HHS Public Access

Author manuscript

J Clin Child Adolesc Psychol. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

J Clin Child Adolesc Psychol. 2018 ; 47(1): 69–78. doi:10.1080/15374416.2016.1212361.

Treatment Precedes Positive Symptoms in the North American Adolescent and Young Adult Clinical High Risk Cohort

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Abstract

Early intervention for psychotic disorders, a growing international priority, typically targets help-seeking populations with emerging psychotic ("positive") symptoms. We assessed the nature of and degree to which treatment of individuals at high risk for psychosis preceded or followed the onset of positive symptoms. The North American Prodrome Longitudinal Study (NAPLS)-2 collected psychosocial treatment histories for 745 (98%) of 764 high-risk participants (mean age = 18.9, 57% male, 57.5% Caucasian, 19.1% Hispanic) recruited from eight North American communities. Similar to prior findings, 82% of participants reported psychosocial treatment prior to baseline assessment, albeit with significant variability across sites (71-96%). Participants first received treatment a median of 1.7 years prior to the onset of a recognizable psychosis-risk syndrome. Only a quarter sought initial treatment in the year following syndrome onset. Although

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mean sample age differed significantly by site, age at initial treatment (M = 14.1, SD = 5.0) did not. High rates of early treatment prior to syndrome onset make sense in light of known developmental precursors to psychotic disorders but are inconsistent with the low rates of treatment retrospectively reported by first episode psychosis samples. Findings suggest that psychosis-risk studies and clinics may need to more actively recruit and engage symptomatic, but non-help-seeking individuals and that community clinicians be better trained to recognize both positive and non-specific indicators of emerging psychosis. Improved treatments for nonspecific symptoms as well as the characteristic attenuated positive symptoms are needed.

Keywords

psychosis; prodromal; help-seeking; psychosocial; NAPLS

Early intervention in schizophrenia and other major psychotic disorders relies on accurate identification of people in the early stages of these illnesses. Current efforts focus on identifying adolescents and young adults (reflecting the period of peak onset) with clinical symptoms, family history, and/or functional decline indicating imminent risk or “clinical high risk” (CHR) for psychosis (see Woodberry, Shapiro, Bryant, & Seidman, 2016 for a comprehensive review). These individuals are identified primarily on the basis of new or worsening “positive” symptoms such as subthreshold paranoia, hallucinations, unusual beliefs, or disorganized speech. The presence of increasing social withdrawal and cognitive, academic, and work impairments is common and often relevant to CHR identification.

In large part, these young people come to the attention of specialized clinical research centers because they are “help-seeking.” A number of studies report long delays from symptom emergence to help-seeking and subsequent recognition of and treatment of psychosis-risk syndromes (Philips et al., 1999; Platz et al., 2006). Thus, many assume that these youth are newly seeking help for emerging difficulties associated with their CHR status (e.g., McGlashan et al., 2007). But is this true?

On the one hand, psychosis is known to be preceded by a number of neurodevelopmental abnormalities and longstanding comorbid disorders (Cannon et al., 2002; Liu, Keshavan, Tronick, & Seidman, 2015; Tarbox et al., 2014) that might prompt help-seeking before the emergence of CHR syndromes. On the other hand, retrospective reports of individuals in a first psychotic episode suggest that help-seeking is uncommon during the premorbid and prodromal phases (Schultze-Lutter et al., 2015). In fact, there is a rich literature on the duration of untreated psychosis (DUP) that suggests that treatment is delayed well beyond the onset of acute psychosis (Perkins, Gu, Boteva & Lieberman, 2005). The bulk of this literature, however, defines the onset of treatment by the start of antipsychotic medications or inpatient hospitalization, and thus does not adequately speak to early psychosocial treatment.

Studies of help-seeking in CHR samples from different continents (e.g., North America, Asia, and Europe) consistently report very high rates (82-86%) of help-seeking prior to assessment in a specialized clinical research setting (Cadenhead et al., 2010; Katsura et al., 2014; Fridgen et al., 2013). This likely reflects CHR criteria requiring distress or impairment

(Miller et al., 2003). Interestingly, initial help-seeking is not only of mental health professionals, but to a large extent of general practitioners or school personnel (e.g., Platz et al., 2006; Stowkowy, Colijn, Addington, 2013).

Consistent with the argument that longstanding issues and nonpsychotic comorbidities might prompt initial treatment, the most commonly reported reasons for help-seeking in CHR are not attenuated positive symptoms, but rather affective symptoms such as depression or anxiety (e.g., 47%, Falkenberg et al., 2015; 60.7% and 22.1%, respectively, Platz et al., 2006). That said, subthreshold psychotic symptoms are reported as the primary reason in a substantial subgroup (40%, Falkenberg, and 2-24% for each of six symptoms in Platz et al., 2006). Negative symptoms (particularly social decline and withdrawal, endorsed by 44% and 34% respectively) and cognitive symptoms (primarily impaired concentration and attention, endorsed by 24% and 10% respectively) are also common precipitants for help-seeking (Platz et al., 2006).

