Precision Measures

to Monitor Progression to Schizophrenia

for Early Detection and Prevention

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AMP SCZ Grants
NIMH U01 MH124629, NIMH U01 MH124631, NIMH U24 MH124639
NIMH U24 MH137171, NIMH U01 MH137298

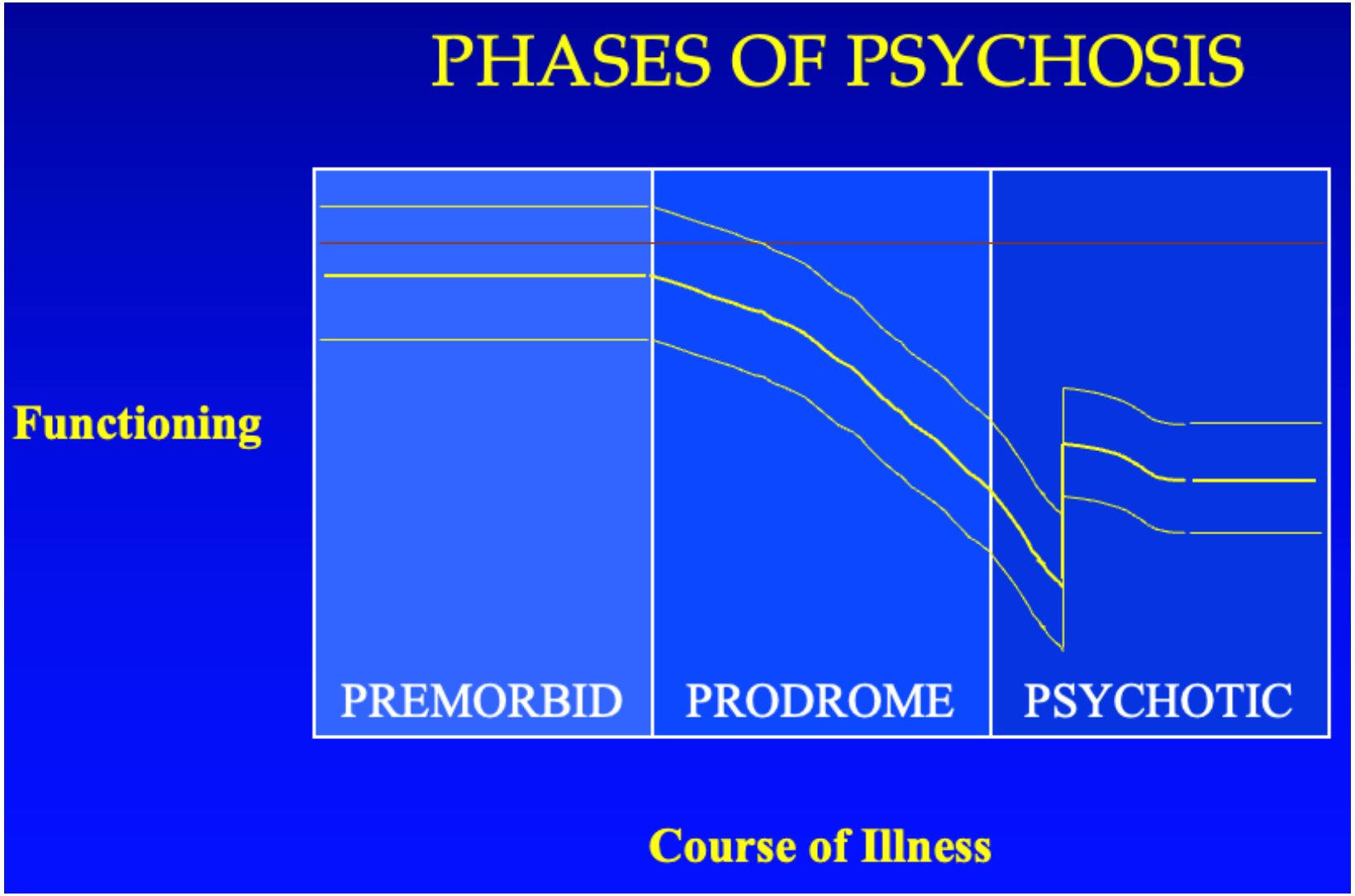
PSYCHS Qualification Grants
FDA U01 FD008131, FDA U01 FD008650

Disclosure

Dr. Woods has received speaking fees from the American Psychiatric Association and from Medscape Features. He has been granted US patent no. 8492418 B2 for a method of treating prodromal schizophrenia with glycine agonists. He is a consultant to and is a partner and owns stock in NW PharmaTech.

