Schizophrenia Bulletin vol. 44 no. 2 pp. 286–296, 2018
doi:10.1093/schbul/sbx080
Advance Access publication July 14, 2017

Latent Profile Analysis and Conversion to Psychosis: Characterizing Subgroups to Enhance Risk Prediction

Kristin M. Healey*[,1], David L. Penn[1,2], Diana Perkins[3], Scott W. Woods[4], Richard S. E. Keefe[5], and Jean Addington[6]

[1]Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, NC; [2]School of Psychology, Australian Catholic University, Melbourne, Australia; [3]Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, NC; [4]Department of Psychiatry, Yale University, New Haven, CT; [5]Department of Psychiatry, Duke University Medical Center, Durham, NC; [6]Department of Psychiatry, Faculty of Medicine, University of Calgary, Calgary, AB, Canada

*To whom correspondence should be addressed; Department of Psychology, University of North Carolina at Chapel Hill, CB #3270, Davie Hall, Chapel Hill, NC 27599-3270, US; tel: 609-468-2857, fax: 919-962-2537, e-mail: healey3@gmail.com

Background: **Groups at clinical high risk (CHR) of developing psychosis are heterogeneous, composed of individuals with different clusters of symptoms. It is likely that there exist subgroups, each associated with different symptom constellations and probabilities of conversion.** ***Method:*** **Present study used latent profile analysis (LPA) to ascertain subgroups in a combined sample of CHR (*n* = 171) and help-seeking controls (HSCs; *n* = 100; PREDICT study). Indicators in the LPA model included baseline Scale of Prodromal Symptoms (SOPS), Calgary Depression Scale for Schizophrenia (CDSS), and neurocognitive performance as measured by multiple instruments, including category instances (CAT). Subgroups were further characterized using covariates measuring demographic and clinical features.** ***Results:*** **Three classes emerged: class 1 (mild, transition rate 5.6%), lowest SOPS and depression scores, intact neurocognitive performance; class 2 (paranoid-affective, transition rate 14.2%), highest suspiciousness, mild negative symptoms, moderate depression; and class 3 (negative-neurocognitive, transition rate 29.3%), highest negative symptoms, neurocognitive impairment, social cognitive impairment. Classes 2 and 3 evidenced poor social functioning.** ***Conclusions: Results*** **support a subgroup approach to research, assessment, and treatment of help-seeking individuals. Class 3 may be an early risk stage of developing schizophrenia.**

Key words: clinical high risk/ultra high risk/ neurocognition/psychosis/functioning/early intervention/negative symptoms

Introduction

Individuals at clinical high risk (CHR) often present with a mixture of difficulties in addition to subthreshold psychotic symptoms, such as neurocognitive decline, premorbid dysfunction, and anxious/mood disorders.[1–4] Heterogeneity impedes research by obscuring potentially discrete subtypes, which hinders clinical research, evaluation, and treatment.

Latent subgroup models are a novel approach in explicating risk in CHR and are within a group of statistical methods known as latent variable mixture modeling (LVMM[5]). LVMM, such as latent profile analysis (LPA), aims to identify homogenous subgroups within heterogeneous cohorts, each with independent symptom constellations and differential associations with conversion and functional ability.[5,6] LVMM may improve accuracy in identifying who among the CHR group will subsequently convert to psychosis. Imaging studies have provided support for latent CHR subgroups, finding significant neurobiological heterogeneity in gray matter volume.[7]

LVMM has been applied in 2 CHR studies with mixed results.[8,9] Velthorst et al[8] used a modified latent class factor analysis to investigate symptom profiles of 288 CHR and unaffected control (UC) individuals. "At risk" and "healthy" classes emerged, but classification did not enhance prediction of conversion. Possible reasons for this include incorporation of UCs with limited variability and lack of diversity in predictive indices.

Valmaggia et al[9] applied a LVMM approach to a sample of 318 CHR individuals' ratings on the Comprehensive Assessment of the At-Risk Mental States.[10] A 4-class model emerged, each associated with different rates of transition to psychosis. The subgroup with the highest transition rate (class 4, 41.2%) was characterized by the highest symptom ratings, lowest overall functioning, and highest unemployment rate. Classes were best separated by differences in negative symptoms and social/role functioning, indicating that these variables

© The Author(s) 2017. Published by Oxford University Press on behalf of the Maryland Psychiatric Research Center.
All rights reserved. For permissions, please email: journals.permissions@oup.com

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

are useful in determining risk. Thus, LVMM identified individuals with a specific constellation of negative symptoms and role impairments that were associated with a higher conversion rate.[9]

The present paper seeks to extend previous LVMM findings through application of LPA in a large group of prospectively identified CHR and help-seeking control (HSC) individuals and build upon Valmaggia et al's[9] model by incorporating measures of pre-morbid, social and role functioning, neurocognition, and social cognition. The aim is to enhance model validity by adding diagnostically relevant clinical and neurocognitive indicators and to further characterize latent subgroups with covariates. Supplementary table 1 defines all acronyms included in the present article.

Methods

Sample

The sample consisted of 171 CHR participants (98 males, 73 females) with a mean age of 19.8 (SD = 4.5) and 100 HSC participants (56 males, 44 females) with a mean age of 19.4 (SD = 3.9) years. Data were collected as a part of National Institute of Mental Health (NIMH) funded, multisite study "Enhancing the Prospective Prediction of Psychosis" (PREDICT). Procedures are described in greater detail in prior publications (eg,[11–14]). PREDICT was conducted at the Universities of North Carolina at Chapel Hill (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[15]). Twenty-nine CHR individuals converted to psychosis (17.0% within CHR; 10.7% within total sample).

The HSC group was comprised of individuals who responded to CHR recruitment, appeared to have prodromal symptoms at phone screen but upon administration of the SIPS did not meet COPS criteria. The HSC group contains the following subgroups: (1) family high risk, no deterioration in Global Assessment of Functioning (n = 16), (2) attenuated symptoms present for more than 1 year (n = 39), (3) current attenuated symptoms but due to another disorder (n = 2), (4) only negative symptoms (n = 4), and (5) attenuated symptoms not meeting severity or frequency criterion (n = 24). HSC individuals were included as a clinically relevant control group, as CHR and HSC individuals are more symptomatically similar to one another than non-psychiatric controls. Inclusion of such self-presenting, help-seeking individuals typically seen at CHR clinics provides greater better representation of clinical realism and diversity. Further, five HSC individuals converted to psychosis (5.0% within HSC; 1.8% within total sample).