One retrospective study of first episode patients examined the timing of psychosocial help-seeking in relation to the CHR phase and found that almost all (95%) patients had sought help for mental problems prior to their first inpatient treatment (Schultze-Lutter et al., 2015). Yet only 23% had sought help prior to the onset of acute psychosis. Just 10% sought help during a retrospectively recognizable CHR phase. The remaining 13% initially sought help for nonpsychotic (“nonspecific”) symptoms in the absence of a CHR syndrome.

Studies of the duration of untreated *illness* (DUI) report delays of weeks to years to the initiation of “appropriate” treatment (e.g., specialized early intervention centers) after the onset of either attenuated positive symptoms or associated nonspecific complaints such as insomnia (Phillips et al., 1999; von Reventlow et al., 2014). Although delays in reaching specialized care are noteworthy, rates of help-seeking in CHR samples are still strikingly high relative to those retrospectively reported by first episode samples. A key unanswered question is whether initial treatment precedes or follows the emergence of CHR syndromes.

The second phase of NAPLS, NAPLS-2, a collaborative multisite consortium, collected detailed psychosocial treatment histories on one of the largest CHR samples to date. The purpose of this paper was to explore the timing of initial treatment in relation to the onset of psychosis-risk syndromes. To examine factors that may have played a role in this relationship and to facilitate comparison with related work, we also report on 1) the nature of psychosocial treatments received and the temporal relationship of psychosocial and psychopharmacological treatments, 2) demographic and clinical characteristics associated with prior treatment, and 3) whether treatment patterns differed across sites or over time (relative to an earlier cohort, NAPLS-1).

Method

Participants

NAPLS-2 participants were recruited from both urban and rural communities surrounding eight research sites across North America and Canada: Emory University, Harvard University/Beth Israel Deaconess Medical Center (BIDMC), University of Calgary,

University of California at Los Angeles (UCLA) and San Diego (UCSD), University of North Carolina (UNC), Yale University, and Zucker Hillside Hospital. Institutional Review Boards at each institution approved the study. CHR status was determined with the Structured Interview of Psychosis-risk Syndromes (SIPS) and clinical consensus review. The SIPS is an internationally recognized interview for assessing CHR status, with established reliability and predictive validity (Miller et al., 2003). For inclusion, participants had to meet the SIPS Criteria of Psychosis-risk Syndromes (COPS) or be under age 19 and meet criteria for schizotypal personality disorder (Youth & Schizotypy) via the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (First, Gibbon, Spitzer, Williams, & Benjamin, 1997). A syndrome onset date was determined for all COPS syndromes. Full details of recruitment, inclusion and exclusion criteria, eligibility procedures, clinical reliability, measures, and clinical procedures have been described elsewhere (Addington et al., 2012; Woods et al., 2013).

Psychosocial Treatment Queries

At baseline assessment, masters and doctoral level clinicians, or trained supervisees, including graduate students, queried participants and/or family members about all current and lifetime psychosocial treatments received since birth. For each treatment received, clinicians asked participants to provide or estimate start and stop dates, modality (individual or group), and the number of sessions. Clinicians inquired about the nature of the therapy to best determine the type (case management, supportive, cognitive behavioral, dynamic, interpersonal, or family therapy, school counseling, or stress management). Interviews were unstructured, but guidelines and training were provided via a manual, annual multi-site meetings, and monthly calls. In contrast to the NAPLS-2 unified protocol, NAPLS-1 retrospectively consolidated and categorized (any therapy, psychotherapy, family therapy, group therapy, or school support) treatment histories collected at independent research sites (Cadenhead et al., 2010).

Analyses

Analyses were conducted using the Statistical Package for the Social Sciences (SPSS, Inc.), version 22. Univariate comparisons of subgroup (e.g., those with and without prior treatment) characteristics were conducted with independent *t* tests for continuous variables and Pearson Chi-Square or Fisher's Exact Test for categorical variables. After dichotomizing categorical variables with multiple levels (e.g., race, education, income), we conducted a bivariate correlational matrix of demographic and clinical variables and entered those variables significantly correlated with a history of prior treatment into a sequential logistic regression to assess the relative strength of association between demographic and clinical characteristics (independent variables: see Supplemental Table 1) and a history of prior treatment (dependent variable). Demographic variables significantly associated with treatment were entered in block one. Clinical variables significantly associated with treatment were entered in block two.

