Independent Versus Joint Effects of Polygenic or Family-Based Schizophrenia Risk in Diverse Ancestry Youth in the ABCD Study

Mahnoor Hyat

A thesis

submitted in partial fulfillment of the

requirements for the degree of

Master of Science

University of Washington

2025

Committee

Jennifer K. Forsyth

Katherine T. Foster

Program Authorized to Offer Degree:

Psychology

University of Washington

Abstract

Independent Versus Joint Effects of Polygenic or Family-Based Schizophrenia Risk in Diverse Ancestry Youth in the ABCD Study

Mahnoor Hyat

Chair of the Supervisory Committee

Jennifer K. Forsyth

Department of Psychology

Background: Behavioral and cognitive signs often precede schizophrenia (SCZ) onset, and measures of SCZ risk, such as family history of psychosis (FH) and SCZ polygenic risk scores (SCZ-PRS), have been linked to cognition and mental health symptoms in childhood. However, studies using SCZ-PRS have largely focused on European ancestry youth. In addition, the extent to which FH reflects common variant based polygenic risk for SCZ, or broader risk factors for SCZ is unclear. We investigated whether SCZ-related behavioral and cognitive signs and symptoms are associated with SCZ-PRS or FH across diverse ancestry children in the Adolescent Brain Cognitive Development (ABCD) study.

Method: Using baseline ABCD data, we analyzed associations of FH and SCZ-PRS, with cognitive, behavioral and emotional measures derived from the NIH-Toolbox, Child Behavior Checklist (CBCL), and Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) for 9,636 children (mean age=9.92 yrs, 47.4% female), specifically 5,636 European, 2,093 African, and 1,477 Admixed American ancestry individuals. SCZ-PRS were refined using PRS-CSx and normalized within ancestry groups, before being assessed for associations with the different phenotypes. Associations were adjusted for age, sex, study site, and genetic relatedness.

Results: FH showed positive associations with SCZ-PRS across all groups, with a significant association in European ancestry youth (b=0.39, FDR-p=0.02). FH was linked to higher CBCL scores across all ancestries (b range=2.90-4.81, FDR-p<0.001), and higher PQB Distress scores in European ancestry youth (b=3.74, FDR-p=0.01). SCZ-PRS was associated with lower NIH-TB total cognition across ancestries (b=-0.43, FDR-p=0.023), particularly in Europeans (b=-0.78, FDR-p=0.001), but not with CBCL or PQB Distress. FH was associated with higher odds of depressive disorders, conduct disorder, anxiety, PTSD, and ADHD (OR=2.17-5.09, FDR-p<0.001), while SCZ-PRS was only linked to a greater likelihood of depressive disorders in Admixed American youth (OR=1.37, FDR-p=0.02). Income-to-needs adjustment slightly altered some associations, but overall patterns remained unchanged.

Conclusion: This study underscores the independent effects of FH and SCZ-PRS on childhood SCZ-related emotional, cognitive and behavioral signs across ancestries. FH was consistently linked to greater psychopathology but not cognitive functioning, while SCZ-PRS showed strong associations with cognition and specific emotional and behavioral symptoms in European ancestry youth. Findings highlight the complementary role of FH and PRS in early SCZ risk assessment and call for improved PRS accuracy across diverse populations.

Introduction

Schizophrenia (SCZ) is a psychiatric disorder impacting roughly 1% of the world with adverse implications, including high unemployment, social disability and elevated suicide rates (Bottlender et al., 2010; Chong et al., 2016; Evensen et al., 2016; Laursen et al., 2014; Kar & Jain, 2016). The economic cost for the US of SCZ due to loss of productivity and healthcare expenses in 2020 was estimated at $281.6 billion (Kadakia et al., 2022). Additionally, the diagnostic criteria are based on the onset of fully formed psychotic symptoms, which leads to treatments being introduced only after severe symptom expression (Tandon et al., 2013).

The concept of clinical staging posits that persistent illness is a late-stage manifestation of an underlying disorder (McGorry et al., 2014). This approach holds promise for SCZ as it assumes that key markers or precursor symptoms may be useful markers of future psychopathology and could guide early interventions to alter illness trajectory (Forsyth & Lewis, 2017). Numerous birth cohort studies have demonstrated that individuals who receive diagnosis of SCZ tend to display behavioral problems, psychopathology, intellectual impairments and language deficits earlier in life (Welham et al., 2009). Impaired cognitive abilities have surfaced as particularly pertinent precursors with SCZ patients showing worse intellectual functioning, working memory, attention, executive functioning, language processing and sensory development long before receiving a diagnosis (Forsyth & Lewis, 2017; Mollon & Reichenberg, 2018; Riglin et al., 2017; Welham et al., 2009). In tandem, dimensional behavioral and emotional problems, such as difficulties in mood regulation and aggressive tendencies, have emerged as potential indicators of future SCZ diagnosis. For example, the Child Behavior Checklist (CBCL) has been used to assess internalizing and externalizing concerns in children with higher scores being linked to the subsequent development of SCZ and psychosis (Hamasaki et al., 2021;

Jansen et al., 2018). Similarly, individuals who later develop SCZ are more likely to meet criteria for diagnosed mental health conditions, such as anxiety and affective disorders, in childhood and adolescence (Maibing et al., 2015). Finally, psychotic-like experiences (PLEs) during childhood and adolescence have been associated with an elevated risk for psychotic disorders, and are thought to capture sub-threshold psychotic symptoms that increase to full psychotic severity for a subset of individuals (Healy et al., 2019; Laurens et al., 2007; Poulton et al., 2000).

Building on this, genetic factors have been shown to significantly contribute to the development of SCZ, with twin studies highlighting the strong hereditary component and an estimated heritability of around 80% (Hilker et al., 2018). Family history of SCZ has long served as a proxy for genetic risk and a means of studying children and adolescents at elevated risk for the disorder (Niemi et al., 2003; Díaz-Castro et al., 2021). A relative risk of 4.87 (4.75–4.99) for SCZ was reported for individuals with first-degree relatives diagnosed with SCZ compared to the general population (Cheng et al., 2018), and having a parent with psychosis was associated with a six-fold increase in risk for psychosis among offspring (Goldstein et al., 2010). Studies using such high-risk design have found that offspring of individuals with SCZ exhibit higher rates of lifetime DSM-IV Axis I disorders, including ADHD and Disruptive Behavior Disorders, compared to children of parents from a community sample (Sanchez-Gistau et al., 2015). High-risk offspring also exhibit cognitive impairments, particularly in attention, social cognition, memory, executive function, and verbal fluency (Erlenmeyer-Kimling et al., 2000; Keshavan, 2009). However, many individuals who develop SCZ do not have an immediate family member with the disorder and sole reliance on family history reports introduces the potential for recall biases (Lu et al., 2018). Additionally, the extent to which family history of SCZ indexes only

shared genetic risk vs broader risk factors is unclear. As a result, alternative methods beyond family history are likely necessary to more accurately capture genetic risk for SCZ.

Fortunately, advancements in genetic analysis have enabled the identification of specific genetic variants linked to SCZ, enhancing the measurement of genetic risk and enabling deeper investigations into its relationship with SCZ and related phenotypes. In particular, the rise of large-scale genome-wide association studies (GWAS) have allowed for the discovery of robust associations between psychiatric disorders including SCZ and hundreds of genetic markers across the genome (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). The most recent GWAS, based on 76,755 patients and 243,649 controls, identified 287 distinct loci that were significantly associated with SCZ (Trubetskoy et al., 2022). This has paved the way for researchers to compute summary-level polygenic risk scores (PRS) which capture each individual's level of genetic risk for the disorder as a weighted sum of risk alleles (Agerbo et al., 2015; Hujoel et al., 2022; Legge et al., 2019), each of which on its own only has a modest impact on risk (Forsyth & Asarnow, 2020). SCZ-PRS, which explain up to 7.3-7.7% of the variance in SCZ case-control status, can then be used to test associations with phenotypes to identify genetically-mediated antecedents of SCZ (Legge et al., 2019; Trubetskoy et al., 2022). For example, SCZ-PRS has been linked to negative symptoms and cognitive impairments, but findings are more mixed for depression and psychotic experiences (Jones et al., 2016; Mistry et al., 2018; Nivard et al., 2017). In addition to equivocal associations between SCZ-PRS and some aspects of psychopathology in childhood, a significant challenge also remains in generating generalizable SCZ-PRS that can be used to identify genetically mediated antecedents of SCZ across global populations. This challenge is due to the over-representation of individuals of European ancestry in existing GWAS, which limits the accuracy of PRS for diverse ancestry

groups. This reduced accuracy is due in part to differences in allele frequency and linkage disequilibrium patterns (Kachuri et al., 2024). Recent efforts to investigate genetic risk for SCZ and other disorders among non-European populations, including individuals of African, Admixed American or East Asian ancestry (Bigdeli et al., 2020; Nguyen et al., 2022) are advancing PRS accuracy across diverse ancestries, alongside improvements in PRS calculation methods. In particular, a novel PRS construction method, PRS-CSx, has been shown to improve cross-population prediction (Ruan et al., 2022). This tool works by leveraging GWAS summary statistics from multiple ancestry groups and ancestry-matched linkage disequilibrium panels to refine allele effect size estimates. This offers important opportunities to enhance the generalizability and clinical utility of PRS, ultimately aiding in the development of more equitable and personalized risk assessment strategies for SCZ and related disorders.

In addition to advances in PRS construction methods, the availability of large-scale, publicly accessible datasets of deeply phenotyped, diverse youth presents valuable opportunities to identify early signs and symptoms linked to genetic risk for SCZ. In particular, the Adolescent Brain Cognitive Development (ABCD) study is the largest, nationally representative, longitudinal study of child development in the US and includes genetic, behavioral, clinical, environmental and neuroimaging information for children and adolescents. Previous studies in ABCD found higher SCZ-PRS linked to worse cognitive functioning, greater attentional variability and severity psychotic-like experiences, but showed mixed results for internalizing and externalizing problems in childhood (Chang et al., 2024; Loughnan et al., 2022; Wainberg et al., 2022). Recent studies also suggest that integrating family history of SCZ and PRS into combined models may enhance disease risk prediction compared to models using each factor alone, thus suggesting that integrating the two when exploring dimensional psychopathology is

likely to yield novel insights (Hujoel et al., 2022; Loughnan et al., 2022; Wainberg et al., 2022). However, these studies tended to restrict primary analyses to European ancestry youth and/or used methods for PRS construction that were not optimized for cross-ancestry PRS accuracy.

Current Study

This study investigates whether early cognitive and behavioral signs and symptoms associated with SCZ reflect common variant based polygenic-specific risk or broader aspects of risk for the disorder, across children from diverse genetic ancestry groups. Specifically, we used ABCD study baseline data to examine the associations of family history of psychosis (FH) and PRS for SCZ (SCZ-PRS) with cognitive, behavioral and emotional signs and symptoms associated with later SCZ in childhood. Additionally, we investigated the extent to which FH and SCZ-PRS associations with these areas of functioning represent independent versus overlapping aspects of risk for SCZ. This study is distinct in its methodological approach. Recognizing the continuous and nuanced nature of family history, we employed a weighted FH measure that accounted for the number and degree of first- and second-degree relatives with SCZ. We also utilized novel PRS construction methods, PRS-CSx, to maximize SCZ-PRS accuracy for diverse ancestries.

Methods and Materials

Sample

This study utilized data collected through the ABCD study which enrolled 11,880 children across 21 research sites across the US, to generate a sample that is representative of the sociodemographic characteristics of the general US population.

We utilized the genetic and phenotypic data provided in the Annual Data Release 4.0 (Yang & Jernigan, Terry, n.d.). Our analysis was focused on the baseline assessment of children

aged 9-10 years old, as this timepoint allows for the exploration of early SCZ-related signs and symptoms that may emerge in childhood. Analyses were conducted for youth of European (*n* = 5,626), African (*n* = 2,093), or Admixed American (*n* = 1,477) ancestry (mean age=9.92 yrs; 47.4% female), as these groups were sufficiently powered for investigation. Some participants had missing data for specific phenotypic measures, as outlined in Table 1.

Measures

SCZ Risk Measures

FH was assessed using data from the caregiver-reported Family History Assessment Survey. This survey collected detailed information on family members' experiences with depression, mania, hallucinations, and related conditions, making it a comprehensive measure of family history. FH was determined by the question: *"Has ANY blood relative of your child ever had a period lasting six months when they saw visions or heard voices or thought people were spying on them or plotting against them?"* Positive responses were followed by a question to identify the relationship of this relative to the child. Responses to this question were used to develop a continuous weighted measure of endorsement, accounting for the degree of relatedness of the affected relative(s) (first- or second-degree relatives).

The second SCZ risk measure was a molecularly defined SCZ-PRS. These scores were derived from the imputed genotyping data that underwent rigorous quality control following the Ricopili pipeline guidelines (Lam et al., 2020; Wainberg et al., 2022). The imputation was completed using the Trans-Omics for Precision Medicine (TOPMed) panels and server (Das et al., 2016; Loh et al., 2016; Taliun et al., 2021). Following ABCD recommendations, we excluded data from plate 461 in the genetic dataset due to a known error associated with this plate. To ensure data quality, we retained only high-quality imputed variants by applying a filter of R2 >

0.8 and minor allele frequency (MAF) > 0.01. To minimize confounding caused by the complex linkage disequilibrium (LD) structure of the major histocompatibility complex (MHC) region, one SNP in the region with the strongest association to SCZ was retained during PRS construction (Loughnan et al., 2022; Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014; Trubetskoy et al., 2022). The final variant count used for PRS construction was 9,621,445.

To derive the SCZ-PRS, we utilized GWAS summary statistics for SCZ from the largest discovery cohorts with diverse ancestries. This included an African American ancestry GWAS, a Latinx ancestry GWAS, and a predominately European ancestry GWAS (Bigdeli et al., 2021; Trubetskoy et al., 2022). PRS-CSx was employed to refine the effect size estimates for each SNP by integrating data from all three GWAS and accounting for the LD patterns across populations. This method was chosen due to its demonstrated accuracy in improving cross-ancestry PRS accuracy compared to many other PRS construction methods (Ruan et al., 2022). The output from PRS-CSx included a meta-analysis file, which provided refined SNP effect size estimates across populations using an inverse-variance-weighted meta-analysis of population-specific posterior effect size estimates, as well as ancestry-specific SNP effect size estimates for each individual GWAS. For the European ancestry group, we used the SNP effect size estimates derived from the predominantly European ancestry GWAS as prior studies suggest that the PRS-CSx meta-analyzed effect sizes typically improve prediction accuracy for non-European groups, which are often underrepresented in GWAS datasets, while ancestry-specific estimates tend to provide greater accuracy for European populations (Ruan et al., 2022). SCZ-PRS, representing the weighted sums of SNP effect sizes, were then generated in PLINK using high-quality imputed SNPs before being standardized within each ancestry group to obtain z-scores.

SCZ-related signs and symptoms

The following dimensional and diagnostic assessments were investigated for association with FH and SCZ-PRS.

I) Dimensional Assessments

A. NIH Cognitive Toolbox

Children completed tasks from the NIH Cognitive Toolbox (NIH-TB) which quantifies cognitive functioning across various domains (Gershon et al., 2013; Weintraub et al., 2013). The tasks administered at baseline include Flanker (inhibitory control), List Sorting (working memory), Picture Sequence (episodic memory), Oral Reading Recognition (language), Picture Vocabulary (language), and Pattern Comparison (processing speed) subtests. The Flanker task tests participants' ability to inhibit attention from irrelevant stimuli. List Sorting requires the participant to recall and sequence different stimuli while Picture Sequence is a test of episodic memory and involves the reproduction of pictures as they had been presented. Both Oral Reading Recognition and Picture Vocabulary assess language skills. The former requires participants to read letters and words aloud, while the latter involves selecting the most fitting picture for a word presented audibly. Lastly, Pattern Comparison measures processing speed by requiring participants to quickly determine whether two stimuli are the same or not. A total composite, age-corrected cognitive score, summarizing functioning across these tasks was used for analysis, after winsorizing scores to account for outliers beyond three standard deviations.

B. Child Behavior Checklist

Primary caregivers completed the Child Behavior Checklist (CBCL) which is a well-validated and widely used assessment involving 113 questions to measure emotional and behavioral problems in children over the past 6 months (Achenbach, 1991). The total composite

score, along with scores for the eight primary subscales: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior severity were used for analysis.

C. Prodromal Questionnaire – Brief Child Version

Children also completed the Prodromal Questionnaire – Brief Child Version (PQ-BC) which is a 21-item scale that assesses the occurrences of psychotic-like experiences (e.g. perceptual abnormalities, and level of distress for any endorsed experience. We generated a summary PQ-BC Distress score by adding the total number of endorsed items weighted by distress (for each item, 0 = did not experience PLE, 1 = experienced PLE with no distress, 2-6 = distressing PLE [+1 to the distress score for the item]) (Chang et al., 2024). The PQ-BC Distress score was used as the measure of psychotic-like experiences (PLEs).

