LATENT PROFILE ANALYSIS AND CONVERSION TO PSYCHOSIS:
CHARACTERIZING SUBGROUPS TO ENHANCE RISK PREDICTION

Kristin M. Healey

A dissertation submitted to the faculty at the University of North Carolina at Chapel Hill in
partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department
of Psychology and Neuroscience (Clinical Psychology).

Chapel Hill
2016

Approved by:

David Penn

Jonathan Abramowitz

Jean Addington

Kathleen Gates

Eric Youngstrom

ABSTRACT

Kristin M. Healey: Latent profile analysis and conversion to psychosis:
Characterizing subgroups to enhance risk prediction
(Under the direction of David L. Penn)

Background: Groups at clinical high risk (CHR) of developing psychosis are
heterogeneous, composed of individuals presenting with several different clusters of diagnostic
symptoms (e.g., affective symptoms, anxiety symptoms, subpsychotic symptoms). It is likely
that there are subgroups within those at CHR, each associated with different constellations of
symptoms and associated probabilities of conversion.

Method: Latent Profile Analysis (LPA) has shown promise in identifying subgroups with
clinically useful profiles of risk indicators among CHR individuals. The current study used a
LPA model to ascertain subgroups in a combined sample of CHR ($n = 171$) and help-seeking
controls (HSC; $n = 100$). Indicators in the LPA model included baseline Scale of Prodromal
Symptoms (SOPS), total depressive symptoms (CDSS), and neurocognitive performance.
Subgroups were further characterized using covariates measuring demographic and clinical
features. General linear mixed models for repeated measures were used to examine within group
change over time and longitudinal subgroup comparisons on a measure of social functioning.

Results: LPA resulted in three classes: class 1 (mild) had the lowest transition risk
(5.6%), the lowest scores across SOPS symptoms and depression scores, and intact
neurocognitive performance; class 2 (positive-depressive) had a transition risk of 14.2%, the
highest positive symptoms, mild or lesser negative symptoms, and moderate depression; class 3
(negative-neurocognitive) had the highest transition risk (29.3%), the highest negative

symptoms, neurocognitive impairment, and social cognitive impairment. Classes 2 and 3 evidenced similarly poor social functioning.

Conclusions: Results support a subgroup approach to the research, assessment, and treatment of help seeking individuals. Three classes emerged with good separation on a majority of indicator variables, including a class that may be an early manifestation of the deficit subtype. Development of efficacious treatments for early neurocognitive deficits and negative symptoms are indicated. Results underline the profound social dysfunction across help seeking individuals and need for improved treatments.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

AIC	Akaike's Information Criteria
ANCOVA	Analysis of covariance
ANOVA	Univariate analyses of variance
AP	Affective Prosody Task
BIC	Bayesian Information Criteria
BLRT	Bootstrapped Likelihood Ratio Test
CAT	Category instances
CDSS	Calgary Depression Scale for Schizophrenia
CHR	Clinical high risk
CPT-IP	Continuous Performance Test-Identical Pairs
DSM	Diagnostic and Statistical Manual of Mental Disorders
EP	Emotion perception
FEDT	Face Emotion Discrimination Task
FEIT	Face Emotion Identification Task
HSC	Help seeking control
IQ	Intelligence quotient
LPA	Latent profile analysis
LVMM	Latent variable mixture modeling
PAS	Premorbid Adjustment Scale
PREDICT	Enhancing the Prospective Prediction of Psychosis
QLS	Heinrichs-Carpenter Quality of Life Scale
RAVLT	Rey Auditory Verbal Learning Test
SFS	Social Functioning Scale
SIPS	Structured Interview for Prodromal Syndromes
SOPS	Scale for Assessment of Prodromal Symptoms

ssa BIC   Sample-size adjusted Bayesian information criteria

TMT   Trail Making Test

ToM   Theory of mind

UC   Unaffected control

WCST   Wisconsin Card Sorting Test

Introduction

The present study investigated a novel latent profile analysis (LPA) methodology to better understand latent subgroups among a heterogeneous group of individuals at clinical high risk (CHR) of developing psychosis. Subgroups have the potential to enhance specificity in predicting who among CHR individuals is at risk of transitioning to a frank psychotic disorder. Early detection and intervention in emerging psychosis is critical to the aim of reducing societal burden associated with psychotic spectrum illnesses. The development of schizophrenia and other psychotic disorders is often associated with significant impairment in individuals diagnosed with schizophrenia, the cost of which amounts to an estimated $30 billion per year and is likely as a result of decline in social and role functioning (Wu et al., 2002). Early intervention may aid in both prevention of frank psychosis and amelioration of dysfunction that precedes the onset of psychosis. To this end, it is crucial to develop both sensitive and specific criteria that enable early identification that generalizes to clinical settings. While current at-risk criteria are the most reliable predictors of psychosis at present, research thus far indicates that such models need improvement (for a review, see Fusar-Poli, Borgwardt, et al., 2013).

A recent meta-analysis indicated that a fraction of prospectively identified individuals have a true vulnerability to developing schizophrenia, as 36% of CHR individuals transitioned to psychosis after three years (e.g., Fusar-Poli, Bonoldi, et al. 2012). To date, studies investigating predictors of conversion to psychosis and variables associated with functional decline have relied upon logistic regression models (e.g., Klosterkötter, Schultze-Lutter, Bechdolf, & Ruhrmann, 2011; Rurhmann et al., 2010; Seidman et al., 2010). Regression models assume that the risk of

developing a psychotic disorder is evenly distributed throughout CHR individuals (Hagenaars &

McCutcheon, 2002). However, CHR groups are psychopathologically heterogeneous, composed

of individuals presenting with several different clusters of diagnostic symptoms (e.g., affective

symptoms, anxiety symptoms, subpsychotic symptoms) (e.g., Fusar-Poli, Bechdolf, et al., 2013;

Salokangas et al., 2012; Wigman et al., 2012). It is likely that there are subgroups within the

heterogeneous CHR group, each associated with different constellations of symptoms and

associated probabilities of conversion. LPA models may ascertain such subgroups and provide a

more accurate model of who is truly at risk of developing schizophrenia, resulting in a clinically

useful profile of risk indicators.

The introduction will provide an overview of the most relevant background concerning

definition and assessment of the prodromal state, rationale for the utility of subgroup analyses in

CHR, characteristics associated with conversion to psychosis, as well as other features associated

with the CHR state. More specifically, the introduction begins with a definition of the prodromal

state, as well as an overview of common methods used to assess risk for psychosis. This will lead

to a brief review of research supporting the heterogeneity of CHR subgroups and resulting utility

of the latent profile approach. Following this review, there will be a synthesis of studies that have

examined clinical, functional, and neurocognitive indices that may predict transition from CHR

to a frank psychotic disorder. This will lead to a discussion of covariates potentially associated

with the CHR state, such as social cognition, internalized stigma, substance use, racial and ethnic

minority status, and premorbid functioning. Functional trajectory in CHR individuals and

determinants of functioning will then be reviewed. The introduction will end with elaboration of

the present study, aims, and hypotheses.

The Prodromal State

Definition and Assessment of the Prodromal State

Central to the task of early detection and intervention is accurate identification of who has entered the prodromal stage of illness and is at risk of developing a psychotic disorder. At present, the field has identified both a later prodromal phase (CHR) and an earlier prodromal phase. The early prodrome predates the CHR stage, and is characterized by distinct subthreshold symptoms (i.e., basic symptoms) that will be discussed below. This section will briefly summarize definitions of the prodromal state and associated psychotic risk assessments to gain a foundation for understanding the present prediction model and associated indices.

The prodrome is broadly defined as a set of changes from a person's premorbid mental and functional state characterized by sub-threshold psychotic symptoms in the period of time preceding onset of psychosis. While the prodrome was first described in 1932 (Mayer-Gross, 1932), it was not until the late 1980's that research groups empirically investigated early signs of psychosis (Huber & Gross, 1989; Riecher et al., 1989). In the first prospective longitudinal study of risk, it was found that 73% of patients reported experiencing subthreshold symptoms consistent with the prodromal phase, which lasted an average of 5 years (Häfner et al., 1992; Häfner et al., 1998). As a result, several research groups developed and validated operational criteria and assessments to reliably detect individuals at an increased risk of developing psychosis, most commonly referred to in the literature as an "at-risk mental state" (ARMS), "ultra-high risk" (UHR) state, and "Clinical High Risk" (CHR) state. For parsimony, the subsequent text will refer to this later prodromal risk state as CHR.

3

Yung and McGorry (1996a; 1996b) were the first to establish psychometrically validated psychosis risk criteria. The first tool to assess prodromal states was the Comprehensive Assessment of At-Risk Mental States (CAARMS), a prospective interview and rating system (Yung & McGorry, 1996a; Yung & McGorry, 1996b). In the CAARMS, individuals are assessed on 27 symptoms across seven core dimensions, including negative symptoms (e.g., avolition), positive symptoms (e.g., perceptual abnormalities), and general symptoms (e.g., impaired tolerance to normal stress). Symptom ratings are used to determine risk status, which can be further delineated into three main subtypes of prodromal syndrome: attenuated positive symptoms (APS), genetic risk and familial risk for psychotic illness with recent decline in functioning (GRD), and brief intermittent psychotic states (BLIPS) (Yung & McGorry, 1996a; Yung & McGorry, 1996b). Early validation studies of CAARMS criteria evidenced enhanced detection rates of individuals at risk of developing a psychotic disorder, with an incidence of psychosis in the CHR group of 30-50% over two years. This provided support for the idea that prodromal individuals are both identifiable and at imminent risk of developing psychosis (Schaffner & McGorry, 2001).

The establishment of formal risk criteria has allowed for continued investigation of the predictive validity of these criteria, which has answered the question of how many individuals "convert" from a CHR state to a full-blown psychotic disorder (Yung & McGorry, 1996a; Yung & McGorry, 1996b). In the high-risk literature, "conversion" has been defined using varying criteria. Criteria tend to be in accordance with those established by Yung and colleagues (1998) as at least one sub-threshold positive symptom reaching a fully psychotic level multiple times per week, for longer than one week. For example, commonly accepted criteria stipulate that the symptom must occur multiple times per week for at least one month, or at least one day if the

symptom is significantly dysfunctional or dangerous (Miller et al., 2003). As such, individuals that progress from a psychometrically determined risk state to a major psychotic diagnosis will be referred to as "converters," and those that do not will be referred to as "nonconverters."

Researchers have also explored prodromal symptoms that emerge prior to CHR, and referred to such symptoms as "basic symptoms" (BS; Klosterkötter, Ebel, Schultze-Lutter, & Steinmeyer, 1996). BS are comprised of subtler alterations from a person's premorbid state, which can include subjective alterations of perception, language, attention, body perception, and thought processing. BS symptoms cluster into two partially overlapping subgroups of items: cognitive-perceptive (COPER) and cognitive (COGDIS) symptoms (Schultze-Lutter, Klosterkötter, Picker, Steinmeyer, & Ruhrmann, 2007). The COGDIS cluster is the most predictive of subsequent psychosis (Schultze-Lutter et al., 2007). BS appear similar to CHR symptoms conceptually, but are distinct in their independence from content related to reality orientation, abnormal thought content, and insight into symptoms' pathological nature. Rather, BS and CHR symptoms and criteria are considered complementary sets of clinical symptoms, thus both tend to be used when assessing the prodromal state to best predict later conversion (Fusar-Poli, Borgwardt, et al., 2013).

While CHR individuals are at increased risk of developing a psychotic disorder, the vast majority of prospectively identified individuals do not convert (Fusar-Poli, Bonoldi et al., 2012). Such a high proportion of false-positives undermine the utility of the CHR status, and calls for enhanced understanding of the CHR state and specificity in predicting conversion.

Potential Subgroups in CHR Populations

Recently, researchers have called for the reconceptualization of the CHR state as a group broadly at risk of developing various forms of psychopathology rather than at specific risk for

schizophrenia (Fusar-Poli, Yung, McGorry, & van Os, 2014). A recent meta-analytic review found that 73% of presenting CHR individuals meet criteria for a comorbid axis I disorder in addition to CHR criteria (Fusar-Poli, Nelson, Valmaggia, Yung, & McGuire, 2014). Individuals at CHR often present with a mixture of psychopathologies in addition to subthreshold psychotic symptoms, such as anxious/mood disorders, personality disorders, and substance use disorders (Salokangas et al., 2012; Wigman et al., 2012; Woods et al., 2009; Yung et al., 2008). CHR groups are characterized by high distress resulting in help-seeking behaviors, though this distress is likely associated with heterogeneous symptom profiles. Heterogeneity impedes research by obscuring potentially discrete subtypes, which then hinders clinical research, evaluation, and treatment. A recent expert consensus paper confirmed that due to the dearth of support for diagnostic reliability and validity, the Attenuated Psychotic Syndrome was not included in the recent Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5; APA) (Yung et al., 2012). While it remains unknown what disorders CHR individuals may develop, accurate risk criteria are needed to ensure that treatment can be appropriately tailored to the emerging diagnosis.

Thus far, psychosis risk assessment research has primarily focused on identifying endophenotypes rather than transdiagnostic symptomatology. While endophenotypic research has identified several key features associated with the CHR state, results have had limited implications for effective treatment and amelioration of dysfunction thus far. Heterogeneity within the CHR population is acknowledged, but the only widely accepted subgroups are dictated by conceptual genetics (i.e., genetic risk and deterioration (GRD) and schizotypal personality disorder, which are presumed to have genetic components). Seeking subgroups to

investigate symptomatic heterogeneity in CHR groups may lead to better identification of who will subsequently convert to a psychotic disorder.

Researchers have called for two different methods of parsing heterogeneity in CHR to create diagnostically meaningful subgroupings, risk stratification models and latent subgroup models. Risk stratification models are well established in medical disease models (e.g., cancer staging, heart disease risk). Such models use available predictive indices to generate a prognostic risk score for each CHR individual. Prognostic risk scores may be stratified into different risk classes, yielding a "prognostic index" with associated likelihood of transition to psychosis. Thus, this process produces specific, individualized hazard rates informing both degree of risk and time to transition (Ruhrmann, Schultze-Lutter, Schmidt, Kaiser, & Klosterkötter, 2014). Staging was first applied to mental illness risk models by Ruhrmann et al. (2010), which used regression to stratify the CHR group by prognostic index into four risk groups, indicating that a differentiated estimation of current risk may further enhance predictive accuracy. This approach has since been replicated with success in large prospective studies of CHR individuals incorporating additional predictor indices (Michel, Ruhrmann, Schimmelmann, Klosterkötter, & Schultze-Lutter, 2014; Nieman et al., 2013). However, risk stratification methods rely on logistic regression, which assumes that the risk of conversion is evenly distributed throughout the sample (Hagenaars & McCutcheon, 2002). Given the heterogeneity of CHR samples, this assumption may be erroneous, and alternate methodological approaches may be warranted.

Latent subgroup models, such as LPA, aim to identify homogenous subgroups within heterogeneous cohorts. Use of such latent subgroups may permit more accurate assessment of true variance, and thus improve measurement of associations between CHR individuals and outcomes of interest (e.g., symptoms and functioning). Latent subgroups may emerge from the

broader CHR cohort, each with independent, specific symptom constellations with differential associations with later conversion and functional ability. Latent subgroup models may provide a possible path to improved accuracy in identifying who among the CHR group will subsequently convert to psychosis. Recent imaging studies have provided support for latent subgroups underlying CHR populations, finding significant neurobiological heterogeneity in gray matter volume within the CHR group (Modinos et al., 2014). Prior to such findings, the field of imaging posited that CHR individuals share similar neuroanatomical alterations. This work underlines heterogeneous psychopathologies' influence on both psychopathological and neurobiological features, with implications for both psychological and psychotropic treatments.

Latent Profile Methods in CHR

Latent subgroup models are a relatively novel approach in explicating risk in CHR groups, and are within a group of statistical methods known as latent variable mixture modeling (Hagenaars & McCutcheon, 2002). LPA is a specific type of latent variable mixture modeling for use with continuous variable indicators. LPA is also referred to in the literature by other names, most commonly "latent class cluster analysis" (LCCA; Vermunt & Magidson, 2002). When categorical variables are used as indicators, the technique is referred to as latent class analysis (LCA), though LPA and LCA are often used interchangeably irrespective of indicator variable type. Latent variable mixture modeling has only been applied in three studies thus far in CHR groups, all of which utilize continuous indicator variables (Raballo et al., 2014; Valmaggia et al., 2013; Velthorst et al., 2013). Two of these studies investigated direct associations between classes and subsequent conversion to psychosis (Valmaggia et al., 2013; Velthorst et al., 2013) while the other did not (Raballo et al., 2015).

Raballo et al. (2014) sought to identify schizophrenia proneness subtypes among a moderately large sample of CHR individuals ($n = 81$) and individuals with first episode psychosis ($n = 86$). LCA applied to the full sample's 17-item schizophrenia checklist scores resulted in a 3-class model, with the class at the highest proneness of developing psychosis characterized by increased paranoid features (e.g., self-referential ideation, persecutory ideation) and increased disturbed subjective experiences (e.g., alterations in perceptual vividness and subclinical hallucinatory experiences). Of note, there was little differentiation between classes on symptoms relating to functionality or affective disturbances. However, this study was limited by its cross-sectional design and authors did not confirm class membership using follow-up predictor and covariate analyses. Instead, conclusions were drawn from inspection of LCA profile plots rather than empirical statistics.

Two studies aimed to improve the prediction of conversion by investigating the latent subgroups among CHR individuals and their associations with subsequent conversion, and these studies found mixed results (Valmaggia et al., 2013; Velthorst et al., 2013). Velthorst et al. (2013) used a modified latent class factor analysis, a combination of factor analysis and LCA, to investigate latent classes underlying the symptom profiles of 288 CHR and healthy control participants. Using a model that investigated how latent classes cluster based upon the continuous latent factor of subthreshold symptom severity, two distinct latent classes emerged: an "at risk" and a "healthy class." The emergence of two qualitatively different latent classes served to separate CHR individuals from healthy controls, but did little to enhance prediction of subsequent conversion. Thus, Velthorst et al. (2013) were unable to find a relationship between symptom constellations and conversion. One possible reason for this finding is the inclusion of

healthy controls with limited variability. Another issue is the limited diversity of predictive

indices, which may have hindered the study's ability to ascertain vulnerability profiles.

Valmaggia et al. (2013) applied a LCCA approach to a sample of 318 CHR individuals'

CAARMS ratings. The LCCA model sought to clarify the constellation of CAARMS symptoms

that was most likely to precede the onset of psychosis. A 4-class model emerged, each associated

with different risks of conversion to psychosis (class 1, 4.9%; class 2, 10.9%; class 3, 11.4%,

class 4, 41.2%). The subgroup with the highest conversion risk (class 4) was characterized by the

highest symptom ratings, lowest overall functioning score, and highest proportion of

unemployed individuals. The four classes could be best separated by differences in negative

symptom ratings (e.g., anhedonia, alogia, avolition) and behavioral change indices (impaired role

functioning, social isolation), indicating that these variables are useful in determining who is at

risk. Items measuring depression, anxiety, or impaired tolerance to normal stress could not

differentiate risk groups, as the entire CHR sample reported high scores in these domains. Thus,

the LCCA model was able to identify individuals with a specific constellation of negative

symptoms and role impairments that were associated with a higher risk of conversion.

The present paper seeks to extend previous latent variable method findings through the

application of LPA in a large group of prospectively identified CHR individuals. Clinical and

neurocognitive indices will be used to generate latent subgroups, and other demographic and

clinical indices will be used to further characterize LPA subgroups. As such, the subsequent

sections will refer to "indicators" and "covariates" in exploring possible variables for

consideration in the model. "Indicators" are indices to be included in the LCA model to generate

subgroups; whereas, "covariates" are indices used to further characterize associated features of

the subgroups.

Predictors of Conversion to Psychosis

A significant goal in CHR research over the past decade has been to determine who will convert from a CHR state to a full-blown psychotic disorder in prospective, longitudinal studies of CHR individuals. To this end, several clinical trials and longitudinal cohort studies have investigated predictors of conversion among help-seeking individuals meeting CHR criteria. Of note, current conversion estimates and predictive models are generated from samples of distressed, impaired, help-seeking individuals who likely have a higher risk of developing psychosis than individuals randomly sampled in the general population. The number of individuals who meet criteria for CHR in the general population remains undetermined (Fusar-Poli, Borgwardt, et al., 2013). Thus, present CHR criteria is based upon and validated among individuals that present to treatment clinics.

The subsequent text will synthesize the existing literature prospectively exploring the predictive validity of clinical and functional characteristics and neurocognitive features. As CHR symptom criteria provides limited specificity in identifying who will likely convert to psychosis, research continues to employ a "close in" strategy, adding additional risk factors to the model to enhance predictive power (Bell et al., 1992). Of particular interest are prospective CHR studies with large samples (n $\geq$ 60) incorporating a broad range of indices in a stepwise multilevel assessment (Riecher-Rössler et al., 2009). When available, data from meta-analytic reviews will be included. The findings of such work informed the selection of clinical indices for inclusion in the present study's model as indicators and covariates.

Clinical Characteristics

Initial studies predicting conversion included individuals meeting CHR symptom criteria (e.g., APS criteria), BS (e.g., COGDIS criteria), or a combination of the two. Each of the following studies' models included different domains of interest and associated psychometric instruments. This has resulted in the generation of distinct predictive models that are difficult to synthesize. All studies used Cox logistic regression, unless otherwise specified.

The Cologne Early Recognition study found that the presence of a specific constellation of BS symptoms (i.e., including thought interference, visual distortions, and disturbances in receptive language) predicted a diagnosis of schizophrenia within 10 years with a probability of 91% (Klosterkötter, Hellmich, Steinmeyer, & Schultze-Lutter, 2001). Importantly, 96% of individuals with an absence of BS did not go on to develop schizophrenia. A recent review of prospective studies using BS found that COGDIS criteria predicted the onset of first-episode psychosis as well as CHR criteria (Schultze-Lutter et al., 2012). Further, meta-analytic findings indicated the addition of individuals meeting BS criteria at baseline assessment was able to identify individuals that transitioned to schizophrenia specifically rather than other affective psychoses, providing support that the BS is associated with diagnostic specificity (Fusar-Poli, Bechdolf, et al., 2013).

Yung and colleagues (2003) conducted the first prospective study of later phase prodromal CHR individuals. The model with the strongest predictive ability was derived from indices of subthreshold positive and negative symptoms, depressive symptoms, duration of the prodrome, baseline overall functioning, and specific symptoms of attention and disorganization (Yung et al., 2003). Mason et al. (2004) attempted to replicate Yung et al. (2003), and found an altered predictive model including the presence of schizotypal personality characteristics and

various symptoms at an item level. Items included those assessing odd beliefs, role functioning, blunted affect, anhedonia/asociality, and auditory hallucinations. Consistent through these models, as well as in findings from the Early Detection and Intervention Evaluation study, is the key role of attenuated positive symptoms in predicting later conversion (Morrison et al., 2004). This initial foundational work led to larger, longitudinal, multisite studies assessing predictors of conversion to psychosis. Three significant samples will be described in the subsequent text: the North American Prodrome Longitudinal Study (NAPLS; Addington et al., 2007), The Personal Assessment and Crisis Evaluation Program (PACE; Thompson, Nelson, & Yung, 2011), and Prospective European Prediction of Psychosis Study (EPOS; Ruhrmann et al., 2010).

NAPLS prospectively followed 291 CHR individuals and found that five clinical predictive variables significantly accounted for unique variance in conversion. Predictive criteria included increased unusual thought content, increased suspiciousness and paranoia, social functioning impairment, history of substance abuse, and presence of genetic risk for schizophrenia with recent decline in overall functioning (Cannon et al., 2008). Contrary to what might be hypothesized given the relationship between cannabis, amphetamines, and psychotic symptom exacerbation, history of alcohol or drug abuse was a relatively weak predictor in this sample. Subsets of the five variables resulted in significantly enhanced predictive power (up to 80%), but led to a higher rate of false negatives (Cannon et al., 2008). NAPLS is a foundational study in prospective prediction research and led to several replication studies.

Other research groups have provided further evidence for predictive relationships established in NAPLS. The Personal Assessment and Crisis Evaluation Program (PACE) was able to replicate findings using a subset of NAPLS indices, finding that unusual thought content, low overall functioning, and genetic risk for schizophrenia with recent decline in overall

functioning each uniquely predicted later conversion (PACE; Thompson, Nelson, et al., 2011).

The Dutch Prediction of Psychosis (DUPS) study also sought to replicate NAPLS prediction

model, finding that social anhedonia and social withdrawal were the two strongest predictors of

subsequent onset (Velthorst et al., 2009). The Prospective European Prediction of Psychosis

Study (EPOS) included individuals meeting CHR criteria and individuals meeting COGDIS

criteria. EPOS results indicated that six variables best predicted conversion, including sleep

disturbance, overall positive symptom score, bizarre thinking, schizotypal personality disorder

diagnosis, overall functioning in the past year, and years of education (Ruhrmann et al., 2010).

Of note, genetic risk for schizophrenia with recent decline in overall functioning was not

predictive in the EPOS sample.

Demjaha and colleagues (2012) sought to investigate a data-driven dimensional model of

prediction through an exploratory factor analysis of clinical symptom scores to ascertain whether

certain symptom dimension scores predicted subsequent conversion to psychosis better than

others. Principal factor analysis yielded a five-factor solution comprised of negative,

disorganization/cognitive, self-harm, anxiety, and manic symptom dimensions. Cox regression

analyses were conducted using summed dimensional scores; results indicated that the negative

and disorganized/cognitive symptom dimensions were most closely associated with subsequent

conversion.

While it is difficult to compare the utility of indices given that studies did not measure the

same sets of variables, certain indices' predictive validity have been well replicated and warrant

summary. The utility of attenuated positive symptoms has been well established, including the

positive symptom subscale total (Morrison et al., 2004; Ruhrmann et al., 2010; Yung et al.,

2003), unusual thought content/odd beliefs symptom ratings (Cannon et al., 2008; Mason et al.,

2004; Thompson, Nelson, et al., 2011; Ruhrmann et al., 2010), and suspiciousness/paranoia symptom ratings (Cannon et al., 2008; Cornblatt et al., 2015). While the general negative symptom subscale total has limited predictive power with only one early study supporting its utility (Yung et al., 2003), specific items measuring anhedonia (Mason et al., 2004; Velthorst et al., 2009), social dysfunction (Cannon et al., 2008), and withdrawal (Velthorst et al., 2009) appear to be predictive of conversion. Fairly consistent evidence is in support of the utility of overall functioning indices (Ruhrmann et al, 2010; Thompson, Nelson, et al., 2011; Yung et al., 2003) as well as overall decline in functioning combined with genetic risk (Cannon et al., 2008; Thompson, Nelson, et al., 2011). Though BS research is more limited, results generally favor the two-stage model of early and late prodromal phase as assessed by BS and CHR, respectively (Klosterkötter et al., 2001; Klosterkötter et al., 2011). Further, work suggests that using both BS (e.g., COGDIS criteria) and CHR criteria enhances prediction of conversion (Ruhrmann et al., 2010).

Mood Symptoms

It is well accepted that affective symptoms co-occur with subpsychotic symptoms in the prodrome (Yung et al., 2008; Woods et al., 2009). In a retrospective accounting of symptoms, a majority of individuals with schizophrenia (73%) reported a prodromal phase consisting of negative symptoms and non-specific affective symptoms lasting an average of five years (Häfner et al., 1992). A study further investigating the chronology and course of depressive symptoms in a sample of adolescent-onset CHR individuals found that depressive symptoms occur at the earliest stage of the prodrome, earlier than the onset of first CHR positive symptoms (Myles-Worsley, Weaver, & Blailes, 2007; Schultze-Lutter, Rurhmann, Berning, Maier, & Klosterkötter,

2010). Further, they found that depressive symptomatology evidenced a linear increase over time among individuals that later converted to psychosis (Schultze-Lutter et al., 2010).

While the association of depression and CHR symptoms is well established, findings are more mixed regarding depressive symptoms and mood diagnoses' ability to predict subsequent conversion to psychosis. A recent meta-analysis ($k = 11$) found that the presence of comorbid depressive and anxiety disorders did not predict subsequent conversion to psychosis over the course of 3.65 years (Fusar-Poli, Nelson, et al., 2014). Instead, authors theorized that mood and anxiety disorders interact with and have causal impact on CHR symptoms, which may eventually lead to transition to psychosis and functional decline (Fusar-Poli, Nelson, et al., 2014). This is consistent with findings from NAPLS, where diagnostic comorbidity, depression symptoms, and mania symptoms did not differentiate converters from nonconverters (Cannon et al., 2008; Cornblatt et al., 2012). However, findings from the large scale longitudinal EPOS study ($n = 245$) found that while several axis I mood and anxiety disorders were prevalent among CHR individuals, comorbid bipolar or unipolar mood disorders predicted conversion to psychosis while anxiety disorders did not (Ruhrmann et al., 2010). Similarly, Michel et al. (2014) found that converters and nonconverters could be differentiated by baseline presence of recurrent brief depressive disorder. Taken together, while findings predicting conversion from the presence of symptoms of depression and mania are mixed, such symptoms may characterize the early prodromal stage and function as a component in a larger constellation of symptoms (Myles-Worsley, Weaver, & Blailes, 2007; Schultze-Lutter et al., 2010). Alternatively, the prodromal phase of bipolar disorder and psychotic spectrum illness share some degree of positive and general symptomatology (e.g., grandiosity, perceptual abnormalities, sleep difficulties; Olvet et al., 2010) and may evidence a similar pattern of neurocognitive impairment after illness onset

(Bora & Pantelis, 2015). While work regarding incidence rates of psychosis vs. other psychiatric disorders in CHR groups is limited, recent findings indicated that emergent psychosis diagnoses were significantly more likely than any nonpsychotic disorder diagnoses in CHR individuals (Webb et al., 2015).

Neurocognitive Ability

Neurocognitive deficits are regarded as a hallmark feature of schizophrenia (Heinrichs, 2005). In the psychosis literature, neurocognitive ability may be understood as neuropsychological performance on a number of different subdomains, including memory, attention, verbal fluency, executive functioning, and psychomotor performance (Marder, Fenton, & Youens, 2004). In the *Diagnostic and Statistical Manual of Mental Health Disorders* (DSM-5) section III, "impaired cognition" was proposed to be one of eight dimensions of psychosis symptom severity (APA; 2013). The extant literature uses both standardized subdomain scores and composite neurocognition scores (i.e., full scale IQ) in models predicting conversion from baseline neurocognitive ability.

A recent meta-analysis found that CHR individuals evidenced small to medium neurocognitive deficits when compared to healthy controls, across neurocognitive domains (Fusar-Poli, Deste, et al., 2012). A notable exception is IQ score, as estimates of general IQ appeared not to differentiate between converters and nonconverters (Giuliano et al., 2012). The longitudinal research on neurocognitive predictors is still in a nascent stage. Across the extant longitudinal literature comparing baseline neurocognitive deficits of converters and nonconverters, the most promising candidate predictors of subsequent conversion appear to be processing speed, verbal memory, verbal fluency, visual memory, and working memory (De Herdt et al., 2013; Fusar-Poli, Deste, et al., 2012; Keefe et al., 2006; Lin et al., 2013; Pukrop et

al., 2007). However, such work does not consider interactions between clinical symptom criteria and neurocognitive ability.

