

Supplemental Material A: Whole Genome Sequencing in Psychiatric Disorders (WGSPD) Summary of Inclusion-Exclusion Criteria for Contributing Studies

Project 1 - Whole Genome Sequencing for Schizophrenia and Bipolar Disorder in the GPC (Boehnke, McCarroll, Pato)

Recruitment generally targeted locations at which health-care services are delivered to people with a history of psychosis, such as hospitals, outpatient centers, Clubhouse programs, and other community programs, as well as through advertisements¹. Eligibility criteria were age 18 or older, capacity to provide written informed consent, no medical cause for the psychosis, and a clinical diagnosis of schizophrenia, schizoaffective disorder, or bipolar disorder substantiated by a psychiatric provider. Individuals meeting eligibility criteria were administered the DI-PAD.

Project 3 - Genomic Strategies to Identify High-Impact Psychiatric Risk Variants (Freimer, Palotie, Geschwind)

Dutch BP study

- Inclusion Criteria
 - Dutch ancestry
 - Premorbid IQ > 80
 - Age ≥ 18
 - Good command of Dutch language
 - For BP: BP I diagnosis, and no compulsory treatment under governmental health act
 - For Relatives: 1st degree relative with BP I diagnosis
 - For Controls: No psychotic or BP diagnosis, and no 1st or 2nd degree relative with psychotic or BP diagnosis
- Exclusion criteria (patients)
 - Somatic illness that could influence the diagnosis of BP

Dutch SCZ study²

- Inclusion criteria for patients and siblings:
 - Age range of 16 to 50 years (extremes included)
 - Good command of the Dutch language
 - Able and willing to give written informed consent.
 - Patients: Diagnosis of non-affective psychotic disorder according to DSM-IV
 - Controls: No lifetime psychotic disorder; No first-degree family member with a lifetime psychotic disorder

Finnish Schizophrenia family study

The Finnish Schizophrenia Family study sample was identified through nationwide health care and population registries. People born between 1940 and 1976 in Finland were screened for schizophrenia, schizoaffective disorder, or schizophreniform disorder diagnosis in three

registers: hospitalization between years 1969 and 1998 from the Hospital Discharge Register, use of free antipsychotic medication from the Medication Reimbursement Register, and disability pension from the Pension Register. The construction of pedigrees was done with the help of National Population Register³.

Two samples of schizophrenia families were recruited: families with at least two affected siblings and families with at least one affected family member from an internal isolate region in Finland with relatively high schizophrenia prevalence⁴.

Psychoses in Finland (PIF, based on Health 2000)

The PIF sample was selected from the Finnish Health 2000 Survey (BRIF8901). Health 2000 is a two-stage stratified cluster sample of the Finnish population⁵ comprising 8028 persons who were 30 years or over and lived in mainland Finland.

The individuals in the survey sample were selected to the Psychoses in Finland substudy if they reported a diagnosed psychotic disorder, received a diagnosis of possible or definite psychotic disorder from the physician conducting the health examination, reported possible psychotic or manic symptoms in the CIDI or had other symptoms suggestive of psychotic disorder. In addition, several registers were used in screening for possible psychotic disorders⁶.

In addition, a random sample of screen negatives were invited to serve as controls. To obtain a control group from a Finnish internal isolate region (Kuusamo), all consenting screen negatives from the isolate region were invited to participate.

Finnish Bipolar Family study

Individuals with a diagnosis of bipolar disorder between the years of 1969 and 1991 inclusive were identified from the Finnish Hospital Discharge Register. Of 7462 such subjects, those with at least two hospitalisations and the first one before the age of 30 years were considered eligible as probands. The first-degree relatives of the probands were identified through the Population Register Centre of Finland. In addition, 62 twin pairs with bipolar disorder were identified in collaboration with the Finnish Twin Cohort. Only those nuclear families in which there are at least two members with a diagnosis of bipolar disorder, type I, or schizoaffective disorder, bipolar type, were considered eligible for molecular research⁷.

Finnish Bipolar Twin study

Patients with a mood disorder diagnosis (ICD-8; World Health Organization codes 296.10 or 296.30 or DSM-III-R codes 296.4, 296.5, or 296.6) during 1969–1991 were identified from the National Hospital Discharge Register. Twins born between 1940 and 1969 were identified using the National Population Register and the Finnish Twin Cohorts^{8,9}. Only patients with bipolar disorder or the manic type of schizoaffective disorder were regarded as eligible probands. All probands, except one who had a secret address and no known current treatment, were invited to participate in the study. The co-twin was also asked to participate¹⁰.