II) Diagnostic Assessments

A. Kiddie schedule for Affective Disorders and Schizophrenia

Caregivers and youth completed a semi-structured, self-administered, computerized version of the validated and reliable KSADS-5 (KSADS-COMP; Kaufman et al., 1997), which assesses current and lifetime history of mental health conditions experienced by the child, including depression, bipolar disorder, anxiety disorders, psychosis, conduct disorder and ADHD. Lifetime history of diagnoses were derived from the caregiver self-administered KSADS-COMP, as they have been shown to have greater concordance with diagnoses derived from gold-standard clinician interviews integrating parent and youth report, compared to diagnoses derived from the youth self-administered KSADS-COMP in a recent study of youth (Townsend et al., 2020). To facilitate comparison with dimensional psychopathology measures derived from the CBCL, analyses of KSADS-derived clinical diagnoses utilized lifetime history

of any depressive disorder, any anxiety disorder (including and excluding PTSD), conduct disorder, and ADHD. Potential issues with ADHD diagnoses via the KSADS-COMP in ABCD have been noted previously due to a modification of the diagnostic criterion to require impairment in two or more settings, which yielded an unexpectedly low endorsement rate (Barch et al., 2021). To address this, we re-coded the variable to include cases with impairment in just one setting, an approach that aligns with both the criterion used in Data Release 3 and methods employed in similar research.

B. CBCL ADHD variable

To facilitate comparison with papers using alternate methods for deriving ADHD diagnoses, we generated an additional ADHD variable using CBCL cut-offs. A T-score of ≥65 on the CBCL Attention Problems scale was established as the threshold for clinical-level attention problems. A key distinction between the diagnostic measures is that the KSADS variables reflect the lifetime prevalence of ADHD, while the CBCL-derived ADHD measure captures symptoms occurring only within the past six months.

Statistical Analysis

Ancestry Principal Components, Ancestry Grouping, and Genetic Relatedness

To create ancestrally homogeneous groups of subjects, we conducted principal components analysis (PCA) using high-quality SNPs from the ABCD dataset merged with HapMap3 data as the reference (The International HapMap 3 Consortium, 2010). HapMap3 includes genotype data from 11 global populations, providing a robust reference for ancestry analysis. To ensure SNP quality, we excluded variants that violated Hardy-Weinberg Equilibrium at a p-threshold of 0.001 during the merging process. We first assessed genetic relatedness using the KING robust algorithm in R with the SNPRelate package (Bigdeli et al., 2020) and then used

PC-Air on the merged data to generate the initial PCs (Conomos et al., 2015). These initial PCs were further refined using the PC-Relate function within the GENESIS package, a method optimized for diverse ancestral groups and high genetic relatedness (Conomos et al., 2016).

We utilized these refined PCs as inputs for a Random Forest classifier to categorize participants into ancestry groups based on HapMap3 super-population labels (Alexander & Lange, 2011). The top eight PCs, which captured the majority of ancestry variance, were used to train the classifier. A probability threshold of 0.7 was applied for ancestry group assignment, leading to a slight reduction in the sample size from 10,979 to 9,365 participants but better grouping accuracy. Figure 1 illustrates the variance explained by the first two PCs.

Association Testing

We employed linear and logistic mixed models to examine associations between FH and SCZ-PRS and the dimensional and diagnostic measures described above. Linear regressions were used to evaluate associations with dimensional variables (i.e., NIH-TB Total Cognition score, CBCL scores, and the PQ-BC Distress score). Logistic regressions assessed associations with clinical diagnoses. Associations between each phenotype and either FH or SCZ-PRS, were first assessed in independent models (e.g., dependent variable ~ FH + covariates or dependent variable ~ SCZ-PRS + covariates), followed by a joint model including both FH and SCZ-PRS (e.g., dependent variable ~ FH + SCZ-PRS + covariates) to refine coefficient estimates for each SCZ risk measure, while accounting for the effect of the other. We first conducted analyses separately for each of the three ancestry groups, followed by a combined analysis using within-ancestry z-scored SCZ-PRS.

The fixed covariates included sex, age, study site, ancestry principal components, and genetic relatedness matrices (GRMs). To optimize computational efficiency, the GRMs were

made sparse by setting a threshold to exclude relationships beyond the fourth-degree relatives. Given the inclusion of GRMs as covariates, we utilized the fitNullModel function within the GENESIS package to perform linear and logistic regressions, as it accommodates matrix covariates. P-values for all dimensional measures were corrected for multiple testing using false discovery rate (FDR) correction within each ancestry group, across both risk SCZ measures. P-values for all diagnostic outcomes were similarly FDR-corrected for multiple testing within each ancestry group, across both risk SCZ measures. We also conducted a sensitivity analysis incorporating income-to-needs ratio as an additional covariate. This ratio was calculated by dividing the median income value within each income band by the federal poverty threshold, adjusted for household size.

Results

We first assessed the associations between FH and SCZ-PRS, and as expected, they showed a positive relationship across groups. This association was significant among European ancestry youth (b=0.39, p=0.01 , FDR p=0.02), but not in the cross-ancestry analysis (b=0.096, p=0.27, FDR p=0.53), or for the African (b=0.07, p=0.53, FDR p=0.53) and Admixed American ancestry groups (b=0.14, p=0.51, FDR p=0.53) alone.

Independent associations between SCZ Risk Measures & Dimensional Measures

Figure 2 and Table 2 summarize the independent associations between the FH and SCZ-PRS risk measures and potential childhood dimensional markers of SCZ.

For FH and NIH-TB total cognition, no significant associations were observed across ancestry groups (b=-1.03, p=0.47, FDR p=0.61), nor in the European, African and Admixed American ancestry groups, when investigated separately. Conversely, greater FH was associated with higher CBCL total problems scores across ancestries (b=9.04, p<0.001, FDR p<0.001) and

within each of the three ancestry groups (*b* range=7.53-10.16, p<=0.002, FDR p<0.001). FH also showed robust associations with all eight CBCL subscales across ancestries and within each of the three groups (*b* range=2.90-4.81, p<0.001, FDR p<0.001). Additionally, individuals with greater FH had higher PQB distress scores across ancestry groups (*b*=3.45, p<0.001, FDR p<0.001) and in the European ancestry group (*b*=3.74, p=0.003, FDR p=0.01).

For the independent models examining associations between dimensional measures of childhood functioning and SCZ-PRS, higher SCZ-PRS was associated with significantly lower NIH-TB total cognition scores across ancestry groups (*b*=-0.43, p=0.01 FDR p=0.02). This relationship was also significant within the European ancestry group (*b*=-0.78, p<0.001, FDR p=0.001) alone, but not in the African or Admixed American groups (*p*s > .05). On the other hand, SCZ-PRS was not significantly associated with CBCL total problems score (*b*=0.08 p=0.52, FDR p=0.64) or scores for any of the 8 subscales (*b* range=-0.09-0.07, p=0.17-0.98, FDR p=0.28-0.98) across ancestries. However, within the European ancestry group alone, higher SCZ-PRS was significantly associated with higher CBCL total problems (*b*=0.33, p=0.03, FDR p=0.04), anxious/depressed (*b*=0.21, p=0.01, FDR p=0.02), rule-breaking behavior (*b*=0.21, p=0.001, FDR p=0.001) and aggressive behavior (*b*=0.16, p=0.02, FDR p=0.04) symptom severity scores. SCZ-PRS and PQB Distress scores were not associated across ancestries (*b*=0.15, p=0.17, FDR p=0.28) or within any of the three ancestry groups (*p*s > .05).

Independent associations between SCZ Risk Measures & Diagnoses in Childhood

Figure 3 and Table 3 illustrate the independent associations between the SCZ risk measures and clinical diagnoses in childhood.

Across ancestry groups, FH was associated with higher likelihood of a depressive disorder (*OR*=2.95 p<0.001, FDR p<0.001), conduct disorder (*OR*=2.18, p<0.001, FDR

p<0.001), anxiety disorder excluding, (*OR*=4.75, p<0.001, FDR p<0.001), or including PTSD (*OR*=5.09, p<0.001, FDR p<0.001), and ADHD (*OR*=2.73, p=, FDR p<0.001). The alternate CBCL-based ADHD diagnosis history was also associated with FH (*OR*=4.41, p<0.001, FDR p<0.001). Associations within specific ancestry groups were similar but did not survive correction for multiple testing for depressive and conduct disorders in European or Admixed American youth.

As illustrated in the heatmap in Figure 3, SCZ-PRS was not significantly associated with lifetime history of the assessed diagnoses across all ancestries or within individual ancestry groups for most disorders. However, there was a significant association between SCZ-PRS and depressive disorders among Admixed American youth (*OR*=1.37, p=0.01, FDR p=0.02).

Joint modeling of SCZ Risk Measures Versus Dimensional Measures

Figure 4 and Table 4 summarize associations between the SCZ risk measures and dimensional phenotypes when modeled jointly. These multivariate associations closely mirrored the patterns observed in the independent models when each risk measure was tested separately.

FH remained unassociated with the NIH-TB total cognition scores across (*b*=-0.98, p=0.49, FDR p=0.64) or within individual ancestry groups, while higher SCZ-PRS was significantly associated with lower cognitive scores across ancestries (*b*=-0.43, p=0.01, FDR p=0.024) and within European ancestry youth (*b*=-0.76, p<0.001, FDR p=0.002).

The joint model also showed strong associations between FH and CBCL total problems across ancestries (*b*=9.03, p<0.001, FDR p<0.001) and within the three ancestry groups. Consistent with the independent model findings, FH showed robust links with the 8 CBCL subscales across ancestries (*b* range=2.89-4.80, p<0.001, FDR p<0.001) as well within the European, African and Admixed American groups. Conversely, SCZ-PRS was not associated

with CBCL total problems (*b*=0.06, p=0.60, FDR p=0.73) or any of the 8 subscale scores (*b* range=-0.09-0.07, p=0.14-0.94, FDR p=0.26-0.94) across ancestries. For the European ancestry group, other associations of SCZ-PRS with CBCL anxious/depressed (*b*=0.20, p=0.02, FDR p=0.03) and rule breaking behavior (*b*=0.20, p=0.001, FDR p=0.003) scores remained significant, whereas the associations with total problems and aggressive behavior were no longer significant after accounting for FH.

Similar to when modeled alone, FH remained significantly associated with PQB Distress scores across ancestries (b=3.44, p<0.001, FDR p<0.001) and within European ancestry youth (b=3.65, p=0.004, FDR p=0.01), but the association did not survive correction for Admixed American youth (b=5.54, p=0.03, FDR p=0.06) and was not nominally significant for African ancestry youth (b=2.62, p=0.11, FDR p=0.24). Similar to when SCZ-PRS was modeled alone, SCZ-PRS was not associated with PQB Distress scores across ancestries (*B*=0.15, p=0.18, FDR p=0.31) or within any of the three groups in models that simultaneously accounted for FH.

Joint associations between SCZ Risk Measures & Diagnostic Measures

Figure 5 and Table 5 summarize associations between the SCZ risk measures and clinical diagnoses in the joint models. Associations between both SCZ risk measures and diagnostic history in childhood were also very similar in the joint versus independent models.

Across ancestry groups, greater FH remained associated with higher likelihood of a history of a depressive disorder (*OR*=2.94, p<0.001, FDR p<0.001), conduct disorder (*OR*=2.17, p<0.001, FDR p<0.001), anxiety disorder excluding (*OR*=4.74, p<0.001, FDR p<0.001), or including PTSD (*OR*=5.07, p<0.001, FDR p<0.001), and ADHD (*OR*=2.72, P<0.001, FDR p<0.001). Results were similar using for CBCL-based current ADHD (*OR*=4.42, p<0.001, FDR p<0.001). As was the case in the independent model, within-ancestry associations of FH with

depressive and conduct disorder did not survive correction for multiple testing for European or American Admixed youth. As in the independent SCZ-PRS models, SCZ-PRS was not significantly associated with history of any clinical diagnoses across all ancestries or within specific ancestry groups after accounting for FH, except for depressive disorders, for which the association with SCZ-PRS among Admixed American youth remained significant (*OR*=1.37, p=0.01, FDR p=0.02).

Sensitivity Analysis Incorporating Income-to-Needs

Analyses including income-to-needs ratio as a covariate revealed a similar pattern, with a few notable exceptions (Tables 6-9). Specifically, in the independent models, the associations between FH and CBCL attention and rule-breaking behavior symptom severity for African ancestry youth, and between FH and CBCL somatic and rule-breaking behavior symptom severity for Admixed American youth were no longer significant. Similarly, FH was no longer significantly associated with conduct disorders in the African and Admixed American ancestry groups or with KSADS or CBCL-based ADHD diagnosis history in African ancestry youth.

In the joint FH and SCZ-PRS models for dimensional phenotypes, the associations across ancestries remained unchanged, but differences emerged within individual ancestry groups. Similar to independent models for FH summarized above when controlling for income-to-needs, associations between FH and CBCL attention and rule-breaking behavior were no longer significant for African ancestry youth, and associations between FH and CBCL somatic and rule-breaking behavior symptom severity no longer survived correction for Admixed American ancestry youth. However, CBCL total and withdrawn symptom severity additionally no longer survived correction for multiple testing when SCZ-PRS was added to the model. Conversely the

pattern of FH and SCZ-PRS associations with lifetime history of clinical diagnoses showed no substantial differences when accounting for income-to-needs.

Discussion

This study demonstrates partially distinct and independent associations of FH and SCZ-PRS with aspects of cognitive, behavioral, and emotional functioning in childhood in the ABCD study. FH showed broad cross-ancestry associations with dimensional and diagnostic markers of psychopathology, such as emotional and behavioral problems, psychotic-like experiences, and an increased likelihood of multiple clinical diagnoses (e.g., depressive, anxiety, conduct disorders, and ADHD) without association to cognitive functioning in the current study. In contrast, SCZ-PRS showed more specific associations to lower cognition functioning across ancestries, and to total and anxious-depressed symptoms, as well as rule-breaking and aggressive behaviors within European ancestry youth only. Notably, when both FH and SCZ-PRS were included in multivariate models, FH retained robust associations across dimensional and diagnostic measures, while SCZ-PRS effects on cognition persisted, underscoring their complementary and domain-specific influences on functioning in childhood.

Across ancestries, greater FH was linked with greater emotional and behavioral problems, more distressing childhood psychotic-like experiences, and higher likelihood of multiple clinical diagnoses, including depressive, conduct, and anxiety disorders (with or without PTSD) and ADHD. These findings align with previous ABCD studies which showed that a binary measure of FH, (i.e., presence of a blood relative with psychosis) was associated with baseline internalizing and externalizing problems, higher psychotic-like symptom and KSADS reports of ADHD and PTSD among youth of European ancestry (Karcher et al., 2020; Loughnan et al., 2022). Interestingly, one prior study in ABCD youth identified significant associations

between FH and KSADS-based depressive and conduct disorders in European ancestry youth, which we did not observe. Conversely, our study found associations between FH and KSADS anxiety disorders for this group, a relationship not reported previously. These differences likely stem from methodological variations, particularly in how FH and socioeconomic status (SES) were measured. Both studies used the same question to assess FH, but our approach employed a weighted measure that accounted for number of affected relatives and degree of relatedness. Similarly, our use of income-to-needs to define SES differed from their usage of parental education and household income. In summary, greater FH was linked to more emotional, behavioral, and clinical problems in childhood with our weighted FH measure providing additional granularity showing novel associations with psychopathology

Associations between SCZ-PRS and psychopathology in childhood were only detected within specific ancestry groups. In European ancestry youth, higher SCZ-PRS was linked to increased severity of CBCL total problems, anxious/depressed, rule breaking, and aggressive behavior symptoms. In Admixed American ancestry youth, SCZ-PRS was associated with KSADS depressive problems. Notably, although SCZ-PRS was associated with some CBCL variables in European ancestry youth, the effect sizes were much smaller compared to the associations between FH and CBCL scores. Nevertheless, we observed more significant associations with emotional and behavioral problems in ABCD study youth at baseline than reported in some recent studies. For example, Wainberg et al. (2022) did not find significant associations between SCZ-PRS and the eight CBCL subscales in European ancestry youth, while Loughnan et al. (2022) noted a significant relationship only with CBCL Rule-Breaking. This may be because our study controlled for additional covariates, such as site and used a GRM to account for family relatedness, which allowed us to include a larger sample than prior studies

that controlled for genetic relatedness by dropping related individuals. Furthermore, differences in PRS generation methods, with our study employing PRS-CSx to maximize PRS accuracy for non-European individuals may have also facilitated our ability to detect these associations. Lastly, while Wainberg et al. (2022) applied Bonferroni correction for multiple comparisons, we used FDR correction. Overall, while SCZ-PRS consistently showed weak associations with psychopathology across ancestries, novel patterns emerged within specific groups.

When looking at overall cognition scores in late childhood, FH was not associated whereas SCZ-PRS showed a consistent association. In particular, SCZ-PRS was associated with poorer overall cognition score in the cross-ancestry sample, as well as within European-ancestry youth specifically. This finding that higher SCZ-PRS predicts poorer cognitive performance aligns with prior research (Loughnan et al., 2022; Mollon & Reichenberg, 2018). The lack of association for FH contrasts prior findings that adolescents and young adults at high risk for psychosis exhibit cognitive deficits when compared to control groups (MacKenzie et al., 2020; Seidman, 2010). However, our findings align with studies using the ABCD sample, which similarly found no significant association between FH and NIH-TB Cognition scores. Weaker associations between FH and cognitive functioning in childhood in the ABCD study may reflect the influence of factors such as normative characteristics of the sample, the reliance on a single-question FH measure, and/or the use of the NIH Toolbox (NIH-TB) as the primary cognitive assessment tool rather than more traditional neurocognitive assessments like the Wechsler Intelligence Scale for Children (WISC). Overall, our results suggest that poorer cognitive function in childhood may more directly reflect consequences of genetic risk for SCZ than the broader FH risk measure. However, this relationship was clearer in European ancestry youth

compared to non-European ancestry groups, which may reflect that our estimates for SCZ-PRS are still not precise enough for non-European ancestry individuals.