Results

Rates of Psychosocial Treatment in the Baseline NAPLS-2 Sample

Of the 764 CHR participants, data on psychosocial treatments received prior to baseline assessment were available for 745 (98%, see Table 1). The vast majority of these (82%, N = 608) reported having received psychosocial treatment during their lifetimes, with a quarter (27%) of these having received two different types, and 9% three or four. At the time of their baseline assessment, almost half (48%, N = 361) were in some form of psychosocial treatment with 7% of these in two or more types. Those in treatment at baseline had already had an average of 34 sessions of these treatments (distribution positively skewed, median = 12), and a total of 64 sessions of any therapy (see Table 2). The mean for the entire sample with prior psychosocial treatment was 56 sessions (median = 20 sessions).

Types of Psychosocial Treatment Received

NAPLS 2 participants received a wide range of psychosocial therapies (see Table 2), roughly half having received supportive therapy. School counseling, case management, cognitive behavioral therapy (CBT), and family therapy were each endorsed by 10-20%. The highest volume of sessions received was in school counseling. Ten percent received treatment in a group format with a mean of 40 sessions.

Relationship to Psychopharmacological Treatment

Of those with data on both psychosocial and psychopharmacological treatments (N = 744), 208 (28%) were both in therapy and on medications at baseline, 410 (55%) had received both forms of treatment prior to baseline assessment, 197 (26%) psychosocial therapy alone, and 51 (7%) medications alone. Only 86 (12%) reported having received neither. Rates of prior medication in the complete sample were comparable to those in the first half of the sample (Woods et al., 2013). Forty-four percent had been treated at some point with antidepressants, 28% with antipsychotics, 22% with stimulants, 12% with benzodiazepines, and 9% with mood stabilizers.

Age and Timing of Treatment

On average, individuals entering the NAPLS-2 study initially sought psychosocial treatment during early adolescence, with a range from infancy to adulthood (age 1-34, see Table 3). Although sample age differed significantly by site, the age at which participants had first received therapy did not. On average, participants entered psychosocial treatment three years prior to the onset of their psychosis-risk (COPS) syndrome and four years prior to study entry (both distributions had positive skew with medians of 1.7 and 2.4 years, respectively, see Figure 1). Half initially began treatment between ages 12 and 18, a quarter (26%) before age 12, and 21% after age 18. Of those treated, 73% were treated *prior* to the onset of a psychosis-risk syndrome. Only 22% sought initial treatment in the year after syndrome onset, the majority (16%) within 6 months. Although the earliest onset of psychopharmacological treatment was age 3, the average age of initial psychiatric medication was 15.0 years (SD = 5.1). Stimulants were prescribed earlier than other medications on average (mean age = 11.6, SD = 4.8).

Demographic Correlates of Prior Psychosocial Treatment

Demographic characteristics of treated and untreated subsamples are reported in Table 1. Rates of psychosocial treatment were significantly higher for younger vs. older participants, for children of more highly educated parents and higher income families, and for Caucasians vs. non-Caucasians. Percentages were lowest for Pacific Islanders and Black participants (66.7 and 68.1% respectively) and highest for Interracial (85.4%), First Nations (84.6%), Caucasian (84.3%), and Asian (82.5%) participants. Rates of treatment did not differ according to Hispanic ethnicity. However, individuals born outside vs. inside the USA or Canada were significantly less likely to have received treatment. Rates also differed by sex, with a significantly greater proportion of the females (86%) than the males (78%) having received psychosocial treatment.

Clinical Correlates of Prior Psychosocial Treatment

Those with and without treatment did not differ on baseline SIPS positive, negative, or total symptom scores or on current GAF scores. However, higher baseline disorganized (D) and general (G) symptom scores and current or lifetime diagnoses of depression or attention-deficit/hyperactivity disorder (ADHD) were associated with significantly higher rates of treatment. Prior treatment was also significantly associated with younger age of psychosis-risk syndrome onset (17.8 vs. 19.1; $t = 3.02$, $p = 0.003$).

Demographic and Clinical Predictors of Prior Treatment

The correlational matrix of primary demographic and clinical variables considered is shown in Supplemental Table 1. Age, sex, household income, highest parental education, whether or not born in the U.S. or Canada, and whether or not Caucasian were entered into the first block of a logistic regression. Sex ($\beta = 0.56$, $p = 0.007$), parental education ($\beta = 0.50$, $p = 0.014$), family income ($\beta = 0.47$, $p = 0.021$), and age ($\beta = 0.05$, $p = 0.017$) remained robustly associated with treatment (Model $\chi^2 = 28.69$, $p < 0.001$; Nagelkerke R Square = 0.064). When clinical variables (Symptoms of Psychosis-risk Syndromes, SOPS, Disorganized, D, and General, G, Symptom totals, age of psychosis-risk syndrome onset, and current or lifetime history of any depressive disorder or ADHD) were entered into the second block of the logistic regression ($N = 699$), sex ($\beta = -0.52$, $p = 0.014$), highest parental education ($\beta = 0.42$, $p = 0.041$), family income ($\beta = 0.42$, $p = 0.046$), and diagnoses of depression ($\beta = 0.72$, $p = 0.001$) and ADHD ($\beta = 0.65$, $p = 0.026$) remained significantly associated with having had prior therapy (Model $\chi^2 = 52.10$, $p < 0.001$; Nagelkerke R Square = 0.115).

