

## Supplementary material

The role of genetic liability in the association of urbanicity at birth and during upbringing with schizophrenia in Denmark

Diana Paksarian, PhD <sup>1</sup>

Betina B Trabjerg, MSc <sup>2,3,4</sup>

Kathleen R. Merikangas, PhD <sup>1</sup>

Ole Mors, PhD<sup>3,5</sup>

Anders D. Børglum, PhD<sup>3,5,6</sup>

David M. Hougaard, DrMedSc<sup>7</sup>

John J. McGrath, MD <sup>2,8</sup>

Carsten B. Pedersen, DrMedSc<sup>2,3,4</sup>

Preben B. Mortensen, DrMedSc<sup>2,3,4</sup>

Esben Agerbo, DrMedSc <sup>2,3,4</sup>

<sup>1</sup> Genetic Epidemiology Research Branch, National Institute of Mental Health, Bethesda, MD, USA

<sup>2</sup> NCCR-National Center for Register-Based Research, Business and Social Sciences, Aarhus University, Denmark

<sup>3</sup> The Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, Copenhagen, Denmark

<sup>4</sup> CIRRAU—Centre for Integrated Register-Based Research, Aarhus University, Denmark

<sup>5</sup> Department P, Aarhus University Hospital, Risskov, Denmark

<sup>6</sup> Department of Biomedicine and Centre for Integrative Sequencing, iSEQ, Aarhus University, Denmark

<sup>7</sup> Danish Center for Neonatal Screening, Statens Serum Institut, Copenhagen, Denmark

<sup>8</sup> Queensland Brain Institute, The University of Queensland, St Lucia, Australia

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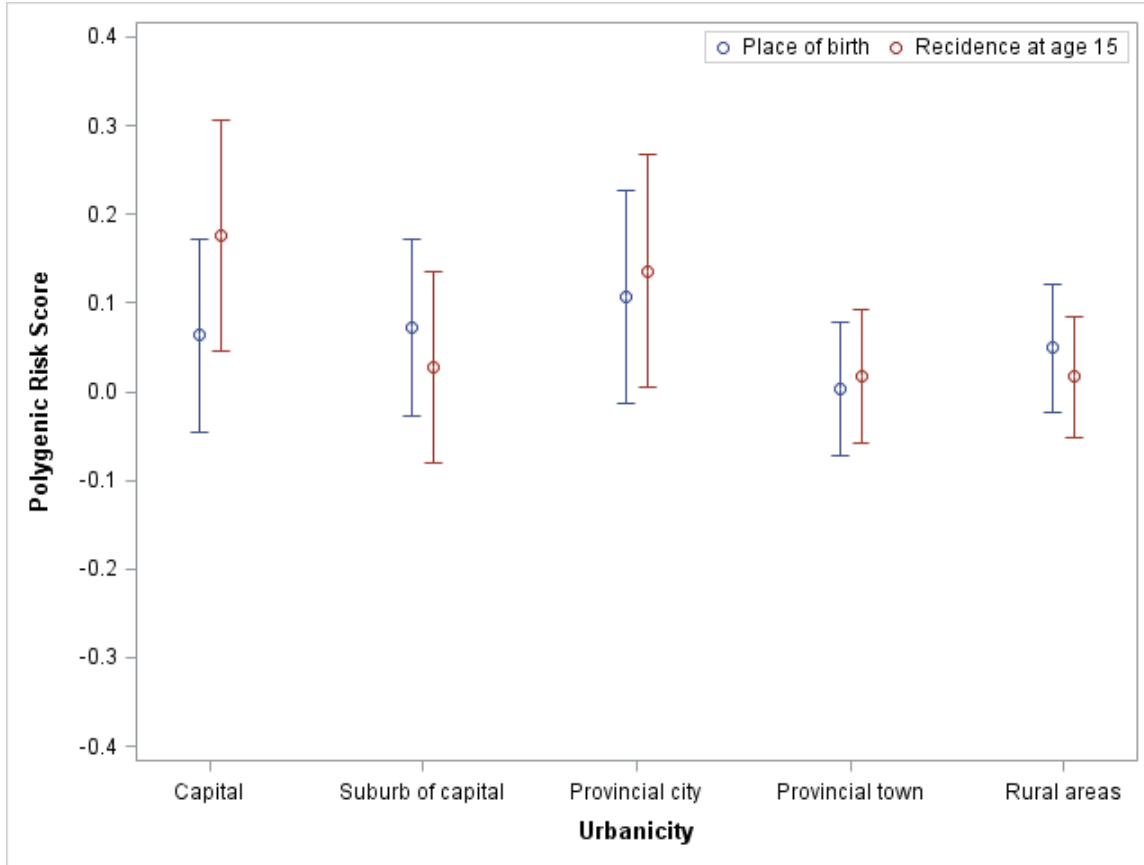
eFigure 1: Mean polygenic risk score for schizophrenia, according to urbanicity at birth and at age 15, among 1 692 cases.

