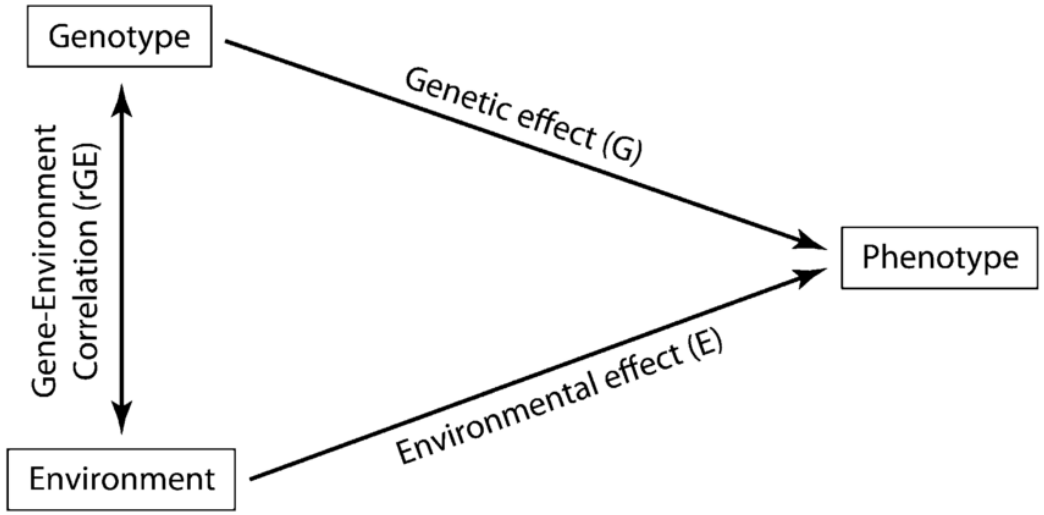
Amsterdam UMC
University Medical Centers

Non-independence of causes of variation: Gene-environment correlations (rGE)

Abdel Abdellaoui



dr_appie
a.abdellaoui@amsterdamumc.nl

GENETICS NETWORK AMSTERDAM

Gene-environment correlation (rGE)

rGE: exposure to environmental condition is associated with genotype

Gene-environment correlation (rGE)

rGE: exposure to environmental condition is associated with genotype

Passive rGE: inherited environment and genotype are correlated
Evocative rGE: environment reacts to genotype
Active rGE: genotype influences behavior to search for an environment

Gene-environment correlation (rGE)

rGE: exposure to environmental condition is associated with genotype

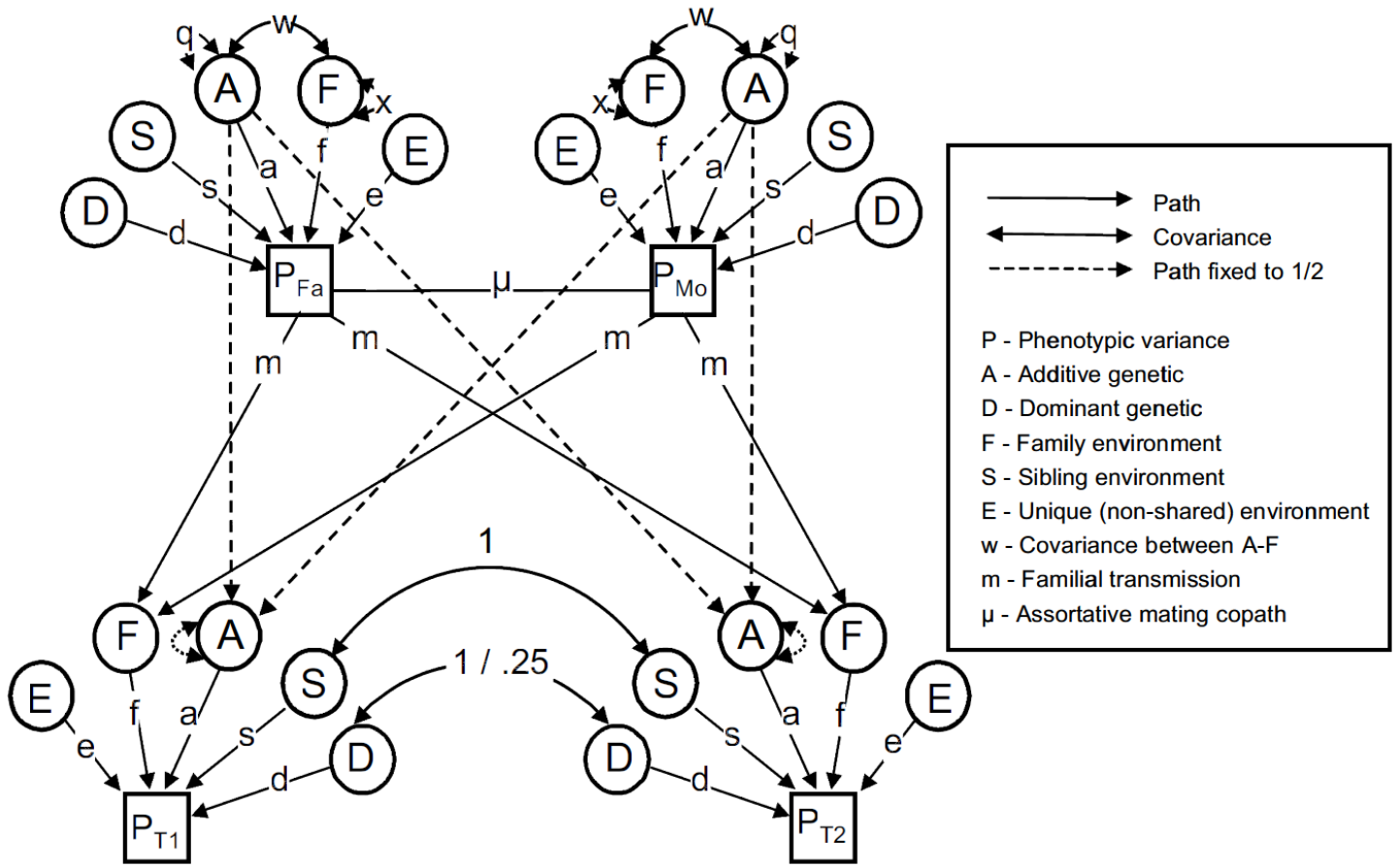
Passive rGE: inherited environment and genotype are correlated
Evocative rGE: environment reacts to genotype
Active rGE: genotype influences behavior to search for an environment

If rGE is ignored in twin models, estimates are biased:

- Correlation between **A** & **C** acts like **C**
- Correlation between **A** & **E** acts like **A**

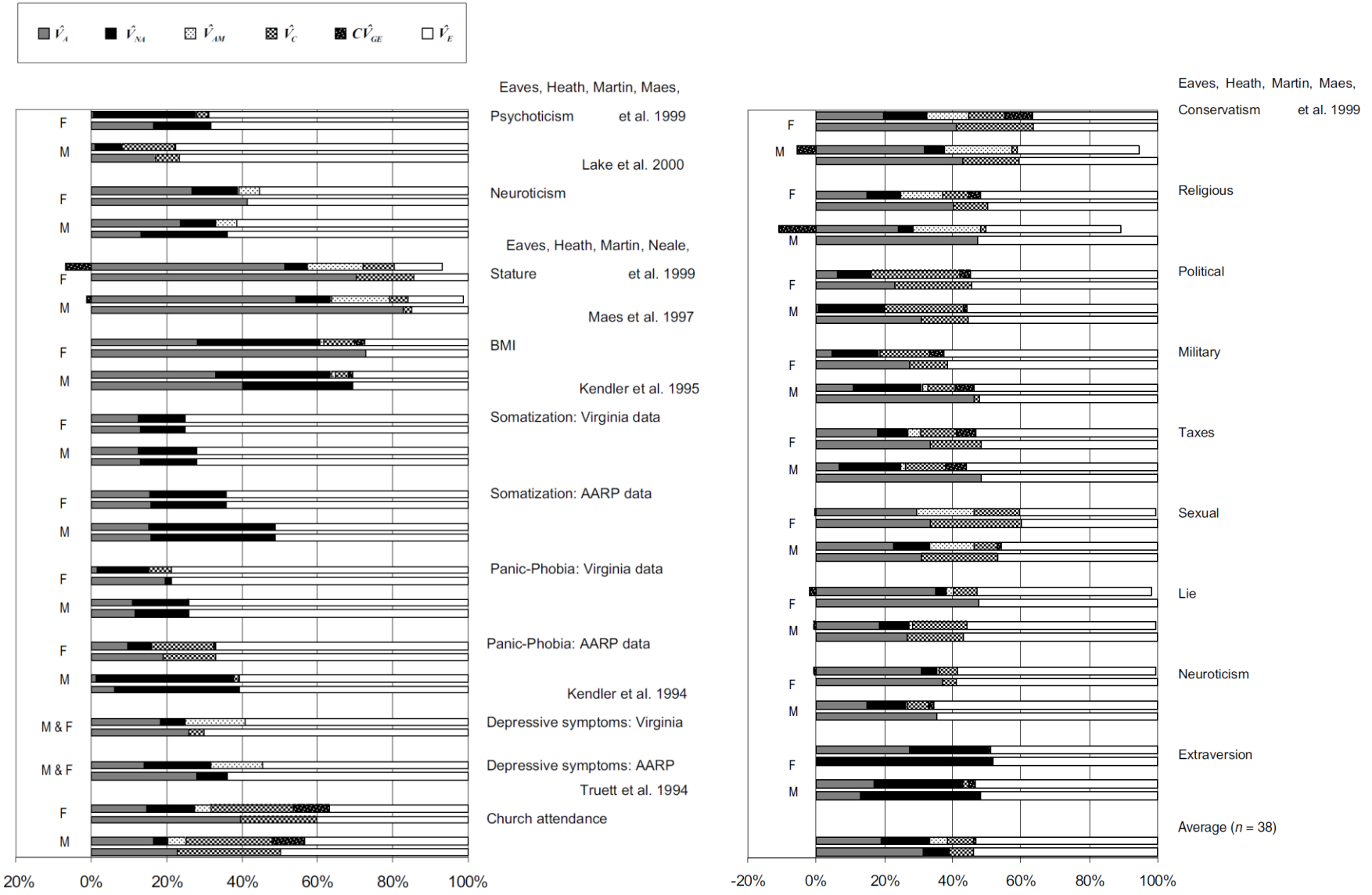
Modeling Extended Twin Family Data I: Description of the Cascade Model