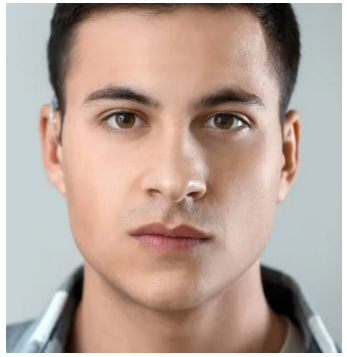
THE CLINICAL HIGH RISK SYNDROME FOR PSYCHOSIS

- Schizophrenia is one of the top 15 most disabling illnesses.
- >75% experience a prodrome prior to onset.
- CHR identifies the SCZ prodrome prospectively.
- CHR is NOT an asymptomatic risk factor.
- The patients are youth and young adults identified by subsyndromal or "attenuated" positive symptoms resembling those in schizophrenia.



CLINICAL HETEROGENEITY IN CHR

Positive Symptom Course (Conversion, Remission)



33384 - age 20

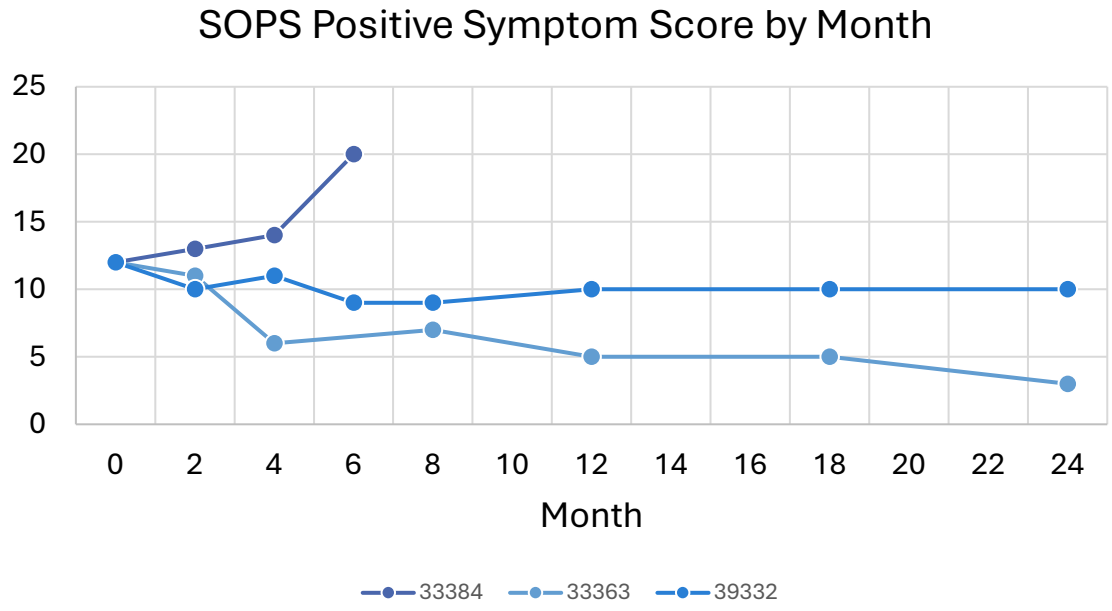
33363 - age 25

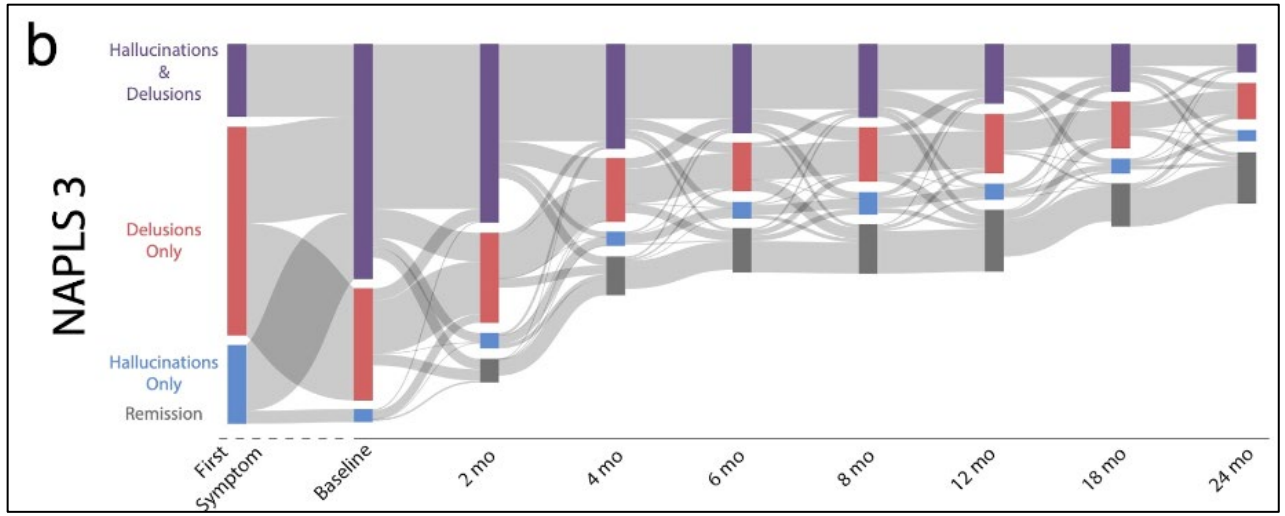
39332 - age 24

Negative Symptom Course
Affective Symptom Course
Functional Course
Cognitive Course

Heterogeneity at and before Baseline

Heterogeneity of Course Within Positive Symptoms