Of particular interest are studies investigating the predictive validity of neurocognitive deficits in regression models by incorporating a broad range of indices measuring both clinical symptomatology and neurocognitive ability (Cornblatt et al., 2015; Keefe et al., 2006; Riecher-Rössler, 2009; Seidman et al., 2010). Früherkennung von Psychosen used a predictive model including indices of executive functioning, working memory, attention, and general ability in combination with basic clinical symptomatology indices. The predictive model with the strongest sensitivity and specificity included items measuring suspiciousness, anhedonia/asociality, and performance on a measure of executive functioning (Riecher-Rössler et al., 2009). The NAPLS team has also explicated the relationship between baseline neurocognitive performance and subsequent conversion to psychosis, finding that impairments were more significant in converters than in nonconverters, but only modestly (composite neurocognitive score, $d = 0.40$) (Seidman et al., 2010). At a domain level, lower baseline verbal memory predicted time to conversion such that it was associated with more rapid conversion. Cox regression models incorporating neurocognitive indices in the prior multivariate NAPLS prediction model (Cannon et al., 2008) found that neurocognitive indicators did not uniquely predict psychosis beyond clinical indices. Conversely, a recent study by Cornblatt et al. (2015) found that impaired verbal memory enhanced a risk model including other clinical variables. Thus, evidence is mixed regarding the utility of neurocognitive indices as compared to other clinical indices.

European researchers have probed neurocognitive impairments among different theorized phases in the prodrome using both COGDIS and CHR criteria (Frommann et al., 2010; Michel et al., 2014). Frommann et al. (2010) found that the early phase prodrome is characterized by

deficits in executive control/processing speed, greater than and independent from deficits in other domains (Cohen's *d* ~ *0*.50). The later phase prodrome is characterized by verbal memory deficits, executive control/processing speed, and to a lesser degree, working memory deficits. Working memory was intact in the early phase prodrome. Thus, it is theorized that deficits in executive control/processing speed predate first subthreshold positive symptoms, while the introduction of verbal memory impairment in later prodrome marks a disease progression. While these data do not shed light on differences between converters and nonconverters, findings indicate that progressive neurocognitive impairment co-occurs with psychotic disease progression (Frommann et al., 2010).

A more recent study extended the investigation of Frommann and colleagues (2010) with comparisons of converters and nonconverters and Cox regression modeling to stratify risk level using both clinical and neurocognitive variables (Michel et al., 2014). Further, neurocognitive deficits were defined relative to age normed data, such that deficits on neurocognitive domains were entered categorically into the predictive model (present, absent). This model found that the risk of conversion was highest in the presence of concomitant factors of APS criteria, COGDIS criteria, and a processing speed deficit as measured by the digit symbol test.

In summary, while meta-analytic studies have indicated that CHR individuals can be characterized by significant deficits across all domains of neurocognition, specific domains appear to be predictive of subsequent conversion to psychosis. Neurocognitive domains that show the strongest ability to predict conversion in models including broader clinical variables are executive functioning (Riecher-Rössler et al., 2009), verbal memory/fluency (Cornblatt et al., 2015; Seidman et al., 2010), and processing speed (Frommann et al., 2010). Further, some work suggests that the early and late prodrome are characterized by different profiles of

neurocognitive deficits, with early deterioration in processing speed ability and working memory

deficits occurring just before onset of frank psychosis (Frommann et al., 2010).

Covariates Characterizing CHR Subgroups

Social Cognition

Social cognition (SC) is best defined as a set of neurocognitive processes related to understanding, recognizing, processing, and appropriately using social stimuli in one's environment (Adolphs, 2009; Penn, Corrigan, Bentall, Racenstein, & Newman, 1997). Social cognition is a multi-faceted construct consisting of several sub-domains. Domains of interest in the present study include emotion perception (EP; the ability to perceive and appropriately use emotions) and theory of mind (ToM; the ability to infer others' mental states) (Pinkham et al., 2013).

There is evidence that as compared to healthy controls, CHR individuals have deficits in some domains of SC more than others (Thompson, Bartholomeusz, & Yung, 2011; van Donkersgoed et al., 2015). Specifically, a meta-analysis showed medium effect sizes differences between CHR and healthy controls in both ToM and EP ($g = 0.43 - 0.45$). In comparisons between converters and nonconverters, ToM also evidenced a medium effect size ($g = .63$), with converters showing significant impairment compared to nonconverters (Lee et al., 2015). Recent findings from baseline measures of the NAPLS 2 cohort found evidence of significant impairment in ToM and EP in CHR individuals, but the EP deficits did not remain statistically significant when controlling for age and IQ (Barbato et al., 2015). Thus, evidence suggests that social cognitive impairments begin during early phases of illness and are differentially associated with basic neurocognition. Regarding whether performance on tasks of SC enhances predictive models of conversion to psychosis, some work suggests that baseline ToM deficits are predictive

of later conversion (Healey, Penn, Perkins, Woods, & Addington, 2013; Kim et al., 2011). These models remained significant even after the addition of neurocognitive predictor variables. Conversely, other work indicates that baseline ToM performance is not predictive of psychosis (Gill et al., 2014). Thus, evidence is mixed in support of SC's predictive validity in CHR individuals.

Meta-analytic findings indicate SC is more proximal to functional outcome than neurocognition in individuals with schizophrenia spectrum illnesses (Fett, Viechtbauer, Penn, van Os, & Krabbendam, 2011). This underlines the importance of investigating SC in CHR individuals as a potential treatment target to mitigate functional decline. Thus far, only two studies have explored associations between neurocognition, social cognition, and social functioning in CHR individuals (Addington, Saeedi, & Addington, 2006; Barbato et al., 2013b). Addington et al. (2006) found that SC mediates the relationship between neurocognition and social functioning. Barbato and colleagues (2013) attempted to replicate this finding, with results suggesting there is a stronger relationship between social cognition and social functioning than neurocognition and social functioning. However, SC did not predict social functioning in a regression model (Barbato et al., 2013b). Further work is thus needed to determine SC's role in CHR individuals and relationship with long term functioning.

Internalized Stigma

It has been argued that labeling young people at risk of developing psychosis may result in internalized stigma and discrimination similar to that associated with a psychotic disorder diagnosis (Yung, Nelson, Thompson, & Wood, 2010). Recent work has supported this, indicating that an individual with a hypothetical "at-risk" diagnosis evoked greater negative stereotyping than individuals with other, non-psychotic diagnoses (Yang et al. 2013). Measures

of internalized stigma have been validated in CHR individuals with success, and this construct has shown significant associations with depression, social anxiety, and suicidal thinking (Pyle et al., 2015). Using the sample of CHR individuals from the present data set, Stowkowy and colleagues (2015) found that a subscale of items concerning an absence of "control over experiences" was associated with conversion to a psychotic disorder (e.g., "I am powerless over my experiences"). This is consistent with other work that has found that "self-disturbance," or a disruption in basic sense of self, is a phenotypic marker of psychotic spectrum illness vulnerability. Disruptions in "mineness" of one's mental content (i.e., feeling that one's thoughts are his/her own) are disrupted in later phases of the prodrome, and is predictive of later transition to psychosis (Nelson, Thompson, & Yung, 2012). Thus, negative beliefs about illness and associated internalized stigma affect course, chronicity, and may be linked to conversion to a full psychotic disorder.

Substance Use

The harmful effect of substance use in early psychosis is well established with evidence linking substance abuse in first-episode psychosis with significantly greater hospitalizations (Haywood, Kravitz, Grossman, & Cavanaugh, 1995) and increased rates of relapse (Malla et al., 2008). Conversely, literature regarding substance use (e.g., alcohol, cannabis, methamphetamine) in CHR individuals is very limited. Some work indicates that cannabis and methamphetamine usage in adolescence incurs a higher risk of developing schizophrenia (Callaghan et al., 2012; Kuepper et al., 2011). Causality of this relationship is debated, as drug use appears to but one component in a constellation of predictors resulting in transition to psychosis (e.g., Arsenault-Lapierre, Kim, & Turecki, 2004). Prospective studies following CHR individuals over time may clarify the role of substance use this vulnerable stage, however this literature is currently very

limited. Substance abuse data is not routinely measured or incorporated in predictive models, and at times individuals meeting substance dependence criteria are excluded from studies to protect validity of neurocognitive data (Addington, Case, et al., 2014).

Of the studies addressing conversion to psychosis, evidence supporting the predictive validity of indices related to substance use is weak. As previously mentioned, results from NAPLS indicated that history of substance use disorder predicted conversion with other indices, though it was not as strong as other clinical predictors (Cannon et al., 2008). Other large longitudinal studies found that substance abuse was not predictive of conversion to psychosis (Auther et al., 2012; Buchy et al., 2015; Ruhrmann et al., 2010) or social/role functioning (Auther et al., 2012). Of note, a study using the same data set as the present study found that low alcohol use predicted subsequent transition, but no other substances at baseline (Buchy et al., 2014). A recent meta-analysis suggested that there is a dose-response relationship between cannabis use and conversion to psychosis, such that current use (i.e., dependence or abuse), but not lifetime cannabis use increased risk of conversion (Kraan et al., 2015). The complicated relationship among substance use and onset of psychosis indicates further prospective investigation may be needed.

Racial and Ethnic Background

Immigrant and visible minority status is associated with an increased risk of developing psychotic spectrum illnesses (e.g., meta analyses: Bourque, Van der Ven, & Malla, 2011; Cantor-Graae & Selten, 2005). African American individuals are three times as likely as Caucasians to receive diagnoses of schizophrenia, and twice as likely after controlling for socioeconomic status (Bresnahan et al., 2007). When compared to the majority population, ethnic minorities are found to have higher rates of schizophrenia spectrum illnesses but lower

rates of bipolar spectrum disorders (Amad et al., 2013; Veldhuizen, 2009). It has been theorized that ethnic minority status incurs specific risk for psychotic disorders. Numerous hypotheses are postulated to explain potential causes, including (1) incorrect diagnosis of psychotic disorders in minorities based on race/ethnicity and/or cultural misinterpretations (Barnes, 2008), and (2) visible minority status leading to increased experiences of discrimination (Berg et al., 2014). Increased perception of discrimination is associated with greater depressive, positive, and delusional symptoms (Berg et al., 2014; Janssen et al., 2003). In individuals with chronic schizophrenia, recent work has investigated the symptom profiles of visible minorities versus all other patients, and has found that visible minorities had significantly higher scores on items measuring delusions and difficulty in abstract thinking (Berg et al., 2014).

It follows then, that increased perception of discrimination associated with one's visible minority status may be associated with increased symptomatology and risk of conversion in the CHR population. While associations between perception of discrimination and transition to psychosis have not yet been explored, there is some evidence that individuals at CHR experience greater discrimination than healthy controls. However, such perceived discrimination was not related to belonging in an ethnic minority group or identifying as an immigrant (Saleem et al., 2014). Research regarding perceived discrimination and racism in particular is in an early stage, as studies tend to match CHR and healthy control groups on racial/ethnic minority status or employ other methodologies to statistically control for the effect of race. It is possible that visible minority status incurs increased risk and specific constellations of symptoms. Subgroup analyses may shed light on such differences.

Premorbid Functional Ability

Functional impairment is a key feature in the phase prior to onset of frank psychosis, as established by studies of first-episode psychosis (MacBeth & Gumley, 2008). Functional deterioration is associated with an earlier age of onset and poorer general prognosis in individuals with established psychotic disorders (e.g., Strous et al., 2004). While evidence supports the predictive validity of indices of baseline functioning in CHR individuals (e.g., Cannon et al., 2008: Mason et al., 2004; Ruhrmann et al., 2010; Thompson, Nelson, et al., 2011; Yung et al., 2003), less work has focused on the predictive validity of premorbid functioning. Premorbid functioning may be defined as functional ability predating the onset of CHR, across different developmental periods (i.e., childhood).

Two studies from the NAPLS sample prospectively investigated the association between deterioration of functioning in the premorbid phase and conversion to psychosis (Tarbox et al., 2013; Tarbox et al., 2014). The Premorbid Adjustment Scale (PAS; Brill, Reichenberg, Weiser, & Rabinowicz, 2008; Cannon-Spoor, Potkin, & Wyatt, 1982) was used to assess premorbid adjustment in social, academic, and overall functioning across four periods of development (age five to adulthood). Comparisons between converters and nonconverters indicated that converters evidenced significantly higher ratings of social maladjustment in early adolescence (age 12-15). After controlling for baseline subthreshold psychotic symptoms, early adolescent social maladjustment continued to uniquely predict conversion over and above all included symptoms. Further, the strongest predictive model including an array of clinical symptoms was comprised of ratings of early adolescent social maladjustment and suspiciousness (Tarbox et al., 2013). An extension of this study found that social maladjustment in late adolescence (15-18) predicted transition specifically to schizophrenia rather than other psychotic spectrum illnesses (Tarbox et

al., 2014). This work is corroborated by findings from the Copenhagen Perinatal Cohort study, which found that teacher-rated measures of social functioning at age 10-13 predicted later transition to psychosis (Tsuji et al., 2013). Thus, social maladjustment from early and late adolescence appears to confer unique risk beyond academic and total maladjustment ratings.

Functional Trajectory

While conversion to psychosis has assumed primacy in early detection and intervention studies, it is becoming increasingly clear that functional outcome is worthy of investigation. CHR individuals that do not go on to convert to a psychotic disorder often continue to experience significant impairment in social and role functioning (e.g., Addington et al., 2011; Schlosser et al., 2012). However, much less is known of nonconverters, as a systematic review indicated nearly half of CHR studies did not provide relevant characteristics of nonconverters (Simon et al., 2011). In the field of CHR research, functioning is typically parsed into social, role, and global functioning, though there is conceptual overlap between these areas. Social functioning may be defined as competencies related to interpersonal communication, independence in activities of daily living, social activities and recreation (Birchwood, Smith, Cochrane, Wetton, & Copestake, 1990). Role functioning may be defined as instrumental role functioning (e.g., role of student, housekeeper, worker), interpersonal relations, and common activities/hobbies.

Of interest is the degree to which functional outcome is independent from conversion to psychosis in CHR groups. If conversion and functional outcome are redundant, there is no utility in further exploring of indices associated with functional outcome. While functioning indices are predictive of subsequent conversion to psychosis (e.g., Cannon et al., 2008; Thompson, Nelson, et al., 2011; Ruhrmann et al., 2010), less work has investigated whether conversion status is predictive of later functional decline in the full CHR sample. This is clinically relevant; if the constellation of factors contributing to poor role and social functioning is different from those

contributing to conversion to a full psychotic disorder, then such symptom constellations may also be prioritized as treatment targets.

Prospective studies including conversion status in models predicting subsequent functional outcome have explicated this relationship with mixed findings. Carrión et al. (2013) included conversion status in a model predicting social and role outcome from indices measuring symptoms and neurocognition. Role outcome was independent of conversion to psychosis, however social outcome was significantly related to conversion. Findings from the EPOS study indicate that approximately one third of the CHR group experienced poor psychosocial outcome, and that conversion to psychosis did not explain functional outcome (Salokangas et al., 2013). Salokangas et al. (2014) found that conversion status was significantly associated with poor functioning at follow-up as measured by the GAF. However, the GAF includes assessment of symptoms, and thus may not be as valid of a measure as other, more specific role/social functional measures.

Though results are mixed, they indicate that conversion and associated symptomatology do not fully account for poor functional outcome in CHR individuals. A recent systematic review revealed that irrespective of conversion to psychosis, individuals with a history of negative symptoms, disorganized symptoms, and cognitive deficits predating the onset of frank psychosis are more likely to have impaired long term functioning (Cotter et al., 2014). Thus, it is useful to investigate variables apart from conversion status, such as symptom constellations and other clinical features, in order to better explicate contributors to subsequent functioning.

The Present Study

The present study aimed to build upon Valmaggia and colleagues' (2013) model, which included only subthreshold psychotic symptoms as measured by the CAARMS and a single overall functional index as measured by the GAF. Their study is limited by the narrow scope of indicators and covariates, such as lacking specific measures of functioning (e.g., social, occupational), neurocognition, and pre-morbid functioning, all of which are associated with later conversion to psychosis in regression models. The present study sought to enhance the validity of the latent model by adding diagnostically relevant clinical and neurocognitive indices as indicators. The current study aimed to extend prior LCA models through the exploration of the functional trajectory of each latent subgroup. Additionally, the current study sought to further characterize latent subgroups with regard to social cognitive ability, premorbid functioning, internalized stigma, substance use, and racial/ethnic composition.

Aims & Hypotheses

Aim 1: Evaluate the latent profile structure of the CHR group. The first aim was to evaluate the latent profile structure of the CHR group using LPA. As previously discussed, CHR groups are diagnostically heterogeneous, composed of individuals presenting with various clusters of symptoms (e.g., affective symptoms, anxiety symptoms, subpsychotic symptoms) (e.g., Salokangas et al., 2012). It is likely that there are subgroups hidden within the heterogeneous CHR group, each associated with different constellations of symptoms and associated probabilities of conversion. LPA models ascertain such subgroups and thus may provide a more accurate model of who is truly at risk of developing schizophrenia, resulting in a

clinically useful profile of risk indicators. As the current study is a data driven statistical model, the number and size of classes were not known a priori (Collins & Lanza, 2010).

Hypothesis: It was hypothesized that LPA methods will reveal homogenous subgroups from the psychopathologically heterogeneous sample. The number and size of classes were not hypothesized.

Aim 2: Evaluate the risk probability of conversion to a psychotic disorder in each latent class. The second aim was to evaluate the probability that each latent class would later convert to a full psychotic disorder (see definition of "conversion" in methods). Hypothesis: It was hypothesized that the subgroup associated with the highest risk of conversion would include high ratings of: attenuated positive psychotic symptoms (e.g., Yung et al., 2003), unusual thought content (e.g., Cannon et al., 2008), suspiciousness (e.g., Cannon et al., 2008), social anhedonia (e.g., Velthorst et al., 2009), occupational functioning impairment (e.g., Mason et al., 2004), and neurocognitive impairment (e.g., processing speed, verbal memory, verbal fluency, and working memory) (e.g., Frommann et al., 2010; Riecher-Rössler et al., 2009; Seidman et al., 2010). There is currently insufficient evidence to hypothesize what constellation of symptoms would characterize latent classes associated with a lower risk of conversion.

Aim 3: Evaluate indicators' importance in the clustering process. The third aim was to examine the indicators' respective contributions to subgrouping. This enables characterization of differences and response patterns among the subgroups, and specifically what patterns of indicators drove the LPA clustering process. Hypothesis: It was hypothesized based upon prior work (Valmaggia et al., 2013) that negative symptoms (e.g., SOPS negative symptom subscale) would be the most influential in the LPA modeling process. Further, it was hypothesized based on extant work using logistic regression that neurocognitive indices (i.e., verbal memory and

31

processing speed) would also be influential in the LCA modeling process (e.g., Frommann et al., 2010; Riecher-Rössler et al., 2009; Seidman et al., 2010).

Aim 4: Evaluate covariates to further characterize subgroups. The fourth aim was to examine associations between covariates and subgroup membership. Covariates of interest have demonstrated patterns of association with the CHR state that warrant further exploration, including social cognition, internalized stigma, substance use, and racial ethnic minority status. Further, prodromal clinic site (Toronto, UNC, Yale) was included as a covariate to assess potential site effects. <u>Hypothesis</u>: It was hypothesized that the subgroup associated with the highest risk of conversion would be further characterized by impairment in ToM, decreased control over experiences, recent cannabis and alcohol abuse, poor premorbid functioning, and racial ethnic minority status (e.g., Bourque et al., 2011; Callaghan et al., 2012; Healey et al., 2013; Kim et al., 2011; Nelson et al., 2012; Tarbox et al., 2013).

Aim 5: Evaluate the functional trajectory of subgroups, and compare subgroups on functioning over time. The fifth aim was to examine the functional trajectory of each subgroup over time. CHR individuals that do not go on to convert to a psychotic disorder often continue to experience significant impairment in social and role functioning (e.g., Addington et al., 2011; Schlosser et al., 2011). Current research indicates that conversion and associated psychotic symptomatology do not fully account for poor functional outcome in CHR individuals (Salokangas et al., 2013; Salokangas et al., 2014). <u>Hypothesis</u>: It was hypothesized that subgroups would evidence significant between group differences across time points on functional indices, and that subgroups would evidence significant within group change over time.

Exploratory Aims

Exploratory Aim 1: Evaluate the covariates that best predict subgroup membership.

Since no current work has explored the set of indices that best predicts subgroup membership given our predictive model, this exploratory aim served to examine covariates that best predict subgroup membership. This is a worthwhile endeavor, as such analyses will encourage further exploration and characterization of subgroups.

Methods

Sample

The sample consisted of 171 participants (98 males, 73 females) at CHR of developing psychosis with a mean age of 19.8 (SD = 4.5) and 100 help-seeking control (HSC) participants (56 males, 44 females) with a mean age of 19.4 (SD = 3.9) years. All data were collected as a part of NIMH funded, multi-site study "Enhancing the Prospective Prediction of Psychosis" (PREDICT). Several studies have been published using this data set (Addington et al., 2008a; Addington et al., 2008b; Addington et al., 2012; Addington & Barbato, 2012; Barbato et al., 2013a; Barbato et al., 2013b; Barbato et al., 2014; Buchy et al., 2014; Callaway et al., 2014; Couture et al., 2008; Hawkins et al., 2008; Healey et al., 2013; Lyngberg et al., 2015; Stowkowy et al., 2015; Stowkowy & Addington, 2012; Yong et al., 2014).

PREDICT was conducted at the Universities of North Carolina at Chapel Hill (UNC-CH; 62 CHR, 24 HSC), Toronto (69 CHR, 45 HSC), and Yale (40 CHR, 31 HSC). All CHR participants met Criteria of Prodromal Syndromes (COPS) derived from the Structured Interview for Prodromal Syndromes (SIPS: McGlashan et al., 2010). The majority of CHR participants (*n* = 168) met criteria for attenuated positive syndrome (APS). Six participants met criteria for genetic risk and deterioration (GRD), which requires either an affected first degree relative or the participant having schizotypal personality disorder and a 30% drop in functioning on the General Assessment of Functioning (GAF) scale in the past 12 months. Schizotypal personality disorder has evidenced a genetic relationship to schizophrenia in samples of twins, adoptees, and first-degree family members (e.g., Kendler, Gruenberg, and Strauss, 1981).

The help-seeking control group (HSC) was comprised of individuals who had (1) responded to CHR recruitment and (2) presented with prodromal symptoms at phone screen but upon administration of the full interview did not meet prodromal criteria. The HSC group contains the following subgroups: (1) family high risk but no deterioration in GAF ($n = 16$) (2) long-standing attenuated symptoms present for 1 year ($n = 39$) (3) current prodromal symptoms but symptoms were clearly due to another disorder ($n = 2$) (4) had only negative symptoms ($n = 4$) and (5) symptoms that did not meet severity or frequency criterion ($n = 24$). HSC individuals were included as a clinically relevant control group that provides a more stringent test of conversion, as CHR and HSC individuals are more symptomatically similar to one another than to non-psychiatric controls.

The Structured Clinical Interview for DSM-IV (SCID-I: First, Spitzer, Gibbon, & William, 1996) was administered to determine the presence of any axis I disorders. Exclusion criterion consisted of any of the following criteria: presence of an axis I psychotic disorder, IQ less than 70, or a past or current of a clinically significant central nervous system disorder that may contribute to or confound CHR symptoms. Individuals were also excluded for past or current use of antipsychotic medication, as the PREDICT study aimed to examine predictors of conversion to psychosis without the confound of antipsychotic medications. After conducting comprehensive clinical assessments to determine inclusion, participants completed other measures and tasks.

Procedures

The PREDICT study was a longitudinal study of predictors of conversion to psychosis. Study protocols and informed consent documents were reviewed and approved by the institutional review boards of the three participating study sites (UNC-CH, University of

Toronto, Yale University). Formal consenting procedures were conducted with all participants.

Testing occurred over two sessions, typically on the same day but consistently within seven days.

Participants were assigned a clinical rater who administered all semi-structured interviews with

that participant. Raters at all three sites underwent a training program developed at Yale to

properly identify the prodromal syndrome with adequate reliability (Miller et al., 2003). All

raters were experienced research clinicians who demonstrated adequate reliability through the

administration of routine reliability checks. Gold standard post-training agreements on the

discrimination between high risk (5) and psychotic (6) levels of intensity on the positive

symptom items (the critical threshold for determining both initial eligibility and subsequent

conversion status) were excellent (kappa = 0.90).

The DSM-IV diagnoses were established with the SCID-I. Interrater reliability was

determined at the start of the study and subsequent annual retesting by 100% agreement on the

diagnosis and at least 80% agreement for symptom presence. JA chaired weekly conference calls

to review inclusion criteria for all CHR individuals that participated the study. JA trained

research assistants in neurocognitive assessments and DP trained research assistants in social

cognitive assessments.

Follow-up Assessments

All participants were contacted to return for follow-up assessments at six-month intervals

over the course of five years. The primary outcome variable for this study was time from initial

evaluation to conversion to psychosis according to SIPS/SOPS criteria. Given significant

attrition, longitudinal functional data will be used from the first two years of testing only.

Conversion data is provided from the full five years. See Appendix A for a full schedule of

assessments and Appendix B reason for dropout by subgroup (CHR and HSC).

Measures

Symptom measures

Clinical high risk (CHR) symptomatology and criteria. Prodromal syndrome and
conversion criteria were assessed using the SIPS (McGlashan et al., 2010). The SIPS interview
assesses information concerning the presence and severity of 19 distinct symptoms of the Scale
of Prodromal Symptoms (SOPS), each rated on a 7-point scale (0-6), with higher ratings
indicating symptomatology associated with greater intensity and frequency. The prodromal range
is generally considered to lie between scores of 3-5, corresponding with anchors moderate-severe
(Corcoran et al., 2011). The SOPS symptoms are categorized across four domains of
psychopathology, including negative, positive, disorganized, and general symptoms, and can be
summarized accordingly for total domain scores (Miller et al., 2003).

The SIPS also assesses information concerning family history, schizotypal personality
disorder, and global functioning. Results of SIPS interview are integrated to determine the
threshold presence of prodromal syndromes. Three prodromal syndromes are operationally
defined, including attenuated positive symptoms syndrome, genetic risk and deterioration
syndrome, and brief intermittent psychotic symptoms. The attenuated positive symptoms
syndrome (APS) consists of the presence of at least one positive symptom (e.g., suspiciousness
or grandiose ideas), but not at a level at or exceeding psychotic ($\geq$ 6). Genetic risk and
deterioration symptoms syndrome consists of a combination of both functional decline and
genetic risk status. Genetic risk is defined by having either schizotypal personality disorder or a
first-degree family member with a schizophrenia spectrum illness. Brief intermittent psychotic
symptoms state consists of one or more positive psychotic symptoms that exceed the threshold
for psychosis, but a frequency too brief to meet criteria for a schizophrenia spectrum illness.

Conversion. Conversion to psychotic disorder is defined as at least one of the five attenuated positive symptoms reaching a psychotic level of intensity (rated 6) for a frequency of ≥ 1 h/day for 4 days/week in the past month, or that symptoms seriously impacted functioning (e.g. severely disorganized or dangerous to self/others) (McGlashan et al., 2010). Symptoms were assessed with the Scale of Prodromal Symptoms (SOPS), which is comprised of 19 items in four symptom domains: positive, negative, general, and disorganized. In the present sample, 29 participants in the CHR group (14 males, 15 females) and 5 participants in the HSC group (2 males, 3 females) converted to psychosis.

Substance use. Substance use was rated using a well-established rating scale, the Alcohol and Drug Use Scale (AUS/DUS) (Drake, Mueser, McHugo, 1996). The AUS/DUS is a 12-item scale that assesses severity of substance use within the past month. Each item is rated on a 5-point scale (1-5) where a rating of 1 is "abstinent," 2 is "use without impairment," 3 is "abuse," 4 is "dependence," and 5 is "severe dependence." Ratings between 3 and 5 are indicative of behaviors associated with DSM-IV diagnoses of substance abuse and dependence. There is one severity rating at baseline for each of the following substances: alcohol, marijuana, cocaine, opiates, PCP, amphetamines, MDMA/ecstasy, GHB, glue/other volatiles, hallucinogens, and other substances.

Mood symptomatology. Calgary Depression Scale for Schizophrenia (CDSS: Addington, Addington, & Maticka-Tyndale, 1993) is a semi-structured interview used to measure depressive symptomatology within the past week. The CDSS has been validated in CHR individuals (Addington, Shah, Liu, & Addington, 2014), and distinguishes depressive symptoms from negative symptoms better than other measures (Addington, Addington, & Maticka-Tyndale, 1994; Collins, Remington, Coulter, & Birkett, 1996). The CDSS is a 9-item scale that assesses

severity of depressive symptoms during the past week. Each item is rated on a 4-point scale (0-3) with low ratings indicating the absence of a symptom and high ratings indicating a severe symptom. Full administration of the CDSS generates a total score (range: 0-27).

The Young Mania Rating Scale (YMRS, Young, Biggs, Ziegler, & Meyer, 1978) is a semi-structured interview to measure mania symptomatology within the past month. The YMRS is an 11-item scale with 7 items measuring the following: elevated mood, increased motor activity, sexual interest, sleep, language—thought disorder, appearance, and insight. Such items are rated on a 5-point scale (0-4) where a rating of 0 is "absent" and a rating of 4 is "severe". The YMRS also includes 4 items measuring the following on a 9-point scale (0-8; absent-severe): irritability, speech (rate and amount), disruptive-aggressive behavior, and content. YMRS administration results in a total score (range: 0-60).

Internalized stigma. Personal Beliefs about Experiences Questionnaire (PBEQ; Morrison et al., 2013; Pyle et al., 2015) is a revised version of the Personal Beliefs about Illness Questionnaire (PBIQ; Birchwood, Mason, MacMillan, & Healy, 1993). The PBIQ evidenced strong reliability (Birchwood et al., 1993). As the PBIQ was developed for individuals with established schizophrenia, items were removed that were unrelated to the CHR population. Items were as follows, "I will always need to be cared for by professional staff", "People like me must be controlled by psychiatric services", and "If I am going to relapse, there is nothing I can do about it".

The PBEQ is a 13-item measure assessing internalized stigma and cognitive appraisals about CHR experiences. It has been validated for use in the CHR population (Pyle et al., 2015). Each item is a statement concerning stereotypical beliefs about psychosis (e.g., "My experiences may mean that I should be kept away from others"). The respondent must rate the degree to

which this statement is true of them on a 4-point scale (1-4); lower ratings indicate strong

disagreement and higher ratings indicate strong agreement. PBEQ administration results in a

total score (range: 13-52). Three items were summed to create the "control over illness"

subscale, consistent with previous work (Birchwood, Jackson, Brunet, Holden, & Barton, 2012;

Stowkowy et al., 2015).