Exclusion criteria included presence of an axis I psychotic disorder, age-scaled intelligence quotient (IQ) < 70, history of a clinically significant central nervous system disorder that may confound/contribute to CHR symptoms, or past/current use of antipsychotics.

Measures

SIPS and Scale for Assessment of Prodromal Symptoms (SOPS[15]) were used to assess criteria for prodromal syndrome, conversion, and severity of attenuated psychotic symptoms. Structured clinical interview for the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV[16]) was used to assess current/lifetime substance abuse/dependence.

Conversion to psychotic disorder is defined as at least 1 of 5 attenuated SOPS positive symptoms reaching a psychotic level of intensity (rated 6) for a frequency of ≥1 h/d for 4 d/wk in the past month. If the symptom meets intensity but not frequency criteria, it must seriously impact functioning (ie, severely disorganized or dangerous to self/others) to be considered conversion.[15]

Calgary Depression Scale for Schizophrenia (CDSS[17]) was used to measure depression and has been validated in CHR individuals.[18]

Neurocognitive Measures. Neurocognitive measures were selected based on demonstrated reliability, validity, absence of ceiling/floor effects in CHR population, ability to discriminate individuals with schizophrenia from UCs, and appropriateness for administration in individuals as young as 14. Verbal fluency was measured with category instances (CAT[19]), executive functioning with Wisconsin Card Sorting Test, 64-card computerized version (WCST[20]) and Trail Making Test B (TMT B[21]), speed of processing with TMT A,[21] verbal explicit memory with Rey Auditory Verbal Learning Test (RAVLT[22]), and attention with Continuous Performance Test-Identical Pairs (CPT-IP[23]). Neurocognitive tests, indices, ranges, and normative UC data are provided in supplementary table 2.

IQ was measured using the Wechsler Adult Intelligence Test or the Wechsler Intelligence Scale for Children-III, depending on the participants' age.[24,25]

Social Cognition. Theory of mind (ToM) was assessed with the "Reading the Mind in the Eyes" Task (Eyes Task[26]), emotion perception (EP) in faces with the Face Emotion Identification Task (FEIT[27]) and the Face Emotion Discrimination Task (FEDT[27]), and EP in voices with the Affective Prosody Task (AP[28]). All social cognitive tests, ranges, and normative data from UC groups are provided in supplementary table 2.

Functioning Measures. Premorbid functioning was assessed using the Premorbid Adjustment Scale (PAS[29]) using administration and scoring procedures outlined by van Mastrigt and Addington.[30] Adult PAS ratings were not included in the present analyses due to young age of the

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

sample (44.6% <19 y). Social functioning was measured using Social Functioning Scale (SFS[31]) with the employment item removed (range: 0–213).[32,33] Role functioning was measured using the employment subscale of the Heinrichs-Carpenter Quality of Life Scales (QLS[34]) (range: 0–18).

Procedures

PREDICT was a longitudinal study of predictors of conversion to psychosis. Study protocols and informed consent documents were reviewed and approved by institutional review boards of the 3 study sites. Formal consent procedures were conducted with participants. Clinical raters were experienced research clinicians who underwent a training program developed at Yale to identify prodromal syndromes with adequate reliability and demonstrated reliability throughout PREDICT.[35] Gold standard post-training agreements were excellent ($\kappa = 0.90$).

JA chaired weekly conference calls with all clinical raters to review inclusion criteria for all participants. Research assistants were trained in neurocognitive assessments by R.S.E.K. and social cognitive assessments by D.L.P.

Statistical Analyses. Data analyses were performed using Mplus version 7 with Mixture Add-On[36] and SPSS version 23.

Model Selection

Number of classes were not estimated a priori, but were ascertained from a combination of model fit statistics and interpretability. Model of best fit was determined from examinations of: (1) Akaike's Information Criteria (AIC[37]), Bayesian Information Criteria (BIC[38]), sample-size adjusted BIC (ssa BIC[39]) (lower values indicate the model of best fit), (2) Bootstrapped Likelihood Ratio Tests (BLRT[40]), (3) Mean estimated average posterior probabilities, and (4) Entropy indices.

An alternative interpretation of information criteria (eg, AIC, BIC, ssa BIC) and log likelihood values is to plot indices against the number of latent classes and examine for the "leveling off" point of the curve (eg, scree plot).[41] The model associated with a subsequent decrease in absolute value of slope may provide a model that balances model fit statistic improvement and parsimony.[41] Substantive interpretability and parsimony of models were considered in model selection.

Data Analytic Plan

Transition rates were computed as the percentage of converters within each class and were compared using χ^2 tests of significance. Separation of LPA model indicators was assessed using univariate ANOVAs and effect sizes as measured by r^2. Indicator profiles were generated depicting estimated sample means. ANOVAs, independent samples t tests, and chi-square tests of significance were conducted to compare classes on covariates. 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 significantly differed.[42,43]

Results

Latent Profile Analysis

LPA Model Selection. Table 1 provides fit indices from the LPA. The AIC, BIC, and ssa BIC values decreased with each class addition and did not readily discriminate a model of best fit. BLRT value remained significant ($P < .0001$) with each class addition. Entropy values remained high for each class model ($k = 2$–5), ranging

Table 1. 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

Note: 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 0.80 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.

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

from 0.88 to 0.93. Fit indices and BLRT alone indicated the 5-class model. However, accepting the model associated with the lowest values does not prioritize model interpretability and parsimony.[44]

Supplementary figure 1 provides scree plots of AIC, BIC, ssa BIC, and log likelihood value. Leveling off point of the curves occurred at 3 classes in each plot, indicating that significant improvements in model fit are not gained through further class additions. Of note, the BIC is considered to be the best of the presently available information criteria,[41] which showed clearest leveling off at 3 classes. The 3-class solution indicated high classification quality, adequate entropy score of 0.88, and mean posterior probabilities ranging from 93.9% to 95.6%. Supplementary table 3 summarizes latent class membership based on estimated posterior probabilities. Indicators evidenced meaningful separation. The 4- and 5-class models were examined and evidenced poor separation across a majority of indicators and thus did not result in substantively meaningful or interpretable class structures.