Site Differences

Rates of prior therapy differed significantly by site with Harvard/BIDMC and Calgary having the highest rates (96 and 90%, respectively) and Emory and Zucker Hillside Hospital having the lowest (72 and 71%, respectively). As illustrated in Table 3, key demographics (age, racial and ethnic distribution, parental education) and clinical characteristics (mean GAF and SIPS total scores) differed by site. Rates of Structured Interview for DSM-IV (SCID) diagnoses differed significantly by site for lifetime or current bipolar and anxiety disorders but not for depression or ADHD. As can be seen in Table 4, the types of therapy received also differed by site.

Psychosocial Treatment in NAPLS-2 Relative to NAPLS-I

The overall percentage of participants with prior treatment was consistent across NAPLS-1 and 2 (82.1% vs. 81.6%, respectively, see Table 1), with younger participants having consistently higher rates of prior treatment than older participants. Although data on prior psychosocial treatment were collected according to a unified procedure in NAPLS-2 and varied by site in NAPLS-1, overall rates of psychotherapy, school counseling, and family therapy were fairly comparable (see Table 2). Sex appeared to be a more significant factor in whether participants received psychosocial treatment in NAPLS-2 relative to NAPLS-1. Racial discrepancies remained largely intact, except for Asian participants, who in NAPLS-2 appeared to have had higher rates of prior psychosocial treatment than in NAPLS-1. Clinically, NAPLS-2 participants with vs. without prior treatment differed only in ratings of disorganized and general symptoms whereas NAPLS-1 participants with prior treatment relative to those without had significantly higher SIPS symptom totals, lower global functioning, and higher rates of schizotypal personality disorder as well.

Discussion

Systematic data on psychosocial treatment prior to enrollment in one of the largest CHR studies confirm that the CHR individuals recruited into this study were not only a “help-seeking” population, but already had received a substantial amount of treatment. Consistent with prior literature, including from NAPLS-1, more than 80% of participants had previously received mental health treatment. Roughly half were in therapy at the time of study entry and a third had already received two or more different types of therapy. These included primarily supportive therapy, school counseling, case management, CBT, and family therapy. Moreover, most had received a substantial dose of therapy, with a mean of 56 and median of 20 sessions. The likelihood of prior therapy was higher for females, those with current or past diagnoses of depression or attention disorders, and those with more highly educated parents and higher income families. Rates of treatment prior to baseline also varied by site, presumably due to differences in area populations, recruitment strategies, and treatments available at and around each site. In contrast to NAPLS-1, total SIPS symptoms, global functioning, and rates of schizotypal personality disorder did not differ between NAPLS-2 participants with and without treatment. These cohort differences may reflect expected study-to-study variation or an overall more diverse sample yielded by expansion of recruitment networks over time.

The timing of help-seeking, albeit consistent with a nascent literature on this topic, may come as a surprise to many in the field. The initial help-seeking of this very large CHR sample was generally not recent nor newly in response to emerging prodromal symptoms. In the vast majority of cases, it began well before the onset of a prodromal syndrome, at least as defined by the SIPS. Unfortunately, it is not possible from these data to know whether this early help-seeking reflects the emergence and distress of non-specific symptoms preceding attenuated psychotic symptoms, the high degree of study recruitment from mental health clinicians (Addington et al., 2012), or the heterogeneity and complexity of referrals made to specialized teams and associated with increased risk for major mental illness. CHR studies may inadvertently select for individuals whose prior treatment was less effective. Given the

potential of psychosocial treatments, in particular, CBT, to significantly reduce the risk for transition to psychosis over 6 to 24 months (van der Gaag et al., 2013), youth who had received effective treatment might have been less likely to be included in NAPLS-2. During the period of enrollment for NAPLS-2, however, the promising specialized psychosocial treatments were available in only a few communities from which NAPLS-2 participants were recruited. It is also possible that better-educated community clinicians were *more* alert to early warning signs and thus more likely to refer to specialized centers. Indeed, a recent meta-analysis of the relationship of recruitment strategies to sample transition risk found higher risk in samples selectively referred by mental health professionals and institutions than those recruited via intensive outreach to the general public (Fusar-Poli et al., 2015).