Courtesy Catalina Mourgues and Albert Powers

Precision Biomarker Measures

Structural MRI

www.nature.com/mp

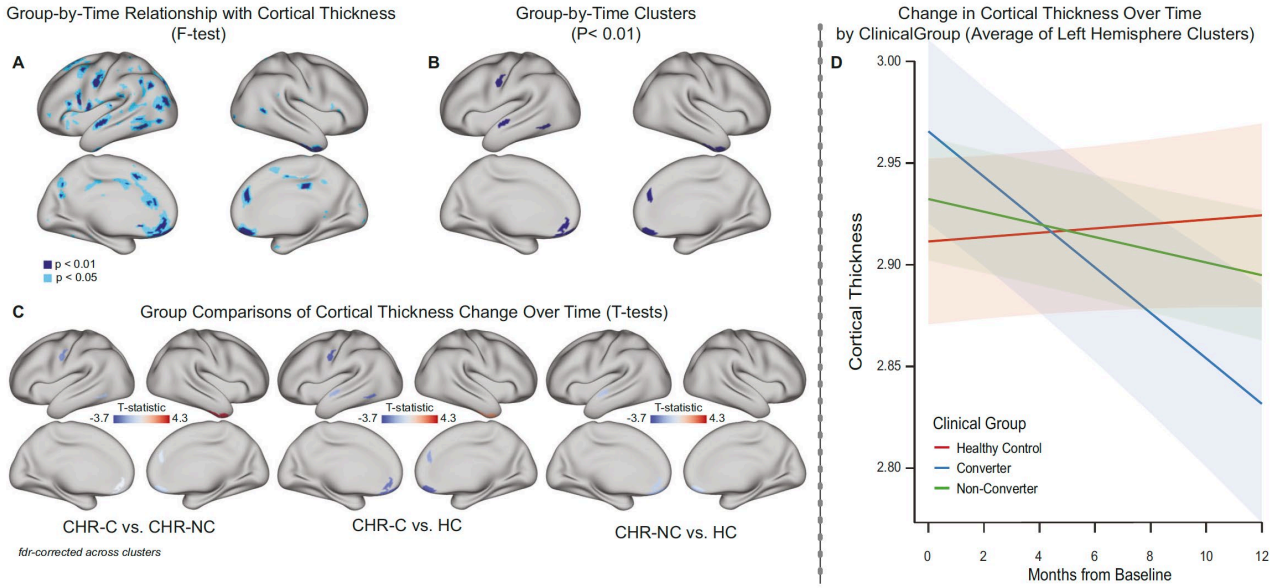
Molecular Psychiatry

ARTICLE OPEN

Check for updates

Accelerated cortical thinning precedes and predicts conversion to psychosis: The NAPLS3 longitudinal study of youth at clinical high-risk

Meghan A. Collins[1✉], Jie Lisa Ji[2,3], Yoonho Chung[4,5], Cole A. Lympus[1], Yvette Afriyie-Agyemang[6], Jean M. Addington[7], Bradley G. Goodyear[8], Carrie E. Bearden[9], Kristin S. Cadenhead[10], Heline Mirzakhanian[10], Ming T. Tsuang[10,11], Barbara A. Cornblatt[12], Ricardo E. Carrión[13,14,15], Matcheri Keshavan[16], Wiliam S. Stone[16], Daniel H. Mathalon[17], Diana O. Perkins[18], Elaine F. Walker[19], Scott W. Woods[2], Albert R. Powers[2], Alan Anticevic[1,2,3] and Tyrone D. Cannon[1,2]