Matthew C. Keller,[1,2] Sarah E. Medland,[3] Laramie E. Duncan,[1] Peter K. Hatemi,[3] Michael C. Neale,[3] Hermine H. M. Maes,[3] and Lindon J. Eaves[3]



Estimating the Extent of Parameter Bias in the Classical Twin Design: A Comparison of Parameter Estimates From Extended Twin-Family and Classical Twin Designs

William L. Coventry[1,2] and Matthew C. Keller[3]

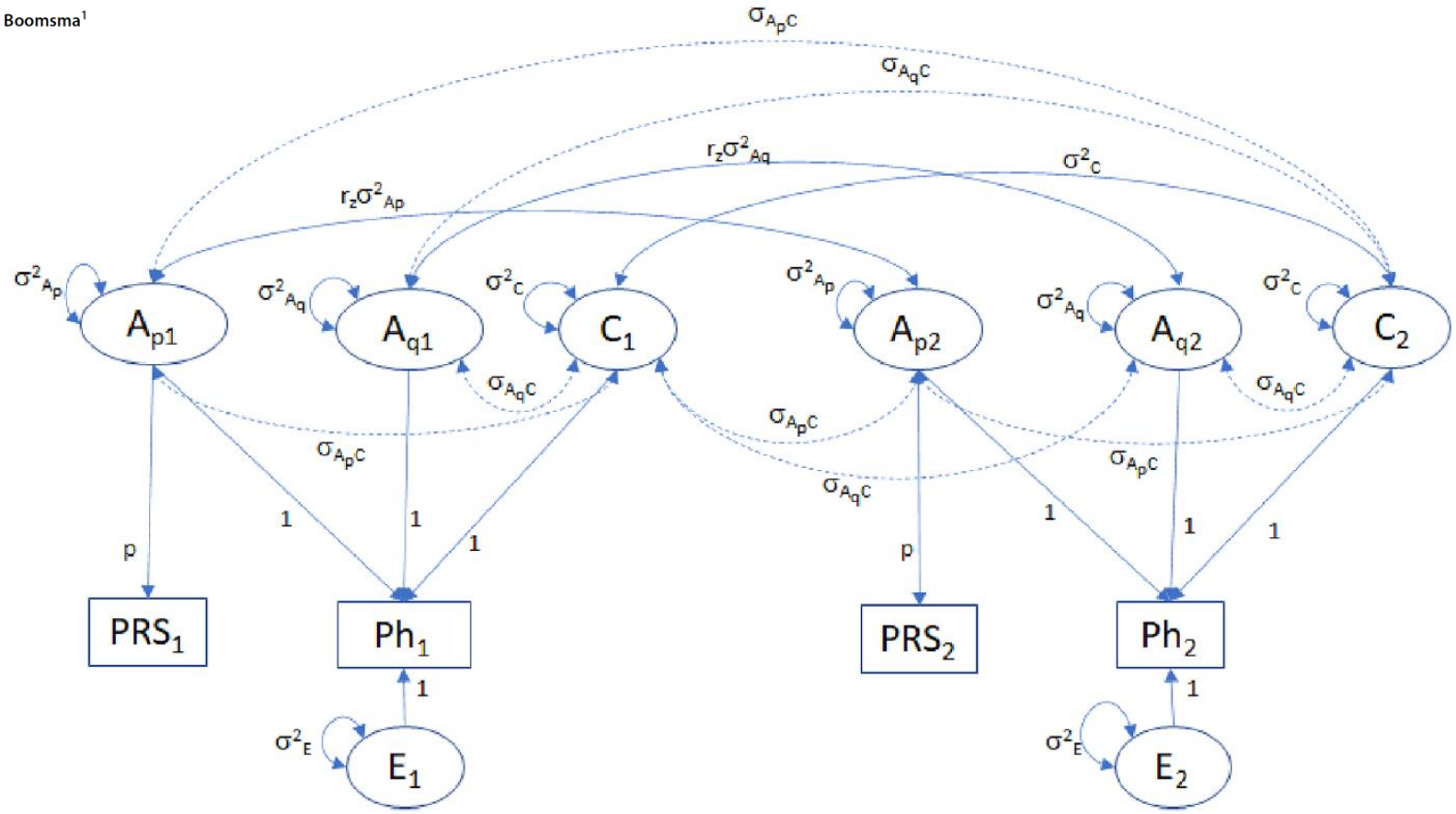


Behavior Genetics (2021) 51:237–249
https://doi.org/10.1007/s10519-020-10035-7

ORIGINAL RESEARCH

Incorporating Polygenic Risk Scores in the ACE Twin Model to Estimate A–C Covariance

Conor V. Dolan[1,4] · Roel C. A. Huijskens[1] · Camelia C. Minică[3,5] · Michael C. Neale[1,2] · Dorret I. Boomsma[1]



Behavior Genetics (2021) 51:154–161
https://doi.org/10.1007/s10519-020-10036-6

ORIGINAL RESEARCH

Direct and Indirect Effects of Maternal, Paternal, and Offspring Genotypes: Trio-GCTA

Espen Moen Eilertsen[1,6,9] · Eshim Shahid Jami[2] · Tom A. McAdams[3,6] · Laurie J. Hannigan[4] · Alexandra S. Havdahl[1,4,5,6] · Per Magnus[9] · David M. Evans[5,7] · Eivind Ystrom[1,6,8]

Behavior Genetics
https://doi.org/10.1007/s10519-019-09969-4

ORIGINAL RESEARCH

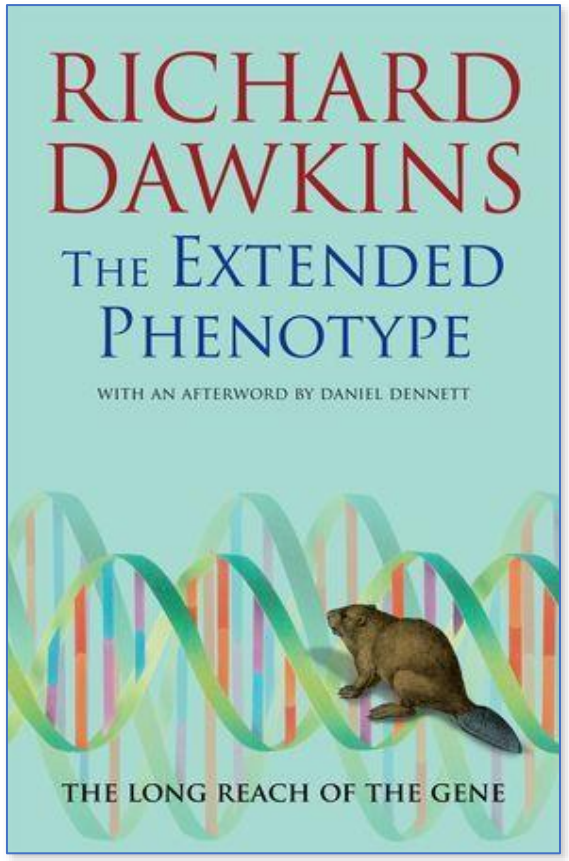
Introducing M-GCTA a Software Package to Estimate Maternal (or Paternal) Genetic Effects on Offspring Phenotypes

Zhen Qiao[1] · Jie Zheng[2,3] · Øyvind Helgeland[4,5] · Marc Vaudel[4] · Stefan Johansson[4,6] · Pål R. Njølstad[4,7] · George Davey Smith[2,3] · Nicole M. Warrington[1,8] · David M. Evans[1,2,3]

Genetic Relationship Matrix (GRM), contains the genetic relationship between **all pairs of individuals** based on **measured SNPs**:

$$\hat{\pi}_{ij} = \frac{1}{N}\sum_k \frac{(x_{ki} - 2p_k)(x_{kj} - 2p_k)}{2p_k(1-p_k)}$$

where x_{ki} is the k^{th} SNP (k=1...N) of the i^{th} person, taking the value of 0, 1, or 2 if it is AA, Aa, aa, and p_k is the frequency of allele a.



"Phenotype" should include all effects that a gene has on its environment, both **inside** and **outside** the body of the individual organism.