In the joint models of FH and SCZ-PRS, the effect sizes and significance levels for the SCZ risk predictors closely mirrored those in the independent models, suggesting that these measures function as largely independent risk factors for youth cognitive, behavioral, and emotional problems. This aligns with recent prior evidence that FH and PRS offer independent yet complementary insights into disease susceptibility for SCZ and other conditions, highlighting the clinical value of combining these measures for early risk assessment (Loughnan et al., 2022; Mars et al., 2022). For example, in a study with 5,959 SCZ cases and 8,717 controls from four Nordic countries, researchers found that in a joint model, the effects of SCZ-PRS remained stable, while the effect of FH was attenuated but remained significant (Lu et al., 2018). These findings also suggest that family history may capture broader vulnerability beyond genetic risk, such as intergenerational exposure to stress (Bowers & Yehuda, 2016; Oliver-Parra et al., 2020). Collectively, the findings underscore the value of combining FH and SCZ-PRS for a broader understanding of SCZ risk in youth.

Although we identified notable association patterns between the risk predictors and SCZ-related signs and symptoms in European ancestry youth, the strength of SCZ-PRS associations in non-European ancestry groups was weaker. These findings underscore the importance of improving PRS accuracy across diverse ancestries through increased representation of diverse ancestry groups large-scale GWAS efforts and continued methods development work to improve the accuracy of PRS across groups. Establishing clear standards for PRS association analyses in diverse ancestry groups to enhance the replicability of findings would also be beneficial for the field. For example, our study used within-ancestry z-scoring, which is a commonly adopted

method but lacks a definitive standard in the field. Support for this approach comes from prior studies that utilize similar scaling methods to create PRS clinical cutoffs or odds ratios across ancestry groups, such as for chronic kidney disease (Khan et al., 2022). Similarly, there have been recent advancements in methods to control for ancestry differences in genetic research that go beyond grouping, such as using covariates that reflect genetic distance for individuals in a new target sample compared to the original discovery GWAS sample, rather than using ancestry PCs (Ding et al., 2023). However, accessible methods for implementing this are evolving and not yet available. In summary, while PRS methodology and inclusion efforts have advanced, ongoing research is needed to establish robust, generalizable, and inclusive standards for cross-ancestry analyses using PRS to enhance our understanding of genetic-mediated precursors for disorders across populations.

Limitations

Some limitations to the current study should be considered when interpreting results. One is the use of the parent-report CBCL and KSADS-COMP to capture dimensional psychopathology and diagnoses. While parent-report measures have generally been found to have greater concurrent validity with gold-standard clinician interviews for diagnoses and symptom severity measures at this age (Townsend et al., 2020; Warnick et al., 2008), reliance on parent-reports also introduces potential bias since they may be influenced by subjective perceptions or sociocultural influences (Robinson et al., 2019). Second, concerns have been raised regarding the psychometric properties of the NIH-TB total cognition score, with some questioning whether it exhibits the same robustness as traditional measures, such as the WISC (Taylor et al., 2022). However, the NIH Toolbox has notable advantages, including ease of administration which makes it scalable and strong predictive validity, making it a reasonably

effective measure of cognition (Distefano et al., 2023). Additionally, while the ABCD study recruited a diverse sample intended to broadly represent demographics of the general U.S. population, it is subject to healthy recruitment bias. This may make it difficult to detect some association patterns, as rates of diagnoses such as SCZ are low. This underscores the importance of testing these associations in samples enriched for psychosis risk.

Conclusion

The current findings highlight the relatively independent effects of FH and SCZ-PRS on cognitive, behavioral, and emotional functioning in childhood across diverse ancestries. By focusing on baseline data when participants were 9-11 years old, we aimed to capture associations that reflect early markers of risk during childhood. FH was consistently associated with greater psychopathology but not cognitive functioning, while SCZ-PRS showed more variable associations, with stronger links to cognition across ancestries and specific emotional and behavioral symptoms in European ancestry youth. These findings underscore the complementary information to be gained from FH and SCZ-PRS in understanding SCZ risk as it manifests across childhood while also emphasizing the need for methodological advancements to improve PRS accuracy across diverse populations. Future research should prioritize inclusive methodologies to improve generalizability, and longitudinal studies to examine the progression of these associations over time.

Tables & Figures

Figure 1. Variance explained by the first 2 ancestry PCs

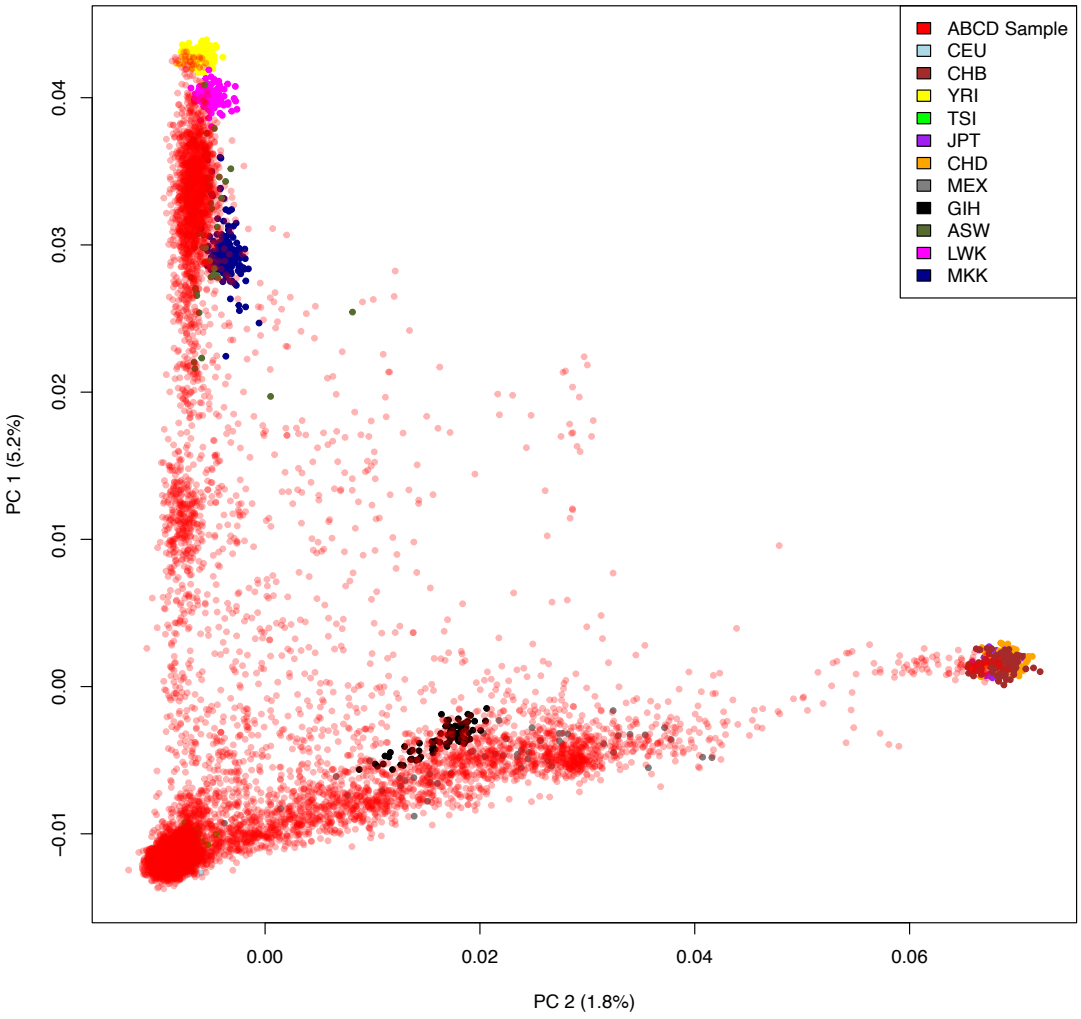

Figure 2. Heatmap of Independent Associations of SCZ-PRS and FH with Dimensional Phenotypes

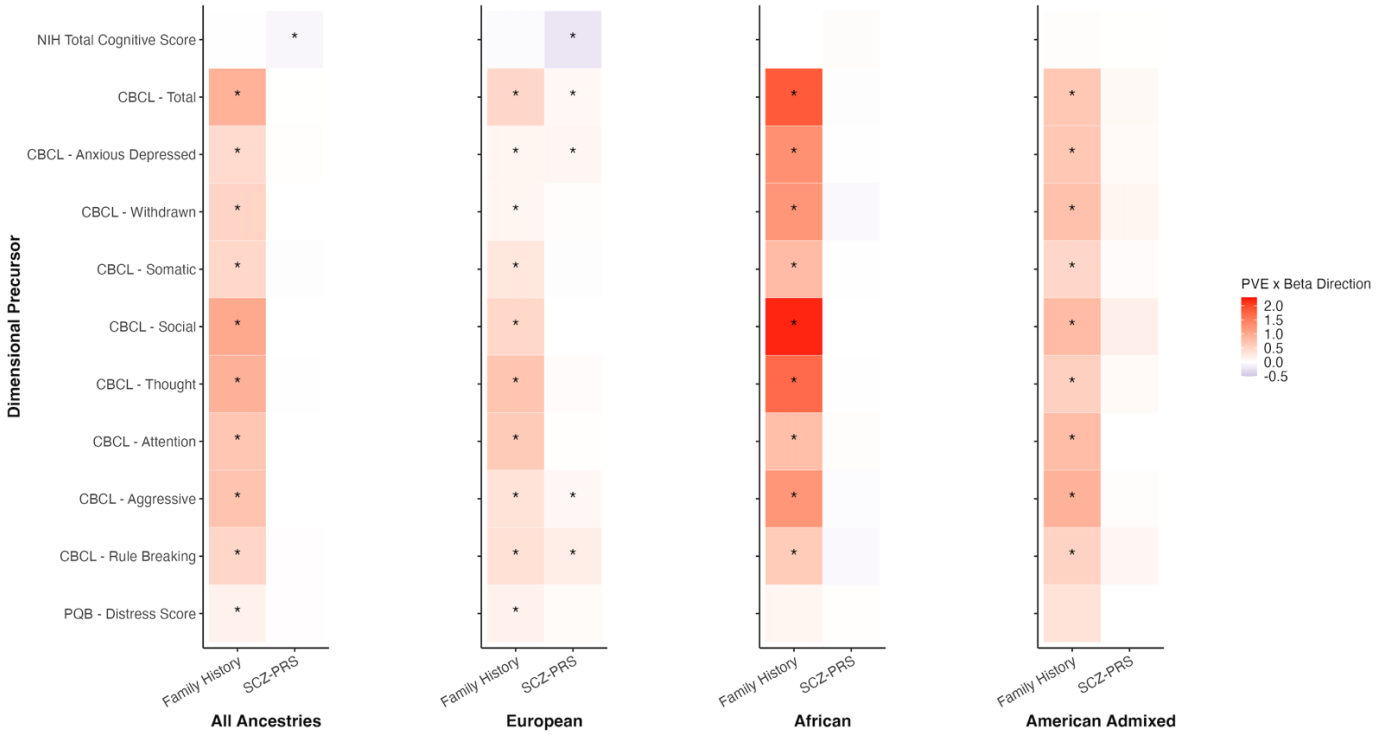

Figure 3. Heatmap of Independent Associations of SCZ-PRS and FH with Diagnostic Phenotypes

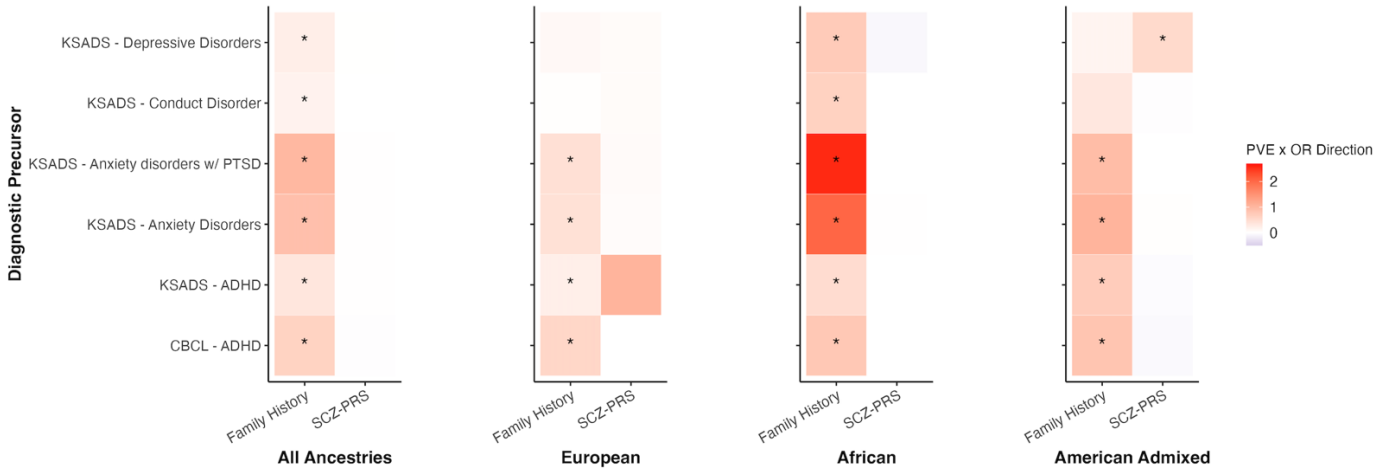

Figure 4. Heatmap of Joint Associations of SCZ-PRS and FH with Dimensional Phenotypes

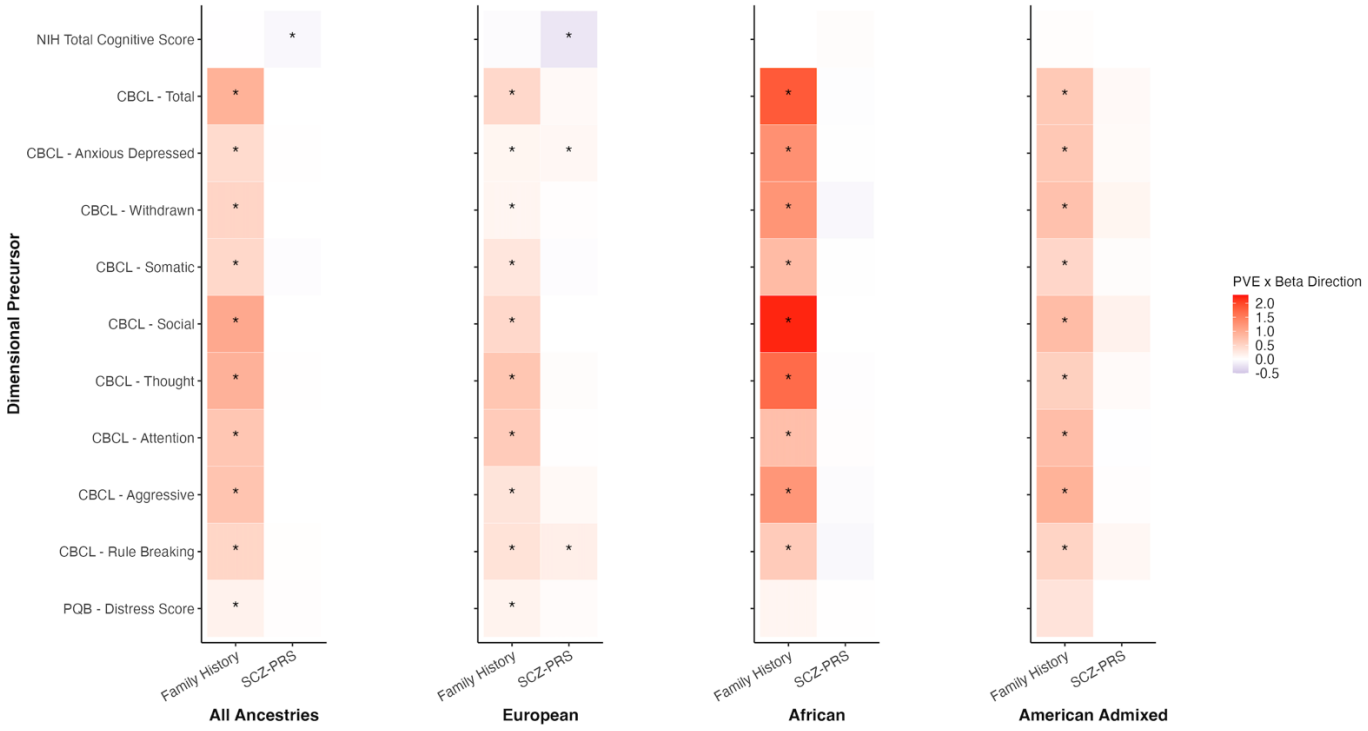

Figure 5. Heatmap of Joint Associations of SCZ-PRS and FH with Diagnostic Phenotypes