Social Cognition Measures

Theory of mind (ToM). ToM was assessed with the "Reading the Mind in the Eyes" task

(Eyes Task: Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), a multiple choice task

requiring the participant to infer mental/emotional states from 36 cropped photos of pairs of

eyes. Participants are instructed to select one of four words that best describe what the person is

thinking or feeling based on their eyes. Participants are given a practice item to ensure

understanding of the task. They are provided with standardized definitions of word choices at

their request. The number of correctly identified faces indexes performance (range: 0-36). The

Eyes Task was selected for its frequent usage in schizophrenia spectrum disorders (Pinkham et

al., 2013).

Emotion perception (EP). Face Emotion Identification Task (FEIT) and the Face

Emotion Discrimination Task (FEDT) were used to measure EP in facial expressions (Kerr &

Neale, 1993). Both tasks are comprised of black and white facial photographs presented using a

DVD. The FEIT contains 19 photographs depicting six basic emotions (happy, sad, afraid, angry,

surprised, and ashamed). Faces are presented for 15 seconds each with 10 seconds of blank

screen separating each presentation. FEIT performance is indexed as the total number of correct

facial emotion identifications (range: 0-19). The FEDT is comprised of 30 pairs of faces,

instructing the participant to judge whether the two faces are displaying the same or different

emotions. Emotions are consistent with those depicted in the FEIT. Pairs of faces are presented for 15 seconds each with 15 seconds of blank screen separating each presentation. FEDT performance is indexed as the total number of correct discriminations (range: 0-30).

The Affective Prosody Task (AP) (Edwards, Pattison, Jackson, & Wales, 2001) was used to assess EP in voices. AP stimuli are comprised of audio recordings of three professional actors speaking four simple sentences ("they must stay here", "we must go there", "she will drive fast", and "he will come soon") in voices expressing fear, sadness, anger, surprise, and neutral (no emotion). Each actor is associated with three practice items and 20 test items, resulting in 60 total items (range: 0-60) indexing performance. Responses are coded as correct or incorrect and correct responses are summed for a total score. The reliability coefficient (Cronbach's Alpha) for AP is .85 (Edwards et al., 2001).

All social cognitive tests, ranges, and normative data from healthy control groups are provided in Table 1.

Functioning measures

Social functioning. Social functioning was measured using the Social Functioning Scale (SFS; Birchwood et al., 1990). The SFS is a self-report measure with well-established psychometric properties in individuals with schizophrenia spectrum illnesses (Birchwood et al., 1990) and is commonly used in CHR samples. The SFS is a self-report questionnaire that generates seven subscale scores in addition to a total score: withdrawal/social engagement, interpersonal communication, independence performance, independence competence, recreation, prosocial behaviors, and employment/occupational. The respondent must rate the degree to which this statement is true of them on a 4-point scale (0-3); lower ratings indicate lower functioning (range: 0-223).

The SFS has been criticized for overlap with measures of occupational functioning and thus not being a pure measure of social functioning (Cornblatt et al., 2007). Pijnenborg et al. (2009) performed a principal components analysis of SFS subscales and found that the SFS employment item is a separable subscale. As the present study is interested more in social functioning rather than a combined measure of social and role functioning, the subscale measuring occupational functioning will be removed from the SFS total score (range: 0-213).

Role functioning. The Heinrichs-Carpenter Quality of Life Scales (QLS) measures role functioning (Heinrichs, Hanlon, & Carpenter, 1984). The QLS is a clinician rated, semi-structured interview. The QLS is frequently used in schizophrenia spectrum illnesses, and has evidenced strong convergent validity in associations with performance-based assessments of functional capacity (Sabbag et al., 2011). The QLS is comprised of four items, each rated on a 7-point (0-6) scale. Lower ratings indicate low quality of life and higher ratings indicate greater quality of life. Full administration of the QLS results in the following 4 domain scores: accomplishment, occupational functioning, underemployment, and satisfaction with occupational functioning. Total score is computed by summing accomplishment, occupational functioning, and underemployment items (range: 0-18). The satisfaction with occupational functioning item is only administered if the occupational functioning item is rated at least 3.

Premorbid functioning. Premorbid functioning was assessed using the Premorbid Adjustment Scale (PAS; Cannon-Spoor et al., 1982), which is a semi-structured interview that measures premorbid functioning retrospectively. Participants are rated on social (i.e., sociability/withdrawal and peer relationships) and academic maladjustment across developmental phases. The PAS has well established predictive and convergent validity (Brill et al., 2008), and is frequently used to measure premorbid functioning in schizophrenia spectrum

illnesses. PAS is comprised of 26 items, each rated on a 7-point scale (0-6), with lower ratings

indicating low maladjustment and higher ratings indicating high maladjustment.

The PAS measures four domains in addition to a total score: sociability/withdrawal, peer

relationships, functional ability apart from nuclear family, and ability to function at a

developmentally appropriate socio-sexual level. Four developmental stages are rated, childhood

(up to age 11), early adolescence (age 12-15), late adolescence (16-18), and adulthood (age 19

and older). Subscale scores are computed by dividing the obtained score by the total possible

score for that developmental stage. Thus, subscale scores are as numbers ranging from 0.0 to 1.0,

with lower numbers representing more "adaptive" levels of functioning. Given the association of

early and late adolescence social maladjustment and subsequent conversion, the present study

will use an overall social maladjustment score composed of an average of early and late

adolescent social maladjustment scores (Tarbox et al., 2013; Tarbox et al., 2014).

General scores were not used, in accordance with administration and scoring procedures

outlined by van Mastrigt and Addington (2002). Adult PAS ratings were not included in the

present analyses given the sample's baseline age (mean: 19.63, SD: 4.29) and lack of utility for

44.6% of the total participants (i.e., individuals under age 19).

Neurocognitive measures

Neurocognitive measures were selected on the basis of demonstrated reliability, validity,

absence of ceiling and floor effects in the CHR population, ability to discriminate individuals

with schizophrenia from healthy controls, and appropriateness for administration in individuals

as young as 14 years of age. For the present study, a subset of neurocognitive indicators were

selected from a larger battery (e.g., Barbato et al., 2013a; Barbato et al., 2013b). Tasks were

selected from domains that have evidenced sensitivity to subsequent conversion to psychosis,

such as verbal memory, verbal fluency, processing speed, attention, and executive functioning (Cornblatt et al., 2015; Frommann et al., 2010; Riecher-Rössler et al., 2009; Seidman et al., 2010). Neurocognitive tests, indices, ranges, and normative data from healthy control groups are provided in Table 1.

This study was developed and data collected prior to the Measurement and Treatment Research to Improve Cognition in Schizophrenia initiative and associated battery, which is currently the gold standard neurocognitive assessment in individuals with schizophrenia spectrum illnesses (Green et al., 2004). However, half of the presently included indices are in the consensus battery (i.e., Trail Making Test A and B, Continuous Performance Test—Identical Pairs).

Intelligence (IQ) was measured using the Wechsler Adult Intelligence Test or the Wechsler Intelligence Scale for Children-III, depending on age of the participant. Age-scaled IQ is computed from the following subtests: block design, arithmetic, digit symbol/coding, vocabulary, and information (Wechsler, 1974; Wechsler, 1981)

Data Analyses

Data analyses were performed using Mplus version 7 (Muthén & Muthén, 2012) and

SPSS version 23. Statistical significance will be defined as $p < .05$ unless otherwise specified.

Latent Profile Analysis

Latent profile analysis (LPA) is useful in situations where a group may be better

represented by distinct subgroups or categories of individuals. LPA is used to identify subtypes

of related cases, also known as latent classes. Classes are latent because they are not directly

observable and must be identified based on a pattern of observable indicators (i.e., previously

referred to as predictive indicators). Use of LPA is appropriate when it is hypothesized that

internally homogenous latent subgroups are present, each subgroup responding similarly to a set

of indicators, but not similarly to individuals in other subgroups. Thus, LPA assumes local

independence of indicators, which can be defined as independence of indicators outside of an

individual's latent class. Subgroups are heterogeneous within the larger sample such that

response patterns to indicators can be distinguished from one another based on subgroup

membership (Collins & Lanza, 2010).

The broad objective of LPA is to capture meaningful response patterns within the data, or

to meaningfully cluster individuals based on their responses on indicators of interest. The

number of distinct response patterns determines the number of classes. Thus, LPA is an analogue

of factor analysis; where factor analysis often investigates the latent structure of variables, LPA

and other finite mixture models investigate the latent structure of cases. Similar to factor

analysis, just as the researcher must assign labels to the factors based on factor structure, the

researcher must assign labels to the latent classes that are generated. Similar to interpreting factor loadings to assign indices to factors, an individual's mean posterior probability of class membership must be examined to determine subgroup membership.

Conceptual underpinnings of latent variable models are such that the *latent variable* (i.e., risk subgroup membership) is what affects *indicators* (e.g., suspiciousness, unusual thought content, neurocognitive impairment, etc.). The causal flow is from the latent variable to the indicator variable. In the present study, subgroup membership associated with higher risk of transition would affect increased symptom ratings. Further, there are two influences that determine an individual's observed response on the indicator variable, the individual's latent class membership (i.e., subgroup membership) and error. As error variance is decreased, there is a greater likelihood that the individual's observed responses on indicators are reflections of the individual's latent class. To this end, it is vital to use indices with strong psychometric properties. An advantage of LPA is that, like other latent variable models, LPA estimates and adjusts for measurement error (Collins & Lanza, 2010).

There are several advantages of using LPA over other statistical approaches in the present study. LPA is able to separate groups even if there is overlap. LPA modeling readily includes cases with missing data. LPA can be used with indicators of different types (e.g., continuous, ordinal, categorical), and covariates can be entered into the LPA model to further characterize classes (Dayton & Macready, 1988). Covariates are a key interpretational tool to assist in the investigation of differences between latent classes. Lastly, mixture models (e.g., LPA) do not assume normality of data, linearity, or homogeneity of variances, but rather assumes that there exist k (clusters) normal distributions within the population. This provides distinct advantages over logistic regression models, which requires assumptions are met of linearity with

transformation, normality of residuals, and homoscedasticity, all of which may be violated if latent subgroups exist among CHR individuals (Collins & Lanza, 2010).

Aims & Hypotheses

Hypothesis 1: It was hypothesized that LPA methods will reveal homogenous subgroups from the psychopathologically heterogeneous sample. To evaluate the first hypothesis, an exploratory LPA was conducted with the full sample (CHR and HSC individuals; $n = 271$). The combined sample was used because 5 individuals converted within the HSC group (14.7% of total converters), thus there may be latent subgroups of interest among HSC individuals. If internally homogenous latent subgroups truly exist among the CHR subgroup, they would be identified in applying LPA to the combined sample. The following continuous indicators were entered in the LPA model: SOPS individual symptoms, CDSS total symptoms, and all neurocognitive indicators included in Table 1.

In the present study, the number of classes were not estimated *a priori,* but were ascertained from a combination of model fit statistics and interpretability. The model of best fit (i.e., number of classes) was determined from examinations of all of the following criteria: (1) Akaike's Information Criteria (AIC; Lin & Dayton, 1997), Bayesian Information Criteria (BIC; Schwarz, 1978), and sample size adjusted BIC (ssa BIC; Sclove, 1987) (lower values are indicative of the model of best fit), (2) Bootstrapped Likelihood ratio tests (BLRT) were used to compare n and n -1 number of classes (McLachlan & Peel, 2000), (3) Mean estimated average posterior probabilities of individual cases belonging to each class, (4) Entropy indices, or probability statistics between 0 and 1 (0 = low classification utility; 1 = higher classification utility). Both (3) and (4) are considered indices of model classification utility and rely on the

estimated posterior probabilities. Substantive interpretability and parsimony of the models were also considered in model selection.

Hypothesis 2: It was hypothesized that the subgroup associated with the highest risk of conversion will include: high attenuated psychotic symptoms (e.g., unusual thought content, suspiciousness, social anhedonia, and occupational functioning), and neurocognitive impairment (e.g., processing speed, verbal memory, verbal fluency, and working memory). To test hypothesis 2, after latent classes were determined using the procedures outlined above, the risk of conversion associated with each subgroup was computed. First, risk was computed as the % of converters in each subgroup out of the total subgroup n, and transition rate was compared across classes using χ^2 tests of significance. Second, risk was computed using Kaplan-Meier survival analysis to investigate rates of conversion over the full five years of assessment (Kaplan & Meier, 1958). To account for attrition and in accordance with statistical procedures as outlined by Kaplan and Meier (1958), study dropouts were counted as "survivors" (nonconverters) and were deleted from the number "at risk" at the following time point. The results of the Kaplan-Meier curve were also interpreted.

Hypothesis 3: It was hypothesized that negative symptoms (i.e., SOPS negative symptom subscale) and neurocognitive indicators (e.g., verbal memory and processing speed) will be the most influential in the LPA modeling process. To test hypothesis 3 and assess the importance of indicators in the LPA process, subgroups were compared on all indicators using univariate analyses of variance (ANOVAs) and effect sizes (r^2). When appropriate, pairwise comparisons were conducted using Bonferroni correction for multiple comparisons. Further, LPA generated an indicator profile depicting all included indices (e.g., SOPS symptoms, CDSS total symptoms, neurocognitive scores) using estimated sample means

from each subgroup. This indicator profile was visually inspected to discern which indicators were influential in the LPA modeling process (Collins & Lanza, 2010).

Hypothesis 4: It was hypothesized that the subgroup associated with the highest risk of conversion would be further characterized by impairment in ToM, decreased control over experiences, recent cannabis and alcohol abuse, poor premorbid functioning, and racial ethnic minority status. To test hypothesis 4, univariate analyses of variance (ANOVAs), independent samples *t* tests, and chi-square tests of significance were conducted to compare the subgroups on the following continuous/categorical covariates: ToM score, facial EP total score, AP score, PBEQ total score, PBEQ "control over experiences" subscale total, AUS/DUS item scores, PAS social and academic maladjustment subscale scores for developmental phase (i.e., child, early adolescent, late adolescent) and combined early/late adolescent social maladjustment score, and self-reported race/ethnicity and other demographic information (e.g., age, sex, parental education). When appropriate, pairwise comparisons were conducted using Bonferroni correction for multiple comparisons. Z-square cell comparison tests with Bonferroni correction were used to probe significant omnibus chi-square tests and determine which groups were significantly different from one another (Goodman, 1969; Sharpe, 2015).

Hypothesis 5: It was hypothesized that subgroups would evidence significant between group differences across time points on functionality, and that functional level will change over time within each subgroup. To test hypothesis 5, longitudinal functioning was investigated in each of the subgroups generated in the LPA model. Prior to this, a test of attrition bias was conducted as this sample evidences significant attrition. Independent samples *t* tests and/or chi-square tests were conducted to compare individuals with and without usable data (e.g., having at least one additional follow up visit) on the following indices: gender, age, parental

education, SOPS positive symptom subscale, total social functioning (SFS) score (without employment item), and total role functioning (QLS) score. Generalized linear mixed models (GLMM) for repeated measures analyses were then used to examine change over time (baseline, 6 months, 12 months, 18 months, 24 months) and group differences for ratings on the functional indices. Least Square Means (LS-Means) were obtained from the mixed models with Hochberg's correction for multiple comparisons. Hochberg's correction was selected for its conservative estimates in GLMM (Hothorn, Bretz, & Westfall, 2008).

Exploratory Analyses

Exploratory Aim 1: Evaluate the covariates that best predicted subgroup membership. Exploratory aim 1 was assessed using multinomial regression analyses. Class membership was the dependent variable, and all LPA covariates evidencing significant group differences (hypothesis 5) were entered as independent variables and regressed on class membership status. As this was an empirically driven aim rather than hypothesis driven, forward stepwise model selection was used to enter predictors into the regression model to assess which indicators explained the most variance in subgroup membership. Wald Chi-square tests of significance were examined to determine which indicators are significantly contributing to subgroup membership. Odds ratios and associated modeled probability table were examined to interpret results.

<center>Results</center>

Primary Analyses

Latent profile analysis (LPA)

LPA model selection. LPA analyses were conducted using Mplus version 7 with Mixture

Add-On (Muthén & Muthén, 2012). Raw scores were used in accordance with recommendations

of Muthén (2001), as variable standardization results in analyses using a correlation matrix,

which are only adequate for scale-free data only (Muthén & Muthén, 2000). Indicators in the

current model are, on the other hand, not scale-free; and rather than seeking to explain a

correlation matrix, LPA seeks to explain the covariance matrix of observed indicators with latent

variables (Muthén & Muthén, 2000). Neurocognitive variables were not age standardized prior to

entry in the LPA model due to non-normal distributions and scarcity of adequate age adjusted

norms. Thus, age was investigated as an inactive descriptive covariate in LPA analyses.

Though a greater number of potential indicators were available for inclusion in the model

(e.g., premorbid functioning), only a subset of the initially proposed indicators were selected.

Balance must be achieved among sample size, number of indicators, and parameters to be

estimated for sufficient statistical power (Tein, Coxe, & Cham, 2013). The addition of redundant

or unnecessary indicators to the LPA model, specifically in a model with a small sample size

(i.e., $n < 1000$), often results in poor and inaccurate model fit. As such, indicators were limited to

those theorized to be most closely influenced by latent subgroup membership (sub-psychotic

symptomatology, neurocognitive performance, depressive symptoms). Neurocognitive indicators

were selected from domains with well-established relationships with conversion to psychosis,

<center>51</center>

such as executive functioning, attention, (e.g., Riecher-Rössler et al., 2009), verbal memory and fluency (Cornblatt et al., 2015; Seidman et al., 2010), and processing speed (Frommann et al., 2010). Twenty-six total indicators were included in the model, including all SOPS symptoms measuring prodromal symptoms (19), CDSS total score measuring depressive symptoms (1), and neurocognitive scores (6).

Table 2 provides the fit indices from the LPA. Five models were estimated specifying between one and five latent classes. The sixth model would not estimate due to too few individuals in class 6 ($n = 8$). The AIC, BIC, and ssa BIC values decreased with each successive class addition and thus did not readily discriminate a model of best fit. The BLRT value remained significant ($p < .0001$) with each class addition to the model. Entropy values remained high for each class model ($k = 2$-5), ranging from 0.88-0.93. Using only available information criteria and likelihood ratio tests, the 5-class test would be selected. However, accepting the model associated with the lowest AIC, BIC, ssa BIC and BLRT values does not prioritize model interpretability and parsimony. Further, the large number of indicators in the present model may artificially result in a large k class model when a more parsimonious model may be better fitting and more clinically meaningful (Tein et al., 2013).

An alternative interpretation of information criteria (e.g., AIC, BIC, ssa BIC) and log likelihood value is to plot the values in graphical form (e.g., scree plot) (Nylund, Asparouhov, & Muthen, 2006). Model fit indices are plotted against the number of latent classes and examined for the "leveling off" point of the curve. Identifying the model associated with a subsequent decrease in slope may provide a model that balances model fit statistics and parsimony (Nylund, Asparouhov, & Muthen, 2006). Models identified through scree plot consensus are then examined for theoretical interpretability and meaningful class separation across indicators.

Figure 1 provides scree plots of AIC, BIC, ssa BIC, and log likelihood value associated with each class model. The leveling off point of the curves occurred at three classes in each of the scree plots, indicating that significant improvements in model fit are not gained with further class additions to the model (i.e., $k > 3$). The three-class solution indicated high quality of classification, with an adequate entropy score of 0.884 and mean posterior probabilities of class membership ranging from 93.9% to 95.6%. Table 3 summarizes the latent class membership based on estimated posterior probabilities. Indicators evidenced meaningful class separation. Interpretability of the model will be discussed in the subsequent sections.

Individuals were assigned to classes as indicated by the highest posterior probability value as such: class 1 (mild symptom cluster) was the largest class with 124 individuals, followed by class 2 (positive-depressive cluster) with 106 individuals, and class 3 (negative-neurocognitive cluster) with 41 individuals.

Classes and risk probability. The overall transition rate in the full combined sample at two years was 12.5% (converters $n = 34$, combined sample $N = 271$). Conversion rate to psychosis significantly differed across groups in the overall model ($\chi^2(2, N = 271) = 16.08$, $p < .001$). Pairwise comparisons indicated that conversion to psychosis was more likely in individuals in class 3 (negative-neurocognitive; transition risk 29.3%, $n = 12$ converters) than class 1 (mild; transition risk 5.6%, $n = 7$ converters) at the $p < .05$ level. There were no significant differences in other pairwise comparisons between class 2 (positive-depressive; transition risk 14.2%, $n = 15$ converters) and class 1 (mild) or class 3 (negative-neurocognitive).

Kaplan-Meier survival curve. Thirty-four of the 271 individuals experienced conversion to psychosis with a mean (SD) time to conversion of 359.3 (319.2) days since baseline (range: 27-1185 days). The nonconverters ($n = 237$) were followed up for a mean (SD)

of 441.1 (461.9) days since baseline. There were no significant differences regarding the age of conversion to psychosis among class 1 (M_1 = 20.01, SD = 2.73), class 2 (M_2 = 21.46, SD = 4.92), and class 3 (M_3 = 19.96, SD = 4.48) ($F(2,31)$ = 0.47, p = 0.629).

The overall model evidenced a significant Breslow (Generalized Wilcoxon) statistic, indicating significant differences early in the survival curves (χ^2(1, N = 271) = 10.97, p < .001). The overall model also evidenced a significant Tarone-Ware test, indicating significant differences in the intermediate area of the survival curves (χ^2(2, N = 271) = 11.45, p < .001). Lastly, the overall Log Rank (Mantel-Cox) comparisons were also statistically significant (χ^2(2, N = 271) = 11.99, p < .001), indicating that the survival curves were significantly different during the later time period of the study.

Figure 2 depicts the results of the Kaplan-Meier survival analysis, plotting the percentage of individuals in each class who did not experience conversion to psychosis (nonconverters) at each assessment during the 5-year follow up period. Individuals who do not experience conversion to psychosis contribute to the survival model until they are no longer available for observation, at which point they are censored.

Areas of increased slope may be interpreted as increased rates of conversion during that time period. Class 3 (negative-neurocognitive) and 2 (positive-depressive) evidenced high rates of transition during the early follow up period (6 months, approximately 10% drop in survival). After 6 months, Class 2 evidenced deceleration in transition rate compared to class 3 (negative-neurocognitive). Class 1 (mild) reached the 10% drop in the survival curve until 18 months, indicating that baseline mild symptoms and minimal neurocognitive impairment are associated with a subsequent transition to psychosis. Class 1 (mild) evidences an overall lower transition rate, with a notable increase at 36 months. Classes are well separated in transition rate in the

intermediate and later areas of the curve. However, given the high rate of attrition in the present sample, the implications of these findings are tentative as the sample size is smaller in the final three years of study and dropouts that may have transitioned to psychosis were censored.

Characteristics of the three-class solution. Table 4 shows the results from the latent profile analysis (i.e., estimated means and standard errors). Figures 3 and 4 show the latent profile plots of the estimated means for each class. To assess the importance of indicators in the latent profile process, we estimated the explained variance using univariate ANOVAs, the results of which are also provided in Table 4. Pairwise comparisons were conducted using Bonferroni correction for multiple comparisons. ANOVA results indicated that all included indicators were influential in the clustering process, with the exception of SOPS symptoms grandiose ideas (P3) and bizarre thinking (D2).

Examinations of the SOPS latent profile plot and pairwise comparisons indicated that class 1 (mild) evidenced the lowest prodromal symptom scores across SOPS symptoms and CDSS total score. Class 1 (mild) largely evidenced SOPS estimated means around a rating of 1, which connotes a symptom that occurs rarely (e.g., less than monthly) and is of questionable presence. Class 1 (mild) evidenced slightly higher ratings (around 2) in symptoms measuring unusual thought content, suspiciousness, and perceptual abnormalities, which suggests such positive symptoms occur monthly and are of mild intensity. Lastly, class 1 (mild) evidenced a level of depression comparable to healthy control sample norms (normative mean: 2.6, SD: 2.7; Müller et al., 2005)

The estimated means associated with class 2 (positive-depressive) were remarkable for having significantly greater ratings on suspiciousness/persecutory ideas (P2) than classes 1 (mild) and 3 (negative-neurocognitive). Class 2 (positive-depressive) evidenced significantly

greater ratings than class 1 (mild) on unusual thought content and perceptual abnormalities, but not class 3 (negative-neurocognitive). While class 2 (positive-depressive) was not statistically significant from class 3 (negative-neurocognitive) in other positive symptom pairwise comparisons, inspection of the latent profile plot indicated that class 2 (positive-depressive) tended to have greater ratings (P1-P4) than classes 1 (mild) and 3 (negative-neurocognitive). Class 2 (positive-depressive) was also noted to have significantly higher ratings of depression, as they had a moderate SOPS dysphoric mood rating and higher CDSS total scores. Individuals in class 2 (positive-depressive) also evidenced significant sleep disturbance compared to other classes. Class 2 (positive-depressive) had negative symptom ratings at or less than a rating of 2 (mild), with the exception of occupational functioning, which neared a rating of 3 (indicating moderate impairment).

Class 3 (negative-neurocognitive) membership was associated with the highest ratings in a majority of symptoms in the negative symptom domain (e.g., ratings between 2-4), and to a lesser degree, was associated with the disorganized symptom domain. This was confirmed statistically through pairwise comparisons, as class 3 (negative-neurocognitive) showed significantly greater ratings than classes 1 (mild) and 2 (positive-depressive) on symptoms of social anhedonia (N1), expression of emotion (N3), ideational richness (N5), and occupational functioning (N6). Classes 2 and 3 evidenced ratings of comparable magnitude in avolition (N2) and decreased experience of emotions (N4). Classes 2 (positive-depressive) and 3 (negative-neurocognitive), on the other hand, were not well distinguished from each other in ratings of disorganized communication (P5), motor disturbances (G3), and impaired tolerance to normal stress (G4).

Regarding neurocognitive performance, classes 1 (mild) and 2 (positive-depressive) performed comparably across indices. On Trails B, class 2 (positive-depressive) evidenced increased performance compared to class 1 (mild), though this finding was no longer significant after correction for multiple comparisons ($p = .054$). Class 3 (negative-neurocognitive) evidenced significant impairment compared to classes 1 (mild) and 2 (positive-depressive) across all measured neurocognitive indices ($p < .05$). As the neurocognitive test scores were not corrected for age before entry into the LPA model, comparisons among classes on neurocognitive indices were also run as analyses of covariance (ANCOVAs) with age entered as a covariate. All overall models remained significant ($p < .001$) and pairwise comparisons using Bonferroni correction for multiple comparisons remained significant ($p < .05$), indicating that classes significantly differed on neurocognitive performance when accounting for variance related to age.

Characterizing the three-class solution with covariates. To further characterize associated features of classes, we conducted ANOVAs and chi-square tests of significance to compare classes on a variety of different covariates. The results of demographic characteristics are provided in Table 5 and clinical covariates are provided in Table 6.

Demographic characteristics. There were significant differences in age and clinic location between the three classes. Pairwise comparisons indicated that individuals in class 3 (negative-neurocognitive) were significantly younger than individuals in class 2 (positive-depressive). Individuals from Yale were more likely to be classified in class 3 (negative-neurocognitive) and less likely to be classified in class 2 (positive-depressive). Conversely, individuals from UNC were more likely to be classified in class 2 (positive-depressive) and less likely to be classified in class 3 (negative-neurocognitive).

Given site effects, comparisons among classes on indicators (SOPS symptoms, CDSS total score, neurocognitive indices) were also run as analyses of covariance (ANCOVAs) with site entered as a covariate. Overall models that had evidenced significance (e.g., Table 4) remained statistically significant ($p < .01$) and all pairwise comparisons using Bonferroni correction for multiple comparisons remained significant ($p<.05$), indicating that classes significantly differed on indicators when accounting for variance related to site.

Classes did not evidence significant differences in racial/ethnic composition, identification as Hispanic/Latino, or parental education. Racial/ethnic background was recoded from a variable with five levels to a dichotomous "white" and "other race" variable. Classes again did not evidence significant differences using recoded variables.

Clinical characteristics. There were significant differences among classes at baseline regarding risk group characterization (HSC vs. CHR). CHR individuals were significantly more likely to be categorized in class 2 (positive-depressive) than individuals in class 1 (mild). Conversely, HSC individuals were more likely to be categorized in class 1 (mild) than class 2 (positive-depressive).

Classes evidenced significant overall models concerning ratings of internalized stigma (PBEQ) total score, the "control over experiences" subscale (PBEQ), and total mania score (YMRS). Classes 2 (positive-depressive) and 3 (negative-neurocognitive) were characterized by significantly greater YMRS total scores and indices of internalized stigma at baseline compared to class 1 (mild). There were no significant differences between classes 2 and 3.

Regarding baseline alcohol and drug use, overall ANOVA models were statistically significant for MDMA/ecstasy and "other" substance usage. Pairwise comparisons for MDMA/ecstasy usage did not reach significance; however, class 2 (positive-depressive) was

significantly more likely to engage in "other" substance use compared to class 1 (mild). The following substances (n = frequency) were reported in class 2 (positive-depressive): ketamine (n = 3), sleeping pills (n = 2), morning glory seeds (n = 1), salvia (n = 1), and nitrous oxide (n = 1).

Functioning. Classes evidenced significant overall group differences across all subscale ratings of premorbid adjustment (PAS). From childhood through early adolescence (i.e., up to age 15), individuals categorized into class 3 (negative-neurocognitive) showed both significant social and academic maladjustment scores compared to classes 1 (mild) and 2 (positive-depressive). Classes 1 (mild) and 2 (positive-depressive) showed comparable levels of impairment during this time period. Regarding late adolescence social maladjustment ratings (i.e., age 16-18), class 3 (negative-neurocognitive) continued to perform at the most impaired level with respect to classes 1 (mild) and 2 (positive-depressive). However, class 2 (positive-depressive) evidenced significant social maladjustment compared to class 1 (mild), thus first began to evidence a pattern of premorbid maladjustment. The averaged early and late adolescence social maladjustment score showed a pattern consistent with late adolescence social maladjustment. This pattern was similar regarding academic maladjustment in late adolescence, as class 3 (negative-neurocognitive) evidenced the greatest impairment; however, the pairwise comparison between class 2 (positive-depressive) and class 1 (mild) only approached significance (p = .059).

Regarding baseline role functioning, class 3 (negative-neurocognitive) evidenced significantly impaired QLS ratings measuring occupational functioning, accomplishment, and underemployment compared to classes 1 (mild) and 2 (negative). Class 2 (positive-depressive) evidenced functional impairment when compared to class 1 (mild) on accomplishment and underemployment and total QLS score. Role satisfaction comparisons were conducted between

classes for individuals who were rated at least 3 on the occupational functioning item (86.7% of class 1, 75.8% of class 2, 57.9% of Class 3). Class 1 (mild) reported significantly greater role satisfaction than class 2 (positive-depressive). The pairwise comparison between class 1 (mild) and class 3 (negative-neurocognitive) only approached significance ($p = .053$), possibly due to the decreased sample size of class 3 ($n = 22$) and associated low power.

