Evaluation of polygenic risk score for schizophrenia among Northern Finland Birth Cohort 1966 data

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Introduction

Psychotic disorders, such as schizophrenia, are severe mental disorders that affect about 3% of the Finnish population [1]. In Northern Finland, the percentage is even higher (4.5%) [2]. Generally, the heritability among psychotic disorders is considered high [3] even though most of the children of parents with psychotic disorder remain without psychotic diagnosis [4]. Using polygenic risk score (PRS) for schizophrenia (SCH), it is possible to estimate personal genetic risk and try to evaluate why only some of the children of parents with psychotic disorder develop psychotic disorder themselves.

Objectives

To calculate PRS for schizophrenia and evaluate it among Northern Finland Birth Cohort 1966 (NFBC1966) data.

Methods

The NFBC1966 is a large longitudinal and still ongoing birth cohort which consists of more than 12 000 cohort members born in 1966 in the Northern Finland.

The calculation of PRS is based on previous results of genome-wide association studies on schizophrenia [5]. Information on psychotic disorders is based on nationwide registers (Care Register for Health Care and the registers from Social Insurance Institution and Finnish Center for Pensions).

Cox regression analysis (Hazard Ratios, HR) was used to estimate association between PRS and psychotic disorder. Kaplan-Meier survival analysis (Mantel-Cox estimate) was used to estimate the incidence of psychotic disorders.

Previously found risk factors (gender, obstetric complications, maternal antenatal depression, unwantedness of a pregnancy, grand multiparity and child's viral central nervous system infection) for psychotic disorders [6] were used as covariates.

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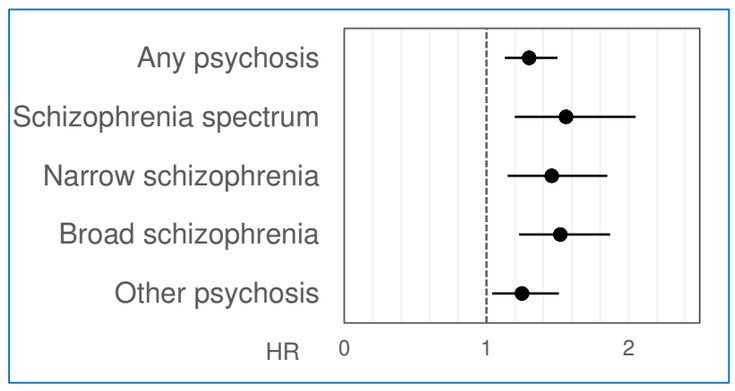
Results

Genetic data was available from 5 363 (48.2% male; 51.8% female) subjects. From them, 3.7% (N=196) was diagnosed with a psychotic disorder. When PRS increased, the risk (adjusted HR) for psychotic disorder was 1.30-fold (95% confidence interval=1.13-1.50, p=0.001). Similar results were found when different psychoses were evaluated separately (Figure 1). Those who had higher than the mean PRS were diagnosed with psychotic disorder more previously and frequently than the others (Mantel-Cox estimate: $\chi 2$=10.4. df=1, p=0.001). Again, similar results occurred while observing different psychoses separately (Figure 2).

Figure 1. Hazard ratios (HR) and their 95% confidence intervals from Cox regression analysis between polygenis risk score (PRS) for schizophrenia and diagnosis of psychoses.