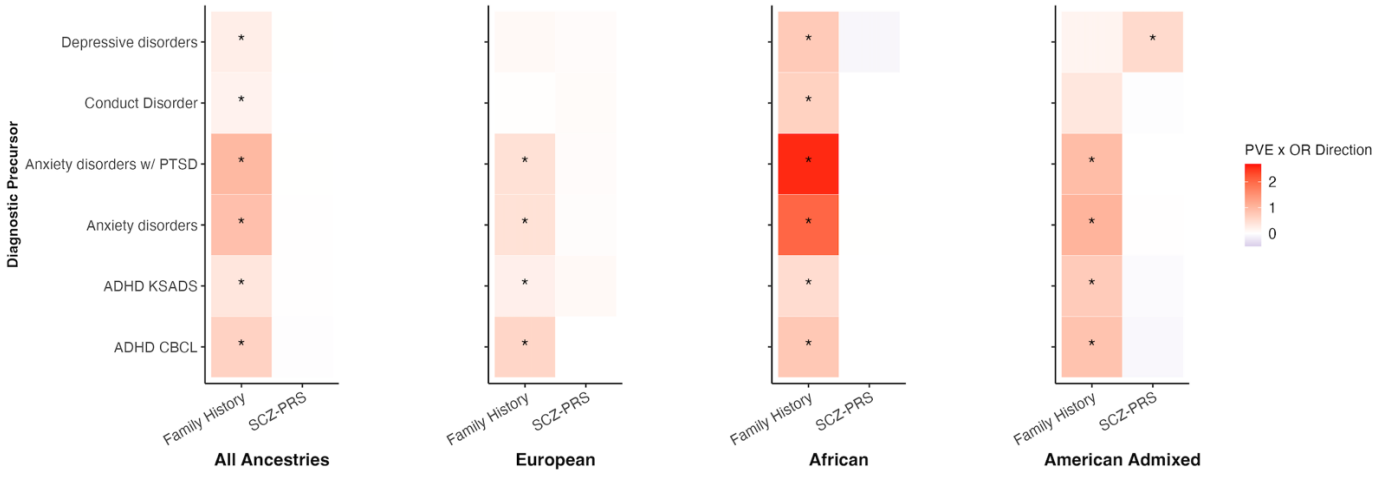

Table 1. The Number of Participants for Whom Data is Available per Phenotype Measure for Each Ancestry Group

Phenotype Measure	European	African	Admixed American	Across Ancestry (Total)
NIH-TB Cognition	5,452	2,020	1,425	8,897
CBCL	5,633	2,093	1,474	9,200
PQB	5,636	2,093	1,477	9,206
KSADS-COMP	5,621	2,087	1,471	9,179

Table 2. Independent Associations of SCZ-PRS and FH with Dimensional Phenotypes

Ancestry	Genetic Risk Measure	Precursor	B	SE	95% CI	Nominal P	FDR P	PVE (%)
All	Family History	NIH Total Cognitive Score	-1.03	1.43	-3.83-1.76	0.469	0.607	0.01
		CBCL - Total	9.04	0.98	7.12-10.95	<0.001	**<0.001**	0.92
		CBCL - Anxious Depressed	3.25	0.51	2.25-4.25	<0.001	**<0.001**	0.44
		CBCL - Withdrawn	3.45	0.50	2.46-4.44	<0.001	**<0.001**	0.51
		CBC - Somatic	3.45	0.52	2.42-4.47	<0.001	**<0.001**	0.47
		CBCL - Social	3.98	0.41	3.19-4.78	<0.001	**<0.001**	1.03
		CBCL - Thought	4.81	0.52	3.79-5.82	<0.001	**<0.001**	0.93
		CBCL - Attention	4.31	0.54	3.24-5.37	<0.001	**<0.001**	0.68
		CBCL - Rule Breaking	2.90	0.43	2.06-3.73	<0.001	**<0.001**	0.50
		CBCL - Aggressive	3.90	0.48	2.96-4.85	<0.001	**<0.001**	0.71
		PQB - Distress Score	3.45	0.90	1.69-5.22	0.0001	**<0.001**	0.16
	SCZ PRS	NIH Total Cognitive Score	-0.43	0.17	-0.77-0.10	0.011	**0.023**	0.07
		CBCL - Total	0.08	0.12	-0.16-0.31	0.520	0.636	0.00
		CBCL - Anxious Depressed	0.07	0.06	-0.05-0.20	0.242	0.354	0.01
		CBCL - Withdrawn	0.01	0.06	-0.11-0.13	0.849	0.889	0.00
		CBC - Somatic	-0.09	0.06	-0.22-0.04	0.170	0.282	0.02
		CBCL - Social	0.01	0.05	-0.09-0.11	0.843	0.889	0.00
		CBCL - Thought	0.06	0.06	-0.06-0.19	0.320	0.440	0.01
		CBCL - Attention	0.00	0.07	-0.13-0.13	0.977	0.977	0.00
		CBCL - Rule Breaking	0.07	0.05	-0.03-0.17	0.179	0.282	0.02
		CBCL - Aggressive	0.02	0.06	-0.09-0.14	0.690	0.799	0.00
		PQB - Distress Score	0.15	0.11	-0.06-0.37	0.168	0.282	0.02
European	Family History	NIH Total Cognitive Score	-3.55	2.27	-8.00-0.9	0.118	0.145	0.04
		CBCL - Total	7.82	1.50	4.88-10.76	<0.001	**<0.001**	0.48
		CBCL - Anxious Depressed	2.18	0.84	0.53-3.83	0.010	**0.017**	0.12
		CBCL - Withdrawn	2.04	0.76	0.54-3.54	0.008	**0.015**	0.13
		CBC - Somatic	3.36	0.83	1.74-4.98	<0.001	**<0.001**	0.29
		CBCL - Social	3.20	0.62	1.98-4.42	<0.001	**<0.001**	0.47
		CBCL - Thought	5.20	0.82	3.58-6.82	<0.001	**<0.001**	0.70
		CBCL - Attention	4.94	0.83	3.31-6.56	<0.001	**<0.001**	0.63
		CBCL - Rule Breaking	2.76	0.61	1.55-3.96	<0.001	**<0.001**	0.36
		CBCL - Aggressive	3.20	0.73	1.77-4.63	<0.001	**<0.001**	0.34
		PQB - Distress Score	3.74	1.26	1.27-6.20	0.003	**0.006**	0.16
	SCZ PRS	NIH Total Cognitive Score	-0.78	0.22	-1.21-0.34	<0.001	**0.0013**	0.22
		CBCL - Total	0.33	0.15	0.04-0.62	0.026	**0.038**	0.09
		CBCL - Anxious Depressed	0.21	0.08	0.04-0.37	0.013	**0.022**	0.11
		CBCL - Withdrawn	0.09	0.08	-0.06-0.24	0.238	0.280	0.02
		CBC - Somatic	-0.08	0.08	-0.24-0.08	0.342	0.380	0.02
		CBCL - Social	0.02	0.06	-0.09-0.14	0.683	0.680	0.00
		CBCL - Thought	0.13	0.08	-0.03-0.29	0.102	0.130	0.05
		CBCL - Attention	0.07	0.08	-0.09-0.23	0.384	0.400	0.01
		CBCL - Rule Breaking	0.21	0.06	0.09-0.33	0.001	**0.001**	0.21
		CBCL - Aggressive	0.16	0.07	0.02-0.30	0.023	**0.036**	0.09
		PQB - Distress Score	0.22	0.12	-0.03-0.46	0.083	0.114	0.05
African	Family History	NIH Total Cognitive Score	-0.25	2.14	-4.45-3.94	0.905	0.946	0.00
		CBCL - Total	10.16	1.62	6.98-13.35	<0.001	**<0.001**	1.85
		CBCL - Anxious Depressed	3.72	0.71	2.32-5.12	<0.001	**<0.001**	1.29
		CBCL - Withdrawn	4.18	0.82	2.58-5.77	<0.001	**<0.001**	1.24
		CBC - Somatic	3.29	0.80	1.73-4.86	<0.001	**<0.001**	0.81
		CBCL - Social	4.63	0.68	3.30-5.96	<0.001	**<0.001**	2.20
		CBCL - Thought	4.88	0.82	3.28-6.48	<0.001	**<0.001**	1.69
		CBCL - Attention	3.66	0.91	1.88-5.44	<0.001	**<0.001**	0.77
		CBCL - Rule Breaking	2.93	0.82	1.33-4.53	<0.001	**<0.001**	0.62
		CBCL - Aggressive	4.26	0.83	2.63-5.90	<0.001	**<0.001**	1.24
		PQB - Distress Score	2.63	1.64	-0.58-5.84	0.109	0.239	0.12
	SCZ PRS	NIH Total Cognitive Score	0.33	0.42	-0.49-1.15	0.431	0.678	0.03
		CBCL - Total	-0.17	0.33	-0.82-0.48	0.600	0.744	0.01

		CBCL - Anxious Depressed	-0.06	0.15	-0.35-0.23	0.676	0.744	0.01
		CBCL - Withdrawn	-0.19	0.17	-0.52-0.14	0.267	0.500	0.06
		CBC - Somatic	-0.07	0.16	-0.39-0.25	0.670	0.744	0.01
		CBCL - Social	-0.01	0.14	-0.28-0.26	0.946	0.946	0.00
		CBCL - Thought	-0.07	0.17	-0.4-0.25	0.657	0.744	0.01
		CBCL - Attention	0.13	0.18	-0.23-0.49	0.475	0.697	0.02
		CBCL - Rule Breaking	-0.18	0.17	-0.5-0.14	0.273	0.500	0.06
		CBCL - Aggressive	-0.13	0.17	-0.47-0.2	0.431	0.678	0.03
		PQB - Distress Score	0.18	0.34	-0.48-0.84	0.598	0.744	0.01
American Admixed	Family History	NIH Total Cognitive Score	2.17	3.46	-4.60-8.95	0.529	0.645	0.03
		CBCL - Total	7.53	2.42	2.80-12.27	0.002	**0.007**	0.66
		CBCL - Anxious Depressed	3.96	1.26	1.49-6.44	0.002	**0.007**	0.67
		CBCL - Withdrawn	4.49	1.36	1.84-7.15	0.001	**0.005**	0.75
		CBC - Somatic	3.64	1.36	0.97-6.32	0.008	**0.019**	0.49
		CBCL - Social	3.59	1.03	1.56-5.61	0.001	**0.005**	0.82
		CBCL - Thought	3.51	1.22	1.13-5.90	0.004	**0.012**	0.57
		CBCL - Attention	4.51	1.32	1.91-7.10	0.001	**0.005**	0.79
		CBCL - Rule Breaking	2.75	0.99	0.81-4.68	0.005	**0.015**	0.53
		CBCL - Aggressive	4.23	1.15	1.97-6.48	<0.001	**0.005**	0.92
		PQB - Distress Score	5.55	2.51	0.63-10.47	0.027	0.060	0.33
	SCZ PRS	NIH Total Cognitive Score	0.11	0.45	-0.76-0.99	0.803	0.844	0.00
		CBCL - Total	0.33	0.31	-0.29-0.94	0.296	0.445	0.07
		CBCL - Anxious Depressed	0.17	0.16	-0.15-0.49	0.304	0.445	0.07
		CBCL - Withdrawn	0.24	0.18	-0.11-0.58	0.176	0.322	0.13
		CBC - Somatic	0.14	0.18	-0.21-0.49	0.428	0.553	0.04
		CBCL - Social	0.21	0.13	-0.05-0.47	0.109	0.219	0.18
		CBCL - Thought	0.15	0.16	-0.16-0.46	0.345	0.474	0.06
		CBCL - Attention	-0.04	0.17	-0.38-0.29	0.806	0.844	0.00
		CBCL - Rule Breaking	0.16	0.13	-0.09-0.41	0.213	0.360	0.11
		CBCL - Aggressive	0.09	0.15	-0.21-0.38	0.557	0.645	0.02
		PQB - Distress Score	0.04	0.32	-0.59-0.68	0.890	0.890	0.00

Table 3. Independent Associations of SCZ-PRS and FH with Diagnostic Phenotypes

Ancestry	Genetic Risk Measure	Precursor	OR	SE	95% CI	Nominal P	FDR P	PVE (%)
All	Family History	KSADS - ADHD	2.73	0.19	1.87-3.98	<0.001	**<0.001**	0.35
		CBCL - ADHD	4.41	0.23	2.78-6.97	<0.001	**<0.001**	0.63
		KSADS - Anxiety Disorders	4.75	0.20	3.20-7.05	<0.001	**<0.001**	0.89
		KSADS - Anxiety Disorders w/ PTSD	5.09	0.20	3.45-7.52	<0.001	**<0.001**	0.99
		KSADS - Depressive Disorders	2.95	0.27	1.75-4.97	<0.001	**<0.001**	0.24
		KSADS - Conduct Disorder	2.18	0.21	1.44-3.30	<0.001	**<0.001**	0.18
	SCZ PRS	KSADS - ADHD	1.03	0.03	0.98-1.08	0.293	0.440	0.01
		CBCL - ADHD	0.96	0.04	0.88-1.04	0.277	0.440	0.02
		KSADS - Anxiety Disorders	1.03	0.03	0.97-1.09	0.356	0.455	0.01
		KSADS - Anxiety Disorders w/ PTSD	1.03	0.03	0.97-1.09	0.379	0.455	0.01
		KSADS - Depressive Disorders	1.03	0.05	0.94-1.13	0.486	0.530	0.01
		KSADS - Conduct Disorder	1.01	0.03	0.95-1.07	0.707	0.707	0.00
European	Family History	KSADS - ADHD	2.81	0.32	1.51-5.22	0.001	**0.003**	0.23
		CBCL - ADHD	6.69	0.40	3.07-14.58	<0.001	**<0.001**	0.57
		KSADS - Anxiety Disorders	4.03	0.32	2.15-7.54	<0.001	**<0.001**	0.43
		KSADS - Anxiety Disorders w/ PTSD	4.06	0.32	2.18-7.57	<0.001	**<0.001**	0.44
		KSADS - Depressive Disorders	2.89	0.54	1.00-8.33	0.050	0.100	0.09
		KSADS - Conduct Disorder	1.41	0.36	0.69-2.86	0.343	0.374	0.02
	SCZ PRS	KSADS - ADHD	1.08	0.03	1.01-1.16	0.024	0.058	1.05
		CBCL - ADHD	1.02	0.06	0.91-1.14	0.720	0.720	0.00
		KSADS - Anxiety Disorders	1.06	0.04	0.99-1.14	0.118	0.142	0.05
		KSADS - Anxiety Disorders w/ PTSD	1.07	0.04	0.99-1.15	0.079	0.130	0.07
		KSADS - Depressive Disorders	1.11	0.07	0.97-1.27	0.115	0.142	0.06
		KSADS - Conduct Disorder	1.07	0.04	0.99-1.15	0.086	0.130	0.06
African	Family History	KSADS - ADHD	2.34	0.29	1.33-4.12	0.003	**0.006**	0.50
		CBCL - ADHD	3.06	0.33	1.60-5.88	0.001	**0.003**	0.78
		KSADS - Anxiety Disorders	5.12	0.31	2.81-9.33	<0.001	**<0.001**	2.05
		KSADS - Anxiety Disorders w/ PTSD	6.13	0.30	3.40-11.08	<0.001	**<0.001**	2.57
		KSADS - Depressive Disorders	3.18	0.35	1.60-6.33	0.001	**0.003**	0.74
		KSADS - Conduct Disorder	2.66	0.30	1.47-4.81	0.001	**0.003**	0.64
	SCZ PRS	KSADS - ADHD	1.01	0.07	0.89-1.15	0.873	0.932	0.00
		CBCL - ADHD	0.98	0.09	0.82-1.17	0.812	0.932	0.00
		KSADS - Anxiety Disorders	1.03	0.08	0.88-1.21	0.698	0.932	0.01
		KSADS - Anxiety Disorders w/ PTSD	1.01	0.08	0.86-1.17	0.932	0.932	0.00
		KSADS - Depressive Disorders	0.89	0.10	0.74-1.08	0.245	0.420	0.08
		KSADS - Conduct Disorder	1.02	0.07	0.88-1.18	0.806	0.932	0.00
American Admixed	Family History	KSADS - ADHD	4.16	0.48	1.61-10.73	0.003	**0.010**	0.72
		CBCL - ADHD	5.95	0.60	1.84-19.25	0.003	**0.010**	0.82
		KSADS - Anxiety Disorders	5.78	0.52	2.08-16.08	0.001	**0.009**	1.05
		KSADS - Anxiety Disorders w/ PTSD	5.25	0.52	1.89-14.59	0.001	**0.009**	0.93
		KSADS - Depressive Disorders	2.73	0.71	0.69-10.88	0.154	0.264	0.16
		KSADS - Conduct Disorder	3.15	0.57	1.02-9.70	0.046	0.092	0.33
	SCZ PRS	KSADS - ADHD	0.95	0.07	0.82-1.10	0.503	0.670	0.04
		CBCL - ADHD	0.91	0.11	0.74-1.13	0.406	0.608	0.06
		KSADS - Anxiety Disorders	1.04	0.091	0.87-1.24	0.657	0.717	0.02
		KSADS - Anxiety Disorders w/ PTSD	1.01	0.09	0.85-1.21	0.873	0.873	0.00
		KSADS - Depressive Disorders	1.37	0.12	1.08-1.74	0.008	**0.020**	0.53
		KSADS - Conduct Disorder	0.96	0.10	0.79-1.15	0.643	0.717	0.02

