Accelerating Medicines Partnership® Schizophrenia
Protocol Summary

Introduction to Accelerating Medicines Partnership - Schizophrenia

The Accelerating Medicines Partnership (AMP®) is a public-private partnership between the National Institutes of Health (NIH), the U.S. Food and Drug Administration (FDA), the European Medicines Agency, and multiple public and private organizations[1]. The goal of the AMP Schizophrenia (AMP SCZ) program, a multi-continent consortium, is to develop a deep biomarker-informed functional characterization and longitudinal clinical profiling of study participants at clinical high risk (CHR) for psychosis. The data will support the development of algorithms of clinical and biological measures to predict the trajectories and outcomes of CHR individuals to identify enriched CHR patient populations to enable proof of principle intervention studies for early intervention in schizophrenia. These tools will allow the assessment of biomarker and outcome measures as early indicators of pharmacologic treatment efficacy.

The AMP SCZ research network will recruit a large cohort of CHR young people aged 12-30 years (n=1,977) and clinical control (CC) participants (n=640) across 42 participating investigative sites from 13 countries (United States, Canada, United Kingdom, Spain, Italy, Switzerland, Netherlands, Germany, Denmark, Australia, Singapore, South Korea, and Chile). CHR participants will complete screening, baseline assessments and a series of follow-up assessments over a period of 24 months. CC participants will complete screening and baseline assessments and a subset (5 per site) will complete month 2, 12 and 24 visits.

Inclusion/Exclusion Criteria

Inclusion Criteria

All Participants

1. Aged 12-30 years inclusive
2. Understand and sign informed consent/assent
3. Meet either CHR or CC criteria

CHR Participants

Meet diagnostic criteria for CHR (Trait/Vulnerability Group; Attenuated Psychotic Symptoms Group; Brief Limited Intermittent Psychotic Symptoms Group) determined using the Positive Symptoms and Diagnostic Criteria for the CAARMS and Harmonized with the SIPS (PSYCHS).

CC Participants

CC participants will be recruited from the community. CC must not meet any of the exclusion criteria and must not:

[1] NIMH » Accelerating Medicines Partnership - Schizophrenia (AMP SCZ) (nih.gov)
https://fnih.org/our-programs/AMP/schizophrenia

1. Meet CHR criteria or have a current or past Cluster A personality disorder.
2. Be receiving any current treatment with psychotropic medication.
3. Have a family history (in first-degree relatives) of psychotic spectrum disorders.

Exclusion Criteria

1. Antipsychotic medication exposure equivalent to a total lifetime haloperidol dose of >50 mg, estimated based on available information (e.g., medical file documentation, patient and family report) or current antipsychotic medication at time of baseline assessment.
2. Documented history of intellectual disability.
3. Past or current clinically relevant central nervous system disorder. When necessary, research assistants will consult with study team investigators (including medical personnel) to determine if the central nervous system disorder is deemed to be clinically relevant.
4. Traumatic brain injury that is rated as 7 or above on the Traumatic Brain Injury screening instrument.
5. Current or past psychotic disorder, verified using the SCID.

Study Design

This is a non-interventional study examining clinical trajectories and predictors of outcomes in the CHR population. The CHR cohort and CCs will be assessed with a core set of measures at baseline and 2 months post-baseline, with additional assessments completed at other timepoints. CHR subjects will be assessed longitudinally for 2 years. Participants who develop first episode psychosis ('converted' cases) during the course of their study participation will continue to be assessed as scheduled. Measures include clinical, cognitive, neurophysiology, neuroimaging, genetics and fluid biomarkers, speech and facial expression (audio/video recordings are optional), and outcome assessments (*see the Assessment Schedule on the next page*). Digital assessments such as daily ecological momentary assessment (daily digital diary entries) and passive sensing measurements (actigraphy and geolocation) are optional.

Schedule of Assessments CHR = CHR Participant CC = CC Participant		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	Conversion
Informed consent																		
Domain	**Instrument/** **Specimen**	**Screening**	**M0**	**M1**	**M2**	**M3**	**M4**	**M5**	**M6**	**M7**	**M8**	**M9**	**M10**	**M11**	**M12**	**M18**	**M24**	
CLINICAL																		
Inclusion/Exclusion criteria	PSYCHS/SOFAS/SCID 5-PD-Schizotypal /FIGS (abbreviated version)/ TBI/medication use (PharmaTreat)	CHR; CC													CC*		CC*	
Medical & psychiatric history	Health and Medical Conditions Questionnaires	CHR; CC	CHR	CHR	CHR; CC	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR; CC	CHR	CHR; CC	
Demographics	Demographics		CHR; CC															
Premorbid functioning	PAS			CHR														
Adverse events	Adverse Events		CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	
Attenuated psychotic symptoms, associated distress, and conversion to psychosis	PSYCHS		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR; CC*	CHR	CHR; CC*	CHR; CC
General psychopathology	BPRS[94]		CHR; CC	CHR	CHR; CC	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	CHR	
Negative symptoms	NSI-PR		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR	CHR	CHR	
Depression	CDSS		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR	CHR	CHR	