Psychological Medicine, 2007, **37**, 615–626. © 2006 Cambridge University Press
doi:10.1017/S0033291706009524 First published online 19 December 2006 Printed in the United Kingdom

REVIEW ARTICLE

Genetic influences on measures of the environment: a systematic review

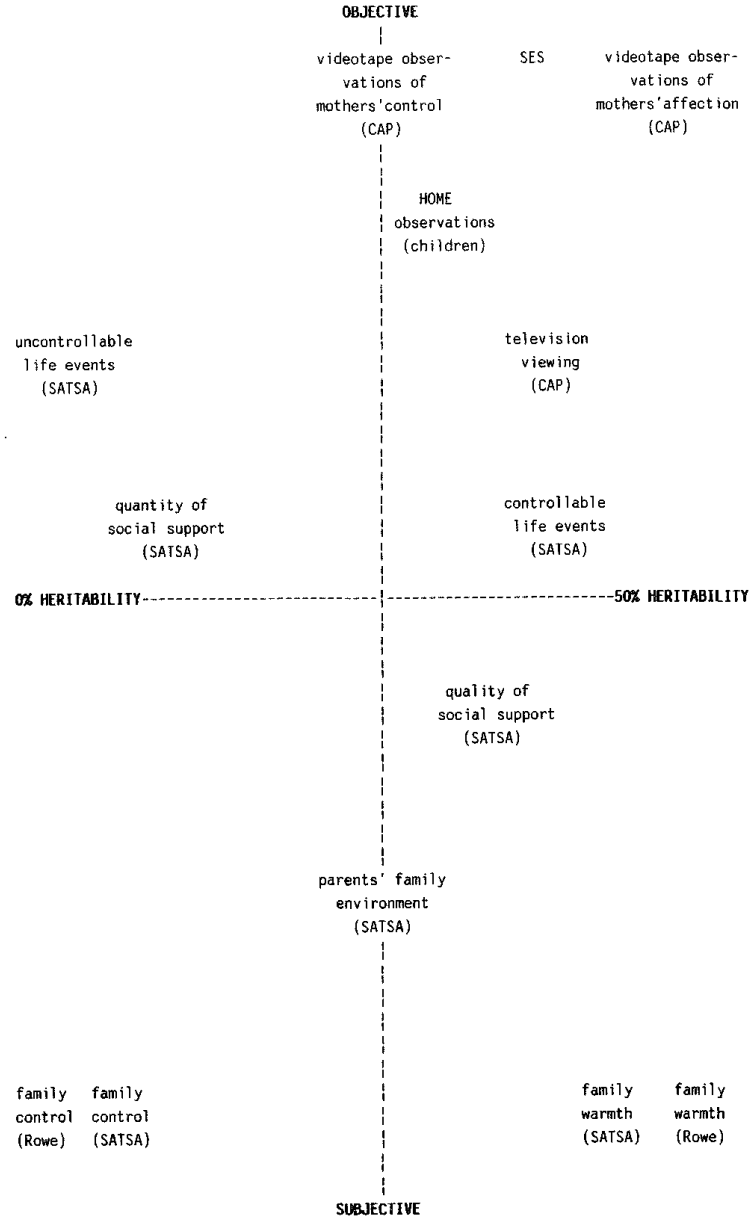
KENNETH S. KENDLER[1,2]* AND JESSICA H. BAKER[1,3]

Constructs	No. studies	Studies included	Total *N*	Weighted mean
Stressful life events				
Total life events	6	Wierzbicki, 1989; Plomin *et al.* 1990; Kendler *et al.* 1993; Thapar & McGuffin, 1996; Bolinskey *et al.* 2004; Wang *et al.* 2005	6197	0·28
Negative life events	3	Plomin *et al.* 1990; Wierzbicki, 1989; Thapar & McGuffin, 1996	731	0·39
Positive life events	3	Plomin *et al.* 1990; Wierzbicki, 1989; Thapar & McGuffin, 1996	731	0·34
Independent life events	6	Plomin *et al.* 1990; Billig *et al.* 1996; Thapar & McGuffin, 1996; Foley *et al.* 1996; Kendler *et al.* 1999; Bolinskey *et al.* 2004	5056	0·17
Dependent life events	5	Plomin *et al.* 1990; Billig *et al.* 1996; Foley *et al.* 1996; Kendler *et al.* 1999; Bolinskey *et al.* 2004	4459	0·31
Selection into trauma	4	Lyons *et al.* 1993; Jang *et al.* 2001; Stein *et al.* 2002; Middeldorp *et al.* 2005	6558	0·36
Selection into non-assaultive trauma	2	Jang *et al.* 2001; Stein *et al.* 2002	569	0·07
Divorce	2	McGue & Lykken, 1992; Middeldorp *et al.* 2005	5692	0·35
Child-based reports of parenting behavior				
Maternal warmth	7	Rowe, 1981; Rende *et al.* 1992; Plomin *et al.* 1994; O'Connor *et al.* 1995; Kendler, 1996; Lichtenstein *et al.* 2003; Neiderhiser *et al.* 2004	3446	0·37
Paternal warmth	5	Rowe, 1981; Plomin *et al.* 1994; O'Connor *et al.* 1995; Kendler, 1996; Lichtenstein *et al.* 2003	2664	0·34
Maternal control	5	Rende *et al.* 1992; O'Connor *et al.* 1995; Kendler, 1996; Lichtenstein *et al.* 2003; Neiderhiser *et al.* 2004	2330	0·15
Paternal control	3	O'Connor *et al.* 1995; Kendler, 1996; Lichtenstein *et al.* 2003	1448	0·17
Paternal negativity	2	Plomin *et al.* 1994; O'Connor *et al.* 1995	377	0·12
Paternal protectiveness	2	Kendler, 1996; Lichtenstein *et al.* 2003	2198	0·20
Maternal protectiveness	2	Kendler, 1996; Lichtenstein *et al.* 2003	2198	0·26
Parent-based reports of parenting behavior				
Parental warmth	4	Perusse *et al.* 1994; Kendler, 1996; Deater-Deckard *et al.* 1999; Deater-Deckard, 2000	1690	0·35
Parental control	3	Kendler, 1996; Losoya *et al.* 1997; Spinath & O'Connor, 2003	433	0·20
Parental protectiveness	3	Perusse *et al.* 1994; Kendler, 1996; Spinath & O'Connor, 2003	1477	0·23
Parental negativity	7	O'Connor *et al.* 1995; Losoya *et al.* 1997; Deater-Deckard *et al.* 1999, 2001; Deater-Deckard, 2000; Neiderhiser *et al.* 2004; Boivin *et al.* 2005	4766	0·19
Family environment				
Cohesion/connectedness	4	Plomin *et al.* 1988, 1989; Jacobson & Rowe, 1999; Jang *et al.* 2001	1911	0·24
Conflict	3	Plomin *et al.* 1988, 1989; Jacobson & Rowe, 1999	1428	0·30
Organization	3	Plomin *et al.* 1988, 1989; Jacobson & Rowe, 1999	1428	0·25
Expressiveness	3	Plomin *et al.* 1988, 1989; Jacobson & Rowe, 1999	1428	0·24
Active	3	Plomin *et al.* 1988, 1989; Jacobson & Rowe, 1999	1428	0·26
Control	3	Plomin *et al.* 1988, 1989; Jacobson & Rowe, 1999	1428	0·18
Social support				
Friend problem	2	Kendler *et al.* 1997; Agrawal *et al.* 2002	2860	0·23
Relative problem	2	Kendler *et al.* 1997; Agrawal *et al.* 2002	2860	0·38
Friend support	3	Kessler *et al.* 1992; Kendler *et al.* 1997; Agrawal *et al.* 2002	4502	0·17
Relative support	3	Kessler *et al.* 1992; Kendler *et al.* 1997; Agrawal *et al.* 2002	4502	0·31
Confidants	3	Kessler *et al.* 1992; Kendler *et al.* 1997; Agrawal *et al.* 2002	4502	0·31
Social integration	2	Kendler *et al.* 1997; Agrawal *et al.* 2002	2860	0·31