Table 4. Joint Model Associations of SCZ-PRS and FH with Dimensional Phenotypes

Ancestry	**Precursor**	**Family History of Psychosis (Joint Model)**						**SCZ PRS (Joint Model)**						**Joint PVE**
		B	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	*B*	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	
All	NIH Total Cognitive Score	-0.978	1.43	-3.77 - 1.82	0.493	0.638	0.01	-0.433	0.17	-0.77 - 0.10	0.012	**0.024**	0.07	0.08
	CBCL - Total	9.03	0.977	7.12 - 10.95	<0.001	**<0.001**	0.92	0.063	0.12	-0.17 - 0.3	0.596	0.729	0.00	0.93
	CBCL - Anxious Depressed	3.24	0.51	2.24 - 4.24	<0.001	**<0.001**	0.44	0.07	0.06	-0.05 - 0.19	0.277	0.406	0.01	0.45
	CBCL - Withdrawn	3.45	0.50	2.46 - 4.44	<0.001	**<0.001**	0.51	0.01	0.06	-0.12 - 0.13	0.921	0.944	0.00	0.51
	CBC - Somatic	3.46	0.52	2.43 - 4.48	<0.001	**<0.001**	0.47	-0.09	0.06	-0.22 - 0.03	0.144	0.264	0.02	0.49
	CBCL - Social	3.98	0.41	3.18 - 4.78	<0.001	**<0.001**	1.03	0.004	0.05	-0.09 - 0.1	0.944	0.944	0.00	1.03
	CBCL - Thought	4.80	0.52	3.79 - 5.82	<0.001	**<0.001**	0.93	0.06	0.06	-0.07 - 0.18	0.380	0.523	0.01	0.94
	CBCL - Attention	4.31	0.54	3.25 - 5.37	<0.001	**<0.001**	0.68	-0.01	0.07	-0.14 - 0.12	0.897	0.944	0.00	0.68
	CBCL - Rule Breaking	2.89	0.43	2.05 - 3.73	<0.001	**<0.001**	0.5	0.07	0.05	-0.04 - 0.17	0.208	0.327	0.02	0.52
	CBCL - Aggressive	3.90	0.48	2.96 - 4.84	<0.001	**<0.001**	0.71	0.02	0.06	-0.10 - 0.13	0.767	0.888	0.00	0.71
	PQB - Distress Score	3.439	0.90	1.68 - 5.20	<0.001	**<0.001**	0.16	0.148	0.11	-0.07 - 0.37	0.184	0.311	0.02	0.18
European	NIH Total Cognitive Score	-3.25	2.27	-7.69 - 1.2	0.153	0.198	0.04	-0.76	0.22	-1.2 - 0.33	<0.001	**0.002**	0.22	0.26
	CBCL - Total	7.70	1.50	4.76 - 10.64	<0.001	**<0.001**	0.46	0.30	0.15	0.01 - 0.59	0.042	0.061	0.07	0.55
	CBCL - Anxious Depressed	2.10	0.84	0.45 - 3.75	0.013	**0.023**	0.11	0.20	0.08	0.03 - 0.36	0.017	**0.029**	0.10	0.22
	CBCL - Withdrawn	2.004	0.76	0.50 - 3.50	0.009	**0.018**	0.12	0.081	0.08	-0.07 - 0.23	0.283	0.312	0.02	0.15
	CBC - Somatic	3.40	0.83	1.78 - 5.02	<0.001	**<0.001**	0.30	-0.09	0.08	-0.25 - 0.07	0.263	0.305	0.02	0.32
	CBCL - Social	3.19	0.62	1.98 - 4.41	<0.001	**<0.001**	0.47	0.01	0.06	-0.11 - 0.13	0.841	0.841	0.00	0.47
	CBCL - Thought	5.15	0.83	3.54 - 6.77	<0.001	**<0.001**	0.69	0.11	0.08	-0.05 - 0.27	0.166	0.202	0.03	0.74
	CBCL - Attention	4.91	0.83	3.29 - 6.54	<0.001	**<0.001**	0.62	0.05	0.08	-0.11 - 0.21	0.527	0.552	0.01	0.64
	CBCL - Rule Breaking	2.68	0.61	1.47 - 3.88	<0.001	**<0.001**	0.34	0.20	0.06	0.08 - 0.32	0.001	**0.003**	0.19	0.55
	CBCL - Aggressive	3.14	0.73	1.71 - 4.57	<0.001	**<0.001**	0.33	0.15	0.07	0.01 - 0.29	0.035	0.056	0.08	0.42
	PQB - Distress Score	3.65	1.26	1.19 - 6.11	0.004	**0.008**	0.15	0.20	0.12	-0.04 - 0.44	0.107	0.147	0.05	0.20
African	NIH Total Cognitive Score	-0.29	2.14	-4.49 - 3.90	0.891	0.891	<0.001	0.33	0.42	-0.49 - 1.15	0.430	0.676	0.03	0.03
	CBCL - Total	10.18	1.62	6.99 - 13.36	<0.001	**<0.001**	1.85	-0.20	0.33	-0.85 - 0.44	0.537	0.690	0.02	1.87
	CBCL - Anxious Depressed	3.73	0.71	2.33 - 5.12	<0.001	**<0.001**	1.29	-0.07	0.15	-0.36 - 0.21	0.625	0.690	0.01	1.30
	CBCL - Withdrawn	4.19	0.81	2.59 - 5.79	<0.001	**<0.001**	1.25	-0.20	0.17	-0.52 - 0.13	0.235	0.458	0.07	1.31
	CBC - Somatic	3.30	0.80	1.74 - 4.86	<0.001	**<0.001**	0.82	-0.08	0.16	-0.39 - 0.24	0.628	0.690	0.01	0.82
	CBCL - Social	4.63	0.68	3.31 - 5.96	<0.001	**<0.001**	2.20	-0.02	0.14	-0.29 - 0.25	0.871	0.891	0.00	2.20
	CBCL - Thought	4.89	0.82	3.29 - 6.49	<0.001	**<0.001**	1.69	-0.09	0.17	-0.41 - 0.24	0.596	0.690	0.01	1.70
	CBCL - Attention	3.65	0.91	1.87 - 5.43	<0.001	**<0.001**	0.77	0.12	0.18	-0.24 - 0.48	0.508	0.690	0.02	0.79
	CBCL - Rule Breaking	2.94	0.82	1.34 - 4.54	<0.001	**<0.001**	0.62	-0.19	0.16	-0.51 - 0.13	0.250	0.458	0.06	0.68
	CBCL - Aggressive	4.27	0.83	2.64 - 5.91	<0.001	**<0.001**	1.24	-0.15	0.17	-0.48 - 0.18	0.387	0.655	0.04	1.27
	PQB - Distress Score	2.62	1.64	-0.60 - 5.83	0.110	0.243	0.12	0.17	0.34	-0.49 - 0.83	0.611	0.690	0.01	0.14
American	NIH Total Cognitive Score	2.16	3.46	-4.61 - 8.94	0.532	0.650	0.03	0.11	0.45	-0.77 - 0.98	0.809	0.848	0.00	0.03
Admixed	CBCL - Total	7.49	2.42	2.75 - 12.23	0.002	**0.007**	0.65	0.31	0.31	-0.30 - 0.92	0.321	0.482	0.07	0.73
	CBCL - Anxious Depressed	3.94	1.26	1.47 - 6.42	0.002	**0.007**	0.66	0.16	0.16	-0.16 - 0.48	0.329	0.482	0.06	0.73
	CBCL - Withdrawn	4.46	1.35	1.80 - 7.12	0.001	**0.005**	0.74	0.23	0.18	-0.12 - 0.57	0.193	0.354	0.11	0.86
	CBC - Somatic	3.62	1.36	0.95 - 6.30	0.008	**0.019**	0.48	0.13	0.18	-0.21 - 0.48	0.455	0.589	0.04	0.52
	CBCL - Social	3.56	1.03	1.54 - 5.58	0.001	**0.005**	0.81	0.20	0.13	-0.06 - 0.46	0.123	0.246	0.16	0.98
	CBCL - Thought	3.50	1.22	1.11 - 5.88	0.004	**0.013**	0.56	0.14	0.16	-0.17 - 0.45	0.371	0.510	0.05	0.62
	CBCL - Attention	4.51	1.33	1.92 - 7.11	0.001	**0.005**	0.79	-0.05	0.17	-0.39 - 0.28	0.758	0.833	0.01	0.79
	CBCL - Rule Breaking	2.73	0.99	0.79 - 4.66	0.006	**0.016**	0.52	0.15	0.13	-0.10 - 0.40	0.230	0.389	0.10	0.62
	CBCL - Aggressive	4.22	1.15	1.96 - 6.47	<0.001	**0.005**	0.91	0.08	0.15	-0.21 - 0.37	0.599	0.693	0.02	0.94
	PQB - Distress Score	5.54	2.51	0.62 - 10.47	0.027	0.060	0.33	0.03	0.32	-0.60 - 0.67	0.919	0.919	0.00	0.33

Table 5. Joint Model Associations of SCZ-PRS and FH with Diagnostic Phenotypes

Ancestry	**Precursor**	**Family History of Psychosis (Joint Model)**						**SCZ PRS (Joint Model)**						**Joint PVE**
		OR	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	*OR*	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	
All	KSADS - ADHD	2.72	0.19	1.87 - 3.97	<0.001	**<0.001**	0.35	1.03	0.03	0.97 - 1.08	0.331	0.497	0.01	0.36
	CBCL - ADHD	4.42	0.23	2.79 - 7.01	<0.001	**<0.001**	0.63	0.95	0.04	0.88 - 1.03	0.252	0.433	0.02	0.65
	KSADS - Anxiety Disorders	4.74	0.20	3.20 - 7.04	<0.001	**<0.001**	0.88	1.02	0.03	0.96 - 1.09	0.435	0.557	0.01	0.89
	KSADS - Anxiety disorders w/ PTSD	5.07	0.20	3.44 - 7.50	<0.001	**<0.001**	0.99	1.02	0.03	0.96 - 1.08	0.465	0.557	0.01	1.00
	KSADS - Depressive Disorders	2.94	0.27	1.75 - 4.96	<0.001	**<0.001**	0.24	1.03	0.05	0.94 - 1.13	0.510	0.557	0.01	0.25
	KSADS - Conduct Disorder	2.17	0.21	1.43 - 3.30	<0.001	**<0.001**	0.18	1.01	0.03	0.95 - 1.07	0.754	0.754	0.00	0.18
European	KSADS - ADHD	2.72	0.32	1.47 - 5.07	0.002	**0.005**	0.21	1.08	0.03	1.01 - 1.15	0.034	0.083	0.09	0.32
	CBCL - ADHD	6.67	0.40	3.06 - 14.55	<0.001	**<0.001**	0.57	1.01	0.06	0.90 - 1.13	0.875	0.875	0.00	0.57
	KSADS - Anxiety Disorders	3.95	0.32	2.11 - 7.40	<0.001	**<0.001**	0.41	1.05	0.04	0.98 - 1.13	0.168	0.202	0.04	0.47
	KSADS - Anxiety disorders w/ PTSD	3.97	0.32	2.12 - 7.41	<0.001	**<0.001**	0.42	1.06	0.04	0.99 - 1.14	0.116	0.175	0.05	0.49
	KSADS - Depressive Disorders	2.78	0.54	0.96 - 8.08	0.060	0.119	0.09	1.11	0.07	0.97 - 1.26	0.134	0.179	0.05	0.15
	KSADS - Conduct Disorder	1.37	0.36	0.67 - 2.79	0.384	0.419	0.02	1.06	0.04	0.99 - 1.15	0.094	0.161	0.06	0.08
African	KSADS - ADHD	2.34	0.29	1.33 - 4.12	0.003	**0.006**	0.50	1.008	0.07	0.89 - 1.15	0.900	0.973	0.00	0.50
	CBCL - ADHD	3.07	0.33	1.60 - 5.90	<0.001	**0.003**	0.78	0.98	0.09	0.82 - 1.16	0.778	0.973	0.00	0.78
	KSADS - Anxiety Disorders	5.11	0.31	2.80 - 9.31	<0.001	**<0.001**	2.04	1.024	0.08	0.87 - 1.20	0.770	0.973	0.01	2.05
	KSADS - Anxiety disorders w/ PTSD	6.14	0.30	3.40 - 11.08	<0.001	**<0.001**	2.57	0.997	0.08	0.85 - 1.16	0.973	0.973	0.00	2.57
	KSADS - Depressive Disorders	3.21	0.35	1.61 - 6.41	<0.001	**0.003**	0.74	0.887	0.1	0.73 - 1.08	0.224	0.384	0.09	0.83
	KSADS - Conduct Disorder	2.66	0.30	1.47 - 4.81	0.001	**0.003**	0.64	1.016	0.08	0.88 - 1.18	0.830	0.973	0.00	0.64
American	KSADS - ADHD	4.18	0.48	1.62 - 10.78	0.003	**0.009**	0.73	0.95	0.07	0.82 - 1.10	0.462	0.616	0.05	0.76
Admixed	CBCL - ADHD	6.05	0.60	1.87 - 19.51	0.003	**0.009**	0.84	0.91	0.11	0.73 - 1.12	0.359	0.539	0.08	0.90
	KSADS - Anxiety Disorders	5.77	0.52	2.07 - 16.08	<0.001	**0.009**	1.05	1.04	0.09	0.87 - 1.24	0.682	0.744	0.01	1.07
	KSADS - Anxiety disorders w/ PTSD	5.24	0.52	1.88 - 14.59	0.002	**0.009**	0.93	1.01	0.09	0.85 - 1.20	0.905	0.905	0.00	0.93
	KSADS - Depressive Disorders	2.70	0.72	0.66 - 11.03	0.167	0.286	0.15	1.37	0.12	1.08 - 1.73	0.009	**0.021**	0.52	0.68
	KSADS - Conduct Disorder	3.17	0.57	1.03 - 9.77	0.044	0.089	0.34	0.95	0.09	0.79 - 1.15	0.601	0.722	0.02	0.36

Table 6. Independent Associations of SCZ-PRS and FH with Dimensional Phenotypes (SES included)

Ancestry	Genetic Risk Measure	Precursor	B	SE	95% CI	Nominal P	FDR P	PVE (%)
All	Family History	NIH Total Cognitive Score	0.83	1.49	-2.08 - 3.75	0.5758	0.6333	0.00
		CBCL - Total	7.19	1.02	5.20 - 9.18	<0.001	**<0.001**	0.60
		CBCL - Anxious Depressed	2.78	0.54	1.72 - 3.84	<0.001	**<0.001**	0.32
		CBCL - Withdrawn	2.10	0.52	1.08 - 3.12	<0.001	**<0.001**	0.20
		CBC - Somatic	2.81	0.55	1.72 - 3.89	<0.001	**<0.001**	0.31
		CBCL - Social	3.58	0.42	2.75 - 4.41	<0.001	**<0.001**	0.85
		CBCL - Thought	4.33	0.55	3.25 - 5.40	<0.001	**<0.001**	0.75
		CBCL - Attention	3.30	0.57	2.18 - 4.42	<0.001	**<0.001**	0.40
		CBCL - Rule Breaking	1.90	0.44	1.04 - 2.77	<0.001	**<0.001**	0.22
		CBCL - Aggressive	3.18	0.51	2.19 - 4.18	<0.001	**<0.001**	0.47
		PQB - Distress Score	3.25	0.94	1.40 - 5.09	<0.001	**0.001**	0.14
	SCZ PRS	NIH Total Cognitive Score	-0.48	0.18	-0.82 - -0.13	0.007	**0.014**	0.09
		CBCL - Total	0.17	0.12	-0.08 - 0.41	0.178	0.245	0.02
		CBCL - Anxious Depressed	0.10	0.07	-0.03 - 0.23	0.129	0.189	0.03
		CBCL - Withdrawn	0.03	0.06	-0.09 - 0.16	0.616	0.646	0.00
		CBC - Somatic	-0.09	0.07	-0.22 - 0.05	0.198	0.256	0.02
		CBCL - Social	0.04	0.05	-0.06 - 0.14	0.429	0.525	0.01
		CBCL - Thought	0.10	0.07	-0.03 - 0.23	0.125	0.189	0.03
		CBCL - Attention	-0.01	0.07	-0.14 - 0.13	0.932	0.932	0.00
		CBCL - Rule Breaking	0.12	0.05	0.01 - 0.22	0.029	0.054	0.06
		CBCL - Aggressive	0.04	0.06	-0.08 - 0.16	0.479	0.555	0.01
		PQB - Distress Score	0.20	0.12	-0.02 - 0.43	0.078	0.132	0.04
European	Family History	NIH Total Cognitive Score	-0.75	2.31	-5.27 - 3.77	0.744	0.779	0.00
		CBCL - Total	6.38	1.53	3.38 - 9.37	<0.001	**<0.001**	0.32
		CBCL - Anxious Depressed	1.96	0.87	0.26 - 3.66	0.024	**0.042**	0.10
		CBCL - Withdrawn	1.08	0.78	-0.44 - 2.60	0.163	0.211	0.04
		CBC - Somatic	2.64	0.85	0.97 - 4.31	0.002	**0.005**	0.18
		CBCL - Social	2.71	0.63	1.48 - 3.95	<0.001	**<0.001**	0.34
		CBCL - Thought	4.89	0.85	3.23 - 6.55	<0.001	**<0.001**	0.62
		CBCL - Attention	4.32	0.85	2.64 - 5.99	<0.001	**<0.001**	0.48
		CBCL - Rule Breaking	2.26	0.62	1.04 - 3.48	<0.001	**<0.001**	0.25
		CBCL - Aggressive	2.88	0.74	1.42 - 4.33	<0.001	**<0.001**	0.28
		PQB - Distress Score	3.51	1.30	0.95 - 6.06	0.007	**0.016**	0.14
	SCZ PRS	NIH Total Cognitive Score	-0.68	0.22	-1.12 - -0.24	0.002	**0.006**	0.18
		CBCL - Total	0.32	0.15	0.03 - 0.61	0.031	**0.049**	0.09
		CBCL - Anxious Depressed	0.20	0.08	0.04 - 0.37	0.017	**0.034**	0.11
		CBCL - Withdrawn	0.10	0.08	-0.05 - 0.24	0.204	0.250	0.03
		CBC - Somatic	-0.09	0.08	-0.25 - 0.08	0.304	0.352	0.02
		CBCL - Social	0.01	0.06	-0.11 - 0.13	0.839	0.839	0.00
		CBCL - Thought	0.14	0.08	-0.02 - 0.30	0.085	0.116	0.06
		CBCL - Attention	0.04	0.08	-0.12 - 0.21	0.588	0.647	0.01
		CBCL - Rule Breaking	0.21	0.06	0.09 - 0.33	<0.001	**0.002**	0.23
		CBCL - Aggressive	0.16	0.07	0.02 - 0.30	0.025	**0.042**	0.09
		PQB - Distress Score	0.23	0.13	-0.02 - 0.48	0.068	0.100	0.06
African	Family History	NIH Total Cognitive Score	1.04	2.25	-3.38 - 5.46	0.644	0.827	0.01
		CBCL - Total	7.91	1.72	4.54 - 11.27	<0.001	**<0.001**	1.24
		CBCL - Anxious Depressed	3.07	0.77	1.57 - 4.58	<0.001	**<0.001**	0.94
		CBCL - Withdrawn	2.42	0.86	0.73 - 4.11	0.005	**0.016**	0.46
		CBC - Somatic	2.86	0.86	1.17 - 4.54	<0.001	**0.003**	0.65
		CBCL - Social	4.10	0.72	2.70 - 5.51	<0.001	**<0.001**	1.89
		CBCL - Thought	4.03	0.88	2.30 - 5.76	<0.001	**<0.001**	1.22
		CBCL - Attention	1.82	0.98	-0.11 - 3.75	0.064	0.176	0.20
		CBCL - Rule Breaking	1.43	0.87	-0.28 - 3.15	0.101	0.246	0.16
		CBCL - Aggressive	3.05	0.92	1.26 - 4.85	<0.001	**0.003**	0.65
		PQB - Distress Score	2.47	1.77	-1.01 - 5.94	0.164	0.328	0.11