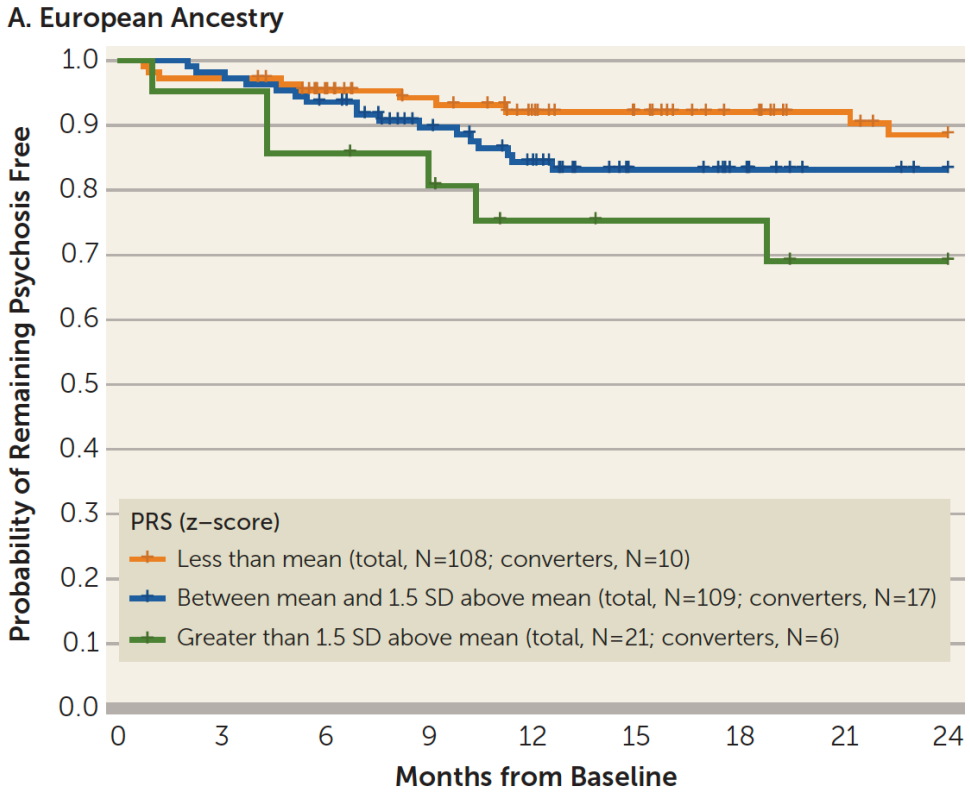


Polygenic Risk

Polygenic Risk Score Contribution to Psychosis Prediction in a Target Population of Persons at Clinical High Risk

Diana O. Perkins, M.D., M.P.H., Loes Olde Loohuis, Ph.D., Jenna Barbee, B.S., John Ford, M.S., Clark D. Jeffries, Ph.D., Jean Addington, Ph.D., Carrie E. Bearden, Ph.D., Kristin S. Cadenhead, M.D., Tyrone D. Cannon, Ph.D., Barbara A. Cornblatt, Ph.D., Daniel H. Mathalon, M.D., Ph.D., Thomas H. McGlashan, M.D., Larry J. Seidman, Ph.D., Ming Tsuang, M.D., Ph.D., Elaine F. Walker, Ph.D., Scott W. Woods, M.D.

FIGURE 2. Kaplan-Meier curves of psychosis conversion stratified by polygenic risk score (PRS) score in Europeans and non-Europeans[a]