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eTable 2: Associations of polygenic risk score for schizophrenia with being born in the capital and living in the capital at age 15, compared to being born or living in rural areas, among controls.

eFigure 1: Mean polygenic risk score for schizophrenia, according to urbanicity at birth and at age 15, among 1 692 cases.



Note: Polygenic risk score adjusted for the first 10 principal components. Only 1 591 cases whose date of matching (case onset) is after the 15<sup>th</sup> birthday and who lived in Denmark at age 15 are used when considering urbanicity at age 15.

eTable 1: Associations of polygenic risk score for schizophrenia with being born in the capital and living in the capital at age 15, compared to being born or living in rural areas, among cases

	Place of birth				
	Capital (n=232) N (%)	Rural areas <sup>a</sup> (n=518) N (%)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
<b>Polygenic risk score<sup>b</sup>, mean (SD)</b>	0.14 (0.89)	-0.01 (0.89)	0.98 (0.81,1.19)	0.93 (0.76,1.13)	0.92 (0.75,1.12)
<b>Parental history of mental disorders</b>					
Schizophrenia or bipolar disorder	29 (12.50)	21 (4.05)	3.30 (1.81,6.09)	3.67 (1.95,6.98)	3.58 (1.88,6.89)
Other mental disorders	51 (21.98)	115 (22.20)	1.15 (0.78,1.68)	1.29 (0.86,1.92)	1.25 (0.82,1.87)
No diagnosis of mental disorders	152 (65.52)	382 (73.75)	1.00 Ref	1.00 Ref	1.00 Ref
	Place of residence at age 15*				
	Capital (n=160) N (%)	Rural areas <sup>a</sup> (n=575) N (%)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
<b>Polygenic risk score<sup>b</sup>, mean (SD)</b>	0.28 (0.92)	-0.03 (0.88)	1.24 (0.99,1.54)	1.18 (0.94,1.48)	1.16 (0.92,1.45)
<b>Parental history of mental disorders</b>					
Schizophrenia or bipolar disorder	17 (10.63)	28 (4.87)	2.61 (1.34,4.96)	2.86 (1.42,5.61)	2.91 (1.43,5.75)
Other mental disorders	46 (28.75)	130 (22.61)	1.53 (1.01,2.29)	1.59 (1.03,2.43)	1.62 (1.04,2.48)
No diagnosis of mental disorders	97 (60.63)	417 (72.52)	1.00 Ref	1.00 Ref	1.00 Ref

\*Note: Associations estimated via logistic regression. Only cases aged 15 or older at the time of matching are considered for the analysis with place of residence at age 15.

Model 1: Adjusted for sex, age, year of birth, and the first 10 principal components.

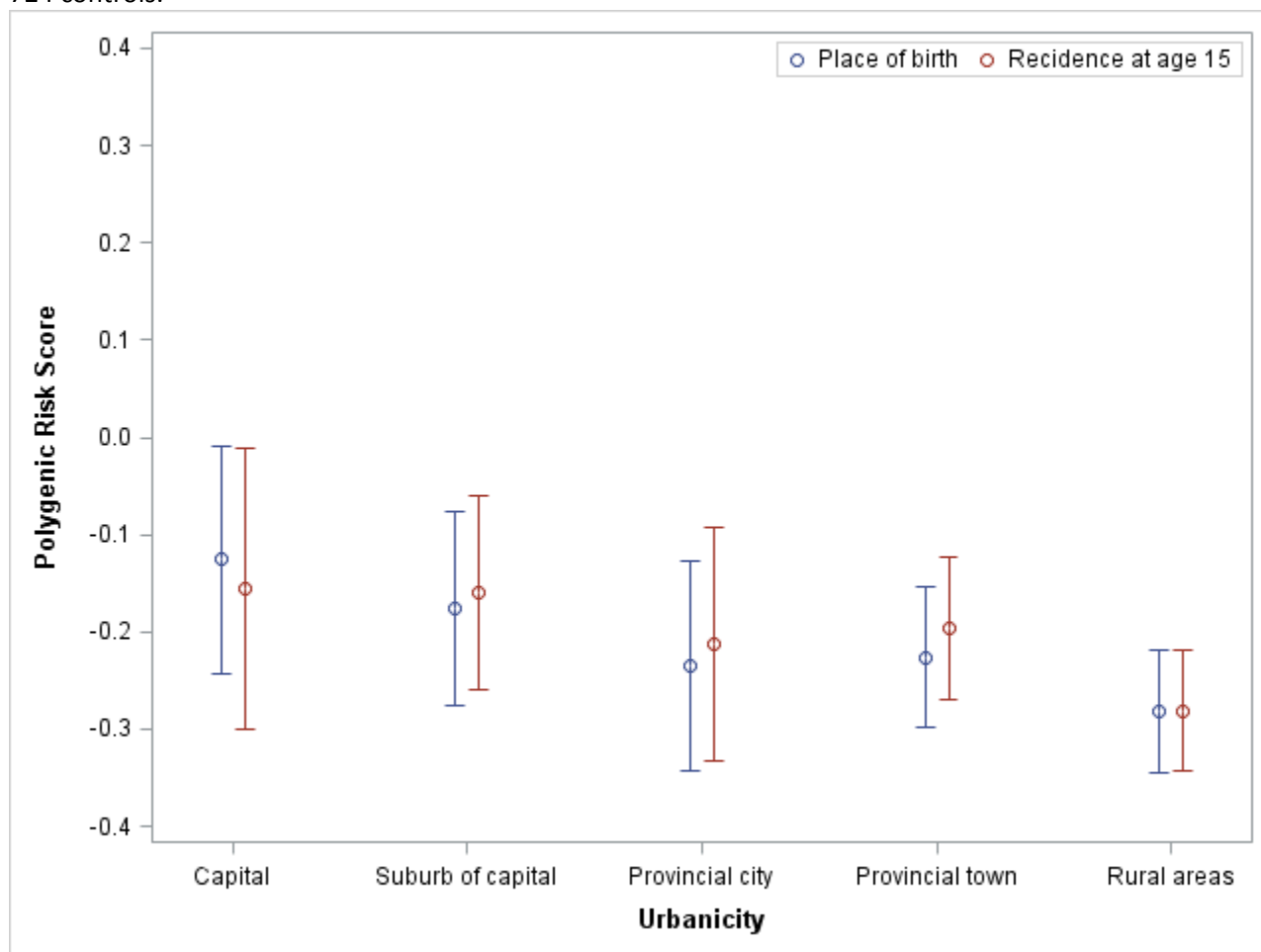
Model 2: Model 1 additionally adjusted for parental history of mental disorder.