Individuals were assigned to classes as indicated by highest posterior probability value as such: class 1 (mild cluster; $n = 124$), class 2 (paranoid-affective cluster; $n = 106$), and class 3 (negative-neurocognitive cluster, $n = 41$).

Classes and Risk Probability. The overall transition rate in the full combined sample of CHRs and HSCs at 2 years was 12.5%. Transition rate significantly differed across groups in the overall model ($\chi^2(2, N = 271) = 16.08$, $P < .001$). Pairwise comparisons indicated that transition to psychosis was more likely in individuals in class 3 (negative-neurocognitive; transition rate 29.3%, $n = 12$ converters) than class 1 (mild; transition rate 5.6%, $n = 7$ converters) at the $P < .05$ level. There were no significant differences in pairwise comparisons between class 2 (paranoid-affective; transition rate 14.2%, $n = 15$ converters) and classes 1 or 3. Diagnoses at transition are provided in Supplementary table 4.

Characteristics of the 3-Class Solution. Table 2 shows results from the LPA and ANOVAs. Figures 1 and 2 show latent profile plots of estimated means. ANOVA results indicated that all indicators were influential in the clustering process, with the exception of SOPS 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 scores across SOPS and CDSS total. Class 1 largely evidenced SOPS estimated means of 1–2, which indicates mild/questionable presence and depression comparable to UC sample norms (normative mean: 2.6, SD: 2.7).[45]

Class 2 (paranoid-affective) estimated means were significantly more severe for suspiciousness/persecutory ideas than classes 1 and 3. Class 2 evidenced significantly more severe ratings than class 1 on unusual thought content and perceptual abnormalities. Class 2 had significantly higher depression ratings (on SOPS dysphoric mood and CDSS total scores) and significant sleep disturbance compared to other classes. Class 2 had mild negative symptom ratings (≤2), with the exception of occupational functioning, which was near moderate (3).

Class 3 (negative-neurocognitive) membership was associated with the highest ratings (between 2–4) in a majority of negative symptoms, and to a lesser degree, disorganized symptoms. This was confirmed through pairwise comparisons. Class 3 evidenced comparable ratings to class 2 on avolition and decreased experience of emotions.

Regarding neurocognitive performance, classes 1 (mild) and 2 (paranoid-affective) performed comparably across indices. Class 3 (negative-neurocognitive) evidenced significant impairment compared to classes 1 and 2 across neurocognitive indices ($P < .05$). As neurocognitive test scores were not age corrected in the LPA model, comparisons among classes on neurocognitive indices were also run as ANCOVAs with age 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 age-related variance.

Characterizing the 3-Class Solution With Covariates. Table 3 provides results from ANOVAs and pairwise comparisons between classes regarding demographics and covariates.

Demographic Characteristics. There were significant differences in age and clinic location between classes. Individuals in class 3 (negative-neurocognitive) were significantly younger than class 2 (paranoid-affective). Individuals from Yale were more likely to be classified in class 3 and less likely to be classified in class 2. Conversely, individuals from UNC were more likely to be classified in class 2 and less likely to be classified in class 3.

Given site effects, comparisons among classes on indicators (SOPS, CDSS total score, neurocognitive indices) were conducted as ANCOVAs with site as a covariate. All results were unchanged, indicating that classes significantly differed on indicators when accounting for site-related variance. Classes showed no significant differences in sex or racial/ethnic composition.

Risk Group. CHR individuals were significantly more likely to be categorized in class 2 (paranoid-affective) than class 1 (mild). Conversely, HSC individuals were more likely to be categorized in class 1 than 2. Supplementary table 5 provides symptom and functional descriptives of risk subgroups within each class.

Premorbid Functioning. Classes had significant overall group differences across PAS subscales. From childhood through early adolescence (age ≤ 15), individuals in class

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

Table 2. Latent Profile Analysis of SOPS, CDSS, and Neurocognition: Estimated Parameters for the 3-Class Solution

Domain	Indicator	Class 1 Mild (n = 124)	Class 2 Paranoid-Affective (n = 106)	Class 3 Negative-Neurocognitive (n = 41)	ANOVA P	Pairwise	Effect Size (r^2)
P.1	Unusual Thought Content/Delusional Ideas	2.4 (0.18)	3.1 (0.15)	2.6 (0.40)	.002	2>1	.05
P.2	Suspiciousness/Persecutory Ideas	1.8 (0.17)	2.7 (0.15)	1.9 (0.37)	$P < .001$	2>1,3	.08
P.3	Grandiose Ideas	1.0 (0.13)	1.0 (0.13)	0.9 (0.23)	.629		.00
P.4	Perceptual Abnormalities/Hallucinations	1.7 (0.17)	2.6 (0.15)	2.2 (0.37)	$P < .001$	2>1	.07
P.5	Disorganized Communication	1.1 (0.14)	1.6 (0.13)	1.7 (0.25)	.001	2,3>1	.06
N.1	Social Anhedonia	0.9 (0.18)	1.8 (0.17)	2.8 (0.68)	$P < .001$	3>1,2; 2>1	.16
N.2	Avolition	0.8 (0.19)	2.3 (0.19)	2.8 (0.45)	$P < .001$	3,2>1	.35
N.3	Decreased Expression of Emotion	0.5 (0.16)	1.1 (0.16)	1.9 (0.46)	$P < .001$	3>1,2; 2>1	.16
N.4	Decreased Experience of Emotions and Self	0.7 (0.12)	1.8 (0.16)	1.5 (0.45)	$P < .001$	2,3>1	.15
N.5	Decreased Ideational Richness	0.4 (0.11)	0.8 (0.11)	2.2 (0.58)	$P < .001$	3>1,2; 2>1	.29
N.6	Occupational Functioning	1.2 (0.42)	2.9 (0.26)	3.8 (0.36)	$P < .001$	3>1,2; 2>1	.25
D.1	Odd Behavior or Appearance	0.5 (0.12)	0.6 (0.11)	2.0 (0.64)	$P < .001$	3>1,2	.20
D.2	Bizarre Thinking	0.7 (0.14)	0.8 (0.11)	1.2 (0.27)	.081		.02
D.3	Trouble with Focus and Attention	1.2 (0.21)	2.3 (0.14)	2.5 (0.24)	$P < .001$	2,3>1	.23
D.4	Impairment in Personal Hygiene	0.3 (0.13)	0.7 (0.14)	1.3 (0.47)	$P < .001$	3>1,2; 2>1	.09
G.1	Sleep Disturbance	0.9 (0.13)	2.5 (0.15)	1.7 (0.47)	$P < .001$	2>1,3; 3>1	.29
G.2	Dysphoric Mood	1.3 (0.20)	3.5 (0.15)	3.0 (0.51)	$P < .001$	2>1,3; 3>1	.44
G.3	Motor Disturbances	0.3 (0.06)	0.8 (0.10)	0.8 (0.40)	$P < .001$	2,3>1	.08
G.4	Impaired Tolerance to Normal Stress	0.8 (0.14)	2.6 (0.18)	2.4 (0.52)	$P < .001$	2,3>1	.30
DEP	CDSS Total Score	2.0 (0.28)	5.8 (0.45)	3.8 (1.15)	$P < .001$	2>1,3; 3>1	.24
NC	CAT Total Score	47.2 (1.62)	49.9 (1.41)	32.5 (2.41)	$P < .001$	1,2>3	.22
NC	WCST Perseverative Errors	6.4 (0.36)	6.8 (0.43)	12.9 (2.68)	$P < .001$	3>1,2	.20
NC	TMT A	26.6 (1.22)	24.2 (0.82)	43.2 (4.91)	$P < .001$	3>1,2	.36
NC	TMT B	62.0 (5.51)	53.8 (1.86)	107.3 (9.90)	$P < .001$	3>1,2	.35
NC	CPT D'3	2.7 (0.09)	2.9 (0.09)	1.8 (0.27)	$P < .001$	1,2>3	.18
NC	RAVLT Total Score	53.52 (2.74)	55.46 (1.05)	43.10 (5.17)	$P < .001$	1,2>3	.21