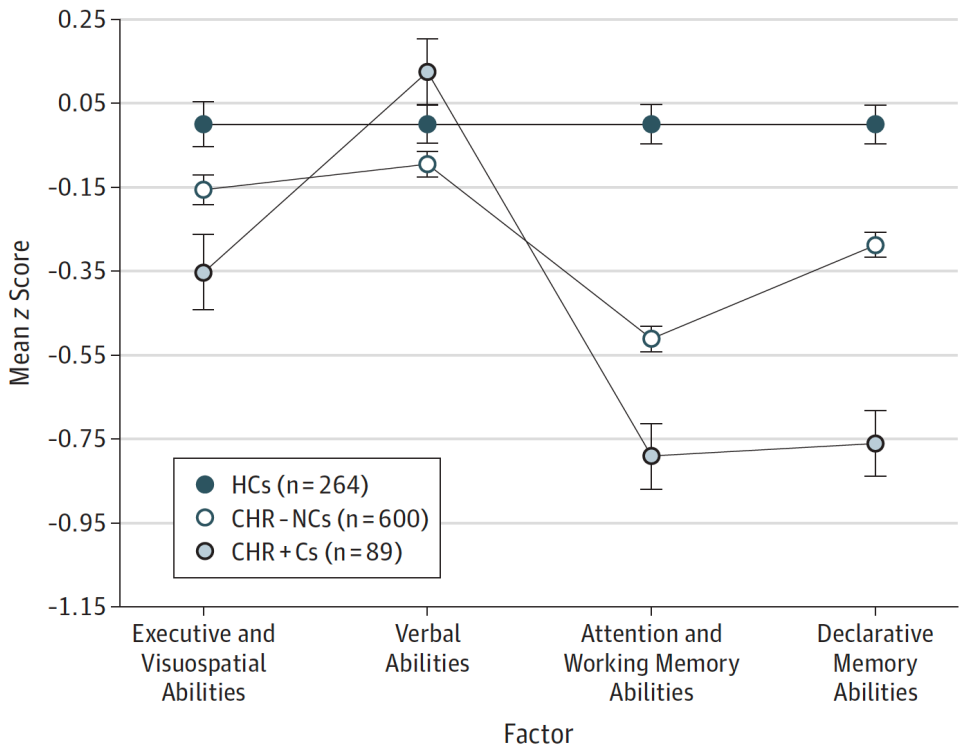
Neurocognition

JAMA Psychiatry | Original Investigation

Association of Neurocognition With Transition to Psychosis
Baseline Functioning in the Second Phase
of the North American Prodrome Longitudinal Study

Larry J. Seidman, PhD; Daniel I. Shapiro, PhD; William S. Stone, PhD; Kristen A. Woodberry, MSW, PhD; Ashley Ronzio, BS; Barbara A. Cornblatt, PhD, MBA; Jean Addington, PhD; Carrie E. Bearden, PhD; Kristin S. Cadenhead, MD; Tyrone D. Cannon, PhD; Daniel H. Mathalon, PhD, MD; Thomas H. McGlashan, MD; Diana O. Perkins, MD; Ming T. Tsuang, MD, PhD, DSc; Elaine F. Walker, PhD; Scott W. Woods, MD

Figure 1. Neuropsychological Profile by Diagnostic Group Adjusted for Age, Site, and Maternal Education