$\quad$ *Social cognition.* Classes evidenced significant overall models measuring group differences in performance on the Eyes Task, FEIT, and AP. The overall model for the FEDT approached statistical significance ($p = .053$). Pairwise comparisons indicated that class 3 (negative-neurocognitive) evidenced significant social cognitive impairment compared to classes 1 (mild) and 2 (positive-depressive) across measures. Class 1 (mild) and 2 (positive-depressive) evidenced no significant differences. Thus, class 3 (negative-neurocognitive) evidenced impairment in both theory of mind and emotion perception.

$\quad$ As social cognitive performance tends to be associated with age, comparisons among classes on social cognitive indices were also run as analyses of covariance (ANCOVAs) with age as a covariate. Overall models for Eyes Task, FEIT, and Affective Prosody Task remained significant ($p < .001$) and pairwise comparisons corrected for multiple comparisons remained significant ($p < .05$), indicating that classes evidenced significant differences in social cognitive performance when accounting for variance related to age.

$\quad$ Social cognitive performance also tends to be associated with neurocognitive ability, thus comparisons among classes on social cognitive indices were also conducted as ANCOVAs with age-scaled IQ score included as a covariate. Overall models for Eyes Task and Affective Prosody task remained significant ($p < .05$); however, FEDT was no longer statistically significant. Pairwise comparisons for Affective Prosody remained significant ($p < .05$). The Eyes Task

contrast between class 2 (positive-depressive) and 3 (negative-neurocognitive) was no longer statistically significant. Results indicate that significant group differences in facial emotion perception performance and ToM may be partially accounted for by neurocognitive ability; however, not affective prosody.

Intelligence. Classes were also compared with respect to age-scaled IQ Score. Classes were significantly different, with specific impairment in class 3 (negative-neurocognitive) compared to classes 1 (mild) and 2 (positive-depressive). Classes 1 (mild) and 2 (positive-depressive) evidenced comparable performance. Results are consistent with those from neurocognitive indicators.

Functional trajectory of subgroups. Two hundred and forty-six total individuals (139 males and 107 females) completed the SFS at baseline. Of those 246 participants, 144 completed the 6-month follow up, 114 completed the 12-month follow up, 84 completed the 18-month follow up, and 59 completed the 24-month follow up. Reasons for dropout are provided in the Appendix B. Given the significant dropout rate in the present sample, a test of attrition bias was conducted to compare individuals with usable longitudinal data (e.g., data from at least baseline and one other time point; "non-dropouts", $n = 173$) and those without usable longitudinal data (e.g., individuals with baseline data only; "dropouts", $n = 73$). Chi-square tests were conducted to compare dropouts and non-dropouts on sex and parental education. Independent samples t-tests were used to compare groups on age, SOPS positive symptom subscale, total social functioning (SFS) score (i.e., without occupational subscale), and total role functioning (QLS) score (items 1-3). There was a significant difference in QLS total score for non-dropouts ($M_{non-dropouts} = 13.11$, SD = 4.72) and dropouts ($M_{dropouts} = 11.34$, SD = 5.16), such that dropouts evidenced significantly impaired role functioning as compared to non-dropouts ($t(244) = -2.61$, p

= .01). There were no other significant differences between groups. Therefore, the subsequent functional trajectory analyses will include only the SFS total score with occupational functioning subscale removed, given significant differences in role functioning between dropouts and non-dropouts.

Table 7 provides the mean estimates, standard error, and n for each class at each time point. Table 8 shows the results from the generalized linear mixed model (GLMM) for repeated measures analysis between groups across time points. At both baseline and the 6-month follow up assessments, class 1 (mild) evidenced significantly higher SFS total score than classes 2 (positive-depressive) and 3 (negative-neurocognitive). There were no significant group differences between the 12-18 month follow up assessments. At 24-month follow up, both classes 1 (mild) and 2 (positive-depressive) evidenced significantly higher SFS total scores than class 3 (negative-neurocognitive).

Table 9 shows the results from the GLMM for repeated measures analysis within groups to assess change over time. Class 2 (positive-depressive) evidenced significant improvement in SFS score between baseline and 24-month follow up. Improvement between baseline and 12-18 months neared significance after correction for multiple comparisons (p = .053 - .082). Classes 1 (mild) and 3 (negative-neurocognitive) evidenced no significant changes in social functioning over time. Figure 5 plots estimated means for each class over time to visually represent the data.

Exploratory Analyses

Contribution of covariates to group membership. To investigate the covariates that best predicted class membership, a multinomial logistic regression (MLR) analysis was conducted with class membership as the dependent variable. To reduce the number of independent variables in the model, covariates were selected that evidenced significant group

differences in prior analyses, and total scores were used when appropriate: YMRS total score, MDMA/ecstasy use, other substance use, PAS subscales (child and early adolescent subscales only), QLS Total score, Eyes Task total score, FEIT total score, and AP total score. Cognitive variables (e.g., IQ score) were not included in the MLR model, as this would be redundant with the neurocognitive indicators entered in the initial LPA model. Forward stepwise selection was used, as this method is suitable for use with a large number of independent variables. Of note, MLR utilizes listwise deletion and missing data was not imputed ($n = 69$), as this is an exploratory analysis. Thus, the sample size is smaller than the original sample (class 1, $n = 96$, 77.4%; class 2, $n = 73$, 68.9%; class 3, $n = 33$, 80.5%).

The overall MLR model was significant, indicating that the current model predicts class membership significantly better than the null model ($\chi^2(14) = 103.43$, $p < .00001$). The best model based on forward stepwise model selection included the following covariates: PAS child academic maladjustment score ($\chi^2(2) = 7.80$, $p = .020$), PAS early adolescent social maladjustment score ($\chi^2(2) = 6.30$, $p = .043$), QLS Total Score ($\chi^2(2) = 27.68$, $p < .001$), Eyes Task total score ($\chi(2) = 14.46$, $p = .001$), FEIT total score ($\chi^2(2) = 5.32$, $p = .070$), and Affective Prosody total score ($\chi^2(2) = 7.13$, $p = .028$). Thus, of the covariates that evidenced significant group differences, indices measuring premorbid maladjustment, role functioning, theory of mind, and emotion perception were most influential in the LPA clustering process. Indices measuring mania and substance use were not selected by the model and did not further the model's ability to predict class membership.

Table 10 provides parameter estimates for classes 2 (positive-depressive) and 3 (negative-neurocognitive) as compared to the reference group, class 1 (mild). The estimated multinomial logistic regression coefficient (B) is provided for the intercept and each predictor

covariate variable selected by the forward stepwise function. The logistic coefficient (B) can be interpreted such that, for one unit change in the independent variable, the logit of the outcome associated with the reference group (class 1) is expected to change by the parameter estimate B. For example, in class 2 (positive-depressive), the B value associated with the PAS early adolescent social maladjustment score is 1.46; this means that if an individual's PAS score was to increase by one unit (i.e., indicating greater premorbid maladjustment), the multinomial log-odds of being classified in class 2 (positive-depressive) instead of class 1 (mild) would be expected to increase by 1.46 units while holding all other variables in the model constant. Positive B values indicated the probability of belonging to the reference group (i.e., class 1) decreases, and negative B values indicated increased probability of belonging to the reference group (class 1). The closer a logistic coefficient is to zero, the less influence the independent variable had in predicting the logit.

Odds ratio values represent the logistic regression odds associated with each predictor variable. Odds ratios greater than one indicate that as the independent variable increases, the individual is x (OR value) times more likely to fall in the comparison group (class 2 or 3) than the referent group (class 1). For example, in class 2 (positive-depressive), the odds ratio value associated with the PAS early adolescent social maladjustment score is 4.31; if two individuals had a one point difference in early adolescent social maladjustment, the individual with the higher score has a relative risk of falling in class 2 (positive-depressive) that is 4.31 times more likely than class 1 (mild) when holding all other variables in the model constant.

To enhance clinical application of the patterns associated with this model, a modeled probability table was computed with MLR results and odds ratios. Table 11 shows the six clinical characteristic indices selected in the forward stepwise model to explain class

membership in the MLR model and associated probabilities of falling into each class depending on a hypothetical index score. Index scores are described as "average," "low," and "high," such that they are the grand mean of that variable, one standard deviation below, and one standard deviation above, respectively. Table 11 can be interpreted such that if an individual performs one standard deviation below the grand mean in total role functioning score (QLS), holding all other indices at their respective grand mean, they are 35.48% likely to fall in class 1 (mild), 52.27% likely to fall in class 2 (positive-depressive), and 12.25% likely to fall in class 3 (negative-neurocognitive). Changes in magnitude within each class for a group of index scores may also be interpreted. For example, as the total role functioning score increased from low to high, the probability of being classified in class 1 (mild) increased substantially, and class 2 (positive-depressive) and 3 (negative-neurocognitive) decreased substantially. Comparatively, little magnitude in change in probability of class membership occurred in classes 1 (mild) and 2 (positive-depressive) as affective prosody score increases from low to high. Average values were the same across all comparisons because they were at the grand mean of that index and all other variables were held constant at their grand mean. Of note, probability was also driven by sample size of each class, thus class 3 ($n = 33$, 16.3% of sample) had lower modeled probabilities overall.

Individuals had a ~50% likelihood or greater of falling into class 1 (mild) with high childhood academic maladjustment, low early adolescent social maladjustment, high role functioning, high theory of mind, high face emotion recognition, and high affective prosody ability. Individuals had a ~50% likelihood or greater of falling into class 2 (positive-depressive) with low childhood academic maladjustment, high early adolescent social maladjustment, low role functioning, and low face emotion recognition. Individuals had a ~10% likelihood or greater

65

of falling into class 3 (negative-neurocognitive) with low role functioning, low theory of mind, and low affective prosody ability.

Discussion

The central aim of the present study was to investigate whether a sample of symptomatically heterogeneous CHR and HSC individuals was comprised of different subgroups, each associated with different rates of transition to psychosis and symptom constellations. Our hypotheses were supported, as meaningful subgroups emerged from LPA analyses. A three-class model was of best fit and evidenced adequate separation across indicators. Our hypothesis was further supported such that each class was associated with different patterns of symptomatology. Class 1 (mild) had few symptoms rated above a "mild", with the exception of one positive symptom (e.g., unusual thought content), and the lowest transition rate (5.6%). Class 2 (positive-depressive) had the greatest positive symptoms of the subgroups, mild or lesser negative symptoms, moderate depression and sleep disturbance, and a greater transition rate (14.2%). Though classes 1 (mild) and 2 (positive-depressive) differed with respect to SOPS symptomatology, they exhibited comparable neurocognitive performance, performing at or near the level of healthy controls according to established norms. Class 3 (negative-neurocognitive), however, had the greatest negative symptoms overall, with positive and depressive symptoms lower than class 2 (positive-depressive). Class 3 (negative-neurocognitive) was found to have the most severe neurocognitive deficits across indices, and was associated with the greatest transition rate (29.3%).

The present study found that classes were best distinguished by separation in negative symptoms (e.g., social anhedonia, occupational functioning, decreased expression of emotion, and decreased ideational richness) and general symptoms (e.g., sleep disturbance, dysphoric

mood). This finding is consistent with prior latent variable work, where classes were clearly separated by differences in negative symptoms and behavioral change variables (e.g., social isolation, impaired role functioning) (Valmaggia et al., 2013). Further consistent with prior work, classes exhibiting the greatest baseline negative symptoms and behavioral change ratings had the highest risk of transition to psychosis (i.e., Class 3) (Valmaggia et al., 2013). These findings are consistent with the growing literature establishing an association between high baseline negative symptoms and subsequent conversion to a psychotic disorder (Alderman et al., 2015; Demjaha et al., 2012; Miller et al., 2003; Lencz et al., 2004; Nelson et al., 2013; Piskulic et al., 2012; Riecher-Rossler et al., 2009; Velthorst et al., 2009; Yung et al., 2003; Yung et al., 2005; Yung et al., 2010; Yung & McGorry 1996b). Class 3 (negative-neurocognitive) was also characterized by significantly impaired neurocognition, performing at least one standard deviation worse than class 1 (mild) and class 2 (positive-depressive) across domains.

While the present study replicated several past findings, it also found a novel latent profile structure, distinct from Valmaggia et al., (2013), that included neurocognitive variables as indicators in the LPA model. The inclusion of neurocognition in the model may have elicited the emergence of class 3 (negative-neurocognitive), a novel subgroup with the highest transition risk that is characterized by negative symptoms and comorbid neurocognitive impairment (i.e., instead of overall high symptom subgroup). To elucidate the possible clinical implications and progression of class 3 (negative-neurocognitive), it is useful to briefly review attempts to parse heterogeneity in established psychoses.

From Bleuler's (1911) first observation of the heterogeneity in the "Group of Schizophrenias," it has been argued that schizophrenia is an umbrella term for several distinct diseases within schizophrenia (Moskowitz & Heim, 2011). Efforts to parse phenomenologically

distinct subgroups resulted in the identification of the deficit and nondeficit subtypes of schizophrenia (Carpenter et al., 1988). Deficit schizophrenia is a well-defined subgroup of schizophrenia characterized by a chronic course of illness, prominent and persistent negative symptoms, and neurocognitive and social cognitive impairment (Kirkpatrick, Buchanan, Ross, & Carpenter, 2001). The deficit subtype has substantial empirical support and clinical utility, with a unique etiology, neurobiology, course/chronicity, and pathological profile (e.g., Ahmed et al., 2014; Kirkpatrick, Buchanan, Ross, & Carpenter, 2001; Voineskos et al., 2013). Current literature indicates that approximately 15-30% of patients meet deficit criteria, and that it is present from the first episode (e.g., Kirkpatrick, Fenton, Carpenter, & Marder, 2006). Further, there is evidence that individuals with persistent negative symptoms (i.e., a key feature of deficit subtype) have a distinct deficit in gray matter volume compared to individuals without persistent negative symptoms (e.g., Buchanan et al., 1993; Lei et al., 2015), as well as white matter abnormalities (Hovington et al., 2015). Deficit schizophrenia, therefore, has been argued to be the most valid taxon amidst a heterogeneous group of psychoses (Ahmed et al., 2014).

The discovery of deficit schizophrenia was considered a paradigm shift within schizophrenia research and the field of psychiatry more broadly (Carpenter, Arango, Buchanan, & Kirkpatrick, 1999), and aspects of this theory have received comparatively scant attention in CHR individuals. The closest analogue of deficit subtype in CHR individuals is Cornblatt and colleagues (2003) proposed "CASIS" model, a two-part explanation of psychosis development. The first dimension of the CASIS model posits that a base biological neurodevelopmental vulnerability to psychosis (e.g., genetic heritability, pre- and perinatal viral infection) underlies the prodrome and affects neurocognitive deficits and functional disability, irrespective of conversion to psychosis. Four domains define the CASIS model, including neurocognitive

deficits, affective disturbance (e.g., depression), negative symptoms of social isolation (i.e., social dysfunction), and school failure (i.e., occupational dysfunction). The second dimension of CASIS regards positive psychotic threshold symptoms, which develop in some individuals who show signs of CASIS, but not all (Cornblatt et al., 2003). While conclusions are tentative, individuals meeting CASIS criteria may be further divided into two putative subgroups based on the present results: (1) class 2 (positive-depressive) experiencing attenuated positive symptoms, moderate affective symptoms, and intact neurocognition, and (2) class 3 (negative-neurocognitive) experiencing moderate negative symptoms, low affective symptoms, and profound neurocognitive deficits (functional deficits to be discussed in subsequent sections).

Further examination of class 3's (negative-neurocognitive) phenotypic presentation shows it may be an early manifestation of the deficit subtype: prominent negative symptoms, significantly impaired neurocognition and social cognition, and poor premorbid functioning. Research related to prominent, early onset negative symptoms further supports a possible CHR deficit subtype classification. In a sample of CHR individuals, negative symptoms had an average age of onset of 11.7 years and a significantly longer duration than positive symptoms (Demmin, Carrion, Auther, McLaughlin, & Cornblatt, 2013).

Despite the utility of the deficit schizophrenia subtype, this has not been added to the DSM-5, because there is currently no valid typification of the remaining heterogeneous nondeficit subtypes (Braff, Ryan, Rissling, & Carpenter, 2013). It follows that characterizing nondeficit subgroup(s) in the present combined CHR and HSC sample proves difficult. Classes were not as clearly separated across the positive symptom subscale, consistent with Valmaggia et al.'s (2013) findings. However, class 2 (positive-depressive) had significantly higher paranoia and unusual thought content, thus, the present study is distinct from prior latent variable models

in that class 2 (positive-depressive) evidences a distinct symptom constellation. Class 2's (positive-depressive) symptom constellation may be best illustrated through SOPS descriptive anchors associated with mean estimate symptom ratings. They had moderate paranoia (e.g., may be mistrustful with SOPS interviewer, feel like others are saying negative things about them), mild negative symptoms such as social anhedonia (e.g., slightly socially awkward and passively goes along with social activities) and moderate occupational dysfunction (e.g., difficulty finishing work tasks or drop in GPA), and mild to moderate general symptoms (e.g., daytime fatigue from mild insomnia, feeling the "blues" have settled in) (McGlashan et al., 2010). Class 2 (positive-depressive) can be further characterized by the highest CDSS scores in the current sample (i.e., increased depressive symptoms); approximately one standard deviation higher than the mean in CHR individuals without mood disorders (Addington, Shah, Liu, & Addington, 2014). CDSS total approached a rating of 6, which is a cutoff associated with major depression in individuals with schizophrenia spectrum illness (Müller et al., 2005). Class 2 (positive-depressive) evidenced intact neurocognition compared to healthy control normed data (Table 1). As such, class 2 (positive-depressive) evidences largely non-specific distress, with a mild emphasis in positive and affective symptoms compared to other classes.

Despite LPA efforts, it is likely that there is limited ability to parse heterogeneity within class 2 (positive-depressive), such that it is comprised of individuals with a broad range of symptomatology that may subsequently transition to mood disorders, anxiety disorders, personality disorders, later onset psychotic disorders, eating disorders, or other diagnoses. Thus, class 2 (positive-depressive) may be at risk for a broad range of psychopathology. However, a recent study incorporating the present sample found that emergent psychosis was significantly more likely than any nonpsychotic disorder (Webb et al., 2015). Given that the inclusion criteria

of this study was one follow up visit (e.g., 6 months), it may be that CHR criteria are sensitive to emergent psychosis for some, but that timing was not sufficient to capture the emergence of nonpsychotic disorders, which take years to manifest past adolescence/early adulthood (e.g., average age range of study was 15.7-19.6 across groups) (Webb et al., 2015). For example, the median age of onset for mood disorders is 30 (Kessler et al., 2005). This is in line with McGorry et al.'s (2006) proposed clinical staging model of prodromal disorders, which posits that non-specific distress crystallizes over time into discrete categorical syndromes. Thus, efforts at identifying homogenous subgroups at this time may be difficult due to the ephemeral nature of distress and symptomatology through adolescence, and the dynamic patterns of psychopathology that manifest through the transition to adulthood (McGorry, Purcell, Goldstone, Amminger, 2011) (see clinical staging model figure in Appendix C). While the clinical staging model continues to exist largely as a theoretical framework instead of a concrete clinical application, it emphasizes the needs for early intervention irrespective of conversion risk, and urges care providers to tailor interventions to presenting symptomatology (McGorry & van Os, 2013).

Rate of Transition to Psychosis

Our hypotheses regarding clinical features associated with the subgroup at the highest risk of transition were partially supported, as class 3 (negative-neurocognitive) had the highest conversion rate (29% transition rate). This is consistent with the broader regression literature and prior latent variable work, where baseline neurocognition and negative symptoms have been associated with subsequent conversion (e.g., Addington & Heinssen, 2012; Valmaggia et al., 2013).

Inconsistent with our hypotheses, the highest risk class (Class 3 – negative-neurocognitive) was not also characterized by significantly greater positive symptoms (e.g.,

unusual thought content, suspiciousness). Class 2 (positive-depressive) was associated with the highest positive symptoms, intact neurocognition, and a lower rate of transition (14.9%). The absence of clear associations between positive symptoms and conversion is inconsistent with the literature, which indicates that higher baseline positive symptoms are associated with subsequent conversion, and that attenuated positive symptoms are the final phase of the prodrome before conversion to psychosis (e.g., Addington & Heinssen, 2012; Cornblatt et al., 2003). However, as previously discussed, regression literature may not be relevant unless it is conducted within putative subgroups, as significant associations would be muted with heterogeneity.

The decreased rate of transition associated with class 2 (positive-depressive) may be related to the subgroup's intact neurocognitive performance, as they performed comparably to non-psychiatric control participants. It is possible that neurocognitive ability is protective against reaching full threshold psychosis, as positive symptoms are less likely to reach a delusional level if one has the ability to correct erroneous beliefs and consider alternative explanations for anomalous experiences (i.e., metacognition) (Beck et al., 2004). Adequate neurocognitive ability is a pre-requisite for the capacity to undertake more complex abilities such as metacognition and cognitive insight in chronic psychoses (Lysaker et al., 2010). Further, lack of cognitive insight is associated with the development and maintenance of positive symptoms of full psychotic disorders (Garety et al., 2001). Class 2's (positive-depressive) intact neurocognition may have facilitated cognitive flexibility and metacognitive functioning, thus enabling the group to be more skeptical of suspicious or unusual thoughts. Further research is required to clarify the relationship amongst neurocognition, cognitive insight, and delusional development in CHR individuals.

Overall, the present study did not clearly enhance the risk prediction model beyond CHR criteria, as the highest risk group is associated with a 29.1% conversion rate, which is nearly identical to the overall rate of conversion in help seeking individuals who meet CHR criteria (29%, Fusar-Poli et al., 2012). However, there is a relatively low rate of conversion in the present study (17% of CHR group), thus a subgroup with a transition rate of 29.1% may still be a meaningful enhancement in specificity. The present study is associated with a lower conversion rate in the highest risk group (Class 3 – negative-neurocognitive), approximately 12% lower than Valmaggia et al.'s (2013) severe symptom group. Differential rates of conversion may be related to methodological differences in subthreshold psychotic symptom scale selection (e.g., SIPS vs. CAARMS); for example, the CAARMS does not include a specific item measuring paranoia/suspiciousness, which was the SOPS item that class 2 (positive-depressive) evidenced significantly higher ratings on. Such difference may have resulted in a different class structure and associated rates of transition compared to Valmaggia et al. (2013).

The Kaplan-Meier survival curves revealed significant group differences. Class 3 (negative-neurocognitive) evidenced the most rapid rate of transition of the three groups. At 24 months, the rate of conversion in classes 1 (mild) and 2 (positive-depressive) largely stalled, while individuals in class 3 (negative-neurocognitive) continued to evidence conversion. Classes were generally well separated in survival rates, indicating that classes have distinct patterns of conversion over time, and thus may be phenomenologically distinct. This is a novel finding, as Valmaggia et al. (2013) found comparable survival curves amidst subgroups with the exception of the severe symptom cluster. Further work would be required to replicate the current class structure and assess survival rate over time to better characterize each subgroup.

Further Characterizing Subgroups with Covariates

Our hypothesis that the subgroup associated with the highest risk of conversion would be further characterized by impairment in ToM, decreased control over experiences (internalized stigma), recent cannabis and alcohol abuse, and racial/ethnic minority status was partially supported.

Class 3 (negative-neurocognitive) had significantly lower social cognitive performance across domains compared to other classes, consistent with the proposed conceptualization of class 3 (negative-neurocognitive) as a CHR analogue of the deficit subgroup. Meta-analytic findings indicate that individuals with deficit schizophrenia have significant social cognitive impairments compared to nondeficit schizophrenia individuals (ES = 0.56, Cohen et al., 2007). Such findings provide further evidence of the possibility that there may exist a pathophysiologically distinct deficit subgroup within the prodome. In contrast, classes 1 (mild) and 2 (positive-depressive) performed comparably to healthy controls on measures of ToM and facial emotion perception according to established norms from age matched healthy controls participants.

Results from a recent meta-analysis evaluating social cognition in individuals at CHR found medium effect sizes for EP ($d = 0.47$) and ToM impairment ($d = 0.44$) (van Donkersgoed et al., 2015). Thus, one would expect class 2 (positive-depressive) to have EP and ToM deficits, given that this class was largely comprised of CHR individuals (74.5%). Further, results comparing CHR and HSC individuals from the current sample found no significant differences in EP or ToM performance (Addington et al., 2008; Healey et al., 2013). Thus, it is possible that deficit subgroups within such help seeking populations are responsible for social cognitive deficits in heterogeneous CHR samples.

There was no differentiation between classes 2 (positive-depressive) and 3 (negative-neurocognitive) in scores pertaining to internalized stigma (PBEQ) and perceived control over experiences subscale (PBEQ). Both classes reported negative beliefs concerning their clinical symptoms and specific absence of control, as they agreed with statements such as, "My experiences frighten me," and "I find it difficult to cope." Prior research has found that negative beliefs are closely associated with negative symptoms, depression, and suspiciousness, which characterize both classes (Pyle et al., 214; Stowkowy et al., 2015). Recent work regarding negative personal beliefs in individuals with more established serious mental illness found that such negative beliefs may be further divided into three distinct factors: external shame, internal shame/defectiveness, and general negative expectations/appraisals (Taylor et al., 2015). Subgroups may be differentially experiencing such negative belief factors, which may have different implications for treatment and amelioration of social dysfunction. The literature on internalized stigma related to clinical experiences is in an early phase, and specific associations with symptom clusters may emerge as future work is undertaken.

Hypotheses regarding cannabis and alcohol abuse in the highest risk class were not supported. It is possible that this lack of an effect is related to restricted range of substance use in the present sample, as scores evidenced high endorsement of abstinence and substance use without impairment. The only notable finding was related to "other" drug use, where class 2 (positive-depressive) had significantly higher use than class 1 (mild). This is in line with some work that indicates individuals with more prominent positive symptoms tend to use more substances (Dominguez, Saka, Lieb, Wittchen, & van Os,, 2010). While substance use may not demonstrate a consistent relationship with transition to psychosis, substance usage in adolescents

may underlie the transdiagnostic risk factor of emotion regulation deficits and thus warrant further exploration in help seeking individuals (Shadur and Lejuez, 2015).

The overall model for symptoms of mania (YMRS) was significantly different and was driven by higher ratings in classes 2 (positive-depressive) and 3 (negative-neurocognitive). While the YMRS has not undergone psychometric validation in CHR individuals, inspection of means and standard deviations from the current study indicates that classes evidenced scores comparable to other outpatient CHR individuals (total score < 4; e.g., Hui et al., 2013). Scores less than four are considered to be in the non-clinical range and not reaching a "mild" threshold of mania (Lukasiewicz et al., 2013). In a sample with more severe psychopathology, inpatient adolescents at CHR and non-CHR did not show significant differences in YMRS total score, indicating that in more severe manifestations of the prodrome, mania symptoms are not unique to CHR individuals (Gerstenberg et al., 2015). Further, baseline mania has not been shown to be predictive of subsequent conversion to psychotic spectrum illnesses, including affective psychoses (e.g., Amminger et al., 2006, Cornblatt et al., 2012). Taken together, YMRS symptom scores appear to be a non-specific indicator of distress in CHR individuals, rather than a key feature of the psychosis prodrome.

We did not find that the group at highest risk of transition to psychosis was comprised of a greater number of ethnic and racial minorities, as we had hypothesized. It is possible that racial ethnic minority status identification is not the variable most proximal to psychosis risk, but, rather, indices of perceived discrimination and salience of racial identity may be more relevant (Kessler, Mickelson, & Williams, 1999). Perceived discrimination spans across various facets of multicultural identity, including skin color, race/ethnicity, socioeconomic status, gender, age, appearance, disability, religion, and sexual orientation, among others. Indeed, recent research has

indicated that CHR individuals report significantly higher perceived discrimination than healthy

controls, and that this is unrelated to attenuated psychotic symptoms (e.g., paranoia) (Saleem et

al., 2014). Future research may investigate the role of perceived discrimination in predicting

subsequent conversion and functional impairment in CHR subgroups.

Regarding demographic characteristics, classes evidenced significant differences

regarding age. The age differences were driven by class 2 (positive-depressive) being

significantly older than class 3 (negative-neurocognitive). Given longitudinal findings indicating

negative symptom onset predates positive symptom onset, it would follow that the youngest

group may be characterized by predominant negative symptoms (Häfner, Maurer, & an der

Heiden, 2013). In a large longitudinal prospective cohort study that used a dimensional approach

towards symptoms (i.e., clustering negative/disorganized symptoms and positive symptoms

separately), negative/disorganized symptoms predicted the occurrence of positive symptoms over

time (Demjaha et al., 2012). Thus, negative/disorganized symptoms may serve as a precursor to

attenuated positive symptoms (Dominguez et al., 2010). Further longitudinal research is required

to establish the pattern of symptom development, and potential differential pattern amongst

putative CHR subgroups.

Classes also had significant differences in clinic of origin, as individuals from UNC-CH

were significantly more likely to be classified in class 1 (mild) and 2 (positive-depressive) than

class 3 (negative-neurocognitive). Individuals from Yale were significantly more likely to be

classified in class 3 (negative-neurocognitive) than classes 1 (mild) and 2 (positive-depressive).

ANOVAs across LPA indicators were repeated as ANCOVAs controlling for the effect of site,

and results were unchanged. Further, each of the three clinics used standardized inclusion

criteria, screening and assessment measures, and recruitment methods, and raters evidenced

significant agreement in routine assessment reliability checks (kappa = 0.90). It is possible that

site differences between classes may be used descriptively to understand possible regional

differences in symptomatology, course, and chronicity. While on the surface, Yale and UNC-CH

are situated in college towns of comparable square mileage; they differ in population density,

climate, and crime rate, among several other factors. Given the relationship between population

density and risk for psychosis (see review: Heinz, Deserno, & Reininghaus, 2013), it is not

surprising that 90% of the sample that comprises highest transition risk class 3 (negative-

neurocognitive) comes from the two sites with the highest population densities (Yale, Toronto).

Class 3 (negative-neurocognitive) exhibited the greatest premorbid academic/social and

baseline role dysfunction across items and subscales, with scores comparable to individuals with

established schizophrenia (Cannon-Spoor et al., 1982). During childhood, classes 1 (mild) and 2

(positive-depressive) both evidenced premorbid functioning comparable to healthy control norms

(Cannon-Spoor et al., 1982). Class 2 (positive-depressive) evidenced functional deterioration

over time, and was statistically comparable to class 3's (negative-neurocognitive) dysfunction in

late adolescent academic maladjustment score, and evidenced significant impairment with

respect to class 1 (mild) in late adolescent social maladjustment, role functioning

accomplishment/unemployment, and role functioning total score. Taken together, class 2

(positive-depressive) had significant social and role impairment, but to a lesser degree and with

later onset than class 3 (negative-neurocognitive). Of note, a recent cluster analysis of premorbid

adjustment scores using the CHR group from the present sample found three unique trajectories

of premorbid functioning (stable-intermediate, stable-good, and deteriorating). Each cluster

evidenced significant differences in negative/disorganized symptoms but not positive symptoms,

providing further evidence of there being an association between negative symptoms and

premorbid dysfunction in CHR individuals (Lyngberg et al., 2015). Such findings are consistent with the literature in established schizophrenia, which have detected an association between poor premorbid functioning and negative symptoms (e.g., Schmael et al., 2007), and continue to fit our conceptualization of class 3 (negative-neurocognitive) as a CHR deficit subtype with marked dysfunction both before and during the prodrome.