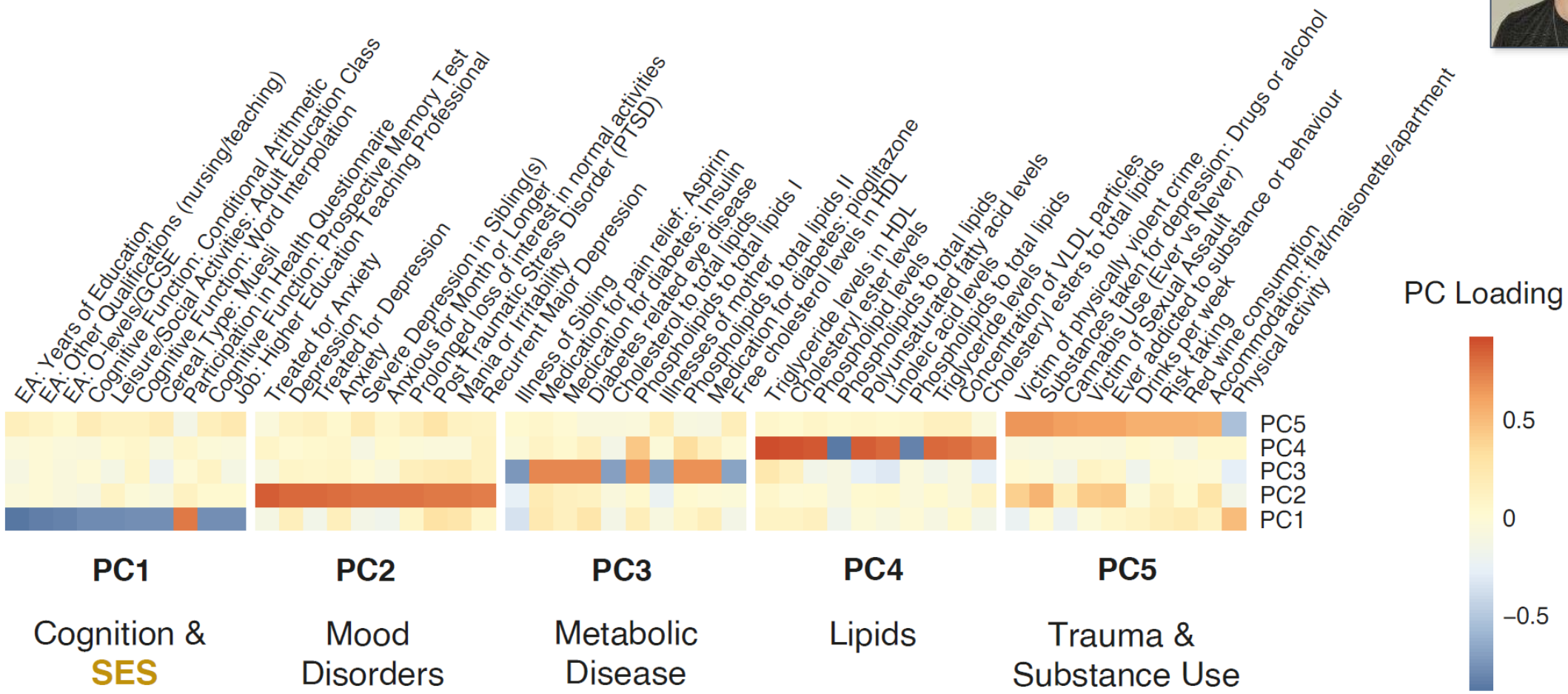
BEHAVIORAL AND BRAIN SCIENCES (1991) 14, 373–427
Printed in the United States of America

The nature of nurture: Genetic influence on "environmental" measures

Robert Plomin[a] and C. S. Bergeman[b]

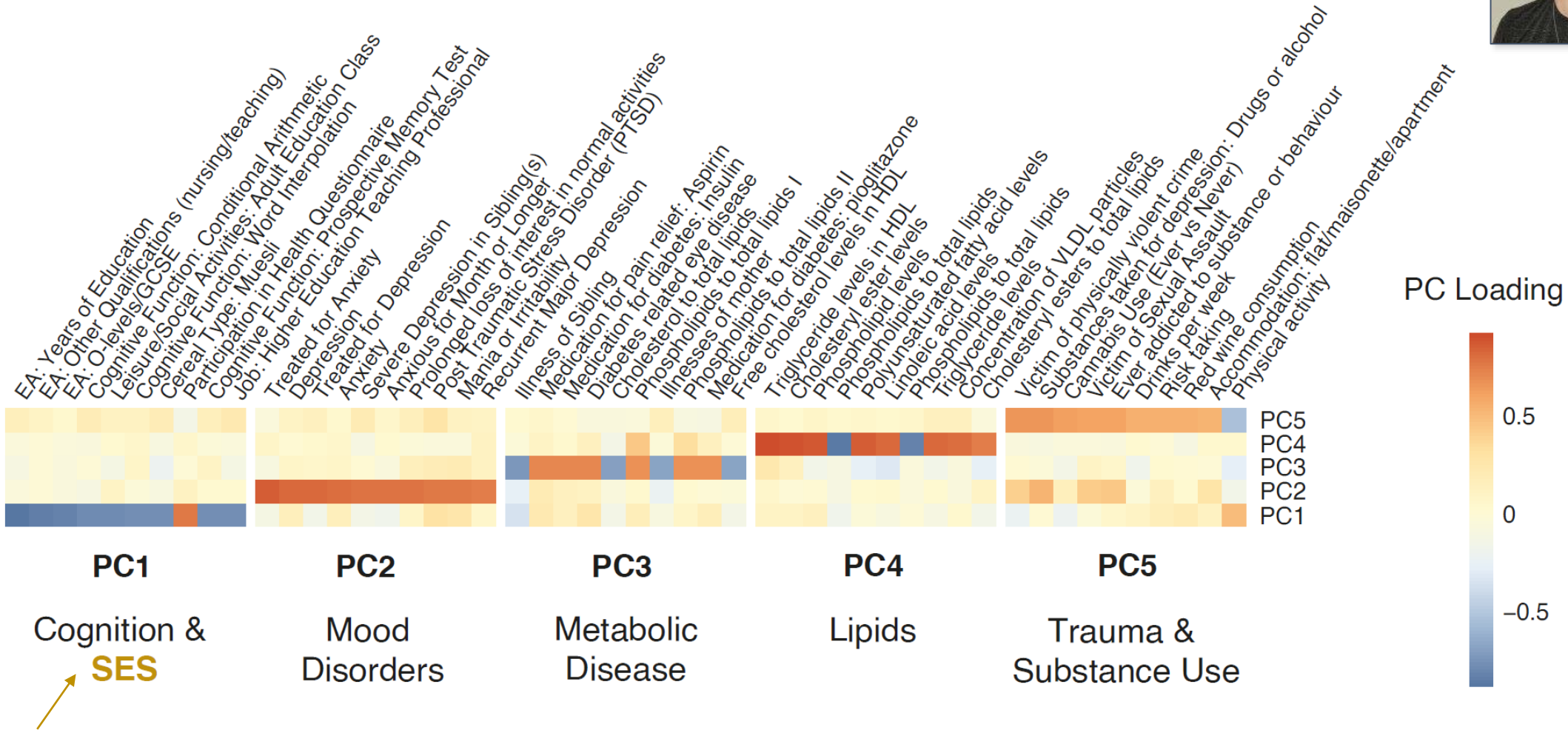


PCA on GWAS summary statistics from GWAS Catalog with N > 50k:



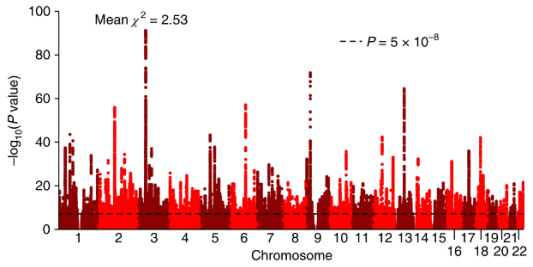
David van den Berg, Karin Verweij, Dirk Smit, Abdel Abdellaoui (2024; unpublished)

PCA on GWAS summary statistics from GWAS Catalog with N > 50k:



Explains 10% of the variance!

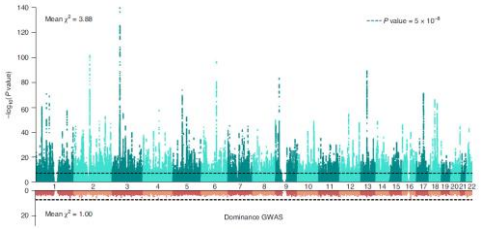
David van den Berg, Karin Verweij, Dirk Smit, Abdel Abdellaoui (2024; unpublished)



ARTICLES
https://doi.org/10.1038/s41588-018-0147-3
nature genetics

Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals

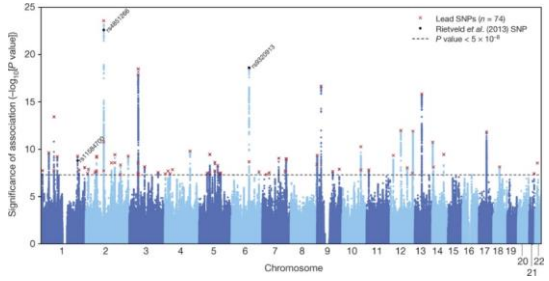
2018 – N = 1,131,881



nature genetics
ARTICLES
https://doi.org/10.1038/s41588-022-01016-z
OPEN

Polygenic prediction of educational attainment within and between families from genome-wide association analyses in 3 million individuals

2022 – N = 3,037,499

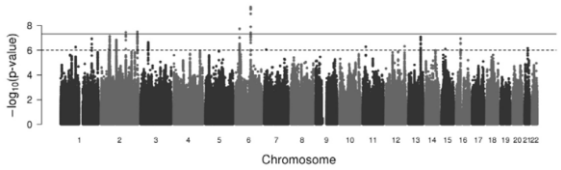


LETTER
doi:10.1038/nature17671

Genome-wide association study identifies 74 loci associated with educational attainment

26 MAY 2016 | VOL 533 | NATURE

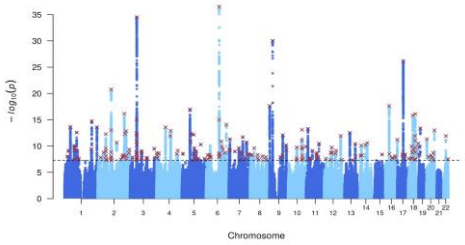
2016 – N = 293,723



SCIENCE VOL 340 21 JUNE 2013

GWAS of 126,559 Individuals Identifies Genetic Variants Associated with Educational Attainment