Note: SOPS, Scale for Assessment of Prodromal Symptoms; CDSS, Calgary Depression Scale for Schizophrenia; P, positive symptom subscale; N, negative symptom subscale; D, disorganized symptom subscale; G, general symptom subscale; DEP, depression symptoms; NC, neurocognition; 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.

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

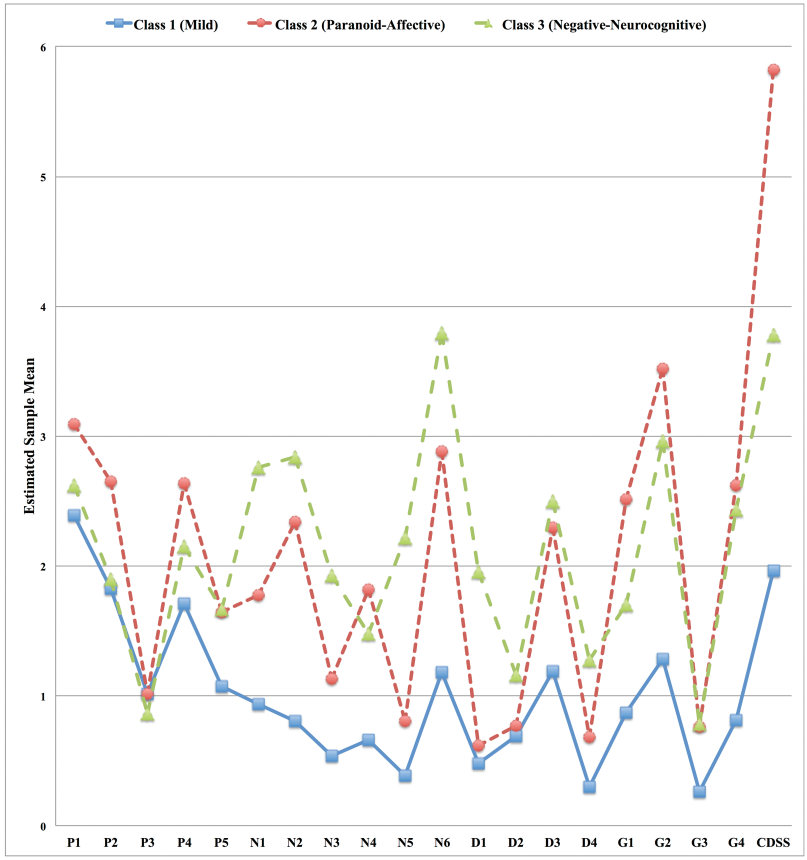

Fig. 1. Latent profile plot of Scale of Prodromal Symptoms (SOPS) and Calgary Depression Scale for Schizophrenia (CDSS) total score.

3 (negative-neurocognitive) showed significant social and academic maladjustment scores compared to classes 1 and 2, whereas classes 1 and 2 had comparable impairment during this time. Regarding late adolescence (age 16–18) social maladjustment ratings, class 3 continued to perform at the most impaired level compared to classes 1 and 2. However, class 2 evidenced significant social maladjustment compared to class 1, suggesting that for class 2, poor functioning begins in late adolescence.

Social Functioning. Classes 2 and 3 had significant impairment on the SFS compared to class 1.

Role Functioning. Class 3 had significant impairment in QLS total score compared to classes 1 and 2. Class 2 evidenced significant impairment in QLS total score compared to class 1.

Social Cognition. Classes had significant overall models measuring group differences on the Eyes Task, FEIT, and AP. The overall model for FEDT approached significance ($P = .053$). Pairwise comparisons indicated that class 3 (negative-neurocognitive) had significant social cognitive deficits compared to classes 1 (mild) and 2 (paranoid-affective) across measures, indicating class 3 was impaired in ToM and EP.

As social cognitive performance tends to be associated with age and IQ,[46] comparisons among classes on social cognition were repeated as ANCOVAs with age as a covariate. Overall models and pairwise comparisons remained significant, indicating that classes evidenced significant differences in social cognitive performance when accounting for age-related variance.

Age-scaled IQ was added as a covariate and overall models for Eyes Task and AP Task remained significant ($P < .05$); however, FEDT was no longer significant. Pairwise comparisons for AP remained significant ($P < .05$). Eyes Task contrast between classes 2 and 3 was no longer significant. Thus, significant group differences in facial EP performance and ToM may be partially accounted for by neurocognitive ability, but not for AP.

Intelligence. Classes were compared across age-scaled IQ. Classes were significantly different, with impairment in class 3 (negative-neurocognitive) compared to classes 1 (mild) and 2 (paranoid-affective).