Consistent with our hypothesis, the class at the greatest risk of transition to psychosis (class 3 – negative-neurocognitive) had the greatest baseline role dysfunction compared to classes 1 (mild) and 2 (positive-depressive). It is of use to contextualize level of role function with respect to healthy individuals and those with psychotic spectrum illnesses. Class 3's (negative-neurocognitive) total QLS score is comparable to that of a sample of individuals with established, multiple episode psychosis (Addington et al., 2008). Class 1 (mild) approached the mean total score from a non-psychiatric control sample (Addington et al., 2008). Class 2 (positive-depressive) evidenced significantly impaired functioning compared to class 1 (mild), with a total score comparable to the general CHR group. Regarding dissatisfaction with one's role functioning, pairwise comparisons indicated that class 2 (positive-depressive) had the greatest dissatisfaction compared to class 1 (mild), while the class 3 (negative-neurocognitive) and class 1 (mild) comparison only approached statistical significance. Taken together, such findings are consistent with the view of class 3 (negative-neurocognitive) as a CHR deficit subgroup with milder depression and lacking in cognitive insight (i.e., related to neurocognitive dysfunction), resulting in less role dissatisfaction despite their having the lowest role functioning overall (Lysaker et al., 2010).

Social Functioning Trajectory Within and Across Classes

Hypotheses related to between group differences in social functioning trajectory were partially supported, as class 1 (mild) evidenced the highest level of social functioning, and more symptomatic classes 2 (positive-depressive) and 3 (negative-neurocognitive) evidenced the lowest level of social functioning. Current literature investigating predictors of social dysfunction in CHR individuals indicates that those with prominent negative symptoms, disorganized symptoms, neurocognitive impairment, and social cognitive impairment have significantly worse social functioning over time (e.g., Carrion et al., 2011; Cotter et al., 2014; Meyer et al., 2014; Milev, Ho, Arndt, & Andreasen, 2005; Pijnenborg et al., 2009). Further, a growing body of research indicates that negative symptoms are responsible for a significant amount of the variance in social functioning, above and beyond neurocognition (Corcoran et al., 2011; Schlosser et al., 2015). Thus, the clinical features of class 3 (negative-neurocognitive) have an established association with subsequent social dysfunction in the literature.

Given the growing literature in support of the relationship between negative symptoms and social functioning, we would expect class 3 (negative-neurocognitive) to perform significantly worse than class 2 (positive-depressive); however, both classes had a similar level of impairment. Of particular interest, class 2 (positive-depressive) evidenced low social functioning despite having intact neurocognition and social cognition, two areas that have been considered key determinants of functional ability in established schizophrenia (meta-analysis: Fett et al., 2011). It is possible that class 2 (positive-depressive) experienced a constellation of mild-moderate clinical symptoms that dynamically interacted with one another to create social dysfunction, rather than individual symptoms of severe intensity that explained significant variance in functioning in a regression model (van Os, 2013). Additionally, some research

81

indicates that depressive symptoms predict social functioning (and role functioning) above and beyond variance explained through negative symptoms (Corcoran et al., 2011; Fulford et al., 2013). Class 2 (positive-depressive) evidenced significantly higher depressive symptomatology than other classes, which may be interacting with other baseline psychopathology (e.g., suspiciousness) to result in isolation and social dysfunction.

Hypotheses related to significant changes over time within each class were only partially supported. Classes 1 (mild) and 3 (negative-neurocognitive) evidenced no significant changes over time, which may indicate that they have stable-intermediate and poor social functioning, respectively. Class 2 (positive-depressive) evidenced a mild degree of SFS improvement over time. Relatedly, class 2 (positive-depressive) evidenced significantly higher SFS scores than class 3 (negative-neurocognitive) at the 24-month follow up assessment. While such longitudinal results must be interpreted with caution given the significant rate of attrition, they are consistent with the extant literature and our present conceptualization of classes 2 (positive-depressive) and 3 (negative-neurocognitive). Class 3 (negative-neurocognitive) would be expected to evidence a more chronic course with persistent functional deficits, in line with the neurodevelopmental hypothesis and CHR-DS presentation. Conversely, symptom heterogeneity of class 2 (positive-depressive) may be associated with ephemeral symptom severity associated with improved functioning.

Contribution of Covariates to Group Membership

An additional exploratory aim was to evaluate the set of indices that best predicted subgroup membership. MLR analyses indicated that functional and social cognitive indices were the best predictors; whereas, covariates measuring substance use and mania were not selected by the forward stepwise model and did not significantly predict subgroup membership. And,

considering both the MLR statistics and modeled probabilities of class assignment based on selected covariates, baseline role functioning appeared to best predict class membership. Results were consistent with the findings of Valmaggia et al. (2013), who found that occupational status and overall functioning score best predicted class membership. Regarding premorbid functioning, a notable finding is that as childhood academic maladjustment increased from low to high, the likelihood of falling in class 2 (positive-depressive) decreased while the likelihood of falling in class 1 (mild) increased. Thus, class 2 (positive-depressive) had intact role functioning in childhood.

Interestingly, performance on social cognitive indices significantly contributed to the model predicting class membership, though the strength of this relationship was not as strong as functional indicators. Significant findings appeared to be driven by class 3 (negative-neurocognitive), as low scores in theory of mind and affective prosody were associated with a higher likelihood of falling into class 3 (negative-neurocognitive), holding all other variables constant.

Limitations and Strengths

As latent variable analyses are influenced by subtle differences in the sample, the present latent structure must be replicated several times to ensure the validity of the putative CHR deficit subgroup. The total sample size did not allow for cross-validation, which would enhance confidence regarding the validity of this taxon. Further, it is possible that the model may have better parsed the heterogeneity within class 2 (positive-depressive) with an increased sample size (Tein et al., 2013). Further, the overall reliability of LPA results may be affected by low prevalence rate of some symptoms (e.g., P5 disorganized communication) in the current sample, which has been influential in predicting conversion and functionality in prior work (e.g.,

Corcoran et al., 2011; Dominguez et al., 2010). Thus, the present findings are tentative until they are replicated using a larger sample.

As previously mentioned, the present class structure revealed significant differences with regard to assessment site. We elected not to include site as a covariate in the LPA model, because in the case of employing a single covariate, the log-linear model is identical whether site is treated as an active covariate or as an additional indicator variable (Clogg, 1981; Hagenaars, 1990; Magidson & Vermunt, 2001). Given that sites did not have significant differences in rates of converters (i.e., latent variable of "risk of psychosis" did not directly affect indicator site membership), we instead elected to use site as an inactive descriptive covariate. Further, significant differences between indicator variables remained when controlling for the effect of site, indicating true variance in symptomatology drove the clustering method. However, we cannot exclude the possibility that there may be differences between the three sites that may have affected differences in symptomatology.

Lastly, the present sample had a high rate of attrition. Given such attrition, it is likely that the longitudinal GLMM was underpowered. However, power analyses were not conducted so this cannot be statistically confirmed. It should be noted that attrition is a common limitation of CHR studies, as it is generally difficult to keep adolescents in longitudinal studies of significant duration. There is evidence that difficulties recontacting members of adolescent and young adult psychiatric cohorts is associated with increased presence of disorder at follow-up (Allott, Chanen, & Yuen, 2006). This is consistent with our findings that dropouts had poorer role functioning than non-dropouts. Thus, it is likely that the present study was not able to capture the most severely ill individuals over time.

Strengths of the present study included the ecological validity in the application of the latent profile analyses to the combined sample. Thus, analyses represent subgroups of self-presenting, help seeking individuals that are realistically seen at CHR clinics. Our use of neurocognitive performance scores as indicators in the latent variable model is novel and the first study to date to utilize such. This is a key strength, as cognitive deficits are a core feature of the CHR state. The current study is further strengthened by inclusion of a broad range of covariates (e.g., functioning, social cognition, internalized stigma) to characterize the subgroups at baseline and over time, which extends previous latent variable models.

Future Directions and Treatment Implications

Detecting putative subgroups within heterogeneous populations improves research, assessment, and encourages more tailored treatment to emergent symptom clusters. The current study was able to parse heterogeneity within the present sample of help seeking individuals. The present results provide further evidence that there may exist a subgroup characterized by predominant negative symptoms, neurocognitive and social cognitive impairment, and poor premorbid and baseline functioning. If such a subgroup exists in the broader population and is replicated in future latent mixture models, CHR subgroups may be considered distinct subclinical entities with different symptom courses and associated treatments.

As class 3 (negative-neurocognitive) was characterized by early functional deterioration, (i.e., during childhood) it may be advantageous to begin risk assessment and treatment at an earlier age to offset persistent dysfunction. Neurocognitive deficits and negative symptoms tend to appear earliest in the course of CHR, and the latter are often difficult to identify (Kahn & Keefe, 2013). Given such difficulties, it is imperative that large-scale awareness campaigns are undertaken to educate individuals throughout various referral pathways (e.g., campus health

clinics, primary care clinics). Education may include topics such as assessment and detection of subthreshold negative psychotic symptoms in adolescents and young adults, and the differential diagnosis between negative symptoms and depressive symptoms (Nelson et al., 2013). Class 3 (negative-neurocognitive) was further characterized by extensive neurocognitive impairments that likely occurred over the course of several years (Kahn & Keefe, 2013). Some researchers have proposed that psychosis is primarily a cognitive disorder, and that early recognition and prevention programs are failing to address the key risk phenotype of cognitive decline or intellectual stagnation that occurs around puberty (Kahn & Keefe, 2013). Large population based studies must be conducted to determine the level and pattern of cognitive underperformance that is associated with later functional decline. Efficacious treatments may then be developed and implemented.

Much of the current neurocognition and negative symptom intervention research has been conducted in older individuals with chronic psychosis and require adaptation for younger populations. To ameliorate neurocognitive deficits, a small number of studies have used cognitive remediation therapy (CRT) in CHR individuals, and found evidence in support of cognitive improvement (Hooker et al., 2014; Loewy et al., in press; Piskulic et al., 2015; Rauchensteiner et al., 2011). However, the tolerability and feasibility of CRT for adolescents is questionable given the high rates of dropout (i.e., 42% in Loewy et al., 2016) compared to similar CRT protocols in individuals with recent-onset schizophrenia. It is therefore imperative to develop rewarding and engaging forms of CRT for this young group to prevent attrition (i.e., incorporating interactive video game style play). Regarding negative symptoms, current treatments of negative symptoms in psychotic spectrum illnesses evidence statistically significant changes in symptoms; however, have not been found to be clinically meaningful (Fusar-Poli et

al., 2015). Thus, it is clear that the field is in great need of efficacious and tolerable treatments for neurocognitive and negative symptoms in individuals at CHR.

Individuals in class 2 (positive-depressive) exhibited a mix of subpsychotic symptomatology, depressive symptoms, and profound social dysfunction. It would be beneficial to conduct longitudinal studies lasting through age 30 to better assess the potential for symptom crossover and illness progression in this class. Treatments may be tailored to emerging diagnoses in line with the clinical staging model (McGorry et al., 2006). Given class 2's (positive-depressive) relative lower risk of transition to psychosis compared to class 3 (negative-neurocognitive), it may be recommended to treat their wide range of symptoms and possible underlying mechanisms rather than specialize in psychosis prevention, as may be indicated for class 3 (negative-neurocognitive).

Finally, given the low level of social functioning across a majority of individuals in the present study, treatments addressing such dysfunction rather than targeting determinants of such may be of interest. Such dysfunction is worthy of intervention in its own right, but also puts individuals at risk for various other forms of psychopathology (Cotter et al., 2014). Broadly, the present study highlights gaps in current knowledge concerning social dysfunction—in particular, causes, correlates, and course. Future research would also benefit from a focus in predictors of functionality and the incorporation of resiliency factors.

Conclusions

Overall, the present results support a subgroup approach to research, assessment, and treatment of help seeking individuals. Three classes emerged with adequate separation on a majority of indicator variables (SOPS symptoms, CDSS total score, neurocognitive scores), including a class that may be an early manifestation of the deficit subtype. Despite the well-

established association between poor outcome and negative symptoms and neurocognitive deficits, such symptom clusters are rarely targeted in CHR individuals. Further, the present findings underline the profound social dysfunction across help seeking individuals and need for improved treatments. We join other researchers who have advocated for a transdiagnostic, heuristic approach to CHR individuals that has been emphasized in understanding the progression to psychosis (Heinssen and Insel, 2015; McGorry et al., 2007).

APPENDIX A: SCHEDULE OF ASSESSMENTS

Study Evaluations	Year 1										Year 2					
	V 1	V 2	V 3	V 4	V 5	V 6	V 7	V 8	V 9	V 10	V 11	V 12	V 13	V 14	V 15	V 16
Cumulative months	0	1	2	3	4	5	6	8	10	12	14	16	18	20	22	24
Symptom Measures																
Structured Interview for Prodromal Syndromes (SIPS), Scale of Prodromal Symptoms (SOPS), and Criteria of Prodromal Syndromes (COPS)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Alcohol/Drug Use Scale (AUS/DUS)	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
Calgary Depression Scale for Schizophrenia (CDSS)	x						x			x			x			x
Young Mania Rating Scale (YMRS)	x						x			x			x			x
Personal Beliefs about Experiences Questionnaire (PBEQ)	x						x			x			x			x
Social Cognitive Measures																
Eyes Task	x						x			x			x			x
Facial Emotion Identification Task (FEIT)	x						x			x			x			x
Facial Emotion Discrimination Task (FEDT)	x						x			x			x			x
Affective Prosody Task (AP)	x						x			x			x			x
Functioning Measures																
Social Functioning Scale (SFS)	x						x			x			x			x
Heinrich Quality of Life (Modified)-Role Functioning (QLS)	x						x			x			x			x
Premorbid Adjustment Scale (PAS)	x															
Neurocognitive Measures																
Neurocognitive Test Battery	x						x			x			x			x

Note. V = visit; x = administered; Cumulative months, 0 = baseline.

APPENDIX B: REASONS FOR DROPOUT

	Assessment (years)								
	0	0.5	1	1.5	2	2.5	3	3.5	4
Clinical High Risk (CHR)									
Completed	171	93	66	43	32	26	17	12	7
Study ended	0	3	22	38	53	64	82	98	106
No Show	0	56	62	66	58	53	44	33	30
Converted	0	19	22	25	29	29	29	29	29
Help seeking controls (HSC)									
Completed	100	61	52	43	32	23	16	6	1
Study ended	0	0	6	13	23	32	49	64	76
No Show	0	38	40	41	41	40	30	25	18
Converted	0	1	2	3	4	5	5	5	5
Combined Sample									
Completed	271	154	118	86	64	49	33	18	8
Study ended	0	3	28	51	76	96	131	162	182
No Show	0	94	102	107	99	93	74	58	48
Converted	0	20	24	28	33	34	34	34	34

(J. Addington, personal communication, March 23, 2016)

APPENDIX C: CLINICAL STAGING MODEL OF PRODROMAL PREVENTION
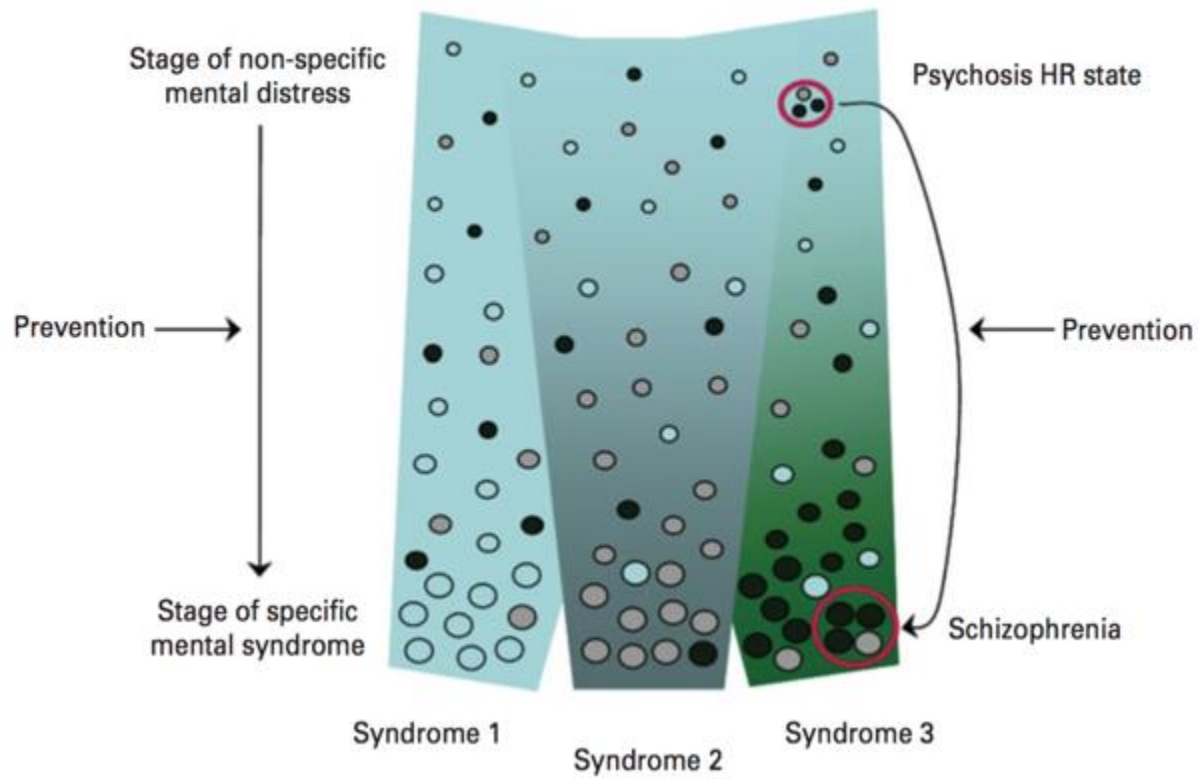
(Figure from Fusar-Poli, Yung, et al., 2014)

APPENDIX D: DSM-IV DIAGNOSIS AT CONVERSION

Conversion Diagnosis	DSM-IV Code	Class 1 (Mild)	Class 2 (Positive-Depressive)	Class 3 (Negative-Neurocognitive)	Total
Schizophrenia	295.00	1	3	2	6
Schizophreniform Disorder	295.40	3	2	5	10
Schizoaffective Disorder	295.70	1	1	0	2
Psychotic Disorder Not Otherwise Specified	298.90	1	6	4	11
Bipolar I with psychotic features	296.04	1	2	1	4
Bipolar II with psychotic features	296.89	0	1	0	1
Total		7	15	12	34

REFERENCES

Addington, D., Addington, J., & Maticka-Tyndale, E. (1993). Assessing depression in schizophrenia: the Calgary Depression Scale. *The British Journal of Psychiatry. Supplement*, *163*(22), 39-44.

Addington, D., Addington, J., & Maticka-Tyndale, E. (1994). Specificity of the Calgary Depression Scale for schizophrenics. *Schizophrenia Research*, *11*(3), 239-244.

Addington, J., & Barbato, M. (2012). The role of cognitive functioning in the outcome of those at clinical high risk for developing psychosis. *Epidemiology and psychiatric sciences*, *21*(04), 335-342.

Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B., McGlashan, T. H., Perkins, D. O., ... & Heinssen, R. (2007). North American Prodrome Longitudinal Study: A collaborative multisite approach to prodromal schizophrenia research. *Schizophrenia Bulletin, 33*(3), 665-672.

Addington, J., Cornblatt, B. A., Cadenhead, K. S., Cannon, T. D., McGlashan, T. H., Perkins, D. O., ... & Heinssen, R. (2011). At clinical high risk for psychosis: outcome for nonconverters. *American Journal of Psychiatry*. *168*(8), 800-805.

Addington, J., Case, N., Saleem, M. M., Auther, A. M., Cornblatt, B. A., & Cadenhead, K. S. (2014). Substance use in clinical high risk for psychosis: a review of the literature. *Early Intervention in Psychiatry*, *8*(2), 104-112.

Addington, J., & Heinssen, R. (2012). Prediction and prevention of psychosis in youth at clinical high risk. *Annual review of clinical psychology*, *8*(2012), 269-289.

Addington, J., Penn, D., Woods, S. W., Addington, D., & Perkins, D. O. (2008a). Facial affect recognition in individuals at clinical high risk for psychosis. *The British Journal of Psychiatry*, *192*(1), 67-68.

Addington, J., Penn, D., Woods, S. W., Addington, D., & Perkins, D. O. (2008b). Social functioning in individuals at clinical high risk for psychosis. *Schizophrenia Research*, *99*(1), 119-124.

Addington, J., Piskulic, D., Perkins, D., Woods, S. W., Liu, L., & Penn, D. L. (2012). Affect recognition in people at clinical high risk of psychosis. *Schizophrenia Research*, *140*(1), 87-92.

Addington, J., Saeedi, H., & Addington, D. (2006). Facial affect recognition: a mediator between cognitive and social functioning in psychosis?. *Schizophrenia Research*, *85*(1), 142-150.

Addington, J., Shah, H., Liu, L., & Addington, D. (2014). Reliability and validity of the Calgary Depression Scale for Schizophrenia (CDSS) in youth at clinical high risk for psychosis. *Schizophrenia Research*, *153*(1), 64-67.

Adolphs, R. (2009). The social brain: neural basis of social knowledge. *Annual Review of Psychology*, *60*, 693-716.

Ahmed, A. O., Strauss, G. P., Buchanan, R. W., Kirkpatrick, B., & Carpenter, W. T. (2014). Are negative symptoms dimensional or categorical? Detection and validation of deficit schizophrenia with taxometric and latent variable mixture models. *Schizophrenia bulletin*, *41*(4), 879-891.

Alderman, T., Addington, J., Bearden, C., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., ... & Woods, S. W. (2015). Negative symptoms and impaired social functioning predict later psychosis in Latino youth at clinical high risk in the North American prodromal longitudinal studies consortium. *Early intervention in psychiatry*, *9*(6), 467-475.

Allott, K., Chanen, A., & Yuen, H. P. (2006). Attrition bias in longitudinal research involving adolescent psychiatric outpatients. *The Journal of nervous and mental disease*, *194*(12), 958-961.

Amad, A., Guardia, D., Salleron, J., Thomas, P., Roelandt, J. L., & Vaiva, G. (2013). Increased prevalence of psychotic disorders among third-generation migrants: results from the French Mental Health in General Population survey. *Schizophrenia Research*, *147*(1), 193-195.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM-5 (5th ed.). Washington, D.C: American Psychiatric Association.

Amminger, G. P., Leicester, S., Yung, A. R., Phillips, L. J., Berger, G. E., Francey, S. M., ... & McGorry, P. D. (2006). Early-onset of symptoms predicts conversion to non-affective psychosis in ultra-high risk individuals. *Schizophrenia research*, *84*(1), 67-76.

Arsenault-Lapierre, G., Kim, C., & Turecki, G. (2004). Psychiatric diagnoses in 3275 suicides: a meta-analysis. *BMC psychiatry*, *4*(1), 37.

Auther, A. M., McLaughlin, D., Carrión, R. E., Nagachandran, P., Correll, C. U., & Cornblatt, B. A. (2012). Prospective study of cannabis use in adolescents at clinical high risk for psychosis: impact on conversion to psychosis and functional outcome. *Psychological Medicine*, *42*(12), 2485-2497.

Barbato, M., Colijn, M. A., Keefe, R. S., Perkins, D. O., Woods, S. W., Hawkins, K. A., ... & Addington, J. (2013a). The course of cognitive functioning over six months in individuals at clinical high risk for psychosis. *Psychiatry research*, *206*(2), 195-199.

Barbato, M., Liu, L., Penn, D. L., Keefe, R. S., Perkins, D. O., Woods, S. W., & Addington, J. (2013b). Social cognition as a mediator between neurocognition and functional outcome in individuals at clinical high risk for psychosis. *Schizophrenia Research*, *150*(2), 542-546.

Barbato, M., Penn, D. L., Perkins, D. O., Woods, S. W., Liu, L., & Addington, J. (2014). Metacognitive Functioning in Individuals at Clinical High Risk for Psychosis. *Behavioural and Cognitive Psychotherapy*, *42*(05), 526-534.

Barnes, A. (2008). Race and hospital diagnoses of schizophrenia and mood disorders. *Social Work*, *53*(1), 77-83.

Baron-Cohen, S., Wheelwright, S., Hill, J., Raste, Y., & Plumb, I. (2001). The "Reading the Mind in the Eyes" test revised version: A study with normal adults, and adults with Asperger syndrome or high-functioning autism. *Journal of Child Psychology and Psychiatry*, *42*(2), 241-251.

Beck, A. T. (2004). A cognitive model of schizophrenia. *Journal of Cognitive Psychotherapy*, *18*(3), 281-288.

Bell, R. Q. (1992). Multiple-risk cohorts and segmenting risk as solutions to the problem of false positives in risk for the major psychoses. *Psychiatry, 55*(4)*, 370-381.

Benjamini, Y., & Hochberg, Y. (1995). Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B (Methodological)*, 57(1), 289-300.

Benton, A. L., Hamsher, K., & Sivan, A. (1989). Multilingual Aphasia Examination. Iowa City, IA: AJA Associates.

Berg, A. O., Andreassen, O. A., Aminoff, S. R., Romm, K. L., Hauff, E., & Melle, I. (2014). The impact of immigration and visible minority status on psychosis symptom profile. *Social Psychiatry and Psychiatric Epidemiology*, *49*(11), 1747-1757.

Birchwood, M., Jackson, C., Brunet, K., Holden, J., & Barton, K. (2012). Personal beliefs about illness questionnaire‐revised (PBIQ‐R): Reliability and validation in a first episode sample. *British Journal of Clinical Psychology, 51*(4), 448-458.

Birchwood, M., Mason, R., MacMillan, F., & Healy, J. (1993). Depression, demoralization and control over psychotic illness: a comparison of depressed and non-depressed patients with a chronic psychosis. *Psychological Medicine*, *23*(02), 387-395.

Birchwood, M., Smith, J. O., Cochrane, R., Wetton, S., & Copestake, S. O. (1990). The Social Functioning Scale. The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *The British Journal of Psychiatry*, *157*(6), 853-859.

Bleuler, E. (1911). Dementia praecox oder Gruppe der Schizophrenien. *Handbuch der psychiatrie*.

Bora, E., & Pantelis, C. (2015). Meta-analysis of cognitive impairment in first-episode bipolar disorder: comparison with first-episode schizophrenia and healthy controls. *Schizophrenia bulletin*, *41*(5), 1095-1104.

Bourque, F., Van der Ven, E., & Malla, A. (2011). A meta-analysis of the risk for psychotic disorders among first-and second-generation immigrants. *Psychological Medicine*, *41*(05), 897-910.

Bresnahan, M., Begg, M. D., Brown, A., Schaefer, C., Sohler, N., Insel, B., ... & Susser, E. (2007). Race and risk of schizophrenia in a US birth cohort: another example of health disparity?. *International Journal of Epidemiology*, *36*(4), 751-758.

Braff, D. L., Ryan, J., Rissling, A. J., & Carpenter, W. T. (2013). Lack of Use in the Literature From the Last 20 Years Supports Dropping Traditional Schizophrenia Subtypes From DSM-5 and ICD-11. *Schizophrenia Bulletin*, *39*(4), 751-753.

Brill, N., Reichenberg, A., Weiser, M., & Rabinowitz, J. (2008). Validity of the premorbid adjustment scale. *Schizophrenia Bulletin*, *34*(5), 981-983.

Buchanan, R. W., Breier, A., Kirkpatrick, B., Elkashef, A., Munson, R. C., Gellad, F., & Carpenter Jr, W. T. (1993). Structural abnormalities in deficit and nondeficit schizophrenia. *American Journal of Psychiatry*, *150*(1), 59-59.

Buchy, L., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., Perkins, D. O., ... & Heinssen, R. (2015). Substance use in individuals at clinical high risk of psychosis. *Psychological medicine*, *45*(11), 2275-2284.

Buchy, L., Perkins, D., Woods, S. W., Liu, L., & Addington, J. (2014). Impact of substance use on conversion to psychosis in youth at clinical high risk of psychosis. *Schizophrenia Research*, *156*(2), 277-280.

Burns, T., & Patrick, D. (2007). Social functioning as an outcome measure in schizophrenia studies. *Acta Psychiatrica Scandinavica*, *116*(6), 403-418.

Callaghan, R. C., Cunningham, J. K., Allebeck, P., Arenovich, T., Sajeev, G., Remington, G., ... & Kish, S. J. (2012). Methamphetamine use and schizophrenia: a population-based cohort study in California. *American Journal of Psychiatry*, *169*(4), 389-396.

Callaway, D. A., Perkins, D. O., Woods, S. W., Liu, L., & Addington, J. (2014). Movement abnormalities predict transitioning to psychosis in individuals at clinical high risk for psychosis. *Schizophrenia Research*, *159*(2), 263-266.

Cannon, T. D., Cadenhead, K., Cornblatt, B., Woods, S. W., Addington, J., Walker, E., ... & Heinssen, R. (2008). Prediction of psychosis in youth at high clinical risk: A multisite longitudinal study in North America. *Archives of General Psychiatry, 65*(1), 28-37.

Cannon-Spoor, H. E., Potkin, S. G., & Wyatt, R. J. (1982). Measurement of premorbid adjustment in chronic schizophrenia. *Schizophrenia Bulletin*, *8*(3), 470.

Cantor-Graae, E., & Selten, J. P. (2005). Schizophrenia and migration: a meta-analysis and review. *American Journal of Psychiatry*, *162*(1), 12-24.

Carpenter, W. T., Arango, C., Buchanan, R. W., & Kirkpatrick, B. (1999). Deficit psychopathology and a paradigm shift in schizophrenia research. *Biological psychiatry*, *46*(3), 352-360.

Carpenter Jr, W. T., Heinrichs, D. W., & Wagman, A. M. (1988). Deficit and nondeficit forms of schizophrenia: the concept. *The American journal of psychiatry*, *145*(5), 578.

Carrión, R. E., Goldberg, T. E., McLaughlin, D., Auther, A. M., Correll, C. U., & Cornblatt, B. A. (2011). Impact of neurocognition on social and role functioning in individuals at clinical high risk for psychosis. *American Journal of Psychiatry*, *168*(8), 806-813.

Carrión, R. E., McLaughlin, D., Goldberg, T. E., Auther, A. M., Olsen, R. H., Olvet, D. M., ... & Cornblatt, B. A. (2013). Prediction of functional outcome in individuals at clinical high risk for psychosis. *JAMA psychiatry*, *70*(11), 1133-1142.

Clogg, C.C. (1981). New Developments in Latent Structure Analysis. In D.J. Jackson and E. F. Borgotta (Eds.). Factor Analysis and Measurement in Sociological Research. Beverly Hills, CA: Sage.

Collins, L. M., & Lanza, S. T. (2010). *Latent class and latent transition analysis: With applications in the social, behavioral, and health sciences* (Vol. 718). Hoboken, New Jersey: John Wiley & Sons.