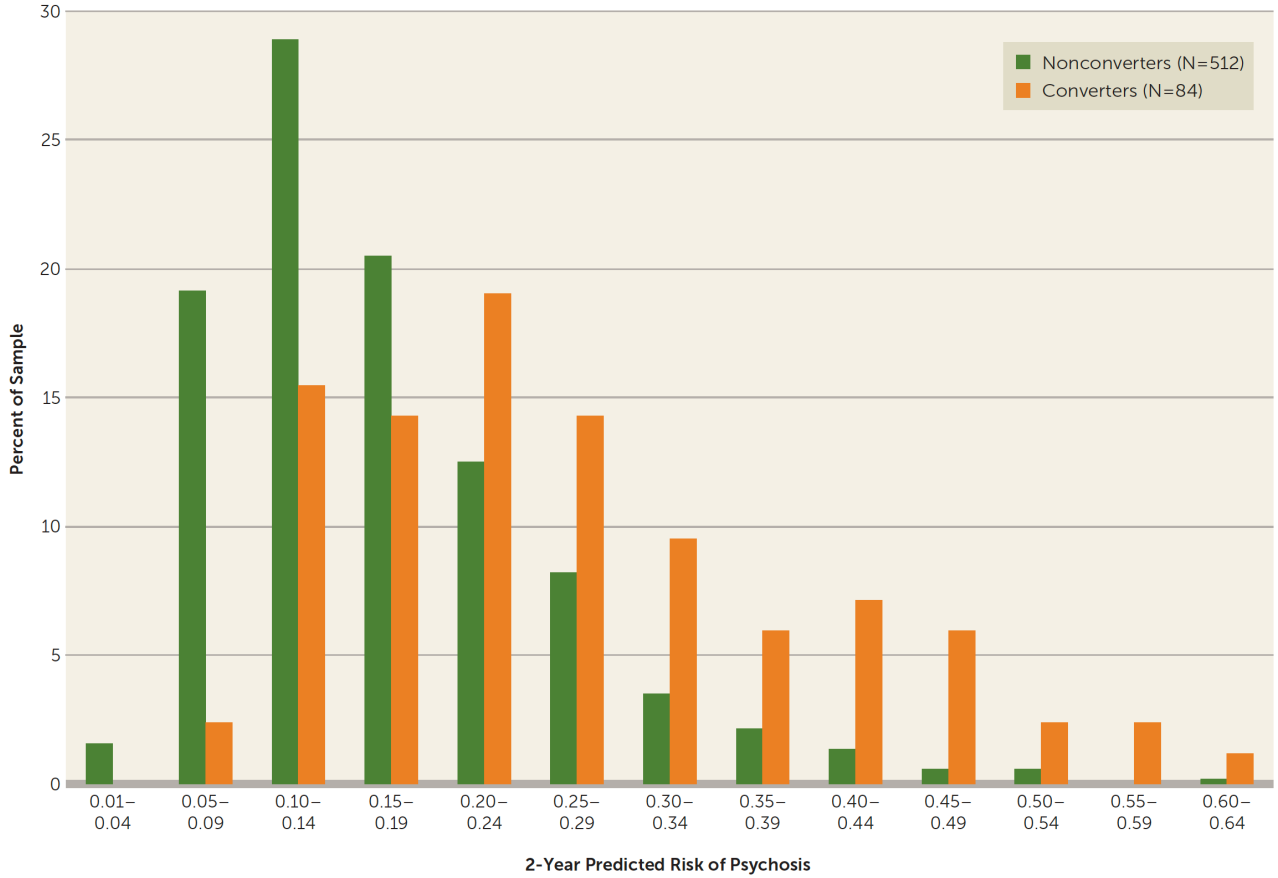


Risk Calculator

An Individualized Risk Calculator for Research in Prodromal Psychosis

Tyrone D. Cannon, Ph.D., Changhong Yu, M.S., Jean Addington, Ph.D., Carrie E. Bearden, Ph.D., Kristin S. Cadenhead, M.D., Barbara A. Cornblatt, Ph.D., Robert Heinssen, Ph.D., Clark D. Jeffries, Ph.D., Daniel H. Mathalon, Ph.D., M.D., Thomas H. McGlashan, M.D., Diana O. Perkins, M.D., M.P.H., Larry J. Seidman, Ph.D., Ming T. Tsuang, M.D., Ph.D., Elaine F. Walker, Ph.D., Scott W. Woods, M.D., Michael W. Kattan, Ph.D.

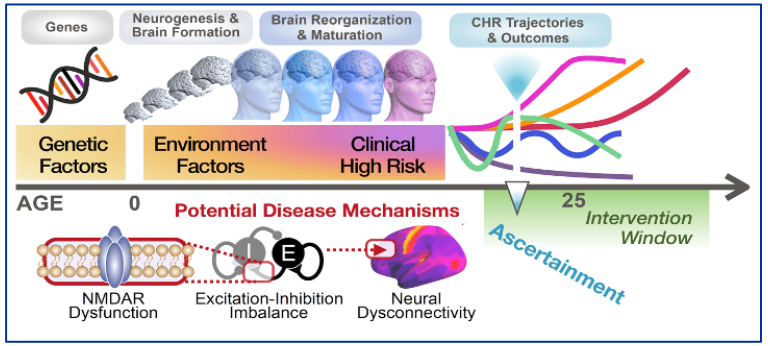
FIGURE 1. Frequency Distributions of Predicted Risks Among Nonconverters and Converters[a]



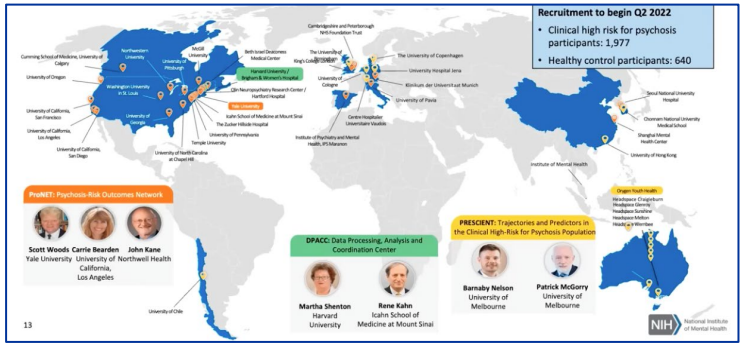
AMP® SCZ LAUNCHED IN JUNE 2022 AFTER A 12-MONTH PLANNING EFFORT LED BY THE FOUNDATION FOR NIH