Discussion

Consistent with prior work, the present study found that classes were best distinguished by separation in negative/

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

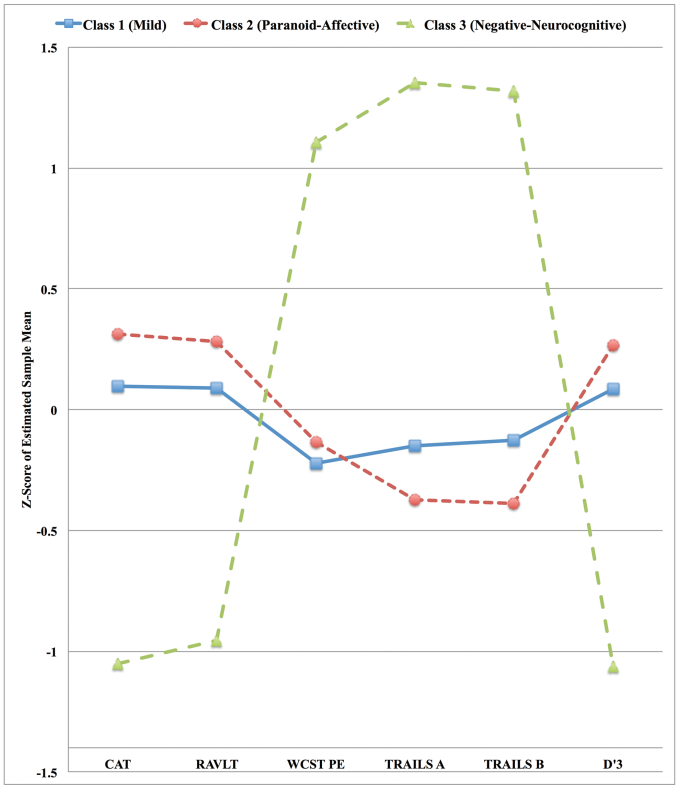

Fig. 2. Latent profile plot of neurocognitive scores. CAT, category instances; RAVLT, Rey Auditory Verbal Learning Test; WCST PE, Wisconsin Cart Sorting Test Perseverative Errors; Trails A, Trail Making Test A; Trails B, Trail Making Test B; D'3, Continuous Performance Test-Identical Pairs (CPT-IP) D'3.

general symptoms and classes that exhibited the greatest baseline negative symptoms and behavioral change ratings had the highest risk of transition to psychosis (ie, class 3).[9] This is consistent with the growing literature establishing an association between high baseline negative symptoms and subsequent conversion to psychosis.[10,35,47–56] Class 3 (negative-neurocognitive) was further characterized by significantly impaired neurocognition. Inclusion of neurocognition in the model may have elicited the emergence of class 3, a novel putative subgroup.

The CHR paradigm was recently conceptually revised into a clinical staging model comprised of subgroups associated with increasing clinical severity and risk of transition.[57] The first stage (CHR−) is characterized by moderate negative symptoms, neurocognitive symptoms, and minimal positive symptoms (none ≥ 3).[58] It is possible that class 3's (negative-neurocognitive) symptomatology is consistent with the CHR− stage and thus they represent a discrete subgroup on the prodromal illness trajectory.

Conversely, class 2 (paranoid-affective) was characterized by significantly higher suspiciousness and CDSS total near the cutoff associated with major depression.[45] Class 2 largely evidenced nonspecific distress, with an emphasis in affective symptoms and sleep disturbance compared to other classes. Class 2 was not clearly consistent with any subgroup in Carrión et al's[58] clinical staging model and instead may be at risk for a broad range of psychopathology (eg, affective disorders). Given that the inclusion criteria of this study was 1 follow-up visit (ie, 6 mo), it may be that CHR criteria are sensitive to emergent psychosis for some, but that timing was insufficient to capture emergence of nonpsychotic disorders, which take years to manifest past adolescence/early adulthood (eg, average age was 15.7–19.6 across classes).[59] This is consistent with clinical staging model theory, which posits that nonspecific distress crystallizes over time into discrete categorical syndromes. Identifying subgroups at this time may be difficult due to the ephemeral nature of distress and symptomatology through adulthood.[60]

Rate of Transition to Psychosis

Class 3 (negative-neurocognitive) had the highest conversion rate (29%) and was not characterized by significantly greater positive symptoms as would be expected based on the clinical staging model.[58] The rate of transition is higher in the present sample (29.3% in class 3) than the comparable class in the clinical staging model (5.9% in CHR−).[58]

Class 2 (paranoid-affective) was associated with the highest suspiciousness, greatest depressive symptoms, intact neurocognition, and lower conversion rate (14.9%). Given that clinical depression is both associated with and predictive of persistent paranoia,[60] it is possible that effective treatment of depression in class 2 may reduce severity of positive symptomatology and prevent subsequent transition to psychosis.

Further Characterizing Subgroups With Covariates

Class 3 (negative-neurocognitive) had significantly lower social cognitive performance consistent with the proposed conceptualization of class 3 as an early risk stage of developing schizophrenia. In contrast, classes 1 and 2 performed comparably to UCs on measures of ToM and facial EP according to norms from age-matched UCs. Results from a meta-analysis of social cognitive performance in CHR individuals found medium effect sizes for EP (d = 0.47) and ToM impairment (d = 0.44).[61] Thus, one would expect class 2 (paranoid-affective) to have EP and ToM deficits, given that CHR individuals comprised 74.5% of this class. Further, results comparing CHR and HSC individuals from this sample found no significant differences in EP or ToM performance.[13,14] Thus, it is possible that specific constellations of symptoms (ie, those associated with class 3) account for social cognitive deficits in heterogeneous CHR samples.