Collins, A. A., Remington, G., Coulter, K., & Birkett, K. (1996). Depression in schizophrenia: a comparison of three measures. *Schizophrenia Research*, *20*(1), 205-209.

Corcoran, C. M., Kimhy, D., Parrilla-Escobar, M. A., Cressman, V. L., Stanford, A. D., Thompson, J., ... & Malaspina, D. (2011). The relationship of social function to depressive and negative symptoms in individuals at clinical high risk for psychosis. *Psychological medicine*, *41*(02), 251-261.

Cornblatt, B. A., Auther, A. M., Niendam, T., Smith, C. W., Zinberg, J., Bearden, C. E., & Cannon, T. D. (2007). Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. *Schizophrenia bulletin*, *33*(3), 688-702.

Cornblatt, B. A., Carrión, R. E., Addington, J., Seidman, L., Walker, E. F., Cannon, T. D., ... & Woods, S. W. (2012). Risk Factors for Psychosis: Impaired Social and Role Functioning. *Schizophrenia Bulletin*, *38*(6), 1247-1257.

Cornblatt, B. A., Carrión, R. E., Auther, A., McLaughlin, D., Olsen, R. H., John, M., & Correll, C. U. (2015). Psychosis prevention: A modified clinical high risk perspective From the Recognition and Prevention (RAP) Program. *American Journal of Psychiatry*. *172*(10), 986-994.

Cornblatt, B. A., & Keilp, J. G. (1994). Impaired attention, genetics, and the pathophysiology of schizophrenia. *Schizophrenia Bulletin*, *20*(1), 31-46.

Cornblatt, B. A., Lencz, T., Smith, C. W., Correll, C. U., Auther, A. M., & Nakayama, E. (2003). The schizophrenia prodrome revisited: a neurodevelopmental perspective. *Schizophrenia bulletin*, *29*(4), 633-651.

Cotter, J., Drake, R. J., Bucci, S., Firth, J., Edge, D., & Yung, A. R. (2014). What drives poor functioning in the at-risk mental state? A systematic review. *Schizophrenia Research*, *159*(2), 267-277.

Couture, S. M., Penn, D. L., Addington, J., Woods, S. W., & Perkins, D. O. (2008). Assessment of social judgments and complex mental states in the early phases of psychosis. *Schizophrenia Research*, *100*(1), 237-241.

Dayton, C. M., & Macready, G. B. (1988). Concomitant-variable latent-class models. *Journal of the American Statistical Association*, *83*(401), 173-178.

De Herdt, A., Wampers, M., Vancampfort, D., De Hert, M., Vanhees, L., Demunter, H., ... & Probst, M. (2013). Neurocognition in clinical high risk young adults who did or did not convert to a first schizophrenic psychosis: a meta-analysis. *Schizophrenia Research*, *149*(1), 48-55.

Demjaha, A., Valmaggia, L., Stahl, D., Byrne, M., & McGuire, P. (2012). Disorganization/cognitive and negative symptom dimensions in the at-risk mental state predict subsequent transition to psychosis. *Schizophrenia Bulletin, 38*(2)*, 351-359.

Demmin, D. L., Carrión, R. E., Auther, A., McLaughlin, D., & Cornblatt, B. A. (2013). Attenuated negative symptoms in individuals at clinical high risk for psychosis. *Comprehensive Psychiatry*, *54*(8), e19.

Dominguez, M. D. G., Saka, M. C., Lieb, R., Wittchen, H. U., & van Os, J. (2010). Early expression of negative/disorganized symptoms predicting psychotic experiences and subsequent clinical psychosis: a 10-year study. *American Journal of Psychiatry*, *167*(9), 1075-1082.

Drake, R., Mueser, K., & McHugo, G. (1996). Clinical Rating Scales. In L. Sederer, B. Dickey (Eds.), *Outcomes Assessment in Clinical Practice* (113-116). Baltimore, MD: Williams and Wilkins.

Edwards, J., Pattison, P. E., Jackson, H. J., & Wales, R. J. (2001). Facial affect and affective prosody recognition in first-episode schizophrenia. *Schizophrenia Research*, *48*(2), 235-253.

Fett, A. K. J., Viechtbauer, W., Penn, D. L., van Os, J., & Krabbendam, L. (2011). The relationship between neurocognition and social cognition with functional outcomes in schizophrenia: a meta-analysis. *Neuroscience & Biobehavioral Reviews*, *35*(3), 573-588.

First, M.B., Spitzer, R.L., Gibbon, M., and Williams, J.B.W. (1996). Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Washington, D.C.: American Psychiatric Press, Inc.

Frommann, I., Pukrop, R., Brinkmeyer, J., Bechdolf, A., Ruhrmann, S., Berning, J., ... & Wagner, M. (2010). Neuropsychological profiles in different at-risk states of psychosis: executive control impairment in the early—and additional memory dysfunction in the late—prodromal state. *Schizophrenia Bulletin*, *37*(4), 861-873.

Fulford, D., Niendam, T. A., Floyd, E. G., Carter, C. S., Mathalon, D. H., Vinogradov, S., ... & Loewy, R. L. (2013). Symptom dimensions and functional impairment in early psychosis: more to the story than just negative symptoms. *Schizophrenia research*, *147*(1), 125-131.

Fusar-Poli, P., Bechdolf, A., Taylor, M. J., Bonoldi, I., Carpenter, W. T., Yung, A. R., & McGuire, P. (2013). At risk for schizophrenic or affective psychoses? A meta-analysis of DSM/ICD diagnostic outcomes in individuals at high clinical risk. *Schizophrenia Bulletin, 39*(4), 923-932.

Fusar-Poli, P., Bonoldi, I., Yung, A. R., Borgwardt, S., Kempton, M. J., Valmaggia, L., ... & McGuire, P. (2012). Predicting psychosis: Meta-analysis of transition outcomes in individuals at high clinical risk. *Archives of General Psychiatry, 69*(3), 220-229.

Fusar-Poli, P., Borgwardt, S., Bechdolf, A., Addington, J., Riecher-Rössler, A., Schultze-Lutter, F., ... & Yung, A. (2013). The psychosis high-risk state: A comprehensive state-of-the-art review. *Journal of American Psychiatry, 70*(1), 107-120.

Fusar-Poli, P., Deste, G., Smieskova, R., Barlati, S., Yung, A. R., Howes, O., ... & Borgwardt, S. (2012). Cognitive functioning in prodromal psychosis: a meta-analysis. *Archives of General Psychiatry*, *69*(6), 562-571.

Fusar-Poli, P., Nelson, B., Valmaggia, L., Yung, A. R., & McGuire, P. K. (2014). Comorbid depressive and anxiety disorders in 509 individuals with an at-risk mental state: impact on psychopathology and transition to psychosis. *Schizophrenia Bulletin*, *40*(1), 120-131.

Fusar-Poli, P., Papanastasiou, E., Stahl, D., Rocchetti, M., Carpenter, W., Shergill, S., & McGuire, P. (2015). Treatments of negative symptoms in schizophrenia: meta-analysis of 168 randomized placebo-controlled trials. *Schizophrenia bulletin, 41*(4), 892-899.

Fusar-Poli, P., Yung, A. R., McGorry, P., & Van Os, J. (2014). Lessons learned from the psychosis high-risk state: Towards a general staging model of prodromal intervention. *Psychological Medicine, 44*(1), 17-24.

Gaddes, W. H., & Crockett, D. J. (1975). The Spreen-Benton aphasia tests, normative data as a measure of normal language development. *Brain and language*, *2*(3), 257-280.

Garety, P. A., Kuipers, E., Fowler, D., Freeman, D., & Bebbington, P. E. (2001). A cognitive model of the positive symptoms of psychosis.*Psychological medicine*, *31*(02), 189-195.

Gerstenberg, M., Hauser, M., Al-Jadiri, A., Sheridan, E. M., Kishimoto, T., Borenstein, Y., ... & Landers, S. E. (2015). Frequency and Correlates of DSM-5 Attenuated Psychosis Syndrome in a Sample of Adolescent Inpatients With Nonpsychotic Psychiatric Disorders. *The Journal of clinical psychiatry*, *76*(11), 1-478.

Gill, K. E., Cressman, V., Poe, S. L., Steinfeld, S., Ben‐David, S., G Keilp, J., ... & Corcoran, C. (2014). Social inference in individuals at clinical high risk for psychosis. *Early Intervention in Psychiatry*. *10*(1), 77-80.

Giuliano, A., Li, H., I Mesholam-Gately, R., M Sorenson, S., A Woodberry, K., & J Seidman, L. (2012). Neurocognition in the psychosis risk syndrome: a quantitative and qualitative review. *Current pharmaceutical design*, *18*(4), 399-415.

Gold, J. M., Carpenter, C., Randolph, C., Goldberg, T. E., & Weinberger, D. R. (1997). Auditory working memory and Wisconsin Card Sorting Test performance in schizophrenia. *Archives of General Psychiatry*, *54*(2), 159-165.

Golden, C. J. (1978). Stroop Color and Word Test: A manual for clinical and experimental uses. *Chicago: Stoelting*, 1-46.

Goodman, L. A. (1969). How to Ransack Social Mobility Tables and Other Kinds of Cross-Classification Tables1. *American Journal of Sociology*, *75*(1), 1-40.

Green, M. F., Nuechterlein, K. H., Gold, J. M., Barch, D. M., Cohen, J., Essock, S., ... & Marder, S. R. (2004). Approaching a consensus cognitive battery for clinical trials in schizophrenia: the NIMH-MATRICS conference to select cognitive domains and test criteria. *Biological psychiatry*, *56*(5), 301-307.

Häfner, H., Riecher-Rössler, A., Hambrecht, M., Maurer, K., Meissner, S., Schmidtke, A., ... & Van der Heiden, W. (1992). IRAOS: an instrument for the assessment of onset and early course of schizophrenia. *Schizophrenia Research, 6*(3), 209-223.

Häfner, H., Maurer, K., & An der Heiden, W. (2013). ABC Schizophrenia study: an overview of results since 1996. *Social psychiatry and psychiatric epidemiology*, *48*(7), 1021-1031.

Häfner, H., Maurer, K., Löffler, W., An der Heiden, W., Munk-Jørgensen, P., Hambrecht, M., & Riecher-Rössler, A. (1998). The ABC Schizophrenia Study: A preliminary overview of the results. *Social Psychiatry and Psychiatric Epidemiology, 33*(8), 380-386.

Hagenaars, J. A. (1990). Categorical Longtidinal Data—Loglinear Analysis of Panel, Trend and Cohort Data. Newbury Park, CA: Sage.

Hagenaars, J. A., & McCutcheon, A. L. (Eds.). (2002). Applied latent class analysis. Cambridge: Cambridge University Press.

Haywood, T. W., Kravitz, H. M., Grossman, L. S., & Cavanaugh Jr, J. L. (1995). Predicting the "revolving door" phenomenon among patients with schizophrenic, schizoaffective, and affective disorders. *The American Journal of Psychiatry*,*152*(6), 856-861.

Healey, K. M., Penn, D. L., Perkins, D., Woods, S. W., & Addington, J. (2013). Theory of mind and social judgments in people at clinical high risk of psychosis. *Schizophrenia Research*, *150*(2), 498-504.

Heinrichs, R. W. (2005). The primacy of cognition in schizophrenia. *American Psychologist*, *60*(3), 229-242.

Heinrichs, D. W., Hanlon, T. E., & Carpenter, W. T. (1984). The Quality of Life Scale: an instrument for rating the schizophrenic deficit syndrome. *Schizophrenia Bulletin*, *10*(3), 388-398.

Heinssen, R. K., & Insel, T. R. (2015). Preventing the onset of psychosis: not quite there yet. *Schizophrenia bulletin*, *41*(1), 28-29.

Heinz, A., Deserno, L., & Reininghaus, U. (2013). Urbanicity, social adversity and psychosis. *World Psychiatry*, *12*(3), 187-197.

Hooker, C. I., Carol, E. E., Eisenstein, T. J., Yin, H., Lincoln, S. H., Tully, L. M., ... & Seidman, L. J. (2014). A pilot study of cognitive training in clinical high risk for psychosis: initial evidence of cognitive benefit. *Schizophrenia research*, *157*, 314-316.

Hothorn, T., Bretz, F., & Westfall, P. (2008). Simultaneous inference in general parametric models. *Biometrical journal*, *50*(3), 346-363.

Hovington, C. L., Bodnar, M., Chakravarty, M. M., Joober, R., Malla, A. K., & Lepage, M. (2015). Investigation of white matter abnormalities in first episode psychosis patients with persistent negative symptoms. *Psychiatry Research: Neuroimaging*, *233*(3), 402-408.

Huber, G., & Gross, G. (1989). The concept of basic symptoms in schizophrenic and schizoaffective psychoses. *Recenti progressi in medicina, 80*, 646-652.

Hui, C., Morcillo, C., Russo, D. A., Stochl, J., Shelley, G. F., Painter, M., ... & Perez, J. (2013). Psychiatric morbidity, functioning and quality of life in young people at clinical high risk for psychosis. *Schizophrenia research*, *148*(1), 175-180.

Janssen, I., Hanssen, M., Bak, M., Bijl, R. V., De Graaf, R., Volbergh, W., ... & Van Os, J. (2003). Discrimination and delusional ideation. *The British Journal of Psychiatry*, *182*(1), 71-76.

Kahn, R. S., & Keefe, R. S. (2013). Schizophrenia is a cognitive illness: time for a change in focus. *JAMA psychiatry*, *70*(10), 1107-1112.

Kahn, P. V., Walker, T. M., Williams, T. S., Cornblatt, B. A., Mohs, R. C., & Keefe, R. S. (2012). Standardizing the use of the Continuous Performance Test in schizophrenia research: A validation study. *Schizophrenia research*, *142*(1), 153-158.

Kaplan, E. L., & Meier, P. (1958). Nonparametric estimation from incomplete observations. *Journal of the American Statistical Association*, *53*(282), 457-481.

Keefe, R. S., Perkins, D. O., Gu, H., Zipursky, R. B., Christensen, B. K., & Lieberman, J. A. (2006). A longitudinal study of neurocognitive function in individuals at-risk for psychosis. *Schizophrenia Research*, *88*(1), 26-35.

Kendler, K. S., Gruenberg, A. M., & Strauss, J. S. (1981). An independent analysis of the Copenhagen sample of the Danish Adoption Study of Schizophrenia: II. The relationship between schizotypal personality disorder and schizophrenia. *Archives of General Psychiatry*, *38*(9), 982-984.

Kerr, S. L., & Neale, J. M. (1993). Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance?. *Journal of Abnormal Psychology*, *102*(2), 312-318.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry*, *62*(6), 593-602.

Kessler, R. C., Mickelson, K. D., & Williams, D. R. (1999). The prevalence, distribution, and mental health correlates of perceived discrimination in the United States. Journal of health and social behavior, *40*(3) 208-230.

Kim, H. S., Shin, N. Y., Jang, J. H., Kim, E., Shim, G., Park, H. Y., ... & Kwon, J. S. (2011). Social cognition and neurocognition as predictors of conversion to psychosis in individuals at ultra-high risk. *Schizophrenia Research*, *130*(1), 170-175.

Kirchner, W. K. (1958). Age differences in short-term retention of rapidly changing information. *Journal of experimental psychology*, *55*(4), 352-358.

Kirkpatrick, B., Buchanan, R. W., Ross, D. E., & Carpenter Jr, W. T. (2001). A separate disease within the syndrome of schizophrenia. *Archives of General Psychiatry*, *58*(2), 165.

Kirkpatrick, B., Fenton, W. S., Carpenter, W. T., & Marder, S. R. (2006). The NIMH-MATRICS consensus statement on negative symptoms. *Schizophrenia bulletin*, *32*(2), 214-219.

Klosterkötter, J., Ebel, H., Schultze-Lutter, F., & Steinmeyer, E. M. (1996). Diagnostic validity of basic symptoms. *European Archives of Psychiatry and Clinical Neuroscience, 246*(3), 147-154.

Klosterkötter, J., Hellmich, M., Steinmeyer, E. M., & Schultze-Lutter, F. (2001). Diagnosing schizophrenia in the initial prodromal phase. *Archives of General Psychiatry, 58*(2), 158-164.

Klosterkötter, J., Schultze-Lutter, F., Bechdolf, A., & Ruhrmann, S. (2011). Prediction and prevention of schizophrenia: what has been achieved and where to go next?. *World Psychiatry, 10*(3), 165-174.

Kongs, S. K., Thompson, L. L., Iverson, G. L., & Heaton, R. K. (2000). Wisconsin card sorting test-64 card version (WCST-64). *Odessa, FL: Psychological Assessment Resources*.

Kraan, T., Velthorst, E., Koenders, L., Zwaart, K., Ising, H. K., van den Berg, D., ... & van der Gaag, M. (2016). Cannabis use and transition to psychosis in individuals at ultra-high risk: review and meta-analysis. *Psychological medicine*, *46*(4), 673-681.

Kuepper, R., van Os, J., Lieb, R., Wittchen, H. U., Höfler, M., & Henquet, C. (2011). Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. *British Medical Journal, 342,* d738-d738.

Lee, T. Y., Hong, S. B., Shin, N. Y., & Kwon, J. S. (2015). Social cognitive functioning in prodromal psychosis: A meta-analysis. *Schizophrenia Research*, *164*(1), 28-34.

Lee, T. Y., Kim, S. N., Correll, C. U., Byun, M. S., Kim, E., Jang, J. H., ... & Kwon, J. S. (2014). Symptomatic and functional remission of subjects at clinical high risk for psychosis: a 2-year naturalistic observational study. *Schizophrenia research*, *156*(2), 266-271.

Lei, W., Deng, W., Li, M., He, Z., Han, Y., Huang, C., ... & Jiang, L. (2015). Gray matter volume alterations in first-episode drug-naïve patients with deficit and nondeficit schizophrenia. *Psychiatry Research: Neuroimaging*, *234*(2), 219-226.

Lencz, T., Smith, C. W., Auther, A., Correll, C. U., & Cornblatt, B. (2004). Nonspecific and attenuated negative symptoms in patients at clinical high-risk for schizophrenia. *Schizophrenia research*, *68*(1), 37-48.

Lin, T. H., & Dayton, C. M. (1997). Model selection information criteria for non-nested latent class models. *Journal of Educational and Behavioral Statistics*, *22*(3), 249-264.

Lin, A., Yung, A. R., Nelson, B., Brewer, W. J., Riley, R., Simmons, M., ... & Wood, S. J. (2013). Neurocognitive predictors of transition to psychosis: medium-to long-term findings from a sample at ultra-high risk for psychosis. *Psychological Medicine*, *43*(11), 2349-2360.

Loewy, R., Fisher, M., Schlosser, D. A., Biagianti, B., Stuart, B., Mathalon, D. H., & Vinogradov, S. (in press). Intensive Auditory Cognitive Training Improves Verbal Memory in Adolescents and Young Adults at Clinical High Risk for Psychosis. *Schizophrenia bulletin*.

Lyons-Warren, A., Lillie, R., & Hershey, T. (2004). Short-and long-term spatial delayed response performance across the lifespan. *Developmental Neuropsychology*, *26*(3), 661-678.

Lukasiewicz, M., Gerard, S., Besnard, A., Falissard, B., Perrin, E., Sapin, H., ... & Azorin, J. M. (2013). Young Mania Rating Scale: how to interpret the numbers? Determination of a severity threshold and of the minimal clinically significant difference in the EMBLEM cohort. *International journal of methods in psychiatric research*, *22*(1), 46-58.

Lyngberg, K., Buchy, L., Liu, L., Perkins, D., Woods, S., & Addington, J. (2015). Patterns of premorbid functioning in individuals at clinical high risk of psychosis. *Schizophrenia research*, *169*(1), 209-213.

Lysaker, P. H., Shea, A. M., Buck, K. D., Dimaggio, G., Nicolò, G., Procacci, M., ... & Rand, K. L. (2010). Metacognition as a mediator of the effects of impairments in neurocognition on social function in schizophrenia spectrum disorders. *Acta Psychiatrica Scandinavica*, *122*(5), 405-413.

MacBeth, A., & Gumley, A. (2008). Premorbid adjustment, symptom development and quality of life in first episode psychosis: a systematic review and critical reappraisal. *Acta Psychiatrica Scandinavica*, *117*(2), 85-99.

Magidson, J., & Vermunt, J. K. (2001). Latent Class Factor and Cluster Models, Bi-Plots, and Related Graphical Displays. *Sociological methodology, 31*(1), 223-264.

Malla, A., Norman, R., Bechard-Evans, L., Schmitz, N., Manchanda, R., & Cassidy, C. (2008). Factors influencing relapse during a 2-year follow-up of first-episode psychosis in a specialized early intervention service. *Psychological Medicine*, *38*(11), 1585-1593.

Marder, S. R., Fenton, W., Youens, K., & Tamminga, C. A. (2004). Schizophrenia, IX. *The American journal of psychiatry*, *161*(1), 25-25.

Mason, O., Startup, M., Halpin, S., Schall, U., Conrad, A., & Carr, V. (2004). Risk factors for transition to first episode psychosis among individuals with 'at-risk mental states'. *Schizophrenia Research, 71*(2), 227-237.

Mayer-Gross, W. (1932). Die Klinik. Berlin: Springer Heidelberg.

McGlashan, T., Walsh, B., & Woods, S. (2010). *The psychosis-risk syndrome: handbook for diagnosis and follow-up*. Oxford University Press.

McGorry, P. D., Hickie, I. B., Yung, A. R., Pantelis, C., & Jackson, H. J. (2006). Clinical staging of psychiatric disorders: a heuristic framework for choosing earlier, safer and more effective interventions. *Australian and New Zealand Journal of Psychiatry*, *40*(8), 616-622.

McGorry, P. D., Purcell, R., Goldstone, S., & Amminger, G. P. (2011). Age of onset and timing of treatment for mental and substance use disorders: implications for preventive intervention strategies and models of care. *Current opinion in psychiatry*, *24*(4), 301-306.

McGorry, P., & van Os, J. (2013). Redeeming diagnosis in psychiatry: timing versus specificity. *The Lancet*, *381*(9863), 343-345.

McKechanie, A. G., Moorhead, T. W., Stanfield, A. C., Whalley, H. C., Johnstone, E. C., Lawrie, S. M., & Owens, D. G. (in press). Negative symptoms and longitudinal grey matter tissue loss in adolescents at risk of psychosis: preliminary findings from a 6-year follow-up study. *The British journal of psychiatry: the journal of mental science*.

McLachlan, G., & Peel, D. (2000). Finite mixture models. New York: John Wiley & Sons.

Meyer, E. C., Carrión, R. E., Cornblatt, B. A., Addington, J., Cadenhead, K. S., Cannon, T. D., ... & Woods, S. W. (2014). The relationship of neurocognition and negative symptoms to social and role functioning over time in individuals at clinical high risk in the first phase of the north american prodrome longitudinal study. Schizophrenia Bulletin, *40*(6), 1452-1461.

Michel, C., Ruhrmann, S., Schimmelmann, B. G., Klosterkötter, J., & Schultze-Lutter, F. (2014). A stratified model for psychosis prediction in clinical practice. *Schizophrenia Bulletin, 40*(6), 1533-1542.

Milev, P., Ho, B. C., Arndt, S., & Andreasen, N. C. (2005). Predictive values of neurocognition and negative symptoms on functional outcome in schizophrenia: a longitudinal first-episode study with 7-year follow-up. *The American journal of psychiatry*, *162*(3), 495-506.

Miller, T. J., McGlashan, T. H., Rosen, J. L., Cadenhead, K., Ventura, J., McFarlane, W., ... & Woods, S. W. (2003). Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: Predictive validity, interrater reliability, and training to reliability. *Schizophrenia Bulletin, 29*(4), 703-715.

Modinos, G., Allen, P., Frascarelli, M., Tognin, S., Valmaggia, L., Xenaki, L., ... & Fusar-Poli, P. (2014). Are we really mapping psychosis risk? Neuroanatomical signature of affective disorders in subjects at ultra high risk. *Psychological Medicine, 44*(16), 3491-3501.

Morrison, A. P., Birchwood, M., Pyle, M., Flach, C., Stewart, S. L., Byrne, R., ... & French, P. (2013). Impact of cognitive therapy on internalised stigma in people with at-risk mental states. *The British Journal of Psychiatry*, *203*(2), 140-145.

Morrison, A. P., French, P., Walford, L., Lewis, S. W., Kilcommons, A., Green, J., ... & Bentall, R. P. (2004). Cognitive therapy for the prevention of psychosis in people at ultra-high risk randomised controlled trial. *The British Journal of Psychiatry*, *185*(4), 291-297.

Müller, M. J., Brening, H., Gensch, C., Klinga, J., Kienzle, B., & Müller, K. M. (2005). The Calgary Depression Rating Scale for schizophrenia in a healthy control group: psychometric properties and reference values. *Journal of affective disorders*, *88*(1), 69-74.

Muthen, B. (2001). Latent variable mixture modeling. In G.A. Marcoulides and Schumacker E. (Eds.), *New developments and techniques in structural equation modeling* (1-33). Mahwah, NJ: Psychology Press.

Muthén, B., & Muthén, L. K. (2000). Integrating person-centered and variable-centered analyses: Growth mixture modeling with latent trajectory classes. *Alcoholism: Clinical and experimental research, 24*(6), 882-891.

Muthén, L. K., & Muthén, B.O. (2012). Mplus. *The comprehensive modelling program for applied researchers: User's guide, 7.*

Myles-Worsley, M., Weaver, S., & Blailes, F. (2007). Comorbid depressive symptoms in the developmental course of adolescent-onset psychosis. *Early Intervention In Psychiatry, 1*(2), 183-190.

Nelson, B., Thompson, A., & Yung, A. R. (2012). Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. *Schizophrenia Bulletin*, *38*(6), 1277-1287.

Nelson, B., Yuen, H. P., Wood, S. J., Lin, A., Spiliotacopoulos, D., Bruxner, A., ... & Francey, S. M. (2013). Long-term follow-up of a group at ultra high risk ("prodromal") for psychosis: the PACE 400 study. *JAMA psychiatry*, *70*(8), 793-802.

Nieman, D. H., Ruhrmann, S., Dragt, S., Soen, F., van Tricht, M. J., Koelman, J. H., ... & de Haan, L. (2013). Psychosis prediction: Stratification of risk estimation with information-processing and premorbid functioning variables. *Schizophrenia Bulletin*, *40*(6), 1482-1490.

Nylund, K. L., Asparouhov, T., & Muthén, B. O. (2007). Deciding on the number of classes in latent class analysis and growth mixture modeling: A Monte Carlo simulation study. *Structural equation modeling*, *14*(4), 535-569.

Oltmanns, T. F., & Neale, J. M. (1975). Schizophrenic performance when distractors are present: attentional deficit or differential task difficulty?. *Journal of abnormal psychology*, *84*(3), 205-209.

Olvet, D. M., Stearns, W. H., McLaughlin, D., Auther, A. M., Correll, C. U., & Cornblatt, B. A. (2010). Comparing clinical and neurocognitive features of the schizophrenia prodrome to the bipolar prodrome. *Schizophrenia research*, *123*(1), 59-63.

Penn, D. L., Corrigan, P. W., Bentall, R. P., Racenstein, J., & Newman, L. (1997). Social cognition in schizophrenia. *Psychological Bulletin*, *121*(1), 114-132.

Pijnenborg, G. H. M., Withaar, F. K., Evans, J. J., Van den Bosch, R. J., Timmerman, M. E., & Brouwer, W. H. (2009). The predictive value of measures of social cognition for community functioning in schizophrenia: implications for neuropsychological assessment. *Journal of the International Neuropsychological Society*, *15*(2), 239-247.

Pinkham, A. E., & Penn, D. L. (2006). Neurocognitive and social cognitive predictors of interpersonal skill in schizophrenia. *Psychiatry research*, *143*(2), 167-178.

Pinkham, A. E., Penn, D. L., Green, M. F., Buck, B., Healey, K., & Harvey, P. D. (2013). The social cognition psychometric evaluation study: results of the expert survey and RAND panel. *Schizophrenia Bulletin*, *40*(4), 813-823.

Piskulic, D., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Heinssen, R., ... & Woods, S. W. (2012). Negative symptoms in individuals at clinical high risk of psychosis. *Psychiatry research*, *196*(2), 220-224.

Piskulic, D., Barbato, M., Liu, L., & Addington, J. (2015). Pilot study of cognitive remediation therapy on cognition in young people at clinical high risk of psychosis. *Psychiatry research*, *225*(1), 93-98.

Pukrop, R., Ruhrmann, S., Schultze-Lutter, F., Bechdolf, A., Brockhaus-Dumke, A., & Klosterkötter, J. (2007). Neurocognitive indicators for a conversion to psychosis: comparison of patients in a potentially initial prodromal state who did or did not convert to a psychosis. *Schizophrenia Research*, *92*(1), 116-125.

Pyle, M., Stewart, S. L., French, P., Byrne, R., Patterson, P., Gumley, A., ... & Morrison, A. P. (2015). Internalized stigma, emotional dysfunction and unusual experiences in young people at risk of psychosis. *Early Intervention in Psychiatry*, *9*(2), 133-140.

Raballo, A., Meneghelli, A., Cocchi, A., Sisti, D., Rocchi, M. B., Alpi, A., ... & Häfner, H. (2014). Shades of vulnerability: Latent structures of clinical caseness in prodromal and early phases of schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience, 264*(2), 155-169.

Rauchensteiner, S., Kawohl, W., Ozgurdal, S., Littmann, E., Gudlowski, Y., Witthaus, H., ... & Juckel, G. (2011). Test-performance after cognitive training in persons at risk mental state of schizophrenia and patients with schizophrenia. *Psychiatry research*, *185*(3), 334-339.

Rausch, F., Eifler, S., Esser, A., Esslinger, C., Schirmbeck, F., Meyer-Lindenberg, A., & Zink, M. (2013). The Early Recognition Inventory ERIraos detects at risk mental states of psychosis with high sensitivity. Comprehensive psychiatry, 54(7), 1068-1076.

Reitan, R. M., & Wolfson, D. (1985). *The Halstead-Reitan neuropsychological test battery: Theory and clinical interpretation* (Vol. 4). Reitan Neuropsychology.

Rey, A. (1958). L'examen clinique en psychologie (The Clinical Examination in Psychology). *Presse Universitaire de France, Paris.*

Riecher-Rössler, A., Pflueger, M. O., Aston, J., Borgwardt, S. J., Brewer, W. J., Gschwandtner, U., & Stieglitz, R. D. (2009). Efficacy of using cognitive status in predicting psychosis: A 7-year follow-up. *Biological Psychiatry, 66*(11), 1023-1030.

Riecher, A., Maurer, K., Löffler, W., Fätkenheuer, B., an der Heiden, W., & Häfner, H. (1989). Schizophrenia—a disease of young single males?. *European Archives of Psychiatry and Neurological Sciences, 239*(3), 210-212.

Ruhrmann, S., Schultze-Lutter, F., Salokangas, R. K., Heinimaa, M., Linszen, D., Dingemans, P., ... & Klosterkötter, J. (2010). Prediction of psychosis in adolescents and young adults at high risk: Results from the prospective European prediction of psychosis study. *Archives of General Psychiatry, 67*(3)*,* 241-251.