Schedule of Assessments CHR = CHR Participant CC = CC Participant		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	Conversion
Anxiety	OASIS[95]		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR	CHR	CHR	
Suicidality	CSSRS		CHR; CC		CHR; CC				CHR						CHR	CHR	CHR	
Sleep disturbance	PROMIS-SD		CHR; CC		CHR; CC				CHR						CHR	CHR	CHR	
Substance use	ASSIST[96]		CHR; CC		CHR				CHR						CHR	CHR	CHR	
DSM diagnoses	SCID-5-RVs[97]		CHR; CC												CHR; CC*	CHR	CHR; CC*	CHR; CC
Patient global impression of severity	PGI-S		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR	CHR	CHR	
Psychosocial functioning	SOFAS[98], GF Social, GF Role		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR; CC*	CHR	CHR; CC*	CHR; CC
Perceived stress scale	PSS		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR	CHR	CHR	
Perceived discrimination questionnaire	PDQ		CHR; CC															
Pubertal development scale	PDS		CHR; CC															
Psychosis polyrisk score	PPS[99]		CHR; CC															
DIGITAL MOMENTARY ASSESSMENTS																		
Daily changes in mental state and context	EMA		CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC			

Schedule of Assessments CHR = CHR Participant CC = CC Participant		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	Conversion
Physical activity, sleep-wake cycles, travel patterns	Passive sensing (actigraphy, geolocation)		CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC			
NEUROCOGNITION																		
Premorbid IQ	WRAT 5 Reading Accuracy		CHR; CC															
Current IQ	WASI-II - 2-subtest version (Vocab & MR)[100]		CHR; CC														CHR	
Processing speed	Digit-Symbol Substitution Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Attention	Continuous Performance Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Working memory	Letter N-Back		CHR; CC		CHR; CC				CHR						CHR		CHR	
Relational memory	Digit-Symbol Substitution Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Spatial memory	Visual Object Learning Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Verbal learning	List Learning Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Emotion recognition	Emotion Recognition Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Motor	Finger Tapping Test		CHR; CC		CHR; CC				CHR						CHR		CHR	
Sensorimotor speed	Motor Praxis*		CHR; CC		CHR; CC				CHR						CHR		CHR	

Schedule of Assessments CHR = CHR Participant CC = CC Participant		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	Conversion
NEUROPHYSIOLOGY (EEG)																		
Mismatch negativity/visual oddball	Mismatch negativity and visual oddball		CHR; CC		CHR; CC													
Auditory oddball	Auditory target/novelty P300 Auditory target/novel alpha desynchronisation		CHR; CC		CHR; CC													
40 HZ auditory steady state response	40Hz inter-trial phase coherence, baseline inter-stimulus interval gamma power		CHR; CC		CHR; CC													
Resting state (eyes open/closed)	Power spectra 1/f slope		CHR; CC		CHR; CC													
BIOSPECIMENS																		
Vital signs	Elevated body mass index, blood pressure, temperature		CHR; CC		CHR; CC													
Current health status and activity	Current illnesses and recent activity		CHR; CC		CHR; CC													
Elevations in white blood cells	Blood sample – CBC with differential		CHR; CC		CHR; CC													
Immune system, coagulation system, complement system, and oxidative stress	Blood sample – plasma, serum (multiplex, ELISA/mass spectrometry)		CHR; CC		CHR; CC													
DNA isolated for microarray/low-pass sequencing	Blood sample – buffy coat		CHR; CC		CHR; CC													

Schedule of Assessments CHR = CHR Participant CC = CC Participant		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14	V15	V16	Conversion
Functional assays for redox dysregulation and cell membranes for lipids (e.g. DHA/EPA/AA)	Whole blood sample (functional assays, mass spectrometry, gas chromatography)		CR; CC		CHR; CC													
Cortisol	Saliva Collection (ELISA)		CHR; CC		CHR; CC													
SPEECH and FACIAL EXPRESSION																		
Language content and structure **Speech acoustics**	Free speech recording (Zoom audio)		CHR; CC		CHR; CC													
Positive SYmptom and diagnostic Criteria for the CAARMS Harmonized with SIPS (PSYCHS)	PSYCHS interview recording		CHR; CC	CHR; CC	CHR; CC	CHR; CC			CHR; CC						CHR; CC	CHR; CC	CHR; CC	CHR; CC
Language content and structure **Speech acoustics**	Audio diaries recorded via smartphone as component of EMA (2 mins daily)		CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC	CHR; CC			
Facial expression	Free speech recording (Zoom video)		CHR; CC		CHR; CC													
NEUROIMAGING (MRI)																		
Structural/functional **(incl resting state)**	T1, T2, diffusion MRI, resting state functional MRI (BOLD)		CHR; CC		CHR; CC													
TREATMENT AND HEALTH SERVICE UTILIZATION	Psychosocial/ pharmacological treatment/service use		CHR; CC	CHR	CHR; CC	CHR			CHR						CHR; CC	CHR	CHR; CC	

** The Baseline visit needs to be conducted within 3 weeks of the screening visit. If not, the screening visit will need to be repeated. The study team will endeavor to schedule all other visits up to month 12 within +/- 1 week of their due date.*

***CC's will be contacted by Research Assistants at Months 12 and 24 and asked about their mood, behavior, emotions, and other experiences since their last assessment (to determine possible onset of CHR status or psychiatric diagnosis). They will also be asked about any contact they may have had with mental health services since last visit. These check-ins will be completed using the PSYCHS, SOFAS, SPD, and the SCID 5 screening questions. If the SCID 5 screening questions indicate presence of a DSM 5 diagnosis, the relevant section of the SCID 5 will be completed. A full conversion to psychosis assessment will be administered if the PSYCHS indicates onset of psychotic disorder. These assessments will be conducted remotely (via phone or video call) and will take around 20-30 minute*