Regarding demographics, class 2 (paranoid-affective) was significantly older than class 3 (negative-neurocognitive). Longitudinal findings indicated negative symptom onset predates positive symptom onset[62] and that

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

Table 3. Associations Between Latent Classes, Demographic Characteristics, and Covariates

	Class 1 (n = 124)	Class 2 (n = 106)	Class 3 (n = 41)	Test	Pairwise
Age	19.48 (4.26)	20.71 (4.03)	17.26 (4.09)	$F_{2,268} = 10.36$, $P < .001$	2>3
Sex, n (% within class)					
Male	69 (55.6)	59 (55.7)	26 (63.4)	$\chi^2_8 = .86$, $P = .65$	
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)	$\chi^2_8 = 8.53$, $P = .38$	
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)	$\chi^2_2 = .11$, $P = .95$	
No	110 (88.7)	95 (89.6)	36 (87.8)		
Clinic, n (% within class)					
UNC Chapel Hill	40 (32.3)$_a$	42 (39.6)$_a$	4 (9.8)$_b$	$\chi^2_4 = 16.90$, $P = .002$	
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)$_b$		
Risk group, n (% within class)					
CHR, n = 171	66 (53.2)$_a$	79 (74.5)$_b$	26 (63.4)$_{a, b}$	$\chi^2_2 = 11.14$, $P = .004$	
HSC, n = 100	58 (46.8)$_a$	27 (25.5)$_b$	15 (36.6)$_{a, b}$		
Functioning, mean (SD)					
PAS Child Social Maladjustment	0.16 (0.20)	0.20 (0.20)	0.30 (0.23)	$F_{2,250} = 7.44$, $P = .001$	3>1,2
PAS Child Acad. Maladjustment	0.17 (0.18)	0.18 (0.19)	0.29 (0.22)	$F_{2,250} = 6.76$, $P = .001$	3>1,2
PAS Early Adol. Social Maladjustment	0.21 (0.20)	0.25 (0.19)	0.36 (0.20)	$F_{2,247} = 8.78$, $P < .001$	3>1,2
PAS Early Adol. Acad. Maladjustment	0.25 (0.21)	0.28 (0.24)	0.40 (0.27)	$F_{2,247} = 7.44$, $P = .001$	3>1,2
PAS Late Adol. Social Maladjustment	0.19 (0.19)	0.30 (0.20)	0.48 (0.29)	$F_{2,187} = 17.58$, $P < .001$	3>1,2; 2>1
PAS Late Adol. Acad. Maladjustment	0.23 (0.21)	0.35 (0.25)	0.48 (0.30)	$F_{2,180} = 10.80$, $P < .001$	2,3>1
SFS total score	123.43 (29.07)	112.38 (25.31)	106.05 (21.07)	$F_{2,242} = 8.05$, $P < .001$	2,3>1
QLS total score	14.19 (3.91)	12.15 (4.83)	8.89 (5.62)	$F_{2,243} = 19.83$, $P < .001$	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)	$F_{2,228} = 29.57$, $P < .001$	1,2>3
FEIT total score	13.23 (2.28)	12.84 (2.12)	10.97 (2.77)	$F_{2,226} = 12.86$, $P < .001$	1,2>3
FEDT total score	25.67 (1.86)	25.80 (1.96)	24.89 (2.08)	$F_{2,227} = 2.97$, $P = .053$	
AP total score	45.90 (5.24)	45.71 (5.27)	37.26 (9.45)	$F_{2,221} = 29.20$, $P < .001$	1,2>3
IQ score, mean (SD)	113.58 (17.22)	115.27 (15.42)	87.10 (12.44)	$F_{2,186} = 27.30$, $P < .001$	1,2>3

Note: CHR, clinical high risk; HSC, help seeking control; PAS, Premorbid Adjustment Scale; SFS, Social Functioning Scale; 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 ($P < .05$).

negative/disorganized symptoms predicted positive symptoms over time.[47] Further, CHR− individuals were the youngest subgroup in the clinical staging model.[58] Thus, it follows that the youngest group may be characterized by predominant negative symptoms.

Classes also had significant differences in clinic of origin. Each of the 3 clinics used standardized inclusion criteria, screening/assessment measures, and recruitment methods, and raters evidenced significant agreement in routine assessment reliability checks. Although such processes were standardized, site differences may be due to selective recruitment processes.

Class 3 (negative-neurocognitive) exhibited the greatest premorbid academic/social and baseline social/role dysfunction, with scores comparable to individuals with established schizophrenia.[29] Class 2 (paranoid-affective) evidenced functional deterioration over time, and was statistically comparable to class 3's dysfunction in late adolescent academic maladjustment score. Class 2 (paranoid-affective) had significant social/role impairment, but to a lesser degree and with later onset than class

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

3. Taken together, such findings are consistent with the view of class 3 as an early risk stage of developing schizophrenia subgroup.

Limitations and Strengths

As LVMM are influenced by subtle sample differences, the present model must be replicated to ensure validity of the present class structure. Sample size prohibited cross-validation, which would enhance confidence regarding taxon validity. However, the present model is complex with several indicator variables and parameters; thus, use of cross-validation procedures would likely generate results with increased error.[63,64] Further, the present model does not include other predictive indicators such as basic symptoms (ie, subtle, subjective disturbances in one's mental processes) and biological markers (eg, electrophysiological, imaging, metabolic, genetic markers).

The present class structure evidenced significant site differences. 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 an additional indicator variable.[65–67] Given that there were no significant site differences in transition rate, we instead used site as an inactive descriptive covariate. Significant differences between indicators remained when controlling for site, indicating true variance in symptomatology drove the LPA.

Strengths of the present study include ecological validity in application of LPA to the combined sample. Our use of neurocognitive scores as indicators is novel and the first study to utilize such. The current study is further strengthened by inclusion of a range of covariates (functioning, social cognition) to characterize subgroups.

Conclusions

Overall, the 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, CDSS, neurocognition). Despite the well-established association between poor outcome, negative symptoms, and neurocognitive deficits, such symptom clusters are insufficiently targeted in CHR individuals. We join other researchers who have advocated for a transdiagnostic, heuristic approach to CHR individuals that has been emphasized in understanding the progression to psychotic and other mental illnesses.[68,69]

Supplementary Material

Supplementary data are available at *Schizophrenia Bulletin* online.

Funding

This study was supported by the following National Institute of Mental Health (NIMH) grants: U01MH066134-02 to J.A., U01MH066069-04 to D.P., and U01MH066160 to S.W.W.

Acknowledgments

K.M.H. conducted analyses and certifies their accuracy. Authors thank statistical consultants Drs Cathy Zimmer and Chris Wiesen for their assistance.