Ruhrmann, S., Schultze-Lutter, F., Schmidt, S. J., Kaiser, N., & Klosterkötter, J. (2014). Prediction and prevention of psychosis: current progress and future tasks. *European Archives of Psychiatry and Clinical Neuroscience, 264*(1), 9-16.

Sabbag, S., Twamley, E. M., Vella, L., Heaton, R. K., Patterson, T. L., & Harvey, P. D. (2011). Assessing everyday functioning in schizophrenia: not all informants seem equally informative. *Schizophrenia Research*, *131*(1), 250-255.

Saleem, M. M., Stowkowy, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., McGlashan, T. H., ... & Woods, S. W. (2014). Perceived discrimination in those at clinical high risk for psychosis. *Early intervention in psychiatry*, *8*(1), 77-81.

Salokangas, R. K. R., Heinimaa, M., From, T., Löyttyniemi, E., Ilonen, T., Luutonen, S., ... & Klosterkötter, J. (2014). Short-term functional outcome and premorbid adjustment in clinical high-risk patients. Results of the EPOS project. *European Psychiatry*, *29*(6), 371-380.

Salokangas, R. K., Nieman, D. H., Heinimaa, M., Svirskis, T., Luutonen, S., From, T., ... & Ruhrmann, S. (2013). Psychosocial outcome in patients at clinical high risk of psychosis: a prospective follow-up. *Social Psychiatry and Psychiatric Epidemiology*, *48*(2), 303-311.

Salokangas, R. K., Ruhrmann, S., von Reventlow, H. G., Heinimaa, M., Svirskis, T., From, T., ... & Klosterkötter, J. (2012). Axis I diagnoses and transition to psychosis in clinical high-risk patients EPOS project: prospective follow-up of 245 clinical high-risk outpatients in four countries. *Schizophrenia Research*, *138*(2), 192-197.

Schaffner, K. F., & McGorry, P. D. (2001). Preventing severe mental illnesses—new prospects and ethical challenges. *Schizophrenia Research, 51*(1), 3-15.

Schlosser, D. A., Campellone, T. R., Biagianti, B., Delucchi, K. L., Gard, D. E., Fulford, D., ... & Vinogradov, S. (2015). Modeling the role of negative symptoms in determining social functioning in individuals at clinical high risk of psychosis. *Schizophrenia research*, *169*(1), 204-208.

Schlosser, D. A., Jacobson, S., Chen, Q., Sugar, C. A., Niendam, T. A., Li, G., ... & Cannon, T. D. (2012). Recovery from an at-risk state: clinical and functional outcomes of putatively prodromal youth who do not develop psychosis. *Schizophrenia Bulletin*, *38*(6), 1225-1233.

Schmael, C., Georgi, A., Krumm, B., Buerger, C., Deschner, M., Nöthen, M. M., ... & Rietschel, M. (2007). Premorbid adjustment in schizophrenia—an important aspect of phenotype definition. *Schizophrenia research*, *92*(1), 50-62.

Schultze-Lutter, F., Klosterkötter, J., Picker, H., Steinmeyer, E. M., & Ruhrmann, S. (2007). Predicting first-episode psychosis by basic symptom criteria. *Clinical Neuropsychiatry, 4*(1), 11-22.

Schultze-Lutter, F., Ruhrmann, S., Berning, J., Maier, W., & Klosterkötter, J. (2010). Basic symptoms and ultrahigh risk criteria: symptom development in the initial prodromal state. *Schizophrenia Bulletin*, *36*(1), 182-191.

Schultze-Lutter, F., Ruhrmann, S., Fusar-Poli, P., Bechdolf, A., G Schimmelmann, B., & Klosterkötter, J. (2012). Basic symptoms and the prediction of first-episode psychosis. *Current Pharmaceutical Design, 18*(4), 351-357.

Schwarz, G. (1978). Estimating the dimension of a model. *The Annals of Statistics*, *6*(2), 461-464.

Sclove, S. L. (1987). Application of model-selection criteria to some problems in multivariate analysis. *Psychometrika*, *52*(3), 333-343.

Seidman, L. J., Giuliano, A. J., Meyer, E. C., Addington, J., Cadenhead, K. S., Cannon, T. D., ... & Cornblatt, B. A. (2010). Neuropsychology of the prodrome to psychosis in the NAPLS consortium: relationship to family history and conversion to psychosis. *Archives of General Psychiatry*, *67*(6), 578-588.

Shadur, J. M., & Lejuez, C. W. (2015). Adolescent Substance Use and Comorbid Psychopathology: Emotion Regulation Deficits as a Transdiagnostic Risk Factor. *Current Addiction Reports*, *2*(4), 354-363.

Sharpe, D. (2015). Your Chi-Square Test is Statistically Significant: Now What?. *Practical Assessment, Research & Evaluation*, *20*(8), 2-12.

Simon, A. E., Velthorst, E., Nieman, D. H., Linszen, D., Umbricht, D., & de Haan, L. (2011). Ultra high-risk state for psychosis and non-transition: a systematic review. *Schizophrenia Research*, *132*(1), 8-17.

Stowkowy, J., & Addington, J. (2012). Maladaptive schemas as a mediator between social defeat and positive symptoms in young people at clinical high risk for psychosis. *Early intervention in psychiatry*, *6*(1), 87-90.

Stowkowy, J., Perkins, D. O., Woods, S. W., Nyman, K., & Addington, J. (2015). Personal Beliefs about Experiences in those at Clinical High Risk for Psychosis. *Behavioural and Cognitive Psychotherapy*, *43*(6), 669-675.

Strauss, E., Sherman, E. M., & Spreen, O. (2006). *A compendium of neuropsychological tests: Administration, norms, and commentary*. Oxford University Press, USA.

Strous, R. D., Alvir, J. M. J., Robinson, D., Gal, G., Sheitman, B., Chakos, M., & Lieberman, J. A. (2004). Premorbid functioning in schizophrenia: relation to baseline symptoms, treatment response, and medication side effects. *Schizophrenia Bulletin*, *30*(2), 265.

Tarbox, S. I., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Perkins, D. O., ... & Woods, S. W. (2013). Premorbid functional development and conversion to psychosis in clinical high-risk youths. *Development and Psychopathology*, *25*(4pt1), 1171-1186.

Tarbox, S. I., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Perkins, D. O., ... & Woods, S. W. (2014). Functional development in clinical high risk youth: prediction of schizophrenia versus other psychotic disorders. *Psychiatry Research*, *215*(1), 52-60.

Taylor, P. J., Pyle, M., Schwannauer, M., Hutton, P., & Morrison, A. (2015). Confirming the structure of negative beliefs about psychosis and bipolar disorder: A confirmatory factor analysis study of the Personal Beliefs about Experience Questionnaire and Personal Beliefs about Illness Questionnaire. *British Journal of Clinical Psychology*, *54*(4), 361-377.

Tein, J. Y., Coxe, S., & Cham, H. (2013). Statistical power to detect the correct number of classes in latent profile analysis. *Structural equation modeling: a multidisciplinary journal*, *20*(4), 640-657.

Thompson, A. D., Bartholomeusz, C., & Yung, A. R. (2011). Social cognition deficits and the 'ultra high risk' for psychosis population: a review of literature. *Early Intervention in Psychiatry*, *5*(3), 192-202.

Thompson, A., Nelson, B., & Yung, A. (2011). Predictive validity of clinical variables in the "at risk" for psychosis population: International comparison with results from the North American Prodrome Longitudinal Study. *Schizophrenia Research, 126*(1), 51-57.

Tombaugh, T. N. (2004). Trail Making Test A and B: normative data stratified by age and education. *Archives of clinical neuropsychology*, *19*(2), 203-214.

Tsai, K. H., López, S., Marvin, S., Zinberg, J., Cannon, T. D., O'Brien, M., & Bearden, C. E. (2014). Perceptions of family criticism and warmth and their link to symptom expression in racially/ethnically diverse adolescents and young adults at clinical high risk for psychosis. *Early Intervention in Psychiatry*. *9*(6), 476-486.

Tsuji, T., Kline, E., Sorensen, H. J., Mortensen, E. L., Michelsen, N. M., Ekstrom, M., ... & Schiffman, J. (2013). Premorbid teacher-rated social functioning predicts adult schizophrenia-spectrum disorder: a high-risk prospective investigation. *Schizophrenia Research*, *151*(1), 270-273.

Uchida, T., Matsumoto, K., Ito, F., Ohmuro, N., Miyakoshi, T., Ueno, T., & Matsuoka, H. (2014). Relationship between cognitive insight and attenuated delusional symptoms in individuals with at-risk mental state. *Psychiatry research*, *217*(1), 20-24.

Valmaggia, L. R., Stahl, D., Yung, A. R., Nelson, B., Fusar-Poli, P., McGorry, P. D., & McGuire, P. K. (2013). Negative psychotic symptoms and impaired role functioning predict transition outcomes in the at-risk mental state: a latent class cluster analysis study. *Psychological Medicine, 43*(11), 2311-2325.

van Donkersgoed, R. J. M., Wunderink, L., Nieboer, R., Aleman, A., & Pijnenborg, G. H. M. (2015). Social cognition in individuals at ultra-high risk for psychosis: a meta-analysis. *PloS one*, *10*(10), e0141075.

van Mastrigt, S., & Addington, J. (2002). Assessment of premorbid function in first-episode schizophrenia: modifications to the Premorbid Adjustment Scale. *Journal of Psychiatry and Neuroscience*, *27*(2), 92-101.

van Os, J. (2013). The dynamics of subthreshold psychopathology: implications for diagnosis and treatment. *American Journal of Psychiatry*, *170*(7), 695-698.

Veldhuizen, S. (2009). Differences in prevalence and treatment of bipolar disorder among immigrants: results from an epidemiologic survey. *Canadian Journal of Psychiatry*, *54*(11), 734-742.

Velthorst, E., Nieman, D. H., Becker, H. E., van de Fliert, R., Dingemans, P. M., Klaassen, R., ... & Linszen, D. H. (2009). Baseline differences in clinical symptomatology between ultra high risk subjects with and without a transition to psychosis. *Schizophrenia Research, 109*(1), 60-65.

Velthorst, E., Derks, E. M., Schothorst, P., Becker, H., Durston, S., Ziermans, T., ... & de Haan, L. (2013). Quantitative and qualitative symptomatic differences in individuals at Ultra-High Risk for psychosis and healthy controls. *Psychiatry Research, 210*(2), 432-437.

Vermunt, J. K., & Magidson, J. (2000). Latent Class Cluster Analysis. In J.A. Hagenaars and A.L. McCutcheon (Eds.), *Advances in Latent Class Analysis* (pp.89-106). Cambridge: Cambridge University Press.

Voineskos, A. N., Foussias, G., Lerch, J., Felsky, D., Remington, G., Rajji, T. K., ... & Mulsant, B. H. (2013). Neuroimaging evidence for the deficit subtype of schizophrenia. *JAMA psychiatry*, *70*(5), 472-480.

Webb, J. R., Addington, J., Perkins, D. O., Bearden, C. E., Cadenhead, K. S., Cannon, T. D., ... & Tsuang, M. T. (2015). Specificity of incident diagnostic outcomes in patients at clinical high risk for psychosis. *Schizophrenia bulletin*, *41*(5), 1066-1075.

Wechsler, D. (1974). Manual for the Wechsler Intelligence Scale for Children- Revised. New York: Psychological Corporation.

Wechsler, D. (1981). Manual for the Wechsler Adult Intelligence Scale-Revised. New York: Psychological Corporation.

Wigman, J. T., van Nierop, M., Vollebergh, W. A., Lieb, R., Beesdo-Baum, K., Wittchen, H. U., & van Os, J. (2012). Evidence that psychotic symptoms are prevalent in disorders of anxiety and depression, impacting on illness onset, risk, and severity—implications for diagnosis and ultra–high risk research. *Schizophrenia Bulletin*, *38*(2), 247-257.

Woods, S. W., Addington, J., Cadenhead, K. S., Cannon, T. D., Cornblatt, B. A., Heinssen, R., ... & McGlashan, T. H. (2009). Validity of the prodromal risk syndrome for first psychosis: Findings from the North American Prodrome Longitudinal Study. *Schizophrenia Bulletin, 35*(5), 894-908.

Wu, E. Q., Birnbaum, H. G., Shi, L., Ball, D. E., Kessler, R. C., Moulis, M., & Aggarwal, J. (2005). The economic burden of schizophrenia in the United States in 2002. *Journal of Clinical Psychiatry, 66*(9)*, 1122-1129.

Yang, L. H., Anglin, D. M., Wonpat-Borja, A. J., Opler, M. G., Greenspoon, M., & Corcoran, C. M. (2014). Public stigma associated with psychosis risk syndrome in a college population: implications for peer intervention. *Psychiatric Services*. *64*(3), 284-288.

Yong, E., Barbato, M., Penn, D. L., Keefe, R. S., Woods, S. W., Perkins, D. O., & Addington, J. (2014). Exploratory analysis of social cognition and neurocognition in individuals at clinical high risk for psychosis. *Psychiatry Research*, *218*(1), 39-43.

Young, R. C., Biggs, J. T., Ziegler, V. E., & Meyer, D. A. (1978). A rating scale for mania: reliability, validity and sensitivity. *The British Journal of Psychiatry*, *133*(5), 429-435.

Yung, A. R., Cotter, J., Wood, S. J., McGorry, P., Thompson, A. D., Nelson, B., & Lin, A. (2015). Childhood maltreatment and transition to psychotic disorder independently predict long-term functioning in young people at ultra-high risk for psychosis. *Psychological medicine*, *45*(16), 3453-3465.

Yung, A. R., & McGorry, P. D. (1996a). The initial prodrome in psychosis: Descriptive and qualitative aspects. *Australian and New Zealand Journal of Psychiatry, 30*(5), 587-599.

Yung, A. R., & McGorry, P. D. (1996b). The prodromal phase of first-episode psychosis: Past and current conceptualizations. *Schizophrenia Bulletin, 22*(2), 353-370.

Yung, A. R., Nelson, B., Stanford, C., Simmons, M. B., Cosgrave, E. M., Killackey, E., ... & McGorry, P. D. (2008). Validation of "prodromal" criteria to detect individuals at ultra high risk of psychosis: 2 year follow-up. *Schizophrenia Research*, *105*(1), 10-17.

Yung, A. R., Nelson, B., Thompson, A. D., & Wood, S. J. (2010). Should a "Risk Syndrome for Psychosis" be included in the DSMV?. *Schizophrenia Research*, *120*(1), 7-15.

Yung, A. R., Phillips, L. J., McGorry, P. D., McFarlane, C. A., Francey, S., Harrigan, S., ... & Jackson, H. J. (1998). Prediction of psychosis: a step towards indicated prevention of schizophrenia. *The British Journal of Psychiatry*. *Supplement*, *172*(33), 14-20.

Yung, A. R., Phillips, L. J., Yuen, H. P., Francey, S. M., McFarlane, C. A., Hallgren, M., & McGorry, P. D. (2003). Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. *Schizophrenia Research*, *60*(1), 21-32.

Yung, A. R., Woods, S. W., Ruhrmann, S., Addington, J., Schultze-Lutter, F., Cornblatt, B. A., ... & McGlashan, T. H. (2012). Whither the attenuated psychosis syndrome?. *Schizophrenia Bulletin*, *38*(6), 1130-1134.

Yung, A. R., Yung, A. R., Pan Yuen, H., Mcgorry, P. D., Phillips, L. J., Kelly, D., ... & Stanford, C. (2005). Mapping the onset of psychosis: the comprehensive assessment of at-risk mental states. *Australian and New Zealand Journal of Psychiatry*, *39*(11-12), 964-971.

Table 1. *Measures of Neurocognition and Social Cognition and Associated Normative Data*

	Domain	Test	Variable employed (range)	Healthy Controls M (SD)
NC	Verbal fluency	Category Instances (CAT) (Benton, Hamsher, & Sivan, 1989)	Mean correct across trials	Not available
NC	Executive functioning	Wisconsin Card Sorting Test, 64-card computerized version (WCST) (Kongs et al., 2000)	Perseverative errors	6.92 (5.04) (Strauss, Sherman, & Spreen, 2006)
		Trail Making Test B (TMT) (Reitan & Wolfson, 1985)	Time to completion (seconds)	49.82 (12.52) (Tombaugh, 2004)
NC	Speed of processing	Trail Making Test A (TMT) (Reitan & Wolfson, 1985)	Time to completion (seconds)	23.66 (7.79) (Tombaugh, 2004)
NC	Verbal explicit memory	Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1958)	Total recall, trials 1-5 (0-75)	54.73 (7.43) (Strauss et al., 2006)
NC	Attention	Continuous Performance Test-Identical Pairs (CPT-IP) (Cornblatt & Keilp, 1994)	Mean response sensitivity (d') 3 digit	3.56 (0.12) (Kahn et al., 2012)
SC	Theory of Mind	Reading the Mind in the Eyes Task (Baron-Cohen et al., 2001)	Total correct (0-36)	26.2 (3.6) (Baron-Cohen et al., 2001)
SC	Emotion Perception	Face Emotion Identification Task (FEIT) (Kerr & Neale, 1993)	Total correct (0-19)	13.42 (2.18) (Pinkham & Penn, 2006)
		Face Emotion Discrimination Task (FEDT) (Kerr & Neale, 1993)	Total correct (0-30)	26.47 (2.30) (Pinkham & Penn, 2006)
		Affective Prosody Task (AP) (Edwards et al., 2001)	Total correct (0-60)	49.46 (6.27) (Edwards et al., 2001)

NC, Neurocognition; SC, Social Cognition

Table 2. *Fit Indices and Class Sizes for the Latent Profile Analysis of SOPS Symptom Scores, CDSS Total Score, and Neurocognitive Scores*

	Number of classes				
	1	2	3	4	5
Loglikelihood	-14339.751	-14026.772	-13839.33	-13729.856	-13644.023
No. of parameters	52	79	106	133	160
AIC	28783.501	28211.544	27890.66	27725.713	27608.047
BIC	28970.812	28496.111	28272.484	28204.795	28184.386
ssa BIC	28805.935	28245.626	27936.39	27783.091	27677.074
Entropy	n/a	0.909	0.884	0.907	0.925
Bootstrap LRT		$p<.0001$	$p<.0001$	$p<.0001$	$p<.0001$
Class size	271	209/62	124/106/41	27/35/110/99	91/27/96/26/31

SOPS: Scale of Prodromal Symptoms; AIC: Akaike's Information Criteria (smaller number suggests a better model); BIC: Bayesian Information Criteria (smaller number suggests a better model); ssa BIC: sample size-adjusted Bayesian Information Criteria (smaller number suggests a better model); Entropy, an overall measure of how well a model predicts class membership, ranging from 0 (no predictive power) to 1 (perfect prediction) (above .80 indicates adequate predictive power); LRT: parametric bootstrapped likelihood ratio test to compare n with $n-1$ classes (significant LRT indicates the n-class solution is better than an $(n-1)$-class solution; Class size, estimated class size based on most likely class membership.

Table 3. *Latent Class Membership Based Upon Estimated Posterior Probabilities*

Class	Based on estimated posterior probability *n* (%)	Based on most likely class membership *n* (%)	Class 1 Mild	Class 2 Positive	Class 3 Negative
1	125.11 (46.2)	124 (45.8)	0.956	0.036	0.008
2	105.71 (39.0)	106 (39.1)	0.048	0.945	0.007
3	40.18 (14.8)	41 (15.1)	0.034	0.027	0.939

The first column indicates class membership based on the mean estimated posterior probability. The second column shows the classification of subjects in each class based on their highest posterior probability (most likely class membership). Columns Class 1-Class 3 indicate the average latent class probabilities for most likely latent class membership (row) by latent class (column). This means that individuals classified into class 1 had an average posterior probability for membership in class one of 95.6%. Individuals classified in class 1 had average posterior probabilities of belonging to class 2 of 4.8% and class 3 of 3.4%.

Table 4. *Latent Profile Analysis of SOPS, CDSS, and Neurocognition: Estimated Parameters for the Three-Class Solution*

Indicator	Class 1 (*n* = 124)	Class 2 (*n* = 106)	Class 3 (*n* = 41)	ANOVA *p*	Pairwise	Effect Size (r^2)
P1: Unusual Thought Content/Delusional Ideas	2.4 (0.18)	3.1 (0.15)	2.6 (0.40)	.002	2>1	0.05
P2: Suspiciousness/Persecutory Ideas	1.8 (0.17)	2.7 (0.15)	1.9 (0.37)	$p<.001$	2>1,3	0.08
P3: Grandiose Ideas	1.0 (0.13)	1.0 (0.13)	0.9 (0.23)	.629		0.00
P4: Perceptual Abnormalities/Hallucinations	1.7 (0.17)	2.6 (0.15)	2.2 (0.37)	$p<.001$	2>1	0.07
P5: Disorganized Communication	1.1 (0.14)	1.6 (0.13)	1.7 (0.25)	.001	2,3>1	0.06
N1: Social Anhedonia	0.9 (0.18)	1.8 (0.17)	2.8 (0.68)	$p<.001$	3>1,2; 2>1	0.16
N2: Avolition	0.8 (0.19)	2.3 (0.19)	2.8 (0.45)	$p<.001$	3,2>1	0.35
N3: Decreased Expression of Emotion	0.5 (0.16)	1.1 (0.16)	1.9 (0.46)	$p<.001$	3>1,2; 2>1	0.16
N4: Decreased Experience of Emotions/Self	0.7 (0.12)	1.8 (0.16)	1.5 (0.45)	$p<.001$	2,3>1	0.15
N5: Decreased Ideational Richness	0.4 (0.11)	0.8 (0.11)	2.2 (0.58)	$p<.001$	3>1,2; 2>1	0.29
N6: Occupational Functioning	1.2 (0.42)	2.9 (0.26)	3.8 (0.36)	$p<.001$	3>1,2; 2>1	0.25
D1: Odd Behavior or Appearance	0.5 (0.12)	0.6 (0.11)	2.0 (0.64)	$p<.001$	3>1,2	0.20
D2: Bizarre Thinking	0.7 (0.14)	0.8 (0.11)	1.2 (0.27)	.081		0.02
D3: Trouble with Focus and Attention	1.2 (0.21)	2.3 (0.14)	2.5 (0.24)	$p<.001$	2,3>1	0.23
D4: Impairment in Personal Hygiene	0.3 (0.13)	0.7 (0.14)	1.3 (0.47)	$p<.001$	3>1,2; 2>1	0.09
G1: Sleep Disturbance	0.9 (0.13)	2.5 (0.15)	1.7 (0.47)	$p<.001$	2>1,3; 3>1	0.29
G2: Dysphoric Mood	1.3 (0.20)	3.5 (0.15)	3.0 (0.51)	$p<.001$	2>1,3; 3>1	0.44
G3: Motor Disturbances	0.3 (0.06)	0.8 (0.10)	0.8 (0.40)	$p<.001$	2,3>1	0.08
G4: Impaired Tolerance to Normal Stress	0.8 (0.14)	2.6 (0.18)	2.4 (0.52)	$p<.001$	2,3>1	0.30
CDSS Total Score	2.0 (0.28)	5.8 (0.45)	3.8 (1.15)	$p<.001$	2>1,3; 3>1	0.24
CAT Total Score	47.2 (1.62)	49.9 (1.41)	32.5 (2.41)	$p<.001$	1,2>3	0.22
WCST Perseverative Errors	6.4 (0.36)	6.8 (0.43)	12.9 (2.68)	$p<.001$	3>1,2	0.20
TMT A	26.6 (1.22)	24.2 (0.82)	43.2 (4.91)	$p<.001$	3>1,2	0.36
TMT B	62.0 (5.51)	53.8 (1.86)	107.3 (9.90)	$p<.001$	3>1,2	0.35
CPT D'3	2.7 (0.09)	2.9 (0.09)	1.8 (0.27)	$p<.001$	1,2>3	0.18
RAVLT Total Score	53.52 (2.74)	55.46 (1.05)	43.10 (5.17)	$p<.001$	1,2>3	0.21

P, positive symptom; N, negative symptom; D, disorganized symptom; G, general symptom; CDSS, Calgary Depression Scale for Schizophrenia; CAT: category instances; WCST, Wisconsin Card Sorting Test; TMT, Trail Making Test; CPT, Continuous Performance Test; RAVLT, Rey Auditory Verbal Learning Test. Mean parameter estimates and associated standard errors for each latent class are provided; mean parameter estimate (standard error). Pairwise comparisons are significant at the $p < .05$ level.

Table 5. *Associations Between Latent Classes and Demographic Characteristics*

	Class 1 ($n = 124$)	Class 2 ($n = 106$)	Class 3 ($n = 41$)	Test
Age, mean (SD)	19.48 (4.26)	20.71 (4.03)	17.26 (4.09)	$F_{2,268} = 10.36, p < 0.001$; pairwise 2>3
Sex, *n* (% within class)				
Male	69 (55.6)	59 (55.7)	26 (63.4)	$\chi^2_2 = .86, p = 0.65$
Female	55 (44.4)	47 (44.3)	15 (36.6)	
Race/ethnicity, *n* (% within class)				
White	93 (75.0)	82 (77.4)	29 (70.7)	$\chi^2_8 = 8.53, p = 0.38$
Black	13 (10.5)	9 (8.5)	7 (17.1)	
Asian	9 (7.3)	8 (7.5)	0 (0.0)	
Native Hawaiian/Pacific Islander	0 (0.0)	1 (0.9)	0 (0.0)	
Mixed	9 (7.3)	6 (5.7)	5 (12.2)	
Hispanic, *n* (% within class)				
Yes	14 (11.3)	11 (10.4)	5 (12.2)	$\chi^2_2 = .11, p = 0.95$
No	110 (88.7)	95 (89.6)	36 (87.8)	
Parental education, *n* (%)				
Did not complete high school	13 (10.6)	6 (5.7)	9 (22.0)	$\chi^2_{16} = 19.78, p = 0.23$
Unknown	16 (13.0)	12 (11.4)	10 (24.4)	
GED or equivalent	18 (14.6)	9 (8.6)	3 (7.3)	
Some college, did not graduate	10 (8.1)	12 (11.4)	1 (2.4)	
Community college or technical school degree	33 (26.8)	31 (29.5)	9 (22.0)	
College graduate	3 (2.4)	4 (3.8)	1 (2.4)	
College graduate and some master's level courses	14 (11.4)	16 (15.2)	5 (12.2)	
Master's degree completed	3 (2.4)	4 (3.8)	1 (2.4)	
Advanced degree courses, did not graduate	13 (10.6)	11 (10.5)	2 (4.9)	
If did not complete HS/GED, # years edu: M (SD)	8.78 (2.91)	10.50 (.58)	9.11 (2.37)	$F_{2,15} = 0.88, p < 0.43$
Clinic, *n* (% within class)				
University of North Carolina at Chapel Hill	40 (32.3)_a	42 (39.6)_a	4 (9.8)_b	$\chi^2_4 = 16.90, p = 0.002$
University of Toronto	52 (41.9)_a	44 (41.5)_a	18 (43.9)_a	
Yale University	32 (25.8)_a	20 (18.9)_a	19 (46.3)_b	

Subscript letters note a class whose column proportions do not differ significantly from each other using z-square cell comparison tests with Bonferroni correction. Differing subscript letters note significant differences between classes ($p < .05$)

118

Table 6. *Associations Between Classes and Covariates*

	Class 1 (n = 124)	Class 2 (n = 106)	Class 3 (n = 41)	Test	Pairwise
Symptomatology					
Risk group, n (% within class)					
Clinical high risk (CHR, n=171)	66 (53.2)$_a$	79 (74.5)$_b$	26 (63.4)$_{a, b}$	$\chi^2_2 = 11.14, p = 0.004$	
Help seeking control (HSC, n=100)	58 (46.8)$_a$	27 (25.5)$_b$	15 (36.6)$_{a, b}$		
YMRS total score, mean (SD)	1.97 (2.80)	3.27 (3.99)	3.88 (4.14)	$F_{2,263} = 6.17, p = 0.002$	2,3>1
Internalized stigma, mean (SD)					
PBEQ total score	27.54 (4.83)	31.63 (4.32)	30.54 (5.59)	$F_{2,237} = 19.13, p < 0.001$	2,3>1
PBEQ "control over experiences" subscale	6.33 (1.90)	7.78 (1.61)	7.15 (2.10)	$F_{2,237} = 15.46, p < 0.001$	2,3>1
Alcohol use/drug use, mean (SD)					
Alcohol	1.58 (0.51)	1.61 (0.58)	1.41 (0.67)	$F_{2,266} = 1.81, p = 0.166$	
Marijuana or THC	1.35 (0.60)	1.42 (0.68)	1.29 (0.75)	$F_{2,266} = .64, p = 0.529$	
Cocaine	1.07 (0.34)	1.09 (0.37)	1.00 (0.00)	$F_{2,266} = 1.05, p = 0.351$	
Opiates	1.04 (0.30)	1.05 (0.35)	1.00 (0.00)	$F_{2,266} = 0.39, p = 0.675$	
Amphetamines	1.03 (0.18)	1.01 (0.10)	1.00 (0.00)	$F_{2,266} = 1.28, p = 0.281$	
MDMA/ecstasy	1.07 (0.26)	1.02 (0.14)	1.00 (0.00)	$F_{2,266} = 3.19, p = 0.043$	
GHB	1.01 (0.09)	1.00 (0.00)	1.00 (0.00)	$F_{2,265} = 0.59, p = 0.556$	
Huffing glue/other volatiles	1.01 (0.09)	1.00 (0.00)	1.00 (0.00)	$F_{2,266} = 0.59, p = 0.554$	
Hallucinogens	1.07 (0.29)	1.11 (0.35)	1.00 (0.00)	$F_{2,266} = 2.26, p = 0.106$	
Other	1.01 (0.09)	1.09 (0.31)	1.00 (0.00)	$F_{2,266} = 4.83, p = 0.009$	2>1
Functioning					
Pre-morbid Adjustment (PAS), mean (SD)					
Child Social Maladjustment	0.16 (0.20)	0.20 (0.20)	0.30 (0.23)	$F_{2,250} = 7.44, p = 0.001$	3>1,2
Child Acad. Maladjustment	0.17 (0.18)	0.18 (0.19)	0.29 (0.22)	$F_{2,250} = 6.76, p = 0.001$	3>1,2
Early Adol. Social Maladjustment	0.21 (0.20)	0.25 (0.19)	0.36 (0.20)	$F_{2,247} = 8.78, p < 0.001$	3>1,2
Early Adol. Acad. Maladjustment	0.25 (0.21)	0.28 (0.24)	0.40 (0.27)	$F_{2,247} = 7.44, p = 0.001$	3>1,2
Late Adol. Social Maladjustment	0.19 (0.19)	0.30 (0.20)	0.48 (0.29)	$F_{2,187} = 17.58, p < 0.001$	3>1,2; 2>1
Late Adol. Acad. Maladjustment	0.23 (0.21)	0.35 (0.25)	0.48 (0.30)	$F_{2,180} = 10.80, p < 0.001$	2,3>1
Early/Late Adol. Social Avg.	0.19 (0.18)	0.27 (0.18)	0.41 (0.24)	$F_{2,187} = 12.10, p < 0.001$	3>1,2; 2>1

Heinrichs-Carpenter QLS					
Occupational functioning	5.13 (1.49)	4.82 (1.81)	3.68 (2.45)	$F_{2,243} = 9.35$, $p < 0.001$	1,2>3
Accomplishment	4.32 (1.45)	3.54 (1.77)	2.42 (1.64)	$F_{2,243} = 20.74$, $p < 0.001$	1,2>3; 1>2
Underemployment	4.74 (1.47)	3.79 (1.77)	2.79 (1.89)	$F_{2,243} = 6.37$, $p = 0.002$	1,2>3; 1>2
Role satisfaction	4.79 (1.65)	3.93 (1.78)	3.82 (1.79)	$F_{2,189} = 21.96$, $p < 0.001$	1>2
QLS total score (1-3)	14.19 (3.91)	12.15 (4.83)	8.89 (5.62)	$F_{2,243} = 19.83$, $p < 0.001$	1,2>3; 1>2
Social cognition, mean (SD)					
Eyes Task total score	26.22 (4.53)	25.77 (4.15)	19.92 (4.55)	$F_{2,228} = 29.57$, $p < 0.001$	1,2>3
FEIT total score	13.23 (2.28)	12.84 (2.12)	10.97 (2.77)	$F_{2,226} = 12.86$, $p < 0.001$	1,2>3
FEDT total score	25.67 (1.86)	25.80 (1.96)	24.89 (2.08)	$F_{2,227} = 2.97$, $p = 0.053$	
AP total score	45.90 (5.24)	45.71 (5.27)	37.26 (9.45)	$F_{2,221} = 29.20$, $p < 0.001$	1,2>3
Neurocognition, mean (SD)					
IQ Score	113.58 (17.22)	115.27 (15.42)	87.10 (12.44)	$F_{2,186} = 27.30$, $p < 0.001$	1,2>3

YMRS, Young Mania Rating Scale; PBEQ, Personal Beliefs about Experiences Questionnaire; QLS, Quality of Life Scale; FEIT, Face Emotion Identification Task; FEDT, Face Emotion Discrimination Task; AP, Affective Prosody Task.