	SCZ PRS	NIH Total Cognitive Score	0.19	0.45	-0.69 - 1.07	0.677	0.827	0.01
		CBCL - Total	-0.09	0.36	-0.79 - 0.62	0.812	0.940	0.00
		CBCL - Anxious Depressed	-0.02	0.16	-0.33 - 0.30	0.924	0.988	0.00
		CBCL - Withdrawn	-0.29	0.18	-0.64 - 0.07	0.114	0.250	0.15
		CBC - Somatic	0.00	0.18	-0.35 - 0.35	0.988	0.988	0.00
		CBCL - Social	0.09	0.15	-0.21 - 0.38	0.571	0.827	0.02
		CBCL - Thought	0.01	0.18	-0.35 - 0.37	0.973	0.988	0.00
		CBCL - Attention	0.09	0.20	-0.30 - 0.49	0.644	0.827	0.01
		CBCL - Rule Breaking	-0.13	0.18	-0.49 - 0.22	0.458	0.725	0.03
		CBCL - Aggressive	-0.17	0.19	-0.54 - 0.21	0.381	0.699	0.05
		PQB - Distress Score	0.28	0.37	-0.46 - 1.01	0.461	0.725	0.03
American Admixed	Family History	NIH Total Cognitive Score	4.28	3.68	-2.93 - 11.48	0.245	0.337	0.11
		CBCL - Total	6.40	2.60	1.30 - 11.49	0.014	**0.044**	0.49
		CBCL - Anxious Depressed	3.93	1.38	1.22 - 6.64	0.004	**0.024**	0.66
		CBCL - Withdrawn	3.57	1.45	0.73 - 6.42	0.014	**0.044**	0.49
		CBC - Somatic	3.26	1.50	0.33 - 6.20	0.029	0.075	0.39
		CBCL - Social	4.16	1.14	1.93 - 6.39	0.000	**0.006**	1.08
		CBCL - Thought	3.42	1.35	0.77 - 6.08	0.011	**0.044**	0.52
		CBCL - Attention	4.70	1.45	1.87 - 7.54	0.001	**0.008**	0.86
		CBCL - Rule Breaking	1.96	1.06	-0.11 - 4.04	0.064	0.106	0.28
		CBCL - Aggressive	4.11	1.26	1.64 - 6.58	0.001	**0.008**	0.86
		PQB - Distress Score	5.39	2.68	0.14 - 10.63	0.044	0.084	0.33
	SCZ PRS	NIH Total Cognitive Score	-0.20	0.47	-1.12 - 0.72	0.670	0.737	0.02
		CBCL - Total	0.67	0.33	0.01 - 1.32	0.046	0.084	0.33
		CBCL - Anxious Depressed	0.28	0.18	-0.07 - 0.63	0.119	0.174	0.20
		CBCL - Withdrawn	0.37	0.19	0.01 - 0.74	0.045	0.084	0.33
		CBC - Somatic	0.12	0.19	-0.26 - 0.49	0.539	0.624	0.03
		CBCL - Social	0.31	0.14	-0.03 - 0.60	0.031	0.075	0.38
		CBCL - Thought	0.17	0.17	-0.17 - 0.51	0.337	0.435	0.08
		CBCL - Attention	0.02	0.19	-0.35 - 0.38	0.921	0.921	0.00
		CBCL - Rule Breaking	0.25	0.14	-0.02 - 0.52	0.067	0.106	0.27
		CBCL - Aggressive	0.12	0.16	-0.20 - 0.44	0.451	0.551	0.05
		PQB - Distress Score	0.07	0.34	-0.60 - 0.75	0.829	0.869	0.00

Table 7. Independent Associations of SCZ-PRS and FH with Diagnostic Phenotypes (SES included)

Ancestry	Genetic Risk Measure	Precursor	OR	SE	95% CI	Nominal P	FDR P	PVE (%)
All	Family History	KSADS - ADHD	2.24	0.21	1.50 - 3.35	<0.001	**<0.001**	0.22
		CBCL - ADHD	2.95	0.26	1.78 - 4.90	<0.001	**<0.001**	0.28
		KSADS - Anxiety Disorders	4.09	0.21	2.69 - 6.22	<0.001	**<0.001**	0.69
		KSADS - Anxiety disorders w/ PTSD	4.25	0.21	2.81 - 6.43	<0.001	**<0.001**	0.74
		KSADS - Depressive Disorders	2.69	0.28	1.55 - 4.66	<0.001	**0.001**	0.19
		KSADS - Conduct Disorder	1.95	0.23	1.25 - 3.05	0.003	**0.006**	0.13
	SCZ PRS	KSADS - ADHD	1.04	0.03	0.98 - 1.09	0.209	0.279	0.02
		CBCL - ADHD	0.95	0.04	0.88 - 1.04	0.276	0.331	0.02
		KSADS - Anxiety Disorders	1.05	0.03	0.98 - 1.11	0.152	0.229	0.03
		KSADS - Anxiety disorders w/ PTSD	1.05	0.03	0.98 - 1.11	0.150	0.229	0.03
		KSADS - Depressive Disorders	1.04	0.05	0.94 - 1.15	0.422	0.422	0.01
		KSADS - Conduct Disorder	1.03	0.03	0.97 - 1.09	0.360	0.393	0.01
European	Family History	KSADS - ADHD	2.46	0.33	1.29 - 4.68	0.006	**0.019**	0.16
		CBCL - ADHD	4.86	0.42	2.14 - 11.04	<0.001	**<0.001**	0.35
		KSADS - Anxiety Disorders	3.68	0.33	1.93 - 7.05	<0.001	**<0.001**	0.36
		KSADS - Anxiety disorders w/ PTSD	3.67	0.33	1.92 - 7.00	<0.001	**<0.001**	0.36
		KSADS - Depressive Disorders	2.42	0.55	0.82 - 7.18	0.110	0.147	0.06
		KSADS - Conduct Disorder	1.36	0.37	0.65 - 2.81	0.413	0.450	0.01
	SCZ PRS	KSADS - ADHD	1.07	0.04	0.99 - 1.15	0.062	0.124	0.08
		CBCL - ADHD	1.01	0.06	0.91 - 1.13	0.802	0.802	0.00
		KSADS - Anxiety Disorders	1.07	0.04	0.99 - 1.15	0.085	0.145	0.07
		KSADS - Anxiety disorders w/ PTSD	1.08	0.04	1.00 - 1.16	0.049	0.118	0.09
		KSADS - Depressive Disorders	1.11	0.07	0.97 - 1.27	0.131	0.157	0.06
		KSADS - Conduct Disorder	1.07	0.04	0.99 - 1.15	0.096	0.145	0.06
African	Family History	KSADS - ADHD	1.86	0.31	1.01 - 3.43	0.047	0.114	0.27
		CBCL - ADHD	1.74	0.41	0.78 - 3.84	0.173	0.347	0.15
		KSADS - Anxiety Disorders	4.26	0.33	2.23 - 8.12	<0.001	**<0.001**	1.62
		KSADS - Anxiety disorders w/ PTSD	4.79	0.32	2.54 - 9.06	<0.001	**<0.001**	1.92
		KSADS - Depressive Disorders	3.18	0.38	1.52 - 6.67	0.002	**0.009**	0.73
		KSADS - Conduct Disorder	2.18	0.33	1.13 - 4.17	0.019	0.058	0.41
	SCZ PRS	KSADS - ADHD	1.05	0.07	0.91 - 1.21	0.502	0.687	0.03
		CBCL - ADHD	0.95	0.10	0.78 - 1.16	0.644	0.749	0.02
		KSADS - Anxiety Disorders	1.04	0.09	0.87 - 1.23	0.687	0.749	0.01
		KSADS - Anxiety disorders w/ PTSD	1.01	0.09	0.86 - 1.20	0.891	0.891	0.00
		KSADS - Depressive Disorders	0.93	0.11	0.75 - 1.15	0.502	0.687	0.03
		KSADS - Conduct Disorder	1.06	0.08	0.90 - 1.24	0.515	0.687	0.03
American Admixed	Family History	KSADS - ADHD	3.66	0.54	1.28 - 10.50	0.016	**0.038**	0.58
		CBCL - ADHD	6.02	0.66	1.65 - 21.94	0.006	**0.029**	0.84
		KSADS - Anxiety Disorders	5.21	0.57	1.70 - 15.99	0.004	**0.029**	0.91
		KSADS - Anxiety disorders w/ PTSD	4.66	0.57	1.52 - 14.31	0.007	**0.029**	0.78
		KSADS - Depressive Disorders	2.64	0.75	0.60 - 11.55	0.199	0.299	0.15
		KSADS - Conduct Disorder	4.17	0.63	1.22 - 14.23	0.022	**0.045**	0.53
	SCZ PRS	KSADS - ADHD	0.97	0.08	0.83 - 1.14	0.740	0.808	0.01
		CBCL - ADHD	0.90	0.12	0.71 - 1.13	0.362	0.434	0.09
		KSADS - Anxiety Disorders	1.13	0.10	0.94 - 1.37	0.200	0.299	0.17
		KSADS - Anxiety disorders w/ PTSD	1.10	0.10	0.91 - 1.32	0.331	0.434	0.10
		KSADS - Depressive Disorders	1.38	0.13	1.07 - 1.77	0.012	**0.036**	0.56
		KSADS - Conduct Disorder	1.02	0.10	0.83 - 1.25	0.874	0.874	0.00

Table 8. Joint Model Associations of SCZ-PRS and FH with Dimensional Phenotypes (SES included)

Ancestry	**Precursor**	**Family History of Psychosis (Joint Model)**						**SCZ PRS (Joint Model)**						**Joint PVE**
		B	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	*B*	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	
All	NIH Total Cognitive Score	0.92	1.49	-1.99 - 3.83	0.536	0.610	0.00	-0.48	0.18	-0.83 - -0.13	0.007	**0.013**	0.09	0.10
	CBCL - Total	7.17	1.02	5.17 - 9.16	<0.001	**<0.001**	0.60	0.15	0.12	-0.09 - 0.39	0.223	0.289	0.02	0.62
	CBCL - Anxious Depressed	2.77	0.54	1.71 - 3.83	<0.001	**<0.001**	0.31	0.09	0.07	-0.04 - 0.22	0.155	0.227	0.02	0.34
	CBCL - Withdrawn	2.10	0.52	1.08 - 3.12	<0.001	**<0.001**	0.19	0.03	0.06	-0.10 - 0.15	0.672	0.704	0.00	0.20
	CBC - Somatic	2.82	0.55	1.74 - 3.91	<0.001	**<0.001**	0.31	-0.09	0.07	-0.23 - 0.04	0.165	0.227	0.02	0.33
	CBCL - Social	3.58	0.42	2.75 - 4.41	<0.001	**<0.001**	0.85	0.03	0.05	-0.07 - 0.13	0.528	0.610	0.00	0.86
	CBCL - Thought	4.31	0.55	3.24 - 5.39	<0.001	**<0.001**	0.74	0.09	0.07	-0.04 - 0.22	0.165	0.227	0.02	0.77
	CBCL - Attention	3.30	0.57	2.18 - 4.42	<0.001	**<0.001**	0.40	-0.01	0.07	-0.15 - 0.12	0.846	0.846	0.00	0.40
	CBCL - Rule Breaking	1.89	0.44	1.02 - 2.75	<0.001	**<0.001**	0.22	0.11	0.05	0.01 - 0.22	0.036	0.066	0.05	0.28
	CBCL - Aggressive	3.18	0.51	2.18 - 4.17	<0.001	**<0.001**	0.47	0.04	0.06	-0.08 - 0.16	0.555	0.610	0.00	0.48
	PQB - Distress Score	3.22	0.94	1.37 - 5.06	0.001	**0.001**	0.14	0.20	0.12	-0.03 - 0.42	0.090	0.152	0.03	0.18
European	NIH Total Cognitive Score	-0.50	2.31	-5.02 - 4.02	0.828	0.867	0.00	-0.68	0.22	-1.12 - -0.24	0.002	**0.006**	0.18	0.18
	CBCL - Total	6.27	1.53	3.27 - 9.26	<0.001	**<0.001**	0.31	0.30	0.15	0.01 - 0.59	0.045	0.070	0.08	0.40
	CBCL - Anxious Depressed	1.88	0.87	0.18 - 3.58	0.030	0.055	0.09	0.19	0.08	0.03 - 0.36	0.021	**0.043**	0.10	0.19
	CBCL - Withdrawn	1.05	0.78	-0.48 - 2.57	0.178	0.230	0.03	0.09	0.08	-0.06 - 0.24	0.224	0.273	0.03	0.06
	CBC - Somatic	2.67	0.85	1.00 - 4.34	0.002	**0.005**	0.18	-0.10	0.08	-0.26 - 0.07	0.251	0.291	0.02	0.20
	CBCL - Social	2.71	0.63	1.48 - 3.95	<0.001	**<0.001**	0.34	0.00	0.06	-0.12 - 0.12	0.967	0.967	0.00	0.34
	CBCL - Thought	4.84	0.85	3.18 - 6.50	<0.001	**<0.001**	0.61	0.12	0.08	-0.04 - 0.29	0.130	0.179	0.04	0.66
	CBCL - Attention	4.31	0.85	2.63 - 5.98	<0.001	**<0.001**	0.47	0.03	0.08	-0.13 - 0.19	0.724	0.796	0.00	0.48
	CBCL - Rule Breaking	2.18	0.62	0.96 - 3.40	<0.001	**0.002**	0.23	0.20	0.06	0.08 - 0.32	<0.001	**0.003**	0.21	0.46
	CBCL - Aggressive	2.82	0.74	1.36 - 4.27	<0.001	**<0.001**	0.27	0.15	0.07	0.01 - 0.29	0.035	0.060	0.08	0.36
	PQB - Distress Score	3.42	1.30	0.86 - 5.97	0.009	**0.019**	0.13	0.22	0.13	-0.03 - 0.47	0.085	0.125	0.06	0.19
African	NIH Total Cognitive Score	1.01	2.25	-3.41 - 5.43	0.653	0.840	0.01	0.18	0.45	-0.70 - 1.06	0.687	0.840	0.01	0.02
	CBCL - Total	7.92	1.72	4.55 - 11.29	<0.001	**<0.001**	1.24	-0.12	0.36	-0.81 - 0.58	0.742	0.859	0.01	1.24
	CBCL - Anxious Depressed	3.07	0.77	1.57 - 4.58	<0.001	**<0.001**	0.94	-0.03	0.16	-0.34 - 0.29	0.865	0.952	0.00	0.94
	CBCL - Withdrawn	2.44	0.86	0.75 - 4.13	0.005	**0.014**	0.47	-0.30	0.18	-0.65 - 0.06	0.102	0.224	0.16	0.62
	CBC - Somatic	2.86	0.86	1.17 - 4.54	<0.001	**0.003**	0.65	-0.01	0.18	-0.36 - 0.33	0.936	0.957	0.00	0.65
	CBCL - Social	4.10	0.72	2.69 - 5.51	<0.001	**<0.001**	1.89	0.07	0.15	-0.22 - 0.36	0.645	0.840	0.01	1.91
	CBCL - Thought	4.03	0.88	2.30 - 5.76	<0.001	**<0.001**	1.22	-0.01	0.18	-0.37 - 0.35	0.957	0.957	0.00	1.22
	CBCL - Attention	1.81	0.98	-0.12 - 3.74	0.065	0.180	0.20	0.09	0.20	-0.31 - 0.48	0.670	0.840	0.01	0.21
	CBCL - Rule Breaking	1.45	0.87	-0.26 - 3.16	0.098	0.224	0.16	-0.14	0.18	-0.49 - 0.21	0.439	0.742	0.04	0.19
	CBCL - Aggressive	3.07	0.92	1.27 - 4.87	<0.001	**0.003**	0.66	-0.18	0.19	-0.55 - 0.19	0.345	0.632	0.05	0.70
	PQB - Distress Score	2.44	1.77	-1.03 - 5.92	0.168	0.098	0.11	0.27	0.37	-0.47 - 1.00	0.476	0.913	0.03	0.14
American Admixed	NIH Total Cognitive Score	4.32	3.68	-2.90 - 11.53	0.241	0.331	0.12	-0.21	0.47	-1.14 - 0.71	0.650	0.715	0.02	0.13
	CBCL - Total	6.26	2.60	1.17 - 11.35	0.016	0.050	0.47	0.64	0.33	-0.01 - 1.30	0.053	0.098	0.30	0.80
	CBCL - Anxious Depressed	3.87	1.38	1.17 - 6.58	0.005	**0.028**	0.64	0.26	0.18	-0.08 - 0.61	0.137	0.200	0.18	0.84
	CBCL - Withdrawn	3.50	1.45	0.65 - 6.34	0.016	0.050	0.47	0.36	0.19	-0.00 - 0.73	0.052	0.098	0.31	0.80
	CBC - Somatic	3.24	1.50	0.30 - 6.18	0.031	0.084	0.38	0.11	0.19	-0.27 - 0.48	0.579	0.670	0.03	0.41
	CBCL - Social	4.09	1.14	1.86 - 6.32	0.000	**0.007**	1.05	0.30	0.14	0.01 - 0.58	0.039	0.096	0.34	1.43
	CBCL - Thought	3.39	1.35	0.74 - 6.04	0.012	0.050	0.51	0.15	0.17	-0.18 - 0.49	0.373	0.482	0.06	0.59
	CBCL - Attention	4.70	1.45	1.86 - 7.54	0.001	**0.009**	0.86	0.00	0.18	-0.36 - 0.36	0.994	0.994	0.00	0.86
	CBCL - Rule Breaking	1.91	1.06	-0.16 - 3.98	0.071	0.118	0.27	0.24	0.14	-0.02 - 0.51	0.075	0.118	0.26	0.54
	CBCL - Aggressive	4.09	1.26	1.62 - 6.56	0.001	**0.009**	0.85	0.11	0.16	-0.21 - 0.43	0.501	0.612	0.04	0.90
	PQB - Distress Score	5.37	2.68	0.13 - 10.62	0.045	0.336	0.33	0.06	0.34	-0.62 - 0.73	0.871	0.748	0.00	0.33