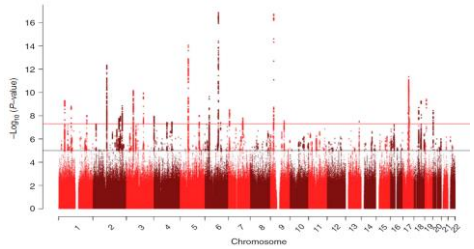
2013 – N = 126,559



bioRχiv
New Results
Follow this preprint

Associations between common genetic variants and income provide insights about the socioeconomic health gradient

2024 – N = 668,288



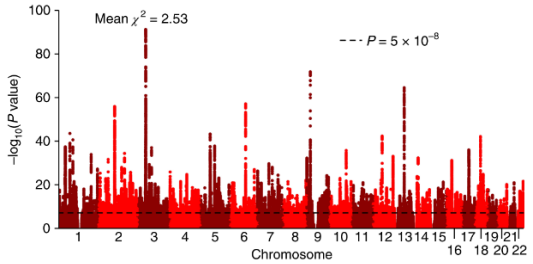
nature COMMUNICATIONS
ARTICLE
https://doi.org/10.1038/s41467-019-13585-5 OPEN

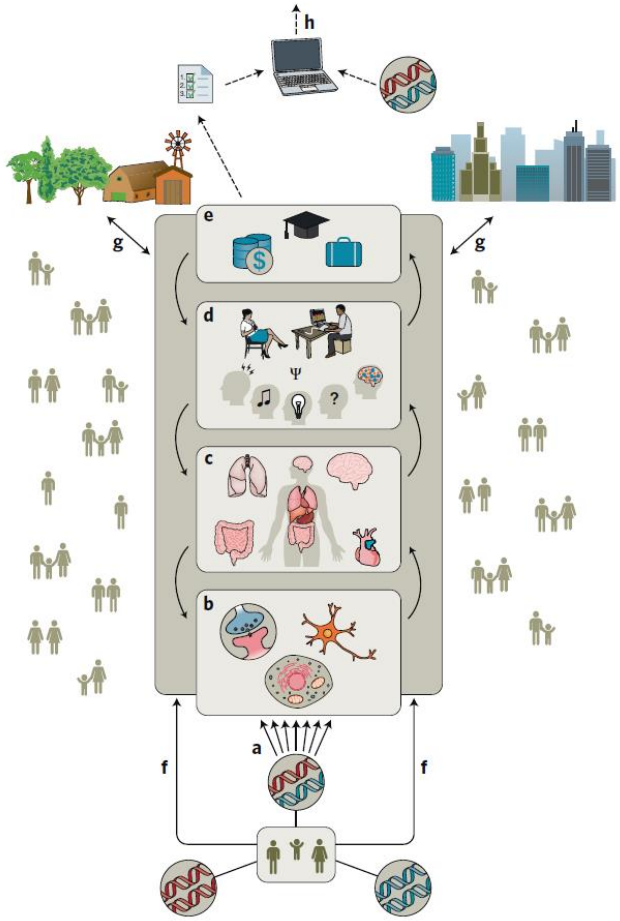
Genome-wide analysis identifies molecular systems and 149 genetic loci associated with income

2019 – N = 286,301

Educational Attainment

Income





GWASs on social outcomes contain signals from **correlated traits** and the **environment**

nature human behaviour
REVIEW ARTICLE
https://doi.org/10.1038/s41562-021-01110-y
Check for updates

Dissecting polygenic signals from genome-wide association studies on human behaviour

Abdel Abdellaoui and Karin J. H. Verweij

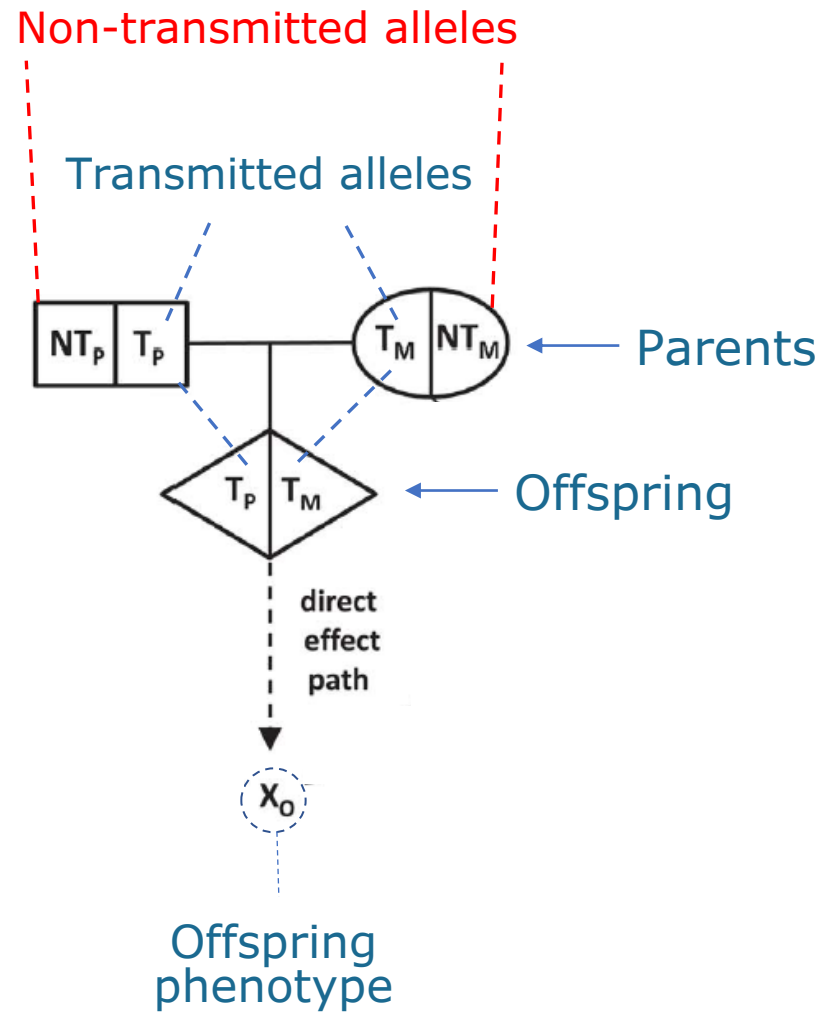
Gene-Environment Correlations - Families

Science **359**, 424–428 (2018)

HUMAN GENOMICS

The nature of nurture: Effects of parental genotypes

Augustine Kong,[1,2,3*] Gudmar Thorleifsson,[1] Michael L. Frigge,[1] Bjarni J. Vilhjalmsson,[4,5] Alexander I. Young,[1,2,6] Thorgeir E. Thorgeirsson,[1] Stefania Benonisdottir,[1] Asmundur Oddsson,[1] Bjarni V. Halldorsson,[1] Gisli Masson,[1] Daniel F. Gudbjartsson,[1,3] Agnar Helgason,[1,7] Gyda Bjornsdottir,[1] Unnur Thorsteinsdottir,[1,8] Kari Stefansson[1,8*]

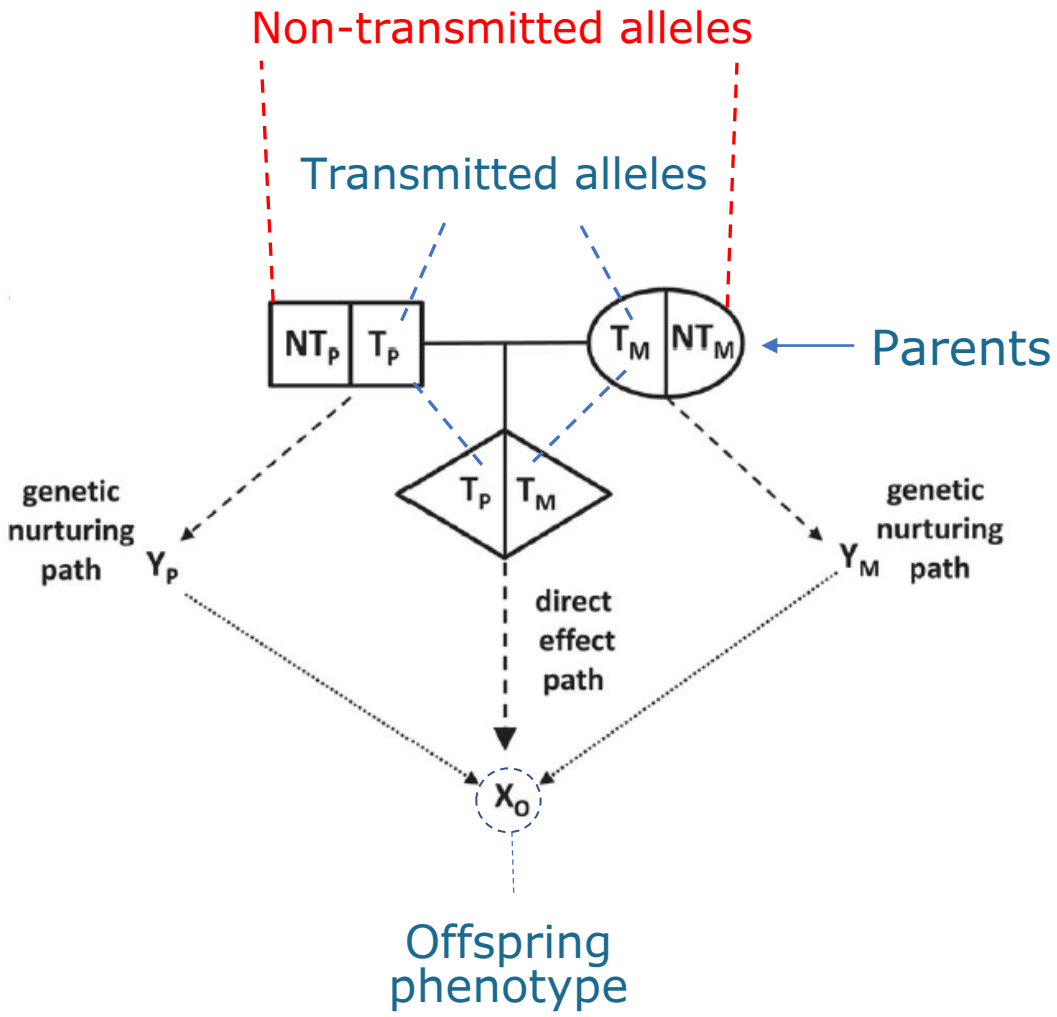


Science **359**, 424–428 (2018)