Subscript letters note a class whose column proportions do not differ significantly from each other using z-square cell comparison tests with Bonferroni correction, while differing subscript letters note significant differences between classes ($p < .05$)

Table 7. *Descriptive Statistics and Mean Estimates of SFS by Class, Across Time Points*

	Mean Estimate	SE	Mean	SD	*n*
Class 1 – Baseline	123.37	2.30	123.43	29.07	113
Class 1 – 6 month	130.57	2.75	132.19	16.01	67
Class 1 – 12 month	127.08	2.93	127.36	17.08	56
Class 1 – 18 month	125.41	3.37	129.26	21.00	38
Class 1 – 24 month	127.53	3.79	133.25	20.52	28
Class 2 – Baseline	112.15	2.53	112.38	25.31	93
Class 2 – 6 month	117.83	3.08	117.36	28.61	53
Class 2 – 12 month	121.84	3.37	120.24	22.87	41
Class 2 – 18 month	122.01	3.61	118.82	20.34	34
Class 2 – 24 month	125.05	4.25	121.18	23.37	22
Class 3 – Baseline	106.05	3.88	106.05	21.07	40
Class 3 – 6 month	112.94	4.64	115.88	23.05	24
Class 3 – 12 month	116.68	5.23	118.41	26.48	17
Class 3 – 18 month	113.39	5.94	115.50	25.99	12
Class 3 – 24 month	102.65	6.62	104.11	19.68	9

SE, Standard Error; SD, Standard Deviation

Table 8. *Generalized Linear Mixed Model Between Classes for SFS Over Time*

	Mean Estimate Difference Between Groups	Standard Error	df	*t*	Uncorrected *p*	Hochberg *p*
Class 1 vs. Class 2						
Baseline: Class 1 vs. Class 2	11.22	3.42	382	3.28	0.001	0.015
6 Month: Class 1 vs. Class 2	12.74	4.13	382	3.09	0.002	0.024
12 Month: Class 1 vs. Class 2	5.24	4.47	382	1.17	0.242	0.664
18 Month: Class 1 vs. Class 2	3.40	4.94	382	0.69	0.491	0.664
24 Month: Class 1 vs. Class 2	2.47	5.69	382	0.43	0.664	0.664
Class 1 vs. Class 3						
Baseline: Class 1 vs. Class 3	17.32	4.51	382	3.84	< 0.000	0.002
6 Month: Class 1 vs. Class 3	17.63	5.39	382	3.27	0.001	0.015
12 Month: Class 1 vs. Class 3	10.40	6.00	382	1.73	0.084	0.664
18 Month: Class 1 vs. Class 3	12.03	6.83	382	1.76	0.079	0.664
24 Month: Class 1 vs. Class 3	24.88	7.63	382	3.26	0.001	0.015
Class 2 vs. Class 3						
Baseline: Class 2 vs. Class 3	6.10	4.63	382	1.32	0.188	0.664
6 Month: Class 2 vs. Class 3	4.88	5.57	382	0.88	0.381	0.664
12 Month: Class 2 vs. Class 3	5.17	6.23	382	0.83	0.407	0.664
18 Month: Class 2 vs. Class 3	8.62	6.95	382	1.24	0.216	0.664
24 Month: Class 2 vs. Class 3	22.40	7.87	382	2.85	0.005	0.047

SFS, Social Functioning Scale; df, degrees of freedom; Mean estimate difference between groups is the absolute value.

Table 9. *Generalized Linear Mixed Model Within Group Analysis for SFS Over Time*

	Change in Mean Estimate	Standard Error	df	*t*	Uncorrected *p*	Hochberg *p*
Class 1: Baseline vs. 6 Month	7.21	2.64	382	-2.73	0.007	0.099
Class 1: Baseline vs. 12 Month	3.71	2.81	382	-1.32	0.186	0.965
Class 1: Baseline vs. 18 Month	2.05	3.26	382	-0.63	0.531	0.965
Class 1: Baseline vs. 24 Month	4.16	3.69	382	-1.13	0.261	0.965
Class 1: 12 Month vs. 18 Month	-1.67	3.49	382	0.48	0.634	0.965
Class 1: 12 Month vs. 24 Month	0.45	3.91	382	-0.11	0.909	0.965
Class 2: Baseline vs. 6 Month	5.68	2.95	382	-1.93	0.055	0.654
Class 2: Baseline vs. 12 Month	9.69	3.26	382	-2.97	0.003	0.053
Class 2: Baseline vs. 18 Month	9.86	3.50	382	-2.81	0.005	0.082
Class 2: Baseline vs. 24 Month	12.91	4.15	382	-3.11	0.002	0.036
Class 2: 12 Month vs. 18 Month	0.17	3.83	382	-0.04	0.965	0.965
Class 2: 12 Month vs. 24 Month	3.21	4.46	382	-0.72	0.471	0.965
Class 3: Baseline vs. 6 Month	6.89	4.39	382	-1.57	0.117	0.965
Class 3: Baseline vs. 12 Month	10.63	5.01	382	-2.12	0.035	0.484
Class 3: Baseline vs. 18 Month	7.34	5.74	382	-1.28	0.202	0.965
Class 3: Baseline vs. 24 Month	-3.40	6.45	382	0.53	0.598	0.965
Class 3: 12 Month vs. 18 Month	-3.29	6.23	382	0.53	0.598	0.965
Class 3: 12 Month vs. 24 Month	-14.02	6.89	382	2.03	0.043	0.554

SFS, Social Functioning Scale; df, degrees of freedom; Change in Mean Estimate is second time point subtracted from first time point.

Table 10. *Class Membership: Results of the Multinomial Regression Analysis of Covariates*

	B (S.E.)	OR (95% CI)	Wald χ^2	p
Class 2				
Intercept	3.08			
Child Academic Maladjustment	-1.89	0.15 (0.02-1.10)	1.01	.062
Early Adolescent Social Maladjustment	1.46	4.31 (0.75-24.65)	2.70	.101
QLS Total Score	-0.11	0.90 (0.83-0.96)	9.03	.003
Eyes Task Total Score	-0.01	0.99 (0.92-1.08)	0.03	.859
FEIT Total Score	-.14	0.87 (0.75-1.01)	3.50	.061
AP Total Score	.00	1.00 (0.94-1.07)	0.01	.930
Class 3				
Intercept	13.67			
Child Academic Maladjustment	1.76	5.82 (0.35-97.72)	1.50	.221
Early Adolescent Social Maladjustment	3.17	23.81 (1.63-347.86)	5.37	.021
QLS Total Score	-0.28	0.76 (0.68-0.86)	20.70	< .001
Eyes Task Total Score	-0.24	0.79 (0.69-0.90)	11.56	.001
FEIT Total Score	-0.23	0.80 (0.63-1.02)	3.32	.069
AP Total Score	-0.11	0.89 (0.82-0.98)	5.52	.019

QLS, Heinrichs-Carpenter Quality of Life Scale; FEIT, Face Emotion Identification Task; AP, Affective Prosody Task; OR, odds ratio; CI, confidence interval; S.E., standard error.
Class 1 (mild) was selected as the reference group.

Table 11. *Modeled Probability (%) of Being Assigned to a Class Based on Covariates*

| Clinical Characteristic	Class 1 (Mild)	Class 2 (Positive-Depressive)	Class 3 (Negative-Neurocognitive)
Low Childhood Academic Maladjustment	44.29	52.94	2.78
Average Childhood Academic Maladjustment	51.75	43.77	4.48
High Childhood Academic Maladjustment	58.20	34.84	6.96
Low Early Adolescent Social Maladjustment	59.76	37.53	2.71
Average Early Adolescent Social Maladjustment	51.75	43.77	4.48
High Early Adolescent Social Maladjustment	43.40	49.43	7.17
Low Role Functioning	35.48	52.27	12.25
Average Role Functioning	51.75	43.77	4.48
High Role Functioning	66.34	32.22	1.44
Low Theory of Mind	46.30	40.62	13.08
Average Theory of Mind	51.75	43.77	4.48
High Theory of Mind	54.28	44.27	1.44
Low Face Emotion Recognition	42.54	51.07	6.39
Average Face Emotion Recognition	51.75	43.77	4.48
High Face Emotion Recognition	60.76	36.21	3.03
Low Affective Prosody Ability	49.59	41.15	9.26
Average Affective Prosody Ability	51.75	43.77	4.48
High Affective Prosody Ability	52.57	45.32	2.11
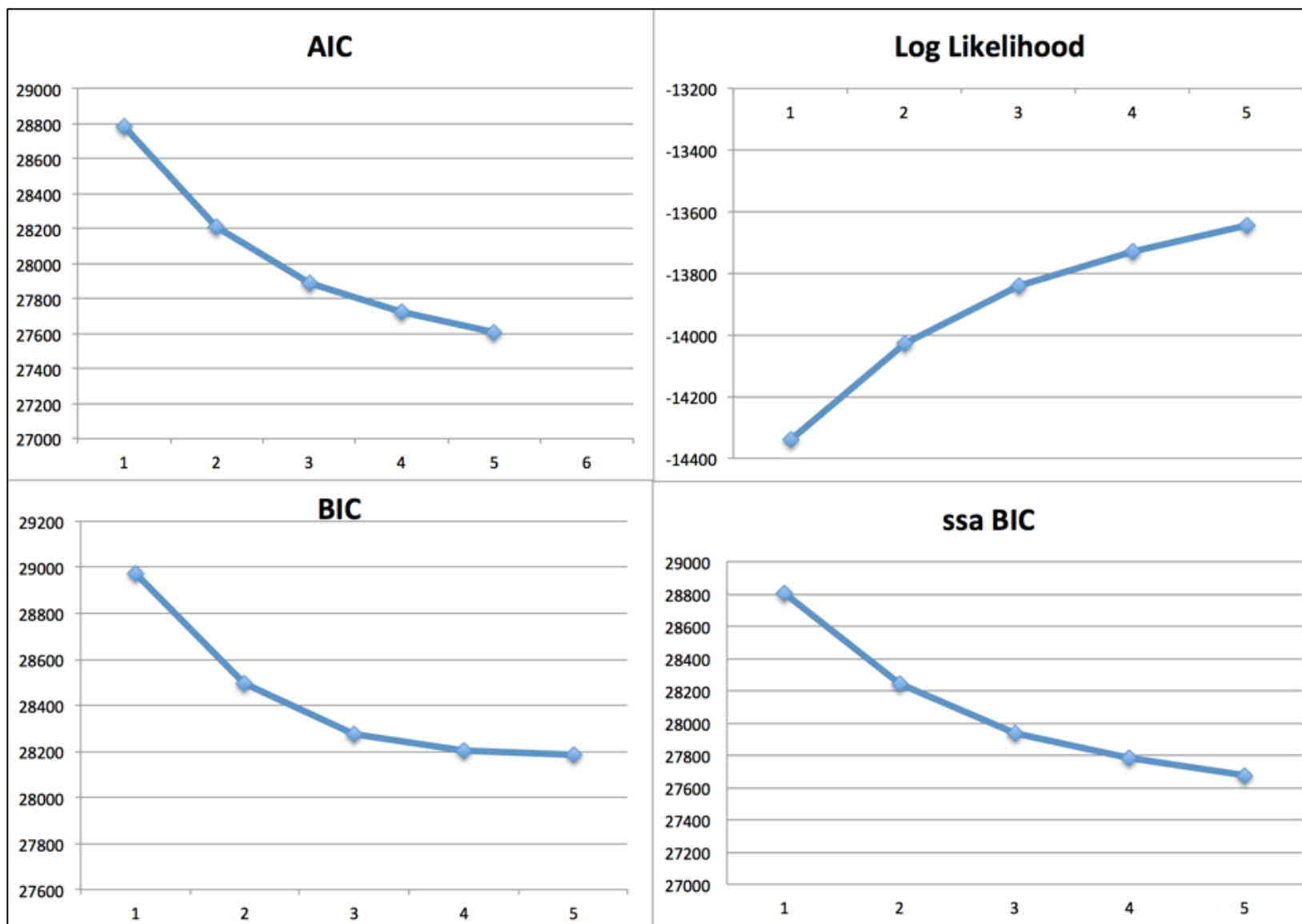
Figure 1. Scree Plots. Y-axis represents information criteria value for each plot (e.g., AIC value). X-axis represents *k* classes. AIC, Akaike's Information Criteria; BIC, Bayesian Information Criteria; ssa BIC, sample size adjusted Bayesian Information Criteria.
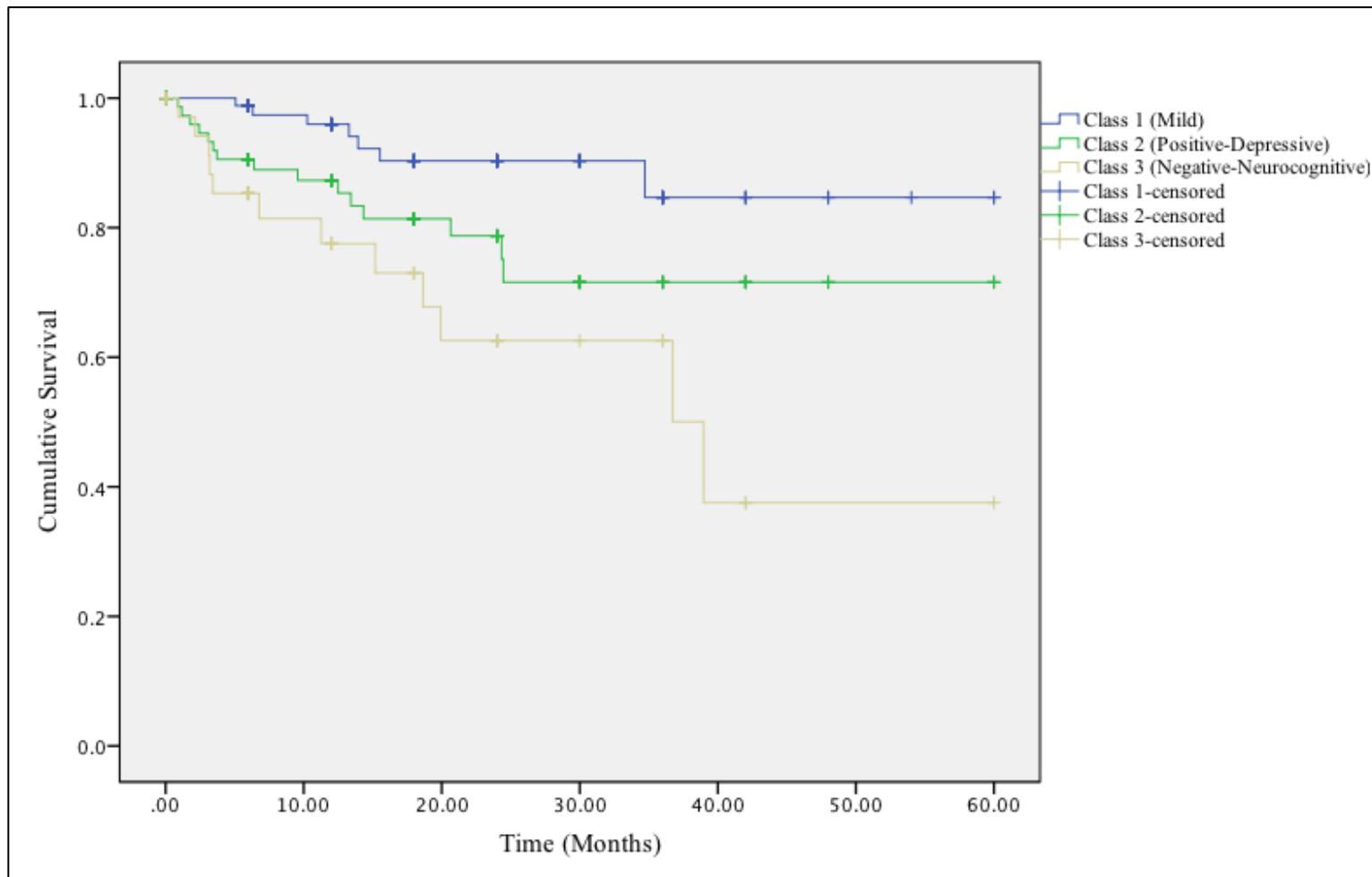
Figure 2. Kaplan-Meier Survival Plot of transition to psychosis within 5 years of referral. Cumulative survival indicates the % of the class that did not transition to psychosis across time.
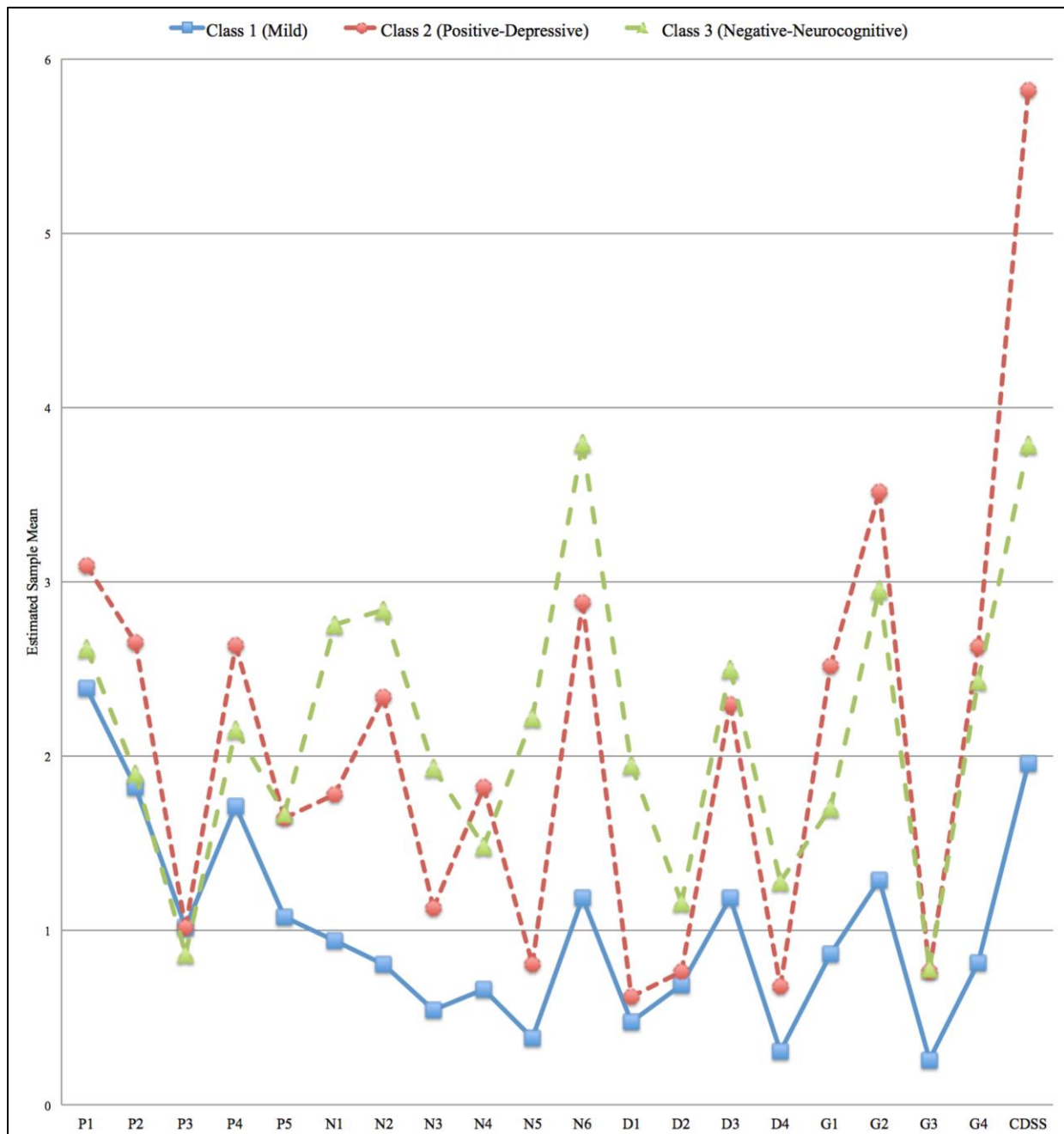
Figure 3. Latent profile plot of Scale of Prodromal Symptoms (SOPS) items and Calgary Depression Scale for Schizophrenia (CDSS) total score. Estimated sample means of each indicator for the three-class model. P1, Unusual Thought Content/Delusional Ideas; P2, Suspiciousness/Persecutory Ideas; P3, Grandiose Ideas; P4, Perceptual Abnormalities/Hallucinations; P5, Disorganized Communication; N1, Social Anhedonia; N2, Avolition; N3, Decreased Expression of Emotion; N4, Decreased Experience of Emotions and Self; N5, Decreased Ideational Richness; N6, Occupational Functioning; D1, Odd Behavior or Appearance; D2, Bizarre Thinking; D3, Trouble with Focus and Attention; D4, Impairment in Personal Hygiene; G1, Sleep Disturbance; G2, Dysphoric Mood; G3, Motor Disturbances; G4, Impaired Tolerance to Normal Stress; CDSS, Calgary Depression Scale for Schizophrenia total score.
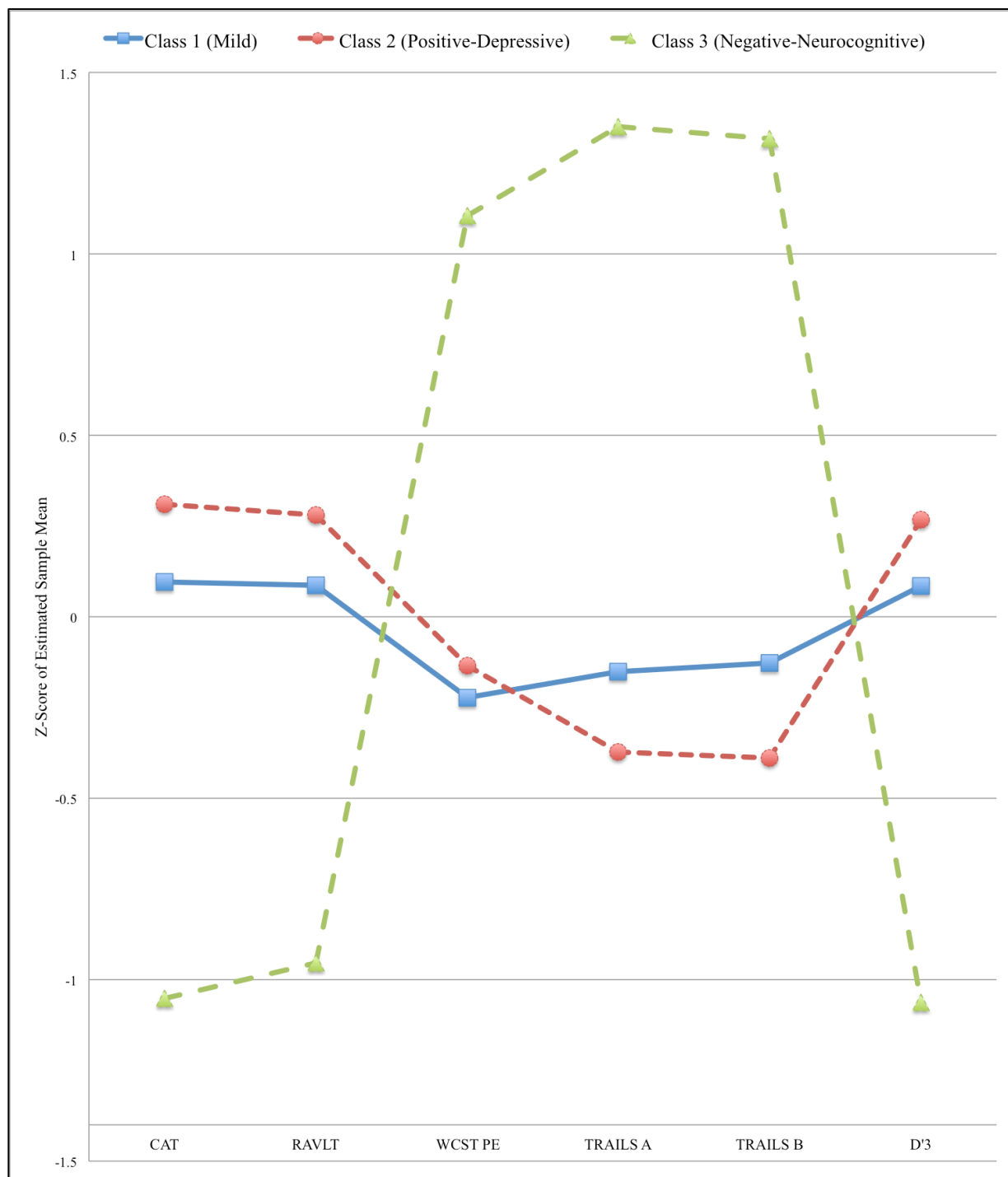
Figure 4. Latent profile plot of neurocognitive scores. CAT, Category Instances; RAVLT, Rey Auditory Verbal Learning Test; WCST PE, Wisconsin Cart Sorting Test Perseverative Errors; Trails A, Trail Making Test A; Trails B, Trail Making Test B; D'3, Continuous Performance Test-Identical Pairs (CPT-IP) D'3.
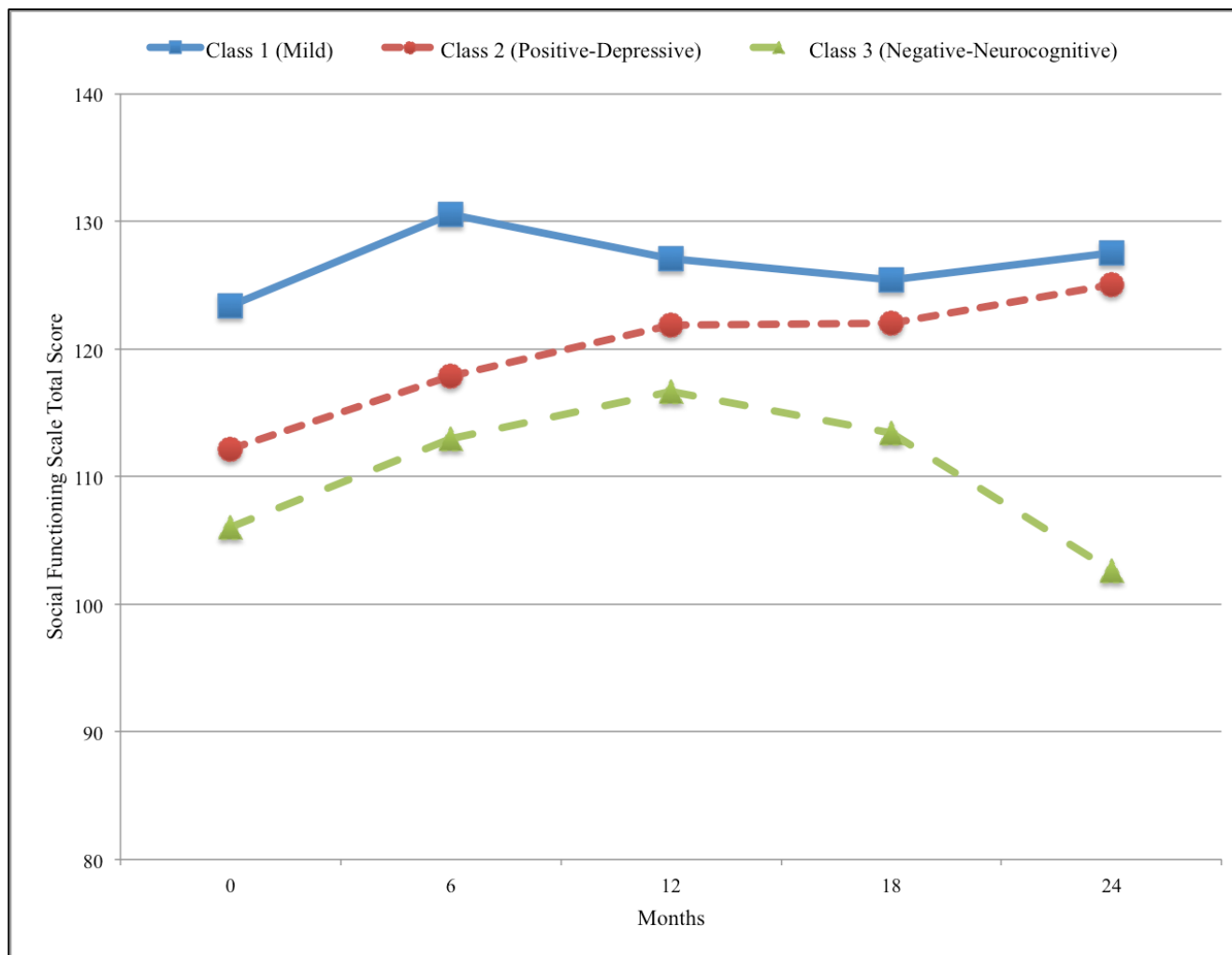
Figure 5. Mean Estimates of Social Functioning Scale (SFS) Over Time by Class.