Table 9. Joint Model Associations of SCZ-PRS and FH with Diagnostic Phenotypes (SES included)

Ancestry	**Precursor**	**Family History of Psychosis (Joint Model)**						**SCZ PRS (Joint Model)**						**Joint PVE**
		OR	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	*OR*	*SE*	*95% CI*	*Nominal P*	*FDR P*	*PVE*	
All	KSADS - ADHD	2.23	0.21	1.49 - 3.34	<0.001	**<0.001**	0.22	1.03	0.03	0.98 - 1.09	0.240	0.302	0.02	0.24
	CBCL - ADHD	2.97	0.26	1.79 - 4.93	<0.001	**<0.001**	0.28	0.95	0.04	0.87 - 1.04	0.252	0.302	0.02	0.30
	KSADS - Anxiety Disorders	4.07	0.21	2.67 - 6.18	<0.001	**<0.001**	0.69	1.04	0.03	0.98 - 1.11	0.198	0.298	0.02	0.89
	KSADS - Anxiety disorders w/ PTSD	4.22	0.21	2.79 - 6.38	<0.001	**<0.001**	0.74	1.04	0.03	0.98 - 1.11	0.197	0.298	0.02	0.77
	KSADS - Depressive Disorders	2.68	0.28	1.54 - 4.64	<0.001	**0.001**	0.19	1.04	0.05	0.94 - 1.15	0.450	0.450	0.01	0.19
	KSADS - Conduct Disorder	1.95	0.23	1.25 - 3.04	0.003	**0.007**	0.13	1.03	0.03	0.97 - 1.09	0.396	0.432	0.01	0.14
European	KSADS - ADHD	2.40	0.33	1.26 - 4.58	0.008	**0.024**	0.16	1.06	0.04	0.99 - 1.14	0.079	0.157	0.07	0.23
	CBCL - ADHD	4.86	0.42	2.14 - 11.03	<0.001	**<0.001**	0.35	1.01	0.06	0.90 - 1.13	0.923	0.923	0.00	0.35
	KSADS - Anxiety Disorders	3.61	0.33	1.88 - 6.91	<0.001	**<0.001**	0.35	1.06	0.04	0.99 - 1.14	0.117	0.167	0.05	0.42
	KSADS - Anxiety disorders w/ PTSD	3.58	0.33	1.87 - 6.83	<0.001	**<0.001**	0.35	1.07	0.04	0.99 - 1.15	0.070	0.157	0.07	0.44
	KSADS - Depressive Disorders	2.35	0.56	0.79 - 7.00	0.125	0.167	0.06	1.11	0.07	0.97 - 1.27	0.146	0.175	0.05	0.11
	KSADS - Conduct Disorder	1.32	0.37	0.64 - 2.74	0.454	0.495	0.01	1.06	0.04	0.99 - 1.15	0.103	0.167	0.06	0.07
African	KSADS - ADHD	1.85	0.31	1.00 - 3.41	0.049	0.117	0.26	1.05	0.07	0.91 - 1.21	0.520	0.714	0.03	0.29
	CBCL - ADHD	1.74	0.41	0.79 - 3.86	0.172	0.344	0.15	0.95	0.10	0.78 - 1.16	0.635	0.762	0.02	0.16
	KSADS - Anxiety Disorders	4.24	0.33	2.22 - 8.10	<0.001	**<0.001**	1.61	1.03	0.09	0.86 - 1.22	0.753	0.821	0.01	1.62
	KSADS - Anxiety disorders w/ PTSD	4.79	0.32	2.54 - 9.06	<0.001	**<0.001**	1.92	1.00	0.09	0.85 - 1.19	0.979	0.979	0.00	1.92
	KSADS - Depressive Disorders	3.21	0.38	1.53 - 6.74	0.002	**0.008**	0.73	0.92	0.11	0.74 - 1.14	0.460	0.714	0.04	0.76
	KSADS - Conduct Disorder	2.17	0.33	1.13 - 4.16	0.020	0.060	0.41	1.05	0.08	0.90 - 1.24	0.535	0.714	0.03	0.44
American Admixed	KSADS - ADHD	3.68	0.54	1.29 - 10.56	0.015	**0.036**	0.59	0.97	0.08	0.83 - 1.13	0.683	0.745	0.02	0.60
	CBCL - ADHD	6.14	0.66	1.69 - 22.26	0.006	**0.031**	0.86	0.89	0.12	0.70 - 1.12	0.324	0.425	0.11	0.95
	KSADS - Anxiety Disorders	5.19	0.57	1.68 - 15.99	0.004	**0.031**	0.89	1.13	0.10	0.93 - 1.36	0.213	0.320	0.15	1.06
	KSADS - Anxiety disorders w/ PTSD	4.63	0.57	1.50 - 14.29	0.008	**0.031**	0.77	1.09	0.09	0.91 - 1.31	0.354	0.425	0.08	0.86
	KSADS - Depressive Disorders	2.60	0.77	0.58 - 11.75	0.213	0.320	0.15	1.37	0.13	1.07 - 1.76	0.012	**0.036**	0.56	0.70
	KSADS - Conduct Disorder	4.16	0.63	1.22 - 14.23	0.023	**0.046**	0.52	1.01	0.10	0.82 - 1.23	0.944	0.944	0.00	0.53

References

Achenbach, T. M. (1991). *Manual for the Child Behavior Checklist/4-18 and 1991 Profiles*. Burlington, VT: Department of Psychiatry, University of Vermont.

Agerbo, E., Sullivan, P. F., Vilhjálmsson, B. J., Pedersen, C. B., Mors, O., Børglum, A. D., Hougaard, D. M., Hollegaard, M. V., Meier, S., Mattheisen, M., Ripke, S., Wray, N. R., & Mortensen, P. B. (2015). Polygenic Risk Score, Parental Socioeconomic Status, Family History of Psychiatric Disorders, and the Risk for Schizophrenia: A Danish Population-Based Study and Meta-analysis. *JAMA Psychiatry*, *72*(7), 635. https://doi.org/10.1001/jamapsychiatry.2015.0346

Alexander, D. H., & Lange, K. (2011). Enhancements to the ADMIXTURE algorithm for individual ancestry estimation. *BMC Bioinformatics*, *12*(1), 246. https://doi.org/10.1186/1471-2105-12-246

Barch, D. M., Albaugh, M. D., Baskin-Sommers, A., Bryant, B. E., Clark, D. B., Dick, A. S., Feczko, E., Foxe, J. J., Gee, D. G., Giedd, J., Glantz, M. D., Hudziak, J. J., Karcher, N. R., LeBlanc, K., Maddox, M., McGlade, E. C., Mulford, C., Nagel, B. J., Neigh, G., … Xie, L. (2021). Demographic and mental health assessments in the adolescent brain and cognitive development study: Updates and age-related trajectories. *Developmental Cognitive Neuroscience*, *52*, 101031. https://doi.org/10.1016/j.dcn.2021.101031

Bigdeli, T. B., Fanous, A. H., Li, Y., Rajeevan, N., Sayward, F., Genovese, G., Gupta, R., Radhakrishnan, K., Malhotra, A. K., Sun, N., Lu, Q., Hu, Y., Li, B., Chen, Q., Mane, S., Miller, P., Cheung, K.-H., Gur, R. E., Greenwood, T. A., … Harvey, P. D. (2021). Genome-Wide Association Studies of Schizophrenia and Bipolar Disorder in a Diverse

Cohort of US Veterans. *Schizophrenia Bulletin*, *47*(2), 517–529. https://doi.org/10.1093/schbul/sbaa133

Bigdeli, T. B., Genovese, G., Georgakopoulos, P., Meyers, J. L., Peterson, R. E., Iyegbe, C. O., Medeiros, H., Valderrama, J., Achtyes, E. D., Kotov, R., Stahl, E. A., Abbott, C., Azevedo, M. H., Belliveau, R. A., Bevilacqua, E., Bromet, E. J., Byerley, W., Carvalho, C. B., Chapman, S. B., … Pato, C. N. (2020). Contributions of common genetic variants to risk of schizophrenia among individuals of African and Latino ancestry. *Molecular Psychiatry*, *25*(10), 2455–2467. https://doi.org/10.1038/s41380-019-0517-y

Bottlender, R., Strauß, A., & Möller, H.-J. (2010). Social disability in schizophrenic, schizoaffective and affective disorders 15years after first admission. *Schizophrenia Research*, *116*(1), 9–15. https://doi.org/10.1016/j.schres.2009.10.008

Bowers, M. E., & Yehuda, R. (2016). Intergenerational Transmission of Stress in Humans. *Neuropsychopharmacology*, *41*(1), 232–244. https://doi.org/10.1038/npp.2015.247

Chang, S. E., Hughes, D. E., Zhu, J., Hyat, M., Salone, S. D., Goodman, Z. T., Roffman, J. L., Karcher, N. R., Hernandez, L. M., Forsyth, J. K., & Bearden, C. E. (2024). Attention-mediated genetic influences on psychotic symptomatology in adolescence. *Nature Mental Health*. https://doi.org/10.1038/s44220-024-00338-7

Cheng, C.-M., Chang, W.-H., Chen, M.-H., Tsai, C.-F., Su, T.-P., Li, C.-T., Tsai, S.-J., Hsu, J.-W., Huang, K.-L., Lin, W.-C., Chen, T.-J., & Bai, Y.-M. (2018). Co-aggregation of major psychiatric disorders in individuals with first-degree relatives with schizophrenia: A nationwide population-based study. *Molecular Psychiatry*, *23*(8), 1756–1763. https://doi.org/10.1038/mp.2017.217

Chong, H. Y., Chaiyakunapruk, N., Teoh, S. L., Wu, D. B.-C., Kotirum, S., & Chiou, C.-F. (2016). Global economic burden of schizophrenia: A systematic review. *Neuropsychiatric Disease and Treatment*, 357. https://doi.org/10.2147/NDT.S96649

Conomos, M. P., Miller, M. B., & Thornton, T. A. (2015). Robust Inference of Population Structure for Ancestry Prediction and Correction of Stratification in the Presence of Relatedness. *Genetic Epidemiology*, *39*(4), 276–293. https://doi.org/10.1002/gepi.21896

Conomos, M. P., Reiner, A. P., Weir, B. S., & Thornton, T. A. (2016). Model-free Estimation of Recent Genetic Relatedness. *The American Journal of Human Genetics*, *98*(1), 127–148. https://doi.org/10.1016/j.ajhg.2015.11.022

Das, S., Forer, L., Schönherr, S., Sidore, C., Locke, A. E., Kwong, A., Vrieze, S. I., Chew, E. Y., Levy, S., McGue, M., Schlessinger, D., Stambolian, D., Loh, P.-R., Iacono, W. G., Swaroop, A., Scott, L. J., Cucca, F., Kronenberg, F., Boehnke, M., … Fuchsberger, C. (2016). Next-generation genotype imputation service and methods. *Nature Genetics*, *48*(10), 1284–1287. https://doi.org/10.1038/ng.3656

Díaz-Castro, L., Hoffman, K., Cabello-Rangel, H., Arredondo, A., & Herrera-Estrella, M. Á. (2021). Family History of Psychiatric Disorders and Clinical Factors Associated With a Schizophrenia Diagnosis. *INQUIRY: The Journal of Health Care Organization, Provision, and Financing*, *58*, 004695802110607. https://doi.org/10.1177/00469580211060797

Ding, Y., Hou, K., Xu, Z., Pimplaskar, A., Petter, E., Boulier, K., Privé, F., Vilhjálmsson, B. J., Olde Loohuis, L. M., & Pasaniuc, B. (2023). Polygenic scoring accuracy varies across the genetic ancestry continuum. *Nature*, *618*(7966), 774–781. https://doi.org/10.1038/s41586-023-06079-4

Distefano, R., Palmer, A. R., Kalstabakken, A. W., Hillyer, C. K., Seiwert, M. J., Zelazo, P. D., Carlson, S. M., & Masten, A. S. (2023). Predictive Validity of the NIH Toolbox Executive Function Measures with Developmental Extensions from Early Childhood to Third Grade Achievement. *Developmental Neuropsychology*, *48*(8), 373–386. https://doi.org/10.1080/87565641.2023.2286353

Erlenmeyer-Kimling, L., Rock, D., Roberts, S. A., Janal, M., Kestenbaum, C., Cornblatt, B., Adamo, U. H., & Gottesman, I. I. (2000). Attention, Memory, and Motor Skills as Childhood Predictors of Schizophrenia-Related Psychoses: The New York High-Risk Project. *American Journal of Psychiatry*, *157*(9), 1416–1422. https://doi.org/10.1176/appi.ajp.157.9.1416

Evensen, S., Wisløff, T., Lystad, J. U., Bull, H., Ueland, T., & Falkum, E. (2016). Prevalence, Employment Rate, and Cost of Schizophrenia in a High-Income Welfare Society: A Population-Based Study Using Comprehensive Health and Welfare Registers. *Schizophrenia Bulletin*, *42*(2), 476–483. https://doi.org/10.1093/schbul/sbv141

Forsyth, J. K., & Asarnow, R. F. (2020). Genetics of Childhood-onset Schizophrenia 2019 Update. *Child and Adolescent Psychiatric Clinics of North America*, *29*(1), 157–170. https://doi.org/10.1016/j.chc.2019.08.007

Forsyth, J. K., & Lewis, D. A. (2017). Mapping the Consequences of Impaired Synaptic Plasticity in Schizophrenia through Development: An Integrative Model for Diverse Clinical Features. *Trends in Cognitive Sciences*, *21*(10), 760–778. https://doi.org/10.1016/j.tics.2017.06.006

Gershon, R. C., Wagster, M. V., Hendrie, H. C., Fox, N. A., Cook, K. F., & Nowinski, C. J. (2013). NIH Toolbox for Assessment of Neurological and Behavioral Function.