An important question raised by this study is whether CHR research studies adequately target and represent the population who will later develop psychosis. In particular, do they adequately sample non-help-seekers, males, individuals from less educated or lower income households, and minority or immigrant groups, all of whom may be less likely to seek or have less access to quality mental health care? New recruitment strategies may be needed to better identify and engage these populations. These might include mobile or remote assessment, more assertive, but gradual engagement, or engagement in conjunction with a known community member. Of course, given lower transition rates in those recruited from outreach to the general public (Fusar-Poli et al., 2015), engagement of non-help-seeking individuals into specialized CHR programs may lead to increased ethical risks (e.g., overpathologizing or creating undue anxiety and burden for individuals with experiences that may remit without treatment, Mittal et al., 2015). Australia provides a model of healthcare reform that enhances early intervention while minimizing these risks (McGorry et al., 2007). *Headspace* offers early mental health intervention in youth-friendly settings that serve as a single entry point for both specific and nonspecific complaints (McGorry et al., 2007). Although broader strategies require mental health system reform and yield samples at overall lower risk for psychosis (Fusar-Poli et al., 2015), they might be more inclusive of the full population that develop psychosis and thus have a greater impact in reducing DUP (Melle et al., 2004).

Alternatively, the fact that many CHR have been in treatment for years might primarily reflect recruitment of younger participants. Retrospective reports of first episode samples often only include those with psychosis onset in adulthood. More effort may be needed to educate child and adolescent providers about risk factors, non-specific symptoms, and early CHR symptoms. The high association of prior treatment with lifetime depressive and ADHD diagnoses highlights these diagnoses as potential early risk factors, risk indicators, or comorbidities. In the Falkenberg et al. study (2015), not only were affective symptoms the most common reason for help-seeking, 59% of these help-seekers met criteria for depressive or anxiety disorders. In fact the vast majority (78%) of CHR who met criteria for depressive or anxiety disorders sought help for affective symptoms. Unfortunately, this study was not able to report on the timing of symptom onset in relation to historical help-seeking. For this, first episode research provides some insight. Psychotic patients have retrospectively reported that affective symptoms were not only the most common and earliest symptoms experienced (Häfner, Maurer, Trendler, an der Heiden & Schmidt, 2005), but were the most common triggers of initial help-seeking (Rietdijk et al., 2011).

Limitations

Several limitations are relevant to interpretating these findings. First, these data were typically not based on treatment records but rather on retrospective report of participants and family members. Second, although written guidelines and training were provided on how to code these data, prior clinician training and setting likely influenced the coding of therapy type, in particular. Third, NAPLS-2 did not collect information on pathways to care, such as who initiated help, for what reasons, or through which networks, or on whether untreated individuals were ever referred for help. Finally, these analyses do not examine the relationship of prior treatment to subsequent transition to psychosis. This will be addressed in future manuscripts.

Clinical Implications and Future Directions

Help-seeking clearly enhances the likelihood that individuals with emerging psychotic symptoms will be identified as early as available science allows. The challenge is to discover and communicate findings relevant to effective screening and intervention to the providers from whom these individuals are likely to seek help. Improved understanding of specific predictors of psychosis in children, adolescents and young adults seeking help for depressive and attention disorders is particularly needed. Further development, testing, and dissemination of psychosocial treatments such as CBT, family therapy, and integrated care, which emerging evidence suggest reduce the short-term risk for acute psychosis, will also be important (van der Gaag et al., 2013). That said, active problem solving with community members to effectively engage non-help-seeking CHR, particularly males and poorer, less educated, and minority and immigrant populations, may prove most critical to overall early detection and prevention efforts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The authors would like to thank J Stowkowy, T Raedler, L McGregor, D Marulanda, L Legere, L Liu, C Marshall, E Falukozi, E Fitton and K Smith (University of Calgary); T Alderman, K Shafer, I Domingues, A Hurria and H Mirzakhanian (UCSD); B Walsh, J Saksa, N Marshman, E Levine and S Tarbox (Yale University); A Giuliano, M Friedman-Yakoobian, W Stone, J Rodenhiser-Hill, A Gnong-Granato, R Serur, G Min and R Szent-Imrey (Beth Israel Deaconess Medical Center/Harvard); P Bachman, J Zinberg, N Hirsh, D, Denneny, L Chang, N Moshfegh and K Young (UCLA); J Brasfield, and H Trotman (Emory University); A Pelletier, K Lansing, H Mates, J Nieri, B Landaas, K Graham, E Rothman, J Hurta, and Y Sierra (University of North Carolina); and A Auther, R Carrion, M McLaughlin, and R Olsen (Zucker Hillside Hospital).