Colombia/Costa Rica studies:

- Inclusion criteria:

- 18 years of age or older
- Member of pedigree heavily loaded for Bipolar Disorder Type I
- Euthymic state
- Exclusion criteria:
 - Poor physical health, or suffering from severe dementia or other neurodegenerative disease
 - Contraindication for MRI
 - Primary diagnosis of substance use disorder

Project 4 - Pedigree Based Whole Genome Sequencing of Affective and Psychotic Disorders (Glahn, Blangero, Gur)

Pennsylvania: **MGI Families** were recruited from according to established procedures and criteria. In brief, probands were >18 years-old, with a consensus best-estimate DSM-IV diagnosis of SCZ. For patients with concomitant psychotic and mood symptoms, hallucinations and delusions must have been present for > 2 weeks in the absence of significant mood symptoms, and the mood component must not have been present for a substantial portion of active and residual illness. We enrolled probands with at least one 1st-degree affected family member with SCZ or SAD. **CC** were recruited from a population-based sample ascertained from the same communities as SCZ families.

- Inclusion criteria
 - ability to provide signed informed consent (for participants 15-18 years-old, assent and parental approval are required),
 - written permission to contact family members,
 - English proficiency, and
 - general good health
 - For CC: Caucasian
- Exclusion criteria
 - mental retardation (estimated IQ < 70 per WRAT-3),
 - significant medical or neurological disorder associated with psychosis, cognitive deficit or neuroanatomic abnormalities,
 - alcohol or substance dependence in the past 6 months,
 - positive drug or alcohol screen at the time of testing,
 - ECT in the past 6 months, and
 - conditions interfering with MRI including metallic inserts, orthopedic circumstances, poor vision, and pregnancy, determined by a serum test in women of child bearing potential.
 - For CC: absence of Cluster A personality disorder and any psychotic disorder in 1st-degree family members.

Texas Study: To be eligible for this study an individual had to be related to someone who previously participated in the San Antonio Family Heart Study or the Genetics of Brain Structure and Function study.

- Inclusion Criteria
 - Related to someone who participated in prior family study
 - Between 18 and 80 years old
 - Proficient in English or Spanish
 - Two or more Hispanic grandparents
- Exclusion Criteria
 - Neurodegenerative disorder
 - History of significant head injury (5 minutes or more) or neurosurgery
 - For MRI: metal implants, surgical clips, certain pacemakers, and exposure to metal shards

¹ Perlman, G., Kotov, R., Fu, J., Bromet, E. J., Fochtmann, L. J., Medeiros, H., ... & Pato, C. N. (2016). Symptoms of psychosis in schizophrenia, schizoaffective disorder, and bipolar disorder: a comparison of African Americans and Caucasians in the Genomic Psychiatry Cohort. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, 171(4), 546-555.

² Korver, N., Quee, P.J., Boos, H.B.M., Simons, C.J.P., de Haan, L., & GROUP Investigators, 2012. Genetic Risk and Outcome of Psychosis (GROUP), a multi site longitudinal cohort study focused on gene-environment interaction: objectives, sample characteristics, recruitment and assessment methods. *International Journal of Methods in Psychiatric Research*, 21, 205-221.

³ Paunio, T., Ekelund, J., Varilo, T., Parker, A., Hovatta, I., Turunen, J. A., ... & Suvisaari, J. (2001). Genome-wide scan in a nationwide study sample of schizophrenia families in Finland reveals susceptibility loci on chromosomes 2q and 5q. *Human molecular genetics*, 10(26), 3037-3048.

⁴ Hovatta, I., Terwilliger, J. D., Lichtermann, D., Mäkiyryö, T., Suvisaari, J., Peltonen, L., & Lönnqvist, J. (1997). Schizophrenia in the genetic isolate of Finland. *American journal of medical genetics*, 74(4), 353-360.

⁵ Aromaa A, Koskinen S (eds): Health and functional capacity in Finland. Baseline results of the Health 2000 health examination survey. Helsinki, Publications of the National Public Health Institute B12/2004. <http://www.terveys2000.fi/julkaisut/baseline.pdf>, 2004.

⁶ Perälä, J., Kuoppasalmi, K., Pirkola, S., Härkänen, T., Saarni, S., Tuulio-Henriksson, A., ... & Suvisaari, J. (2010). Alcohol-induced psychotic disorder and delirium in the general population. *The British Journal of Psychiatry*, 197(3), 200-206.

⁷ Soronen, P., Silander, K., Antila, M., Palo, O. M., Tuulio-Henriksson, A., Kieseppä, T., ... & Hennah, W. (2008). Association of a nonsynonymous variant of DAOA with visuospatial ability in a bipolar family sample. *Biological psychiatry*, 64(5), 438-442.

⁸ Kaprio, J., Sarna, S., Koskenvuo, M., & Rantasalo, I. (1978). The Finnish twin registry: formation and compilation, questionnaire study, zygosity determination, procedures and research program. *Twin Research*, 179-184.

⁹ Kaprio, J., Koskenvuo, M., & Rose, R. J. (1990). Change in cohabitation and intrapair similarity of monozygotic (MZ) cotwins for alcohol use, extraversion, and neuroticism. *Behavior Genetics*, 20(2), 265-276.

¹⁰ Kieseppä, T., Partonen, T., Kaprio, J. & Lönnqvist, J. (2000). Accuracy of register- and record-based bipolar I diagnoses in Finland – a study of twins. *Acta Neuropsychiatrica* 12, 106–109.