Accelerating Medicines Partnership®
SCHIZOPHRENIA

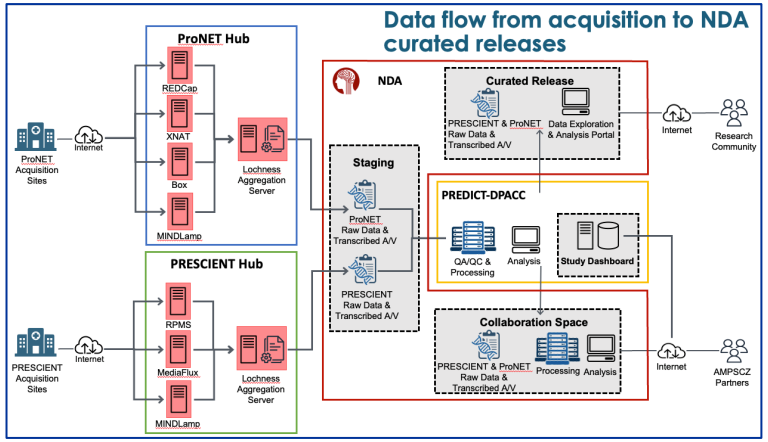
- The overall aim of the AMP SCZ **Observational Study** is to provide tools to parse heterogeneity and improve success in developing pharmacologic treatments for patients with CHR for psychosis.
- Three grants: ProNET, PRESCIENT, PREDICT DPACC, including 43 sites on 5 continents.
- **Met and surpassed recruitment goals**: 2034 CHR and 652 HC to be followed over 2 years.
- MRI, EEG, fluids, digital, and language biomarkers.
- Data deposited in NIMH Data Archive.
- 3 Public sector partners. Private partners include: 3 non-profit partners, 2 private foundations, and 3 industry partners.



Courtesy Alan Anticevic



Courtesy AMP SCZ



Courtesy PREDICT DPACC

Precision Outcome Measures

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DOI: 10.1111/eip.13457

ORIGINAL ARTICLE

WILEY

Development of the PSYCHS: Positive SYmptoms and Diagnostic Criteria for the CAARMS Harmonized with the SIPS

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Abstract

Aim: To harmonize two ascertainment and severity rating instruments commonly used for the clinical high risk syndrome for psychosis (CHR-P): the Structured

Individual names of AMP SCZ collaborators are listed in the Acknowledgment.
Accelerating Medicines Partnership Schizophrenia (AMP SCZ) authors are listed in the section Appendix A.
For affiliations refer to page 12

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PSYCHS Roles in Drug Development

1. **Ascertainment**
   a. Excludes frank psychosis
   b. Includes CAARMS CHR
   c. Includes SIPS CHR

   } Context of Use (COU)

2. **Clinical Outcome Assessment (COA)**
   a. Attenuated positive symptom severity defined by:
      i. PSYCHS severity scale (15 items, each rated 0-6, highest over past 4 weeks)
      ii. SIPS
      iii. CAARMS
   b. Conversion to psychosis
   c. Remission from CHR

Used in the Accelerating Medicines Partnership® Schizophrenia

- CHR Observational Study
- CHR Proof-of-Principle Trials

Clinically Meaningful Change in PSYCHS at 12 Weeks for Endpoint Analysis

A decrease of 5 points in the overall PSYCHS severity score indicates a clinically meaningful change when analyzed against the Patient Global Impression and the overall BPRS score.

Table 1. Distribution of PSYCHS Total Score Change-From-Baseline Scores at 12 Weeks for AMP SCZ CHR Patients With a 1-Category Improvement in Patient Global Impression of Severity. Negative values indicate improvement.

PGI-S at Baseline	N (%)	Change in PSYCHS Total Score from Baseline to 12 Weeks				
		10th Percentile	25th Percentile	50th Percentile	75th Percentile	90th Percentile
Mild	14 (28.5)	0.4	-2.5	**-6.5**	-8	-12.2
Moderate	28 (57.1)	1	-2.5	**-5.0**	-9	-11.5
Severe	7 (14.7)	2.8	0	**-8.0**	-11.5	-13.4

The PGI-S is a single-item PRO for CHR whose content is related to, but not a direct reflection of, the severity of attenuated positive symptoms : "Please choose the response that best describes the overall severity of your mental health symptoms over the past 7 days." Its recall period is 7 days, while the PSYCHS recall period is the highest severity over the past month.

Table 2. Distribution of PSYCHS Total Score Change-From-Baseline Scores at 12 Weeks for AMP SCZ CHR Patients With an 8-12 Point Improvement in BPRS-total. Negative values indicate improvement

BPRS total at Baseline	N (%)	Change in PSYCHS Total Score from Baseline to 12 Weeks				
		10th Percentile	25th Percentile	50th Percentile	75th Percentile	90th Percentile
Tertile 1 (34-38)	8 (33.3)	-13.30	-10.0	**-6.0**	-2.25	0.3
Tertile 2 (39-41)	9 (37.5)	-14.2	-10.0	**-5.0**	-4.0	-0.4
Tertile 3 (43-51)	7 (29.2)	-10.4	-6.5	**-4.0**	2.0	6.4