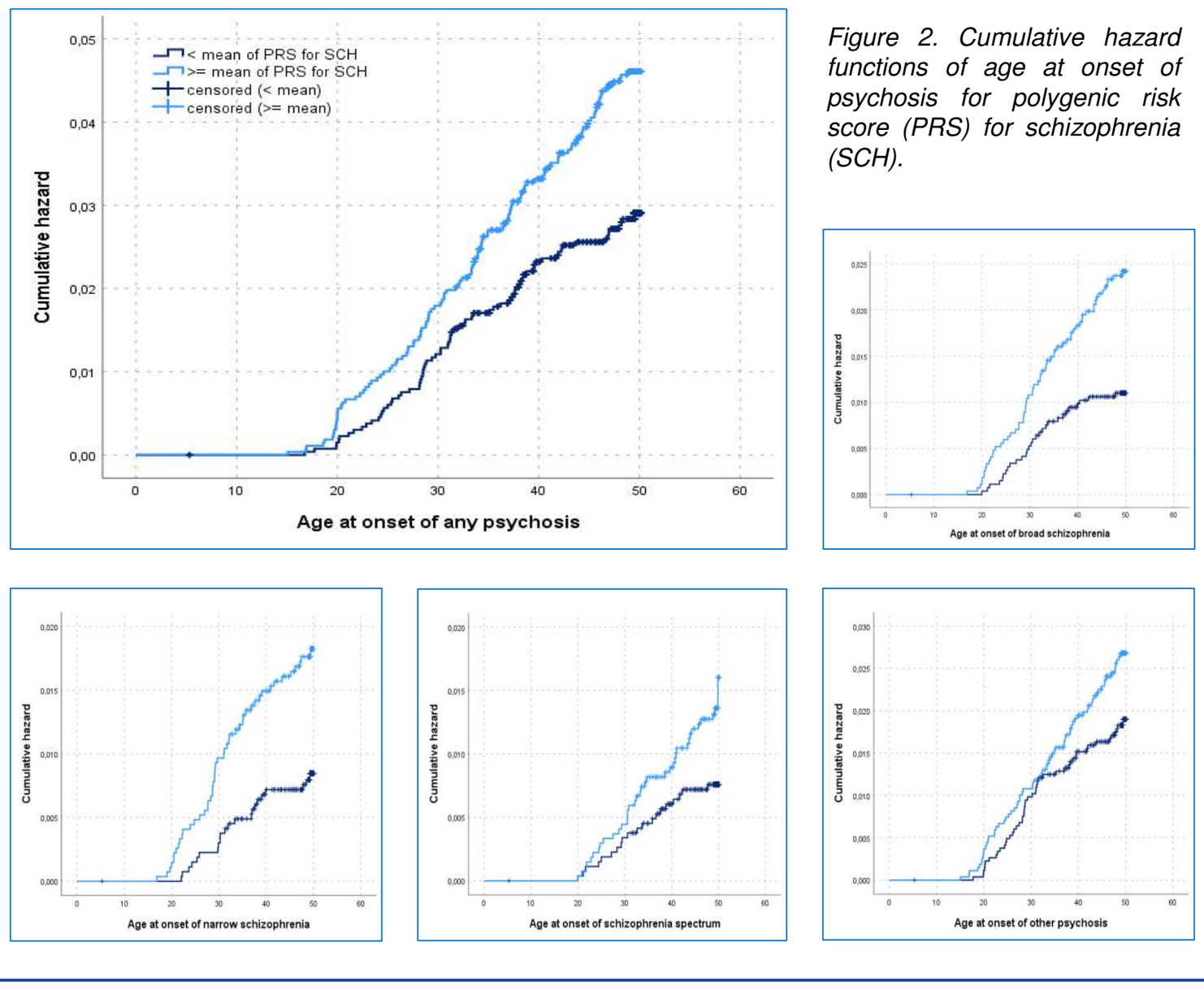


The association pf PRS for schzophrenia is adjusted with gender, obstetric complications, maternal antenatal depression, unwantedness of a pregnancy, grand multiparity and child's viral central nervous system infection.

Conclusions

PRS for schizophrenia is a sufficient estimate of personal genetic risk for a psychotic disorder among NFBC1966. People with higher PRS were diagnosed more often and earlier with psychotic disorder than people with lower PRS.

Figure 2. Cumulative hazard functions of age at onset of psychosis for polygenic risk score (PRS) for schizophrenia (SCH).



References

[1] Perälä J, Suvisaari J, Saarni SI, Kuoppasalmi K, Isometsä E, Pirkola S, Partonen T et al. Arch Gen Psychiatry 2007, 64(1):19-28. [2] Perälä J, Saarni SI, Ostamo A, Pirkola S, Haukka J, Härkänen T, Koskinen S et al. Schizophr Res 2008, 106:337-347. [3] Cardno AG, Marshall EJ, Coid B, Macdonald AM, Ribchester TR, Davies NJ, Venturi P et al. Arch Gen Psychiatry 1999, 56(2):162-168. [4] Svrakic DM, Zorumski CF, Svrakic NM, Zwir I, Cloninger CR. Curr Opin Psychiatry 2013, 26:188-195. [5] Schizophrenia Working Group of the Psychiatric Genomics Consortium. Nature 2014, 511:421-427. [6] Jääskeläinen E, Haapea M, Rautio N, Juola P, Penttilä M, Nordström T, Rissanen I et al. Schizophr Res Treatment 2015, 2015:524875.

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