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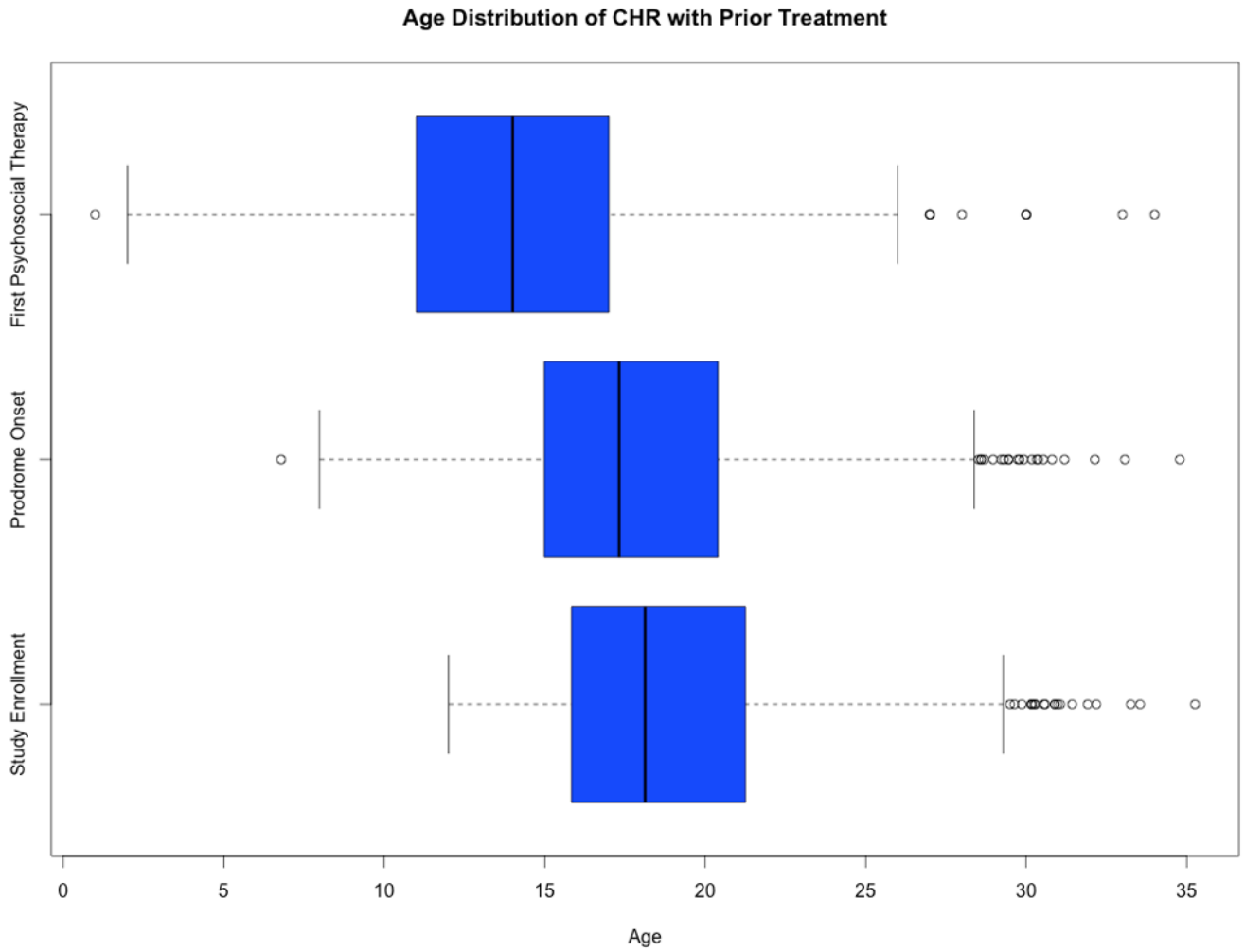

Fig 1.

Boxplots ($N = 591$) of age at initial treatment (First Psychosocial Therapy), psychosis-risk syndrome onset (Prodrome Onset), and NAPLS-2 baseline assessment (Study Enrollment)

Table 1

Demographic and Clinical Characteristics for NAPLS-1 and NAPLS-2 With and Without Lifetime Psychosocial Treatment