HUMAN GENOMICS

The nature of nurture: Effects of parental genotypes

Augustine Kong,[1,2,3*] Gudmar Thorleifsson,[1] Michael L. Frigge,[1] Bjarni J. Vilhjalmsson,[4,5] Alexander I. Young,[1,2,6] Thorgeir E. Thorgeirsson,[1] Stefania Benonisdottir,[1] Asmundur Oddsson,[1] Bjarni V. Halldorsson,[1] Gisli Masson,[1] Daniel F. Gudbjartsson,[1,3] Agnar Helgason,[1,7] Gyda Bjornsdottir,[1] Unnur Thorsteinsdottir,[1,8] Kari Stefansson[1,8*]



Science **359**, 424–428 (2018)

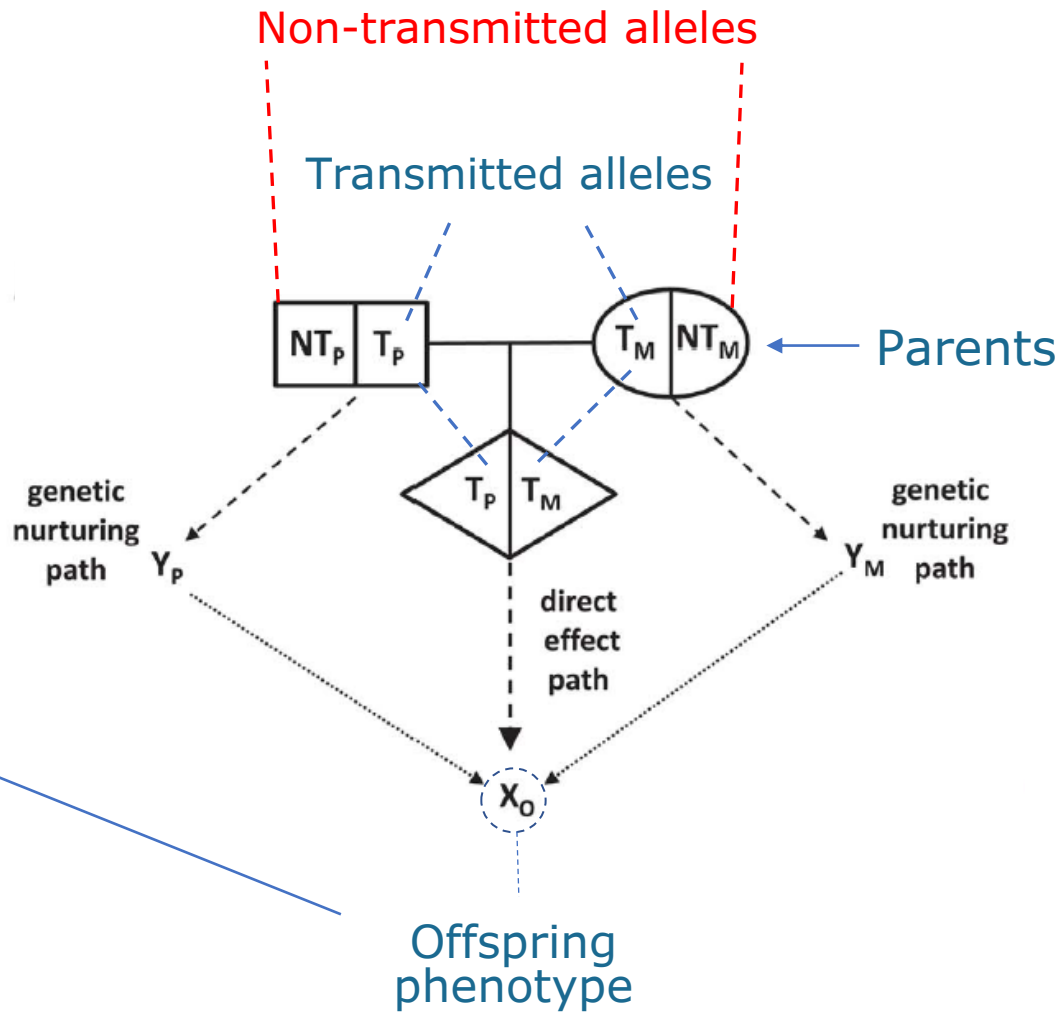
HUMAN GENOMICS

The nature of nurture: Effects of parental genotypes

Augustine Kong,[1,2,3*] Gudmar Thorleifsson,[1] Michael L. Frigge,[1] Bjarni J. Vilhjalmsson,[4,5] Alexander I. Young,[1,2,6] Thorgeir E. Thorgeirsson,[1] Stefania Benonisdottir,[1] Asmundur Oddsson,[1] Bjarni V. Halldorsson,[1] Gisli Masson,[1] Daniel F. Gudbjartsson,[1,3] Agnar Helgason,[1,7] Gyda Bjornsdottir,[1] Unnur Thorsteinsdottir,[1,8] Kari Stefansson[1,8*]

Non-transmitted educational attainment alleles are associated with:

- Educational attainment
- Age at first child
- High-density lipoprotein (HDL)
- BMI
- Fasting glucose level
- Height
- Cigarettes per day
- Overall health



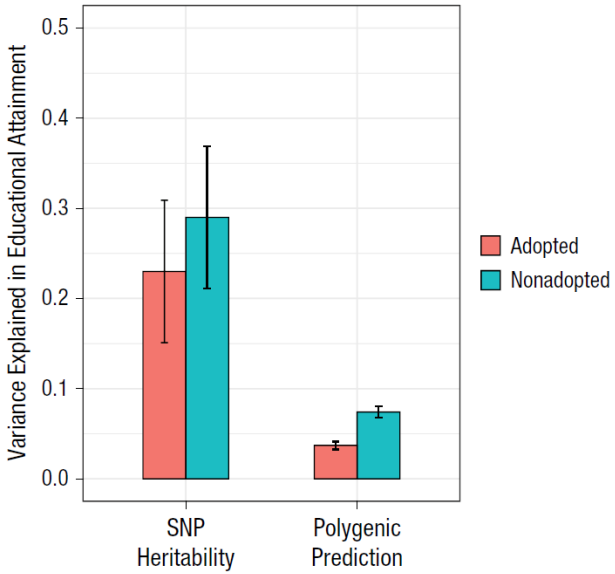
Research Article

Comparison of Adopted and Nonadopted Individuals Reveals Gene–Environment Interplay for Education in the UK Biobank

Rosa Cheesman[1], Avina Hunjan[1,2], Jonathan R. I. Coleman[1,2], Yasmin Ahmadzadeh[1], Robert Plomin[1], Tom A. McAdams[1], Thalia C. Eley[1,2], and Gerome Breen[1,2]

Psychological Science
2020, Vol. 31(5) 582–591

Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/0956797620904450
www.psychologicalscience.org/PS

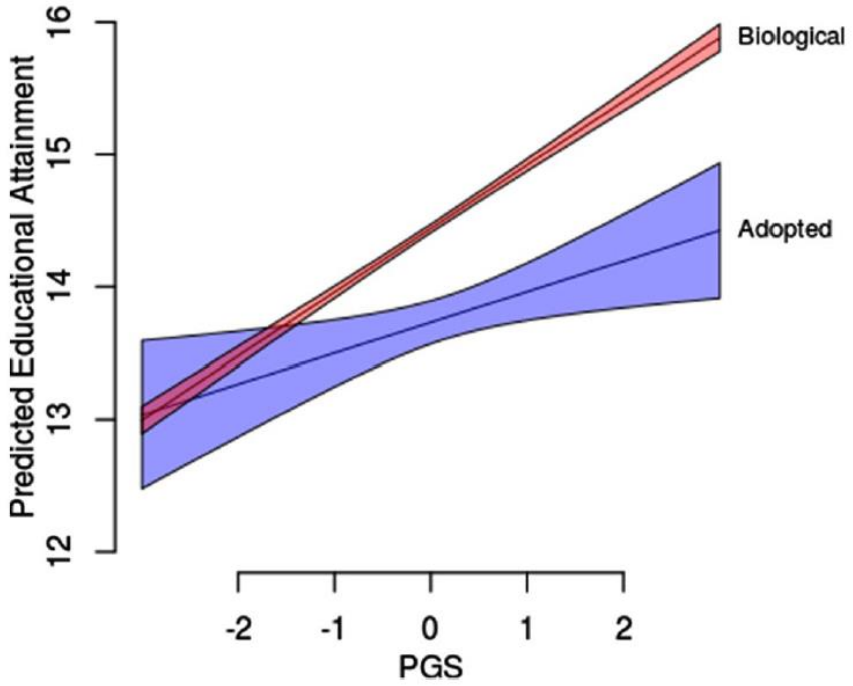


Behavior Genetics
https://doi.org/10.1007/s10519-020-10000-4

ORIGINAL RESEARCH

Separating Measured Genetic and Environmental Effects: Evidence Linking Parental Genotype and Adopted Child Outcomes