Figure 2. Change-From-Baseline Scores at 12 Weeks, N=231

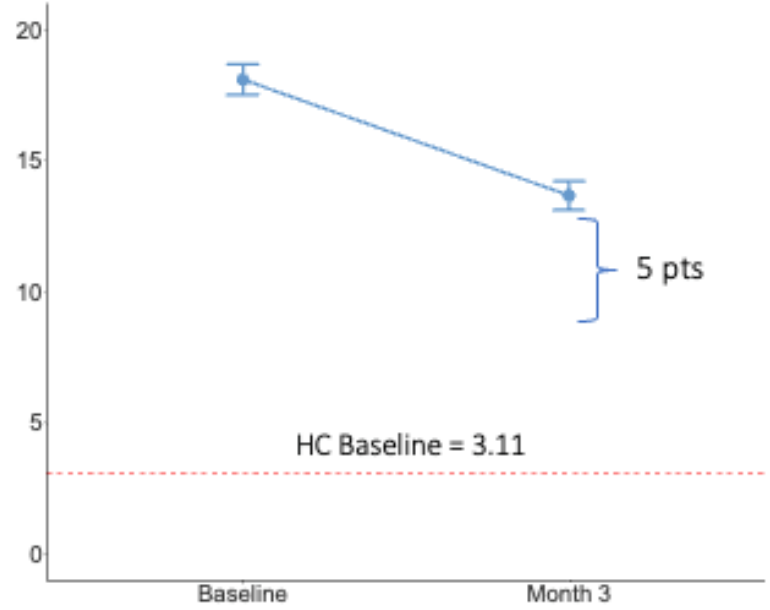

Table 3. Descriptives Total PSYCHS severity scores at Baseline and 12 weeks follow up.

	Mean	Sd	Median	Min	Max
Baseline	18.1	8.88	17	0	43
Month 3	13.7	8.27	13	0	39

SUBSTANTIAL UNMET CLINCIAL NEED IN CHR

- Identifiable with high reliability and validity based on attenuated positive symptoms (Woods et al 2019).
- No unique billing code, but listed in DSM-5 among three other disorders under 298.8. DSM-5 recommends ICD-10 F28.
- Common: Point prevalence at 1.7% of the general youth population and 19.2% of the population of youth presenting for psychiatric care (Salazar de Pablo et al 2021).
- Impairment: Typically distressed by symptoms and show moderate functional impairment.
- Cognitive deficits on average (Seidman et al 2016).
- Affective and anxiety symptoms and comorbid diagnoses.
- ~20% eventually convert to syndromal psychosis (Fusar-Poli et al 2020), on average in 1-2 years (Powers et al 2020).
- Patients who do not convert often have ongoing symptoms and impairment (Addington et al 2019).
- Being treated: More than 100 CHR specialty clinics in multiple countries on six continents (Kotlicka-Antczak et al 2020). An additional ~35 CHR clinics in the US funded by SAMHSA.

- No approved pharmacologic therapies.

AMP® SCZ Proof-of-Principle Trials Launched in February 2026

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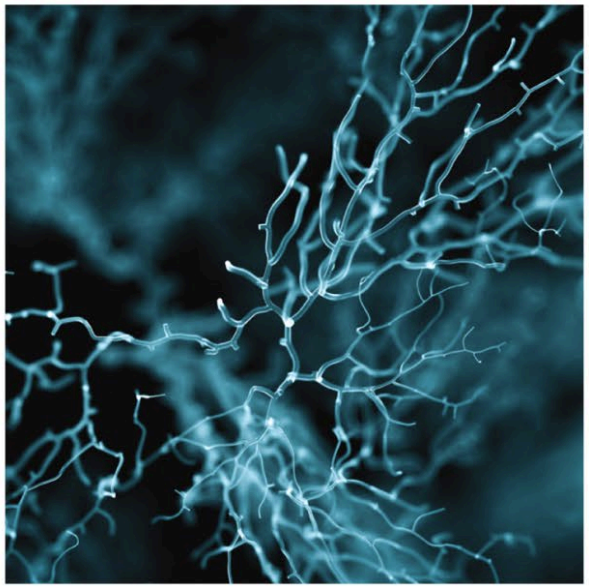

Monument Therapeutics Announces Partnership with Foundation for the National Institutes of Health for Clinical Trial of MT1988, a Novel Treatment for Schizophrenia

August 19, 2025

AMP SCZ: https://fnih.org/our-programs/accelerating-medicines-partnership-amp/amp-schizophrenia/
MT: https://monumenttx.com/news/

THANK YOU