Measure	NAPLS-1 (1998-2005)[a]			NAPLS-2 (2008-2013)		
	Total Sample (372[b])	Yes (257)	No (56)	Total Sample (745[c])	Yes (608[d])	No (137[e])
Demographic						
Age, *M* (range, *SD*)	18.2 (4.7)	18.0 (4.8)	19.8 (4.7)**	18.9 (4.3)	18.7 (4.1)	20.1 (4.7)**
% with age <18				48.6	50.8	38.7*
% male	62.1	61.5	55.2	57.0	54.8	67.2**
Race %*						
First Nations				1.7	1.8	1.5
Asian	4.3	(66.7)[f]	(33.3)[f]	7.6	7.8	7.3
Pacific Islander	0.3			0.4	0.3	0.7
Black	9.1	(62.5)[f]	(37.5)[f]	15.2	12.7	26.3*
Central/South American				4.6	4.4	5.1
Caucasian	77.7	(85.3)[f]	(14.7)[f]	57.5	59.5	48.9*
Mixed race	5.9			12.9	13.5	10.2
Ethnicity (% Hispanic)	15.2	14.8	12.5	19.1	18.4	21.9
% Parents College Graduates				64.6	67.1	53.7**
Clinical						
Global functioning *M* (*SD*)		44.9 (11.1)	53.6 (12.7)**	48.43 (10.68)	48.23 (10.7)	49.36 (10.6)
SIPS Symptom Total		38.5 (13.9)	34.1 (15.6)**	38.0 (12.1)	38.3 (12.3)	36.9 (11.3)
Positive Symptom Total		11.8 (3.9)	11.8 (4.5)	11.9 (3.8)	11.9 (3.7)	11.8 (4.2)
Negative Symptom Total		11.9 (6.6)	10.5 (7.4)	11.9 (6.1)	11.8 (6.1)	12.07 (5.7)
Disorganized Symptom Total		6.8 (3.9)	5.0 (3.8)**	5.2 (3.1)	5.3 (3.2)	4.5 (2.6)**
General Symptom Total		8.2 (4.4)	6.8 (4.6)*	9.2 (4.3)	9.3 (4.3)	8.5 (4.3)*
Inclusion diagnosis SPD *N* (%)		(32.4)	(9.1)**	(9.7)	(10.5)	(5.8)
DSM-IV bipolar disorder				56 (7.7)	43 (7.2)	13 (9.6)

Measure	NAPLS-1 (1998-2005)[a]			NAPLS-2 (2008-2013)		
	Total Sample (372[b])	Yes (257)	No (56)	Total Sample (745[c])	Yes (608[d])	No (137[e])
DSM-IV nonBP depressive *N*(%)		(26.5)	(20.0)	443 (60.4)	380 (63.7)	63 (46.3)***
DSM-IV anxiety disorder *N*(%)				412 (56.3)	339 (56.9)	73 (53.7)
DSM-IV ADHD *N*(%)				160 (21.9)	143 (24.0)	17 (12.5)**

Note. Yes: Had any psychosocial treatment prior to baseline assessment; No: Had no prior psychosocial treatment; Inclusion diagnosis SPD: under age 19 with schizotypal personality disorder; DSM-IV: Diagnostic and Statistical Manual of Mental Disorders (4th ed.); nonBP depressive: nonbipolar depressive disorder, ADHD: Attention Deficit Hyperactivity Disorder (all types).

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$ for comparison of subgroups with vs. without lifetime psychosocial treatment

[a] Data from Cadenhead, K.S., Addington, J., Cannon, T., Cornblatt, B., McGlashan, T., Perkins, D., … Heinssen, R. (2010). Treatment history in the psychosis prodrome: characteristics of the North American Prodrome Longitudinal Study Cohort. *Early Intervention in Psychiatry*, *4*(3), 220-226.

[b] Full sample. Treatment data missing for 15.9%.

[c] Sample with psychosocial treatment data.

[d] Missing data on specific variables ranged from 0-3%.

[e] Data on specific variables missing for one participant (< 1%).

[f] Percentages listed here are the percent of the subgroup rather than the entire sample.

Table 2

Psychosocial Therapies Received Prior to and Concurrent with Baseline Assessment

	NAPLS 1 (*N*=372)[a]		NAPLS 2 (*N*=745)			
	Proportion Receiving		Proportion Receiving % (*N*)		No of sessions, mean (*SD*)	
	Lifetime	Baseline	Lifetime	Baseline	Lifetime	Baseline
Any Therapy	82.1	55.0	81.6 (608)	48.5 (361)	56 (96)	64 (96)
Psychotherapy	73.7	46.3	62.8 (468)	33.5 (250)	43 (68)	29 (48)
Group Therapy	5.5	1.9	10.1 (75)	3.5 (26)	40 (80)	32 (44)
Supportive			52.5 (391)	26.0 (194)	42 (66)	29 (43)
School Counseling	15.9	8.3	17.4 (130)	6.7 (50)	59 (114)	61 (118)
Case Management			13.0 (97)	8.1 (60)	22 (51)	13 (31)
Cognitive Behavior Therapy (CBT)			11.4 (85)	5.0 (37)	28 (44)	20 (21)
Family Therapy	8.1	4.2	11.1 (83)	2.7 (20)	27 (57)	29 (61)
Interpersonal			7.4 (55)	3.8 (28)	45 (73)	44 (88)
Stress Management			3.1 (23)	1.1 (8)	14 (15)	19 (19)
Dynamic			2.3 (17)	0.9 (7)	20 (25)	22 (18)

[a]NAPLS 1 *N*=372 but with missing data for 15.9-17.5%. Data from Cadenhead, K.S., Addington, J., Cannon, T., Cornblatt, B., McGlashan, T., Perkins, D., … Heinssen, R. (2010). Treatment history in the psychosis prodrome: characteristics of the North American Prodrome Longitudinal Study Cohort. *Early Intervention in Psychiatry*, *4*(3), 220-226.