Benjamin W. Domingue[1] · Jason Fletcher[2]

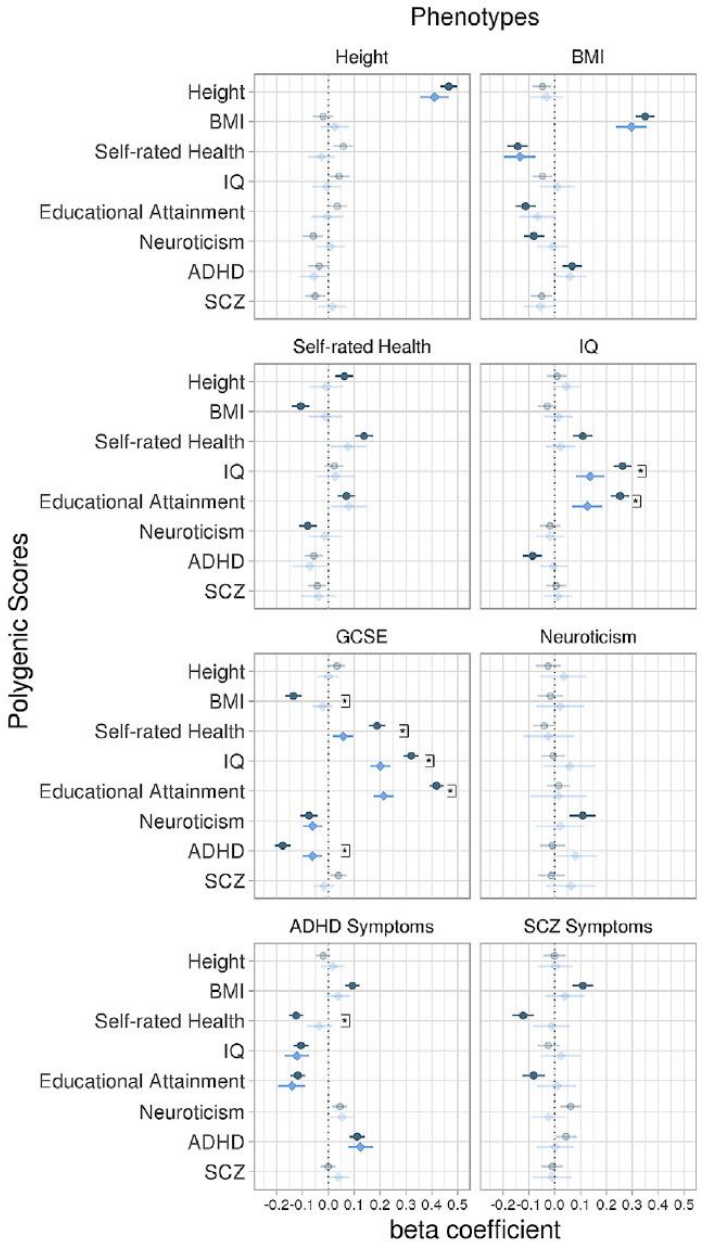


The American Journal of Human Genetics *105*, 351–363, August 1, 2019 **ARTICLE**

Comparing Within- and Between-Family Polygenic Score Prediction

Saskia Selzam,[1,*] Stuart J. Ritchie,[1] Jean-Baptiste Pingault,[1,2] Chandra A. Reynolds,[3] Paul F. O'Reilly,[1,4] and Robert Plomin[1]

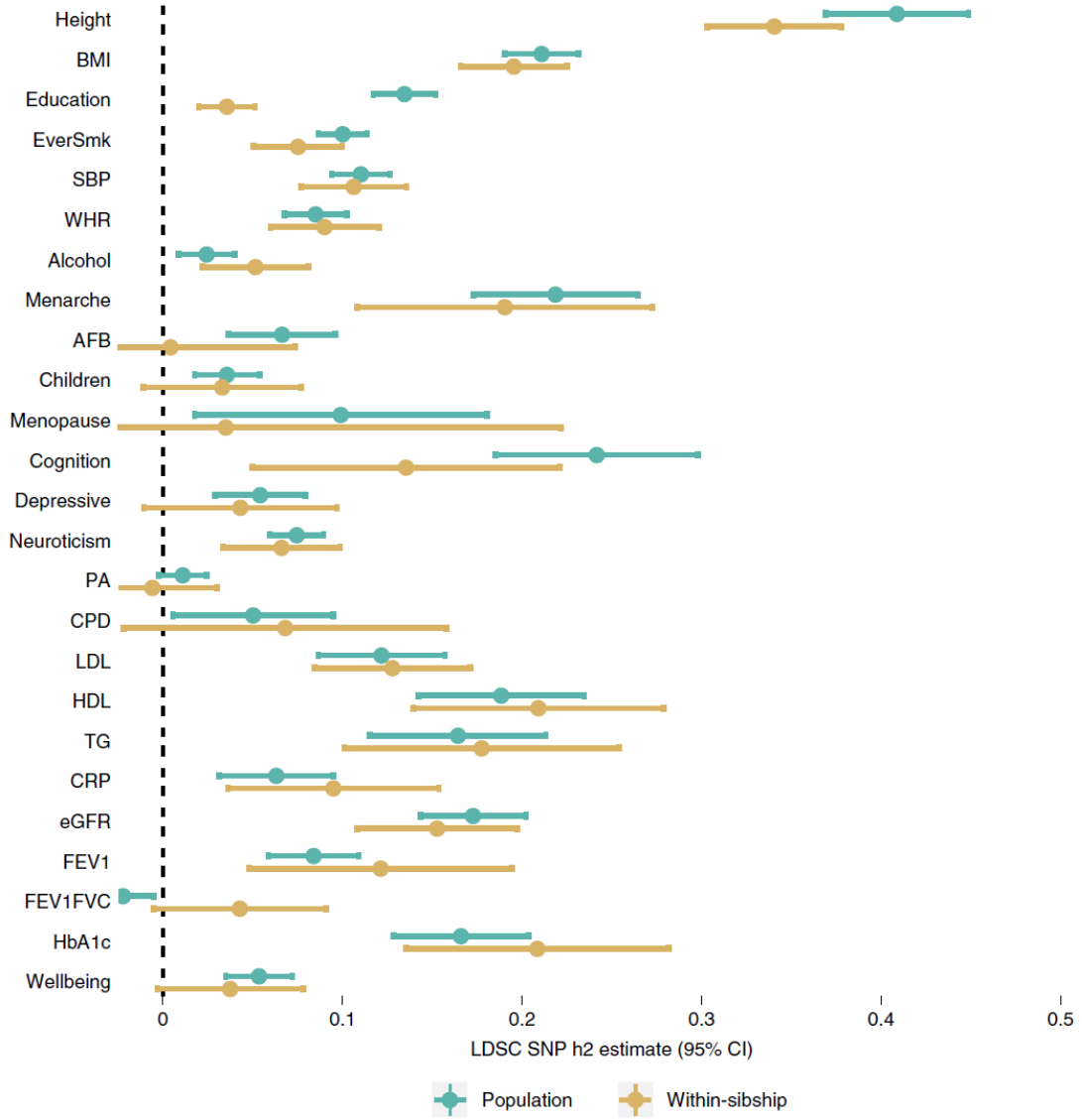
Predictive power of polygenic scores of cognitive traits (intelligence & education) was 60% greater between families than within families.



nature genetics
ARTICLES
https://doi.org/10.1038/s41588-022-01062-7
Check for updates