References

1. Salokangas RK, Ruhrmann S, von Reventlow HG, et al.; EPOS group. 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. *Schizophr Res*. 2012;138:192–197.
2. Wigman JT, van Nierop M, Vollebergh WA, et al. 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. *Schizophr Bull*. 2012;38:247–257.
3. Woods SW, Addington J, Cadenhead KS, et al. Validity of the prodromal risk syndrome for first psychosis: findings from the North American Prodrome Longitudinal Study. *Schizophr Bull*. 2009;35:894–908.
4. Yung AR, Nelson B, Stanford C, et al. Validation of "prodromal" criteria to detect individuals at ultra high risk of psychosis: 2 year follow-up. *Schizophr Res*. 2008;105:10–17.
5. Hagenaars JA, McCutcheon AL. *Applied Latent Class Analysis*. Cambridge, UK: Cambridge University Press; 2002.
6. Vermunt JK, Magidson J. Latent class cluster analysis. In: Hagenaars JA, McCutcheon AL, eds. *Advances in Latent Class Analysis*. Vol 11. Cambridge, MA: Cambridge University Press; 2002:89–106.
7. Modinos G, Allen P, Frascarelli M, et al. Are we really mapping psychosis risk? Neuroanatomical signature of affective disorders in subjects at ultra high risk. *Psychol Med*. 2014;44:3491–3501.
8. Velthorst E, Derks EM, Schothorst P, et al. Quantitative and qualitative symptomatic differences in individuals at ultra-high risk for psychosis and healthy controls. *Psychiatry Res*. 2013;210:432–437.
9. Valmaggia LR, Stahl D, Yung AR, et al. Negative psychotic symptoms and impaired role functioning predict transition outcomes in the at-risk mental state: a latent class cluster analysis study. *Psychol Med*. 2013;43:2311–2325.
10. Yung AR, Yuen HP, McGorry PD, et al. Mapping the onset of psychosis: the comprehensive assessment of at-risk mental states. *Aust N Z J Psychiatry*. 2005;39:964–971.
11. Addington J, Penn D, Woods SW, Addington D, Perkins DO. Facial affect recognition in individuals at clinical high risk for psychosis. *Br J Psychiatry*. 2008;192:67–68.
12. Addington J, Penn D, Woods SW, Addington D, Perkins DO. Social functioning in individuals at clinical high risk for psychosis. *Schizophr Res*. 2008;99:119–124.

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

13. Addington J, Piskulic D, Perkins D, Woods SW, Liu L, Penn DL. Affect recognition in people at clinical high risk of psychosis. *Schizophr Res*. 2012;140:87–92.
14. Healey KM, Penn DL, Perkins D, Woods SW, Addington J. Theory of mind and social judgments in people at clinical high risk of psychosis. *Schizophr Res*. 2013;150:498–504.
15. McGlashan T, Walsh B, Woods S. *The Psychosis-Risk Syndrome: Handbook for Diagnosis and Follow-Up.* New York, NY: Oxford University Press; 2010.
16. First MB, Spitzer RL, Gibbon M, Williams JB. *User's Guide for the Structured Clinical Interview for DSM-IV Axis I Disorders SCID-I: Clinician Version*. New York, NY: American Psychiatric Pub; 1997.
17. Addington D, Addington J, Maticka-Tyndale E. Assessing depression in schizophrenia: the calgary depression scale. *Br J Psychiatry*. 1993;163(suppl 22):39–44.
18. Addington J, Shah H, Liu L, Addington D. Reliability and validity of the Calgary Depression Scale for Schizophrenia (CDSS) in youth at clinical high risk for psychosis. *Schizophr Res*. 2014;153:64–67.
19. Benton AL, Hamsher KD, Sivan A. *Multilingual Aphasia Examination.* Iowa City, IA: AJA Associates; 1989.
20. Kongs SK, Thompson LL, Iverson GL, Heaton RK. *Wisconsin Card Sorting Test-64 Card Version (WCST-64)*. Odessa, FL: Psychological Assessment Resources; 2000.
21. Reitan RM, Wolfson D. *The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation*. Vol 4. Tucson, AZ: Reitan Neuropsychology; 1985.
22. Lezak MD. *Neuropsychological Assessment*. 3rd ed. New York, NY: Oxford University Press; 1995.
23. Cornblatt BA, Keilp JG. Impaired attention, genetics, and the pathophysiology of schizophrenia. *Schizophr Bull*. 1994;20:31–46.
24. Wechsler D. Manual for the wechsler intelligence scale for children - revised. New York, NY: Psychological Corporation; 1974.
25. Wechsler D. *Manual for the Wechsler Adult Intelligence Scale - Revised*. New York, NY: Psychological Corporation; 1981.
26. Baron-Cohen S, Wheelwright S, Hill J, Raste Y, Plumb I. The "Reading the Mind in the Eyes" test revised version: a study with normal adults, and adults with Asperger syndrome or high-functioning autism. *J Child Psychol Psychiatry*. 2001;42:241–251.
27. Kerr SL, Neale JM. Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance? *J Abnorm Psychol*. 1993;102:312–318.
28. Edwards J, Pattison PE, Jackson HJ, Wales RJ. Facial affect and affective prosody recognition in first-episode schizophrenia. *Schizophr Res*. 2001;48:235–253.
29. Cannon-Spoor HE, Potkin SG, Wyatt RJ. Measurement of premorbid adjustment in chronic schizophrenia. *Schizophr Bull*. 1982;8:470–484.
30. van Mastrigt S, Addington J. Assessment of premorbid function in first-episode schizophrenia: modifications to the premorbid adjustment scale. *J Psychiatry Neurosci*. 2002;27:92–101.
31. Birchwood M, Smith J, Cochrane R, Wetton S, Copestake S. The social functioning scale. The development and validation of a new scale of social adjustment for use in family intervention programmes with schizophrenic patients. *Br J Psychiatry*. 1990;157:853–859.
32. Cornblatt BA, Auther AM, Niendam T, et al. Preliminary findings for two new measures of social and role functioning in the prodromal phase of schizophrenia. *Schizophr Bull*. 2007;33:688–702.
33. Pijnenborg GH, Withaar FK, Evans JJ, van den Bosch RJ, Timmerman ME, Brouwer WH. The predictive value of measures of social cognition for community functioning in schizophrenia: implications for neuropsychological assessment. *J Int Neuropsychol Soc*. 2009;15:239–247.
34. Heinrichs DW, Hanlon TE, Carpenter WT Jr. The quality of life scale: an instrument for rating the schizophrenic deficit syndrome. *Schizophr Bull*. 1984;10:388–398.
35. Miller TJ, McGlashan TH, Rosen JL, et al. Prodromal assessment with the structured interview for prodromal syndromes and the scale of prodromal symptoms: predictive validity, interrater reliability, and training to reliability. *Schizophr Bull*. 2003;29:703–715.
36. Muthén LK, Muthén BO. *Mplus: Statistical Analysis with Latent Variables: User's Guide*. 7th ed. Los Angeles, CA: Muthén & Muthén; 2012.
37. Lin TH, Dayton CM. Model selection information criteria for non-nested latent class models. *J Educ Behav Stat*. 1997;22:249–264.
38. Schwarz G. Estimating the dimension of a model. *Ann Stat*. 1978;6:461–464.
39. Sclove SL. Application of model-selection criteria to some problems in multivariate analysis. *Psychometrika*. 1987;52:333–343.
40. McLachlan G, Peel D. *Finite Mixture Models*. New York, NY: John Wiley & Sons; 2004.
41. Nylund KL, Asparouhov T, Muthén BO. Deciding on the number of classes in latent class analysis and growth mixture modeling: a monte carlo simulation study. *Struct Equ Model*. 2007;14:535–569.
42. Goodman LA. How to ransack social mobility tables and other kinds of cross-classification tables. *Am J Sociol*. 1969;75:1–40.
43. Sharpe D. Your chi-square test is statistically significant: now what? *Pract Assess Res Eval*. 2015;20:1–10.
44. Tein JY, Coxe S, Cham H. Statistical power to detect the correct number of classes in latent profile analysis. *Struct Equ Modeling*. 2013;20:640–657.
45. Müller MJ, Brening H, Gensch C, Klinga J, Kienzle B, Müller KM. the calgary depression rating scale for schizophrenia in a healthy control group: psychometric properties and reference values. *J Affect Disord*. 2005;88:69–74.
46. Penn DL, Sanna LJ, Roberts DL. Social cognition in schizophrenia: an overview. *Schizophr Bull*. 2008;34:408–411.
47. Alderman T, Addington J, Bearden C, et al. 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 Interv Psychiatry*. 2015;9:467–475.
48. Demjaha A, Valmaggia L, Stahl D, Byrne M, McGuire P. Disorganization/cognitive and negative symptom dimensions in the at-risk mental state predict subsequent transition to psychosis. *Schizophr Bull*. 2012;38:351–359.
49. Lencz T, Smith CW, Auther A, Correll CU, Cornblatt B. Nonspecific and attenuated negative symptoms in patients at clinical high-risk for schizophrenia. *Schizophr Res*. 2004;68:37–48.
50. Nelson B, Yuen HP, Wood SJ, et al. Long-term follow-up of a group at ultra high risk ("prodromal") for psychosis: the PACE 400 study. *JAMA Psychiatry*. 2013;70:793–802.
51. Piskulic D, Addington J, Cadenhead KS, et al. Negative symptoms in individuals at clinical high risk of psychosis. *Psychiatry Res*. 2012;196:220–224.