Table 3

NAPLS-2 Sample Characteristics by Site for those with Lifetime Psychosocial Treatment (*N* = 608)

Measure	UCLA	Emory	Harvard	ZHH	UNC	UCSD	Calgary	Yale
Age, *M* (*SD*) ***	18.5 (4.4)	21.5 (5.2)	18.8 (3.5)	16.7 (2.0)	20.5 (3.3)	18.2 (3.7)	18.0 (3.6)	18.2 (4.8)
Age Prodrome *M* (*SD*) ***	17.8 (4.6)	20.7 (5.3)	17.3 (4.6)	15.8 (2.3)	18.8 (3.8)	17.7 (3.7)	17.1 (3.5)	17.0 (4.8)
Age at 1st Treatment	15.1 (5.5)	13.9 (5.3)	14.4 (4.3)	12.5 (3.7)	14.9 (5.2)	13.9 (4.8)	13.8 (4.7)	14.2 (5.3)
% with age <18 ***	57.8	31.7	42.3	68.3	20.3	51.5	61.2	62.2
% male	57.8	38.1	55.8	53.3	55.4	61.8	51.5	64.9
Race (%) ***								
American Indian	1.2	0.0	3.8	0.0	1.4	6.0	2.2	0.0
Asian	4.8	8.0	9.5	13.3	4.1	10.5	8.2	5.5
Pacific Islander	2.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
African American *	7.2	39.7	17.3	13.3	18.9	6.0	0.7	13.5
Central/So. American	13.3	1.6	0.0	8.3	2.7	3.0	3.0	2.7
Caucasian *	55.4	42.9	57.7	51.7	68.9	44.8	70.1	70.3
Mixed race *	15.7	7.9	11.5	13.3	4.1	29.9	15.7	8.1
Ethnicity (% Hispanic) ***	34.9	12.7	11.5	25.0	9.5	41.2	3.7	18.9
% Parent College Grad ***	62	58	78	66	81	53	74	60
GAF *M* (*SD*) ***	46.9 (11.4)	48.6 (8.7)	47.6 (8.6)	43.8 (9.1)	50.4 (13.2)	46.5 (6.6)	52.0 (12.0)	46.1 (9.3)
SIPS Total *M* (*SD*) ***	37.1 (12.6)	39.4 (10.4)	39.9 (12.4)	43.4 (12.2)	38.0 (11.3)	35.5 (12.9)	35.1 (13.3)	41.7 (9.9)
Inclusion SPD ***	14.5	28.6	3.8	11.7	8.1	7.4	9.0	2.7
% DSM-IV Bipolar **	1.4	6.3	15.7	13.3	12.2	7.4	3.8	4.0
% DSM-IV Depression	68.1	57.1	64.7	70.0	51.4	70.6	63.4	65.3
% DSM-IV Anxiety ***	61.1	31.7	64.7	71.7	59.5	52.9	48.1	73.3
% DSM-IV ADHD	22.5	17.5	33.3	30.0	25.7	16.2	23.9	25.3

Note. Age Prodrome: Age at onset of initial prodromal syndrome according to the SIPS; Central/So. American: Central or South American; % Parent College Grad: % with at least one parent who was a college graduate; GAF: Global Assessment of Functioning; SIPS: Structured Interview of Psychosis-Risk Syndromes; Inclusion SPD: Included based on age <19 and meeting criteria for schizotypal personality disorder. Data missing on specific variables: 0-3%.

* $p < 0.05$,

** $p < 0.01$,

*** $p < 0.001$ for differences by site

Table 4

Percent of Site Samples with Psychosocial Data who had Received Specific Psychosocial Therapies Prior to Baseline

	UCLA *N* = 102	Emory *N* = 88	Harvard *N* = 54	ZHH *N* = 84	UNC *N* = 85	UCSD *N* = 89	Calgary *N* = 149	Yale *N* = 94
Any Therapy (%) *	81.4	71.6	96.3	71.4	87.1	76.4	89.9	78.7
Supportive (%) *	50.0	33.0	74.1	20.2	70.6	61.8	49.0	70.2
School Counseling (%) *	12.7	9.1	27.8	20.2	8.2	7.9	38.3	6.4
Case Management (%) *	11.8	18.2	14.8	3.6	1.2	4.5	33.6	3.2
Cognitive Behavioral (CBT, %) *	24.5	12.5	18.5	17.9	12.9	1.1	7.4	1.1
Family Therapy (%)	10.8	11.4	9.3	3.6	16.5	4.5	16.1	12.8
Interpersonal (%) *	6.9	9.1	3.7	29.8	3.5	5.6	2.0	2.1
Stress Management (%)	1.0	4.5	1.9	0.0	8.2	0.0	3.4	5.3
Dynamic (%)	4.9	3.4	7.4	1.2	1.2	0.0	1.3	1.1

* $p < 0.05$ for differences by site