	Effect Size
	Mean (SD)		*t*	*d*
Age in years	19.65 (4.67)	18.45 (4.23)	3.74**	0.26
Years of education	12.68 (3.58)	11.28 (2.82)	5.90**	0.41
	Number (%)		X^2	*Cramer's V*
Sex				
Male	141 (50.4%)	436 (57.1%)	3.73	0.06
Female	139 (49.6%)	328 (42.9%)		
Race				
First Nations	4 (1.4%)	13 (1.7%)	5.24	0.07
Asian	30 (10.7%)	54 (7.1%)		
Black	49 (17.5%)	118 (15.5%)		
Latin America/Middle East/White	167 (59.6%)	478 (62.6%)		
Native Hawaiian or Pacific Islander	1 (0.4%)	3 (0.4%)		
Interracial	29 (10.4%)	97 (12.7%)		
Hispanic or Latino				
Yes	50 (17.9%)	142 (18.6%)	0.08	0.01
No	230 (82.1%)	621 (81.4%)		
Father's highest level of formal education				
No or primary school			10.13*	0.10
Some high school	7 (2.6%)	35 (4.9%)		
High school and/or some college	13 (4.8%)	72 (10.0%)		
College graduate	117 (42.9%)	280 (38.9%)		
	136 (49.8%)	333 (46.2%)		
Mother's highest level of formal education				
No or primary school			17.13**	0.13
Some high school	4 (1.4%)	32 (4.3%)		
High school and/or some college	8 (2.9%)	59 (7.9%)		
College graduate	99 (35.6%)	283 (38.1%)		
	167 (60.1%)	370 (49.7%)		
Marital Status				
Single never married	266 (95.0%)	720 (94.9%)	0.01	0.003
Other	14 (5.0%)	39 (5.1%)		
Current living arrangement				

Variable	Controls *n* = 280	Prodromal *n* = 764	Test Statistic	Effect Size
	Mean (SD)		*t*	*d*
Living with family	177 (63.2%)	576 (75.9%)	25.06**	0.16
Living with spouse/partner	18 (6.4%)	38 (5.0%)		
Living on own in apartment/house	31 (11.1%)	40 (5.3%)		
Living in group/rooming home	4 (1.4%)	20 (2.6%)		
Living with others, not spouse/partner	41 (14.6%)	68 (9.0%)		
Living in a shelter	0 (0.0%)	2 (0.3%)		
Living on the street	0 (0.0%)	0 (0.0%)		
Other	9 (3.2%)	15 (2.0%)		
Currently working				
Yes	129 (46.1%)	189 (25.0%)	42.65**	0.20
No	151 (53.9%)	567 (75.0%)		
Highest level of formal education obtained				
High school incomplete			78.81**	0.27
High school graduate	101 (36.1%)	399 (52.7%)		
High school and above	92 (32.9%)	289 (38.2%)		
	87 (31.1%)	69 (9.1%)		
Currently enrolled as a student				
Yes	227 (81.1%)	624 (82.3%)	0.22	0.01
No	53 (18.9%)	134 (17.7%)		

*** p<0.001

* p<0.05

** p<0.01

Table 2

Frequency and Proportion of Prodromal Syndromes within the Clinical High Risk Sample.

Prodromal Criteria	Number	%
Attenuated Psychotic Symptom Syndrome (APSS)	641	83.9
Genetic Risk and Deterioration (GRD)	34	4.4
Brief Intermittent Psychotic Symptoms (BIPS)	6	0.8
Under 19 plus Schizotypal Personality Disorder	21	2.7
APSS plus GRD	48	6.3
BIPS plus APSS	12	1.6
BIPS plus APSS plus GRD	2	0.3
Total	764	100%

Table 3

Frequency at Baseline of the Number of Clinical High Risk Participants Endorsing Each of the 19 Symptoms on the Scale of Prodromal Symptoms (N=744)

Symptom	Mean (SD)	Number (percent) endorsing this symptom >2
Positive Symptoms		
Unusual thought content/delusional ideas	3.34 (1.33)	609 (79.6)
Suspiciousness/persecutory ideas	2.76 (1.51)	498 (65.1)
Grandiosity	1.00 (1.30)	121 (15.8)
Perceptual abnormalities/hallucinations	3.07 (1.50)	568 (74.2)
Disorganized communication	1.75 (1.47)	227 (29.7)
Negative Symptoms		
Social anhedonia	2.36 (1.74)	314 (42.3)
Avolition	2.45 (1.62)	384 (52.4)
Expression of emotion	1.36 (1.52)	188 (25.7)
Experience of emotions and self	1.75 (1.68)	283 (38.7)
Ideational richness	1.16 (1.31)	142 (19.4)
Occupational functioning	2.84 (2.01)	414 (56.4)
Disorganization Symptoms		
Odd behavior or appearance	0.84 (1.20)	94 (12.8)
Bizarre thinking	0.91 (1.20)	91 (12.4)
Trouble with focus and attention	2.64 (1.28)	434 (59.2)
Impairment in personal hygiene	0.76 (1.21)	77 (10.5)
General Symptoms		
Sleep disturbance	2.32 (1.56)	384 (52.3)
Dysphoric mood	3.34 (1.61)	507 (67.9)
Motor disturbances	0.83 (1.06)	45 (6.1)
Impaired tolerance to normal stress	2.70 (1.88)	381 (52.0)

Table 4

Clinical Outcome of Clinical High Risk Participants at End of Study

	IN REMISSION	SYMPTOMATIC	PRODROMAL PROGRESSION	PSYCHOTIC
	n (%)	n (%)	n (%)	n (%)
2 YEARS	109/367[a] (29.7%)	93/367 (25.3%)	72/367 (19.6%)	93/367 (25.3%)
LOCF	171/613[b] (27.9%)	186/613 (30.3%)	163/613 (26.6%)	93/613 (15.2%)

LOCF - Last assessment carried forward

[a] 367 is the number of converters plus the CHR participants who completed a 2 year followup

[b] 613 is the number of converters plus the CHR participants who completed at least one followup

Table 5

Post Hoc Analyses of the Baseline Differences between the Clinical Outcome Groups

BASELINE SOPS SYMPTOM	LOCF CLINICAL OUTCOME	24 MONTH CLINICAL OUTCOME
P1 - Unusual thought content	Psychotic > Remission***	Psychotic > Remission***
	Psychotic > Symptomatic**	Psychotic > Symptomatic**
	Psychotic >Prodromal Progression*	Prodromal Progression > Remission**
	Prodromal Progression > Remission*	
	Prodromal Progression > Symptomatic*	
P2 - Suspiciousness	Remission < Symptomatic***	Remission < Symptomatic**
	Remission < Prodromal Progression**	Remission < Psychotic***
	Remission < Psychotic***	
P5 - Disorganization	Psychotic > Remission***	Psychotic > Remission**
	Psychotic >Symptomatic*	Psychotic >Prodromal Progression**
	Psychotic >Prodromal Progression***	
N2 - Avolition	Remitted < Symptomatic*	NS
Positive total	Remission < Symptomatic***	Remission < Symptomatic**
	Remission < Prodromal Progression*	Remission < Prodromal Progression*
	Remission < Psychotic***	Remission < Psychotic***
	Symptomatic < Psychotic*	
	Prodromal Progression < Psychotic**	
Disorganization total	Psychotic > Remission***	Psychotic > Remission***
	Psychotic > Prodromal Progression**	
	Psychotic > Symptomatic*	

LOCF=Last observation carried forward

* p<0.05

** p<0.01

*** p<0.001