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021

52. Riecher-Rössler A, Pflueger MO, Aston J, et al. Efficacy of using cognitive status in predicting psychosis: a 7-year follow-up. *Biol Psychiatry*. 2009;66:1023–1030.
53. Velthorst E, Nieman DH, Becker HE, et al. Baseline differences in clinical symptomatology between ultra high risk subjects with and without a transition to psychosis. *Schizophr Res*. 2009;109:60–65.
54. Yung AR, Phillips LJ, Yuen HP, et al. Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. *Schizophr Res*. 2003;60:21–32.
55. Yung AR, Nelson B, Thompson AD, Wood SJ. Should a "Risk Syndrome for Psychosis" be included in the DSMV? *Schizophr Res*. 2010;120:7–15.
56. Yung AR, McGorry PD. The prodromal phase of first-episode psychosis: past and current conceptualizations. *Schizophr Bull*. 1996;22:353–370.
57. Fusar-Poli P. The clinical high-risk state for psychosis (CHR-P), version II. *Schizophr Bull*. 2017;43:44–47.
58. Carrión RE, Correll CU, Auther AM, Cornblatt BA. A severity-based clinical staging model for the psychosis prodrome: longitudinal findings from the New York recognition and prevention program. *Schizophr Bull*. 2017;43:64–74.
59. Webb JR, Addington J, Perkins DO, et al. Specificity of incident diagnostic outcomes in patients at clinical high risk for psychosis. *Schizophr Bull*. 2015;41:1066–1075.
60. Salokangas RK, Schultze-Lutter F, Hietala J, et al.; EPOS Group. Depression predicts persistence of paranoia in clinical high-risk patients to psychosis: results of the EPOS project. *Soc Psychiatry Psychiatr Epidemiol*. 2016;51:247–257.
61. van Donkersgoed RJ, Wunderink L, Nieboer R, Aleman A, Pijnenborg GH. Social cognition in individuals at ultra-high risk for psychosis: a meta-analysis. *PLoS One*. 2015;10:e0141075.
62. Häfner H, Maurer K, an der Heiden W. ABC Schizophrenia study: an overview of results since 1996. *Soc Psychiatry Psychiatr Epidemiol*. 2013;48:1021–1031.
63. Browne MW, Cudeck R. Single sample cross-validation indices for covariance structures. *Multivariate Behav Res*. 1989;24:445–455.
64. Bollen KA, Long JS. *Testing Structural Equation Models*. Newbury Park, CA: SAGE; 1993.
65. Clogg CC. Factor analysis and measurement in sociological research. In: Jackson DJ, Borgotta EF, eds. *New Developments in Latent Structure Analysis*. Beverly Hills, CA: Sage; 1981:215–246.
66. Hagenaars JA. *Categorical Longitudinal Data—Loglinear Analysis of Panel, Trend and Cohort Data*. Newbury Park, CA: Sage; 1990.
67. Magidson J, Vermunt JK. Latent class factor and cluster models, bi-plots, and related graphical displays. *Sociol Methodol*. 2001;31:223–264.
68. Heinssen RK, Insel TR. Preventing the onset of psychosis: not quite there yet. *Schizophr Bull*. 2015;41:28–29.
69. McGorry P, van Os J. Redeeming diagnosis in psychiatry: timing versus specificity. *Lancet*. 2013;381:343–345.

Downloaded from https://academic.oup.com/schizophreniabulletin/article/44/2/286/3964615 by University of North Carolina at Chapel Hill user on 18 October 2021