Model 3: Model 2 additionally adjusted for parental place of birth and paternal age at childbirth.

<sup>a</sup> Municipalities in Denmark where largest town has less than 10 000 inhabitants.

<sup>b</sup> Normalized to the sample

eFigure 2: Mean polygenic risk score for schizophrenia, according to urbanicity at birth and at age 15, among 1 724 controls.



Note: Polygenic risk score adjusted for the first 10 principal components. Only 1 609 controls whose date of matching (case onset) is after the 15<sup>th</sup> birthday and who lived in Denmark at age 15 are used when considering urbanicity at age 15.

eTable 2: Associations of polygenic risk score for schizophrenia with being born in the capital and living in the capital at age 15, compared to being born or living in rural areas, among controls

	Place of birth				
	Capital (N=181) N (%)	Rural areas <sup>a</sup> (N=621) N (%)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
<b>Polygenic risk score<sup>b</sup>, mean (SD)</b>	-0.05 (0.88)	-0.33 (0.79)	1.29 (1.03,1.61)	1.30 (1.04,1.63)	1.30 (1.04,1.64)
<b>Parental history of mental disorders</b>					
Schizophrenia or bipolar disorder	3 (1.66)	13 (2.09)	0.88 (0.20,2.80)	0.85 (0.19,2.80)	0.99 (0.22,3.30)
Other mental disorders	32 (17.68)	56 (9.02)	2.17 (1.34,3.46)	2.00 (1.19,3.30)	1.93 (1.14,3.22)
No diagnosis of mental disorders	146 (80.66)	552 (88.89)	1.00 Ref	1.00 Ref	1.00 Ref
	Place of residence at age 15*				
	Capital (N=117) N (%)	Rural areas <sup>a</sup> (N=639) N (%)	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
<b>Polygenic risk score<sup>b</sup>, mean (SD)</b>	-0.08 (0.86)	-0.33 (0.78)	1.20 (0.92,1.57)	1.20 (0.92,1.57)	1.21 (0.92,1.59)
<b>Parental history of mental disorders</b>					
Mental disorder <sup>c</sup>	21 (17.95)	76 (11.89)	1.58 (0.91,2.65)	1.40 (0.76,2.46)	1.34 (0.72,2.39)
No diagnosis of mental disorders	96 (82.05)	563 (88.11)	1.00 Ref	1.00 Ref	1.00 Ref

\*Note: Associations estimated via logistic regression. Only controls aged 15 or older at the time of matching are considered for the analysis with place of residence at age 15.

Model 1: Adjusted for sex, age, year of birth, and the first 10 principal components.

Model 2: Model 1 additionally adjusted for parental history of mental disorder.

Model 3: Model 2 additionally adjusted for parental place of birth and paternal age at childbirth.

<sup>a</sup> Municipalities in Denmark where largest town has less than 10 000 inhabitants.

<sup>b</sup> Normalized to the sample

<sup>c</sup> Schizophrenia, bipolar and other psychiatric disorders.