Neurology, *80*(Issue 11, Supplement 3), S2–S6. https://doi.org/10.1212/WNL.0b013e3182872e5f

Goldstein, J. M., Buka, S. L., Seidman, L. J., & Tsuang, M. T. (2010). Specificity of Familial Transmission of Schizophrenia Psychosis Spectrum and Affective Psychoses in the New England Family Study's High-Risk Design. *Archives of General Psychiatry*, *67*(5), 458. https://doi.org/10.1001/archgenpsychiatry.2010.38

Hamasaki, Y., Nakayama, T., Hikida, T., & Murai, T. (2021). Combined pattern of childhood psycho-behavioral characteristics in patients with schizophrenia: A retrospective study in Japan. *BMC Psychiatry*, *21*(1), 57. https://doi.org/10.1186/s12888-021-03049-w

Healy, C., Brannigan, R., Dooley, N., Coughlan, H., Clarke, M., Kelleher, I., & Cannon, M. (2019). Childhood and adolescent psychotic experiences and risk of mental disorder: A systematic review and meta-analysis. *Psychological Medicine*, *49*(10), 1589–1599. https://doi.org/10.1017/S0033291719000485

Hilker, R., Helenius, D., Fagerlund, B., Skytthe, A., Christensen, K., Werge, T. M., Nordentoft, M., & Glenthøj, B. (2018). Heritability of Schizophrenia and Schizophrenia Spectrum Based on the Nationwide Danish Twin Register. *Biological Psychiatry*, *83*(6), 492–498. https://doi.org/10.1016/j.biopsych.2017.08.017

Hujoel, M. L. A., Loh, P.-R., Neale, B. M., & Price, A. L. (2022). Incorporating family history of disease improves polygenic risk scores in diverse populations. *Cell Genomics*, *2*(7), 100152. https://doi.org/10.1016/j.xgen.2022.100152

Jansen, P. R., Polderman, T. J. C., Bolhuis, K., Ende, J., Jaddoe, V. W. V., Verhulst, F. C., White, T., Posthuma, D., & Tiemeier, H. (2018). Polygenic scores for schizophrenia and educational attainment are associated with behavioural problems in early childhood in the

general population. *Journal of Child Psychology and Psychiatry*, *59*(1), 39–47. https://doi.org/10.1111/jcpp.12759

Jones, H. J., Stergiakouli, E., Tansey, K. E., Hubbard, L., Heron, J., Cannon, M., Holmans, P., Lewis, G., Linden, D. E. J., Jones, P. B., Davey Smith, G., O'Donovan, M. C., Owen, M. J., Walters, J. T., & Zammit, S. (2016). Phenotypic Manifestation of Genetic Risk for Schizophrenia During Adolescence in the General Population. *JAMA Psychiatry*, *73*(3), 221. https://doi.org/10.1001/jamapsychiatry.2015.3058

Kachuri, L., Chatterjee, N., Hirbo, J., Schaid, D. J., Martin, I., Kullo, I. J., Kenny, E. E., Pasaniuc, B., Polygenic Risk Methods in Diverse Populations (PRIMED) Consortium Methods Working Group, Auer, P. L., Conomos, M. P., Conti, D. V., Ding, Y., Wang, Y., Zhang, H., Zhang, Y., Witte, J. S., & Ge, T. (2024). Principles and methods for transferring polygenic risk scores across global populations. *Nature Reviews Genetics*, *25*(1), 8–25. https://doi.org/10.1038/s41576-023-00637-2

Kadakia, A., Catillon, M., Fan, Q., Williams, G. R., Marden, J. R., Anderson, A., Kirson, N., & Dembek, C. (2022). The Economic Burden of Schizophrenia in the United States. *The Journal of Clinical Psychiatry*, *83*(6). https://doi.org/10.4088/JCP.22m14458

Kar, S. K., & Jain, M. (2016). Current understandings about cognition and the neurobiological correlates in schizophrenia. *Journal of Neurosciences in Rural Practice*, *07*(03), 412–418. https://doi.org/10.4103/0976-3147.176185

Karcher, N. R., Loewy, R. L., Savill, M., Avenevoli, S., Huber, R. S., Simon, T. J., Leckliter, I. N., Sher, K. J., & Barch, D. M. (2020). Replication of Associations With Psychotic-Like Experiences in Middle Childhood From the Adolescent Brain Cognitive Development

(ABCD) Study. *Schizophrenia Bulletin Open*, *1*(1), sgaa009. https://doi.org/10.1093/schizbullopen/sgaa009

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, C., Moreci, P., Williamson, D., & Ryan, N. (1997). Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL): Initial Reliability and Validity Data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*(7), 980–988. https://doi.org/10.1097/00004583-199707000-00021

Keshavan, M. S. (2009). Premorbid cognitive deficits in young relatives of schizophrenia patients. *Frontiers in Human Neuroscience*, *3*. https://doi.org/10.3389/neuro.09.062.2009

Khan, A., Turchin, M. C., Patki, A., Srinivasasainagendra, V., Shang, N., Nadukuru, R., Jones, A. C., Malolepsza, E., Dikilitas, O., Kullo, I. J., Schaid, D. J., Karlson, E., Ge, T., Meigs, J. B., Smoller, J. W., Lange, C., Crosslin, D. R., Jarvik, G. P., Bhatraju, P. K., … Kiryluk, K. (2022). Genome-wide polygenic score to predict chronic kidney disease across ancestries. *Nature Medicine*, *28*(7), 1412–1420. https://doi.org/10.1038/s41591-022-01869-1

Lam, M., Awasthi, S., Watson, H. J., Goldstein, J., Panagiotaropoulou, G., Trubetskoy, V., Karlsson, R., Frei, O., Fan, C.-C., De Witte, W., Mota, N. R., Mullins, N., Brügger, K., Lee, S. H., Wray, N. R., Skarabis, N., Huang, H., Neale, B., Daly, M. J., … Ripke, S. (2020). RICOPILI: Rapid Imputation for COnsortias PIpeLIne. *Bioinformatics*, *36*(3), 930–933. https://doi.org/10.1093/bioinformatics/btz633

Laurens, K., Hodgins, S., Maughan, B., Murray, R., Rutter, M., & Taylor, E. (2007). Community screening for psychotic-like experiences and other putative antecedents of schizophrenia in children aged 9–12 years. *Schizophrenia Research*, *90*(1–3), 130–146. https://doi.org/10.1016/j.schres.2006.11.006

Laursen, T. M., Nordentoft, M., & Mortensen, P. B. (2014). Excess Early Mortality in Schizophrenia. *Annual Review of Clinical Psychology*, *10*(1), 425–448. https://doi.org/10.1146/annurev-clinpsy-032813-153657

Legge, S. E., Jones, H. J., Kendall, K. M., Pardiñas, A. F., Menzies, G., Bracher-Smith, M., Escott-Price, V., Rees, E., Davis, K. A. S., Hotopf, M., Savage, J. E., Posthuma, D., Holmans, P., Kirov, G., Owen, M. J., O'Donovan, M. C., Zammit, S., & Walters, J. T. R. (2019). Association of Genetic Liability to Psychotic Experiences With Neuropsychotic Disorders and Traits. *JAMA Psychiatry*, *76*(12), 1256. https://doi.org/10.1001/jamapsychiatry.2019.2508

Loh, P.-R., Danecek, P., Palamara, P. F., Fuchsberger, C., A Reshef, Y., K Finucane, H., Schoenherr, S., Forer, L., McCarthy, S., Abecasis, G. R., Durbin, R., & L Price, A. (2016). Reference-based phasing using the Haplotype Reference Consortium panel. *Nature Genetics*, *48*(11), 1443–1448. https://doi.org/10.1038/ng.3679

Loughnan, R. J., Palmer, C. E., Makowski, C., Thompson, W. K., Barch, D. M., Jernigan, T. L., Dale, A. M., & Fan, C. C. (2022). Unique prediction of developmental psychopathology from genetic and familial risk. *Journal of Child Psychology and Psychiatry*, *63*(12), 1631–1643. https://doi.org/10.1111/jcpp.13649

Lu, Y., Pouget, J. G., Andreassen, O. A., Djurovic, S., Esko, T., Hultman, C. M., Metspalu, A., Milani, L., Werge, T., & Sullivan, P. F. (2018). Genetic risk scores and family history as predictors of schizophrenia in Nordic registers. *Psychological Medicine*, *48*(7), 1201–1208. https://doi.org/10.1017/S0033291717002665

MacKenzie, L. E., Howes Vallis, E., Rempel, S., Zwicker, A., Drobinin, V., Pavlova, B., & Uher, R. (2020). Cognition in offspring of parents with psychotic and non-psychotic severe

mental illness. *Journal of Psychiatric Research*, *130*, 306–312. https://doi.org/10.1016/j.jpsychires.2020.08.019

Maibing, C. F., Pedersen, C. B., Benros, M. E., Mortensen, P. B., Dalsgaard, S., & Nordentoft, M. (2015). Risk of Schizophrenia Increases After All Child and Adolescent Psychiatric Disorders: A Nationwide Study. *Schizophrenia Bulletin*, *41*(4), 963–970. https://doi.org/10.1093/schbul/sbu119

Mars, N., Lindbohm, J. V., Della Briotta Parolo, P., Widén, E., Kaprio, J., Palotie, A., & Ripatti, S. (2022). Systematic comparison of family history and polygenic risk across 24 common diseases. *The American Journal of Human Genetics*, *109*(12), 2152–2162. https://doi.org/10.1016/j.ajhg.2022.10.009

McGorry, P., Keshavan, M., Goldstone, S., Amminger, P., Allott, K., Berk, M., Lavoie, S., Pantelis, C., Yung, A., Wood, S., & Hickie, I. (2014). Biomarkers and clinical staging in psychiatry. *World Psychiatry*, *13*(3), 211–223. https://doi.org/10.1002/wps.20144

Mistry, S., Harrison, J. R., Smith, D. J., Escott-Price, V., & Zammit, S. (2018). The use of polygenic risk scores to identify phenotypes associated with genetic risk of schizophrenia: Systematic review. *Schizophrenia Research*, *197*, 2–8. https://doi.org/10.1016/j.schres.2017.10.037

Mollon, J., & Reichenberg, A. (2018). Cognitive development prior to onset of psychosis. *Psychological Medicine*, *48*(3), 392–403. https://doi.org/10.1017/S0033291717001970

Nguyen, V. T., Braun, A., Kraft, J., Ta, T. M. T., Panagiotaropoulou, G. M., Nguyen, V. P., Nguyen, T. H., Trubetskoy, V., Le, C. T., Le, T. T. H., Pham, X. T., Heuser-Collier, I., Lam, N. H., Böge, K., Hahne, I. M., Bajbouj, M., Zierhut, M. M., Hahn, E., & Ripke, S. (2022). Increasing sample diversity in psychiatric genetics – Introducing a new cohort of

patients with schizophrenia and controls from Vietnam – Results from a pilot study. *The World Journal of Biological Psychiatry*, *23*(3), 219–227. https://doi.org/10.1080/15622975.2021.1951474

Niemi, L. T., Suvisaari, J. M., Tuulio-Henriksson, A., & Lönnqvist, J. K. (2003). Childhood developmental abnormalities in schizophrenia: Evidence from high-risk studies. *Schizophrenia Research*, *60*(2–3), 239–258. https://doi.org/10.1016/S0920-9964(02)00234-7

Nivard, M. G., Gage, S. H., Hottenga, J. J., van Beijsterveldt, C. E. M., Abdellaoui, A., Bartels, M., Baselmans, B. M. L., Ligthart, L., Pourcain, B. S., Boomsma, D. I., Munafò, M. R., & Middeldorp, C. M. (2017). Genetic Overlap Between Schizophrenia and Developmental Psychopathology: Longitudinal and Multivariate Polygenic Risk Prediction of Common Psychiatric Traits During Development. *Schizophrenia Bulletin*, *43*(6), 1197–1207. https://doi.org/10.1093/schbul/sbx031

Oliver-Parra, A., Dalmau-Bueno, A., Ruiz-Muñoz, D., & García-Altés, A. (2020). Relationship between parents' mental disorders and socioeconomic status and offspring's psychopathology: A cross-sectional study. *PLOS ONE*, *15*(10), e0240681. https://doi.org/10.1371/journal.pone.0240681

Poulton, R., Caspi, A., Moffitt, T. E., Cannon, M., Murray, R., & Harrington, H. (2000). Children's Self-Reported Psychotic Symptoms and Adult Schizophreniform Disorder: A 15-Year Longitudinal Study. *Archives of General Psychiatry*, *57*(11), 1053. https://doi.org/10.1001/archpsyc.57.11.1053

Riglin, L., Collishaw, S., Richards, A., Thapar, A. K., Maughan, B., O'Donovan, M. C., & Thapar, A. (2017). Schizophrenia risk alleles and neurodevelopmental outcomes in

childhood: A population-based cohort study. *The Lancet Psychiatry*, *4*(1), 57–62. https://doi.org/10.1016/S2215-0366(16)30406-0

Robinson, M., Doherty, D. A., Cannon, J., Hickey, M., Rosenthal, S. L., Marino, J. L., & Skinner, S. R. (2019). Comparing adolescent and parent reports of externalizing problems: A longitudinal population-based study. *British Journal of Developmental Psychology*, *37*(2), 247–268. https://doi.org/10.1111/bjdp.12270

Ruan, Y., Lin, Y.-F., Feng, Y.-C. A., Chen, C.-Y., Lam, M., Guo, Z., Stanley Global Asia Initiatives, Ahn, Y. M., Akiyama, K., Arai, M., Baek, J. H., Chen, W. J., Chung, Y.-C., Feng, G., Fujii, K., Glatt, S. J., Ha, K., Hattori, K., Higuchi, T., … Ge, T. (2022). Improving polygenic prediction in ancestrally diverse populations. *Nature Genetics*, *54*(5), 573–580. https://doi.org/10.1038/s41588-022-01054-7

Sanchez-Gistau, V., Romero, S., Moreno, D., De La Serna, E., Baeza, I., Sugranyes, G., Moreno, C., Sanchez-Gutierrez, T., Rodriguez-Toscano, E., & Castro-Fornieles, J. (2015). Psychiatric disorders in child and adolescent offspring of patients with schizophrenia and bipolar disorder: A controlled study. *Schizophrenia Research*, *168*(1–2), 197–203. https://doi.org/10.1016/j.schres.2015.08.034

Schizophrenia Working Group of the Psychiatric Genomics Consortium. (2014). Biological insights from 108 schizophrenia-associated genetic loci. *Nature*, *511*(7510), 421–427. https://doi.org/10.1038/nature13595

Seidman, L. J. (2010). Neuropsychology of the Prodrome to Psychosis in the NAPLS ConsortiumRelationship to Family History and Conversion to PsychosisNeuropsychology of Prodrome to Psychosis. *Archives of General Psychiatry*, *67*(6), 578. https://doi.org/10.1001/archgenpsychiatry.2010.66

Taliun, D., Harris, D. N., Kessler, M. D., Carlson, J., Szpiech, Z. A., Torres, R., Taliun, S. A. G., Corvelo, A., Gogarten, S. M., Kang, H. M., Pitsillides, A. N., LeFaive, J., Lee, S., Tian, X., Browning, B. L., Das, S., Emde, A.-K., Clarke, W. E., Loesch, D. P., … Abecasis, G. R. (2021). Sequencing of 53,831 diverse genomes from the NHLBI TOPMed Program. *Nature*, *590*(7845), 290–299. https://doi.org/10.1038/s41586-021-03205-y

Tandon, R., Gaebel, W., Barch, D. M., Bustillo, J., Gur, R. E., Heckers, S., Malaspina, D., Owen, M. J., Schultz, S., Tsuang, M., Van Os, J., & Carpenter, W. (2013). Definition and description of schizophrenia in the DSM-5. *Schizophrenia Research*, *150*(1), 3–10. https://doi.org/10.1016/j.schres.2013.05.028

Taylor, B. K., Frenzel, M. R., Eastman, J. A., Wiesman, A. I., Wang, Y.-P., Calhoun, V. D., Stephen, J. M., & Wilson, T. W. (2022). Reliability of the NIH toolbox cognitive battery in children and adolescents: A 3-year longitudinal examination. *Psychological Medicine*, *52*(9), 1718–1727. https://doi.org/10.1017/S0033291720003487

The International HapMap 3 Consortium. (2010). Integrating common and rare genetic variation in diverse human populations. *Nature*, *467*(7311), 52–58. https://doi.org/10.1038/nature09298

Townsend, L., Kobak, K., Kearney, C., Milham, M., Andreotti, C., Escalera, J., Alexander, L., Gill, M. K., Birmaher, B., Sylvester, R., Rice, D., Deep, A., & Kaufman, J. (2020). Development of Three Web-Based Computerized Versions of the Kiddie Schedule for Affective Disorders and Schizophrenia Child Psychiatric Diagnostic Interview: Preliminary Validity Data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(2), 309–325. https://doi.org/10.1016/j.jaac.2019.05.009

Trubetskoy, V., Pardiñas, A. F., Qi, T., Panagiotaropoulou, G., Awasthi, S., Bigdeli, T. B., Bryois, J., Chen, C.-Y., Dennison, C. A., Hall, L. S., Lam, M., Watanabe, K., Frei, O., Ge, T., Harwood, J. C., Koopmans, F., Magnusson, S., Richards, A. L., Sidorenko, J., … Van Os, J. (2022). Mapping genomic loci implicates genes and synaptic biology in schizophrenia. *Nature*, *604*(7906), 502–508. https://doi.org/10.1038/s41586-022-04434-5

Wainberg, M., Jacobs, G. R., Voineskos, A. N., & Tripathy, S. J. (2022). Neurobiological, familial and genetic risk factors for dimensional psychopathology in the Adolescent Brain Cognitive Development study. *Molecular Psychiatry*, *27*(6), 2731–2741. https://doi.org/10.1038/s41380-022-01522-w

Warnick, E. M., Bracken, M. B., & Kasl, S. (2008). Screening Efficiency of the Child Behavior Checklist and Strengths and Difficulties Questionnaire: A Systematic Review. *Child and Adolescent Mental Health*, *13*(3), 140–147. https://doi.org/10.1111/j.1475-3588.2007.00461.x

Weintraub, S., Dikmen, S. S., Heaton, R. K., Tulsky, D. S., Zelazo, P. D., Bauer, P. J., Carlozzi, N. E., Slotkin, J., Blitz, D., Wallner-Allen, K., Fox, N. A., Beaumont, J. L., Mungas, D., Nowinski, C. J., Richler, J., Deocampo, J. A., Anderson, J. E., Manly, J. J., Borosh, B., … Gershon, R. C. (2013). Cognition assessment using the NIH Toolbox. *Neurology*, *80*(Issue 11, Supplement 3), S54–S64. https://doi.org/10.1212/WNL.0b013e3182872ded

Welham, J., Isohanni, M., Jones, P., & McGrath, J. (2009). The Antecedents of Schizophrenia: A Review of Birth Cohort Studies. *Schizophrenia Bulletin*, *35*(3), 603–623. https://doi.org/10.1093/schbul/sbn084

Yang, R. & Jernigan, Terry. (n.d.). *Adolescent Brain Cognitive Development Study (ABCD)—Annual Release 4.0* [Dataset]. NIMH Data Repositories. https://doi.org/10.15154/1523041