OPEN

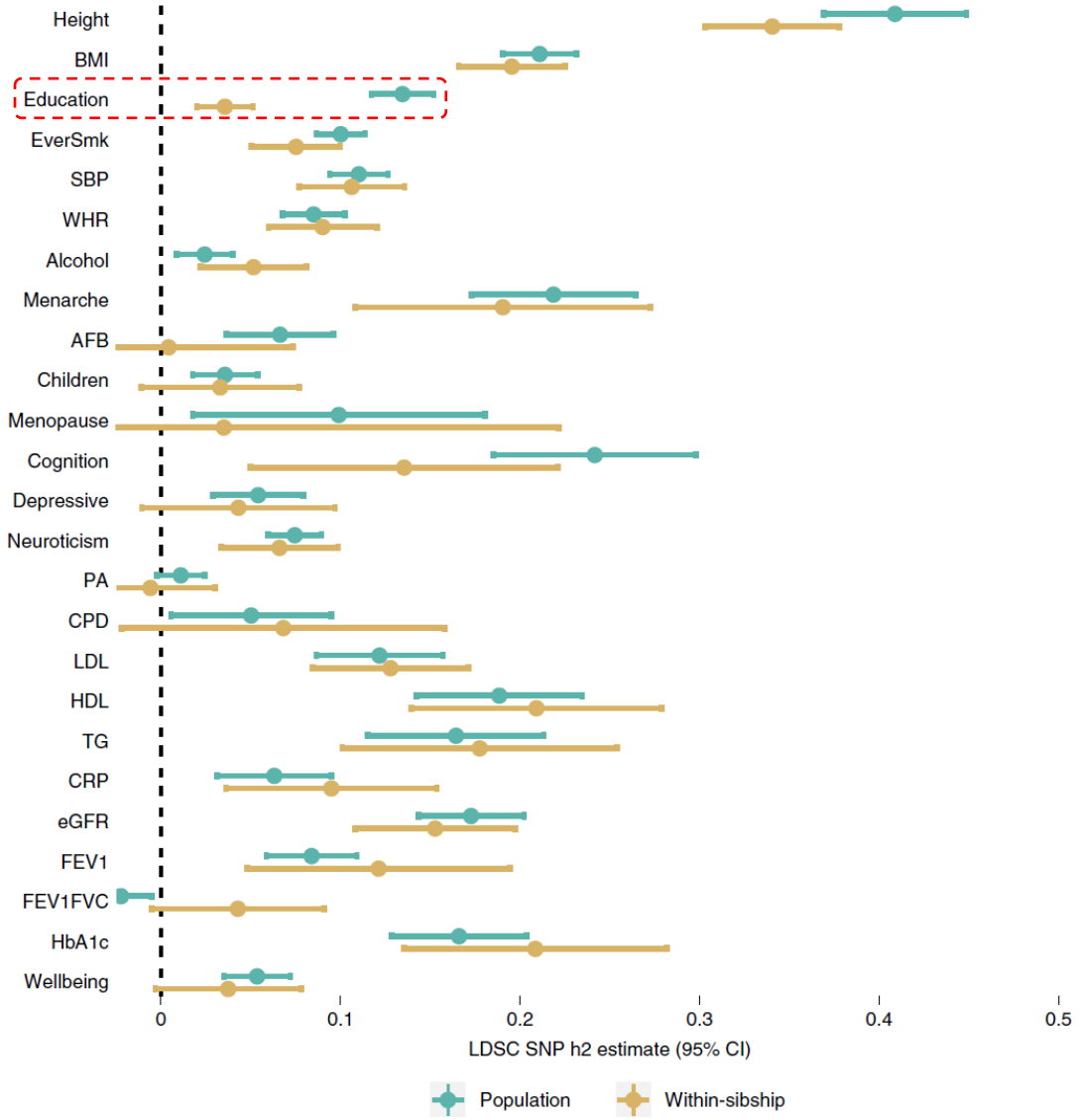
Within-sibship genome-wide association analyses decrease bias in estimates of direct genetic effects



nature genetics
ARTICLES
https://doi.org/10.1038/s41588-022-01062-7
Check for updates

OPEN

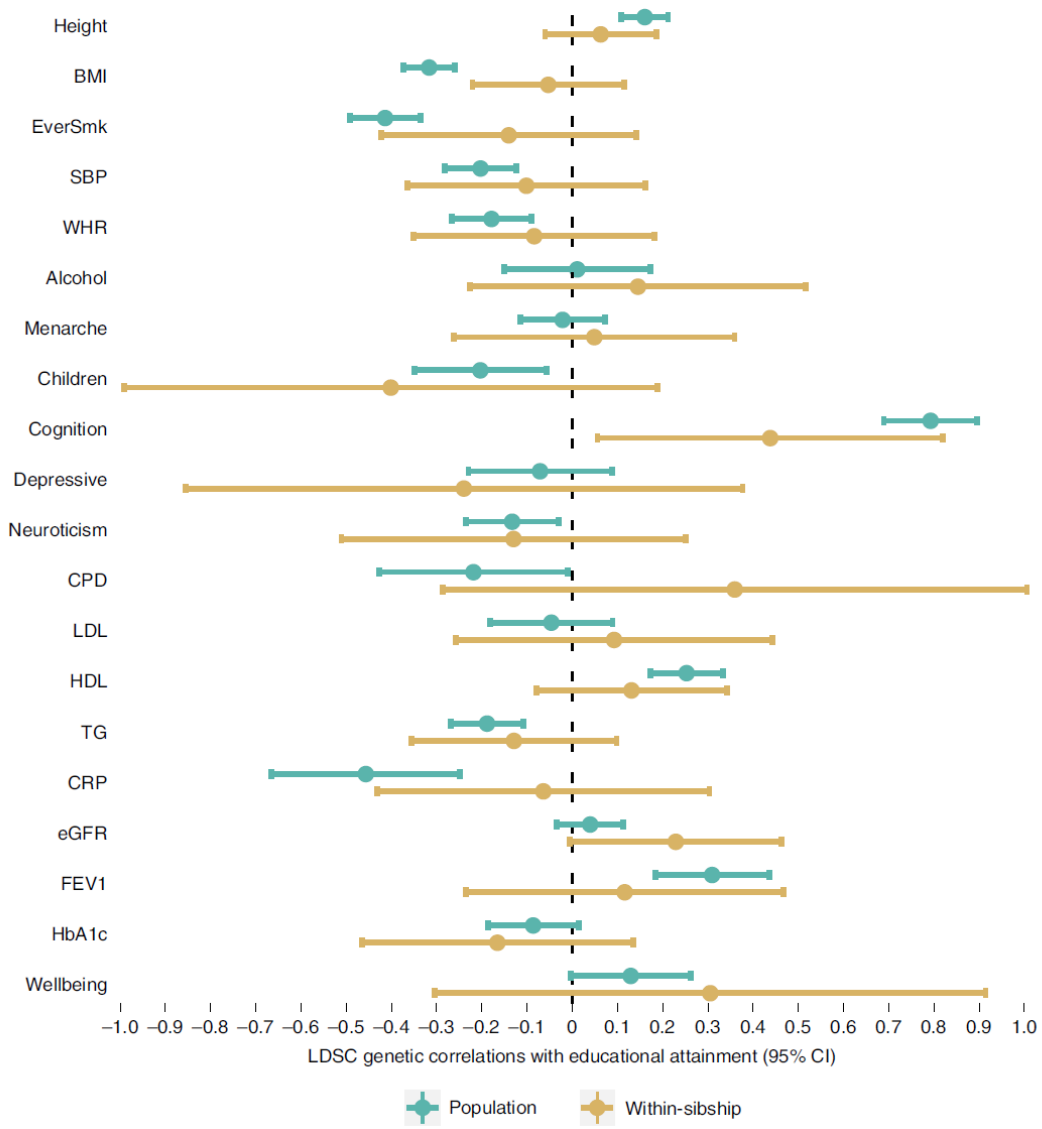
Within-sibship genome-wide association analyses decrease bias in estimates of direct genetic effects



nature genetics
ARTICLES
https://doi.org/10.1038/s41588-022-01062-7
Check for updates

OPEN

Within-sibship genome-wide association analyses decrease bias in estimates of direct genetic effects



nature human behaviour

Article

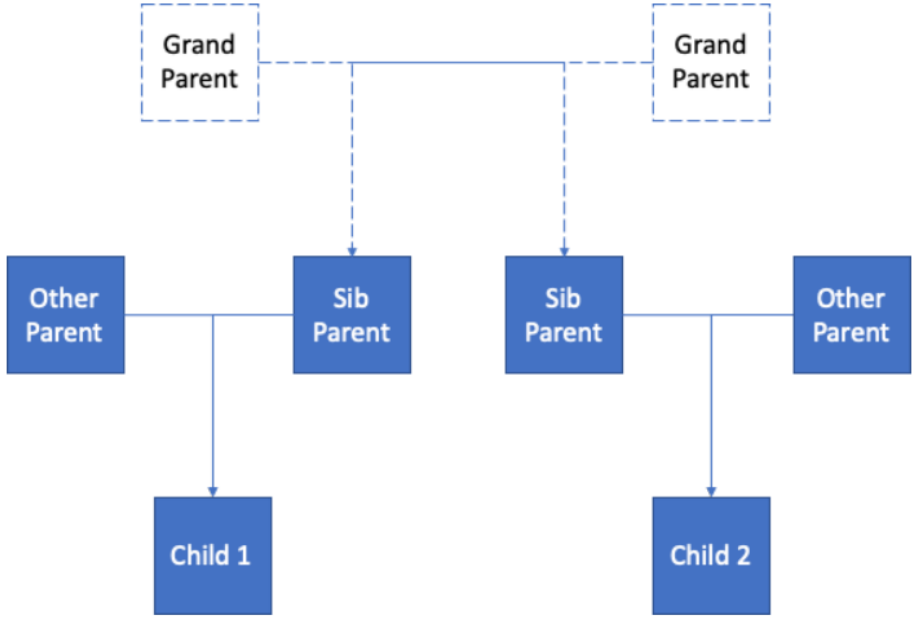
More than nature and nurture, indirect genetic effects on children's academic achievement are consequences of dynastic social processes

Received: 12 May 2022

Accepted: 29 November 2023

Published online: 15 January 2024

Michel G. Nivard[1,2], Daniel W. Belsky[3,4], K. Paige Harden[5,6], Tina Baier[7], Ole A. Andreassen[8,9], Eivind Ystrøm[10,11], Elsje van Bergen[1,2,12] & Torkild H. Lyngstad[7]



Blue squares indicate MoBa participants. White squares (grandparents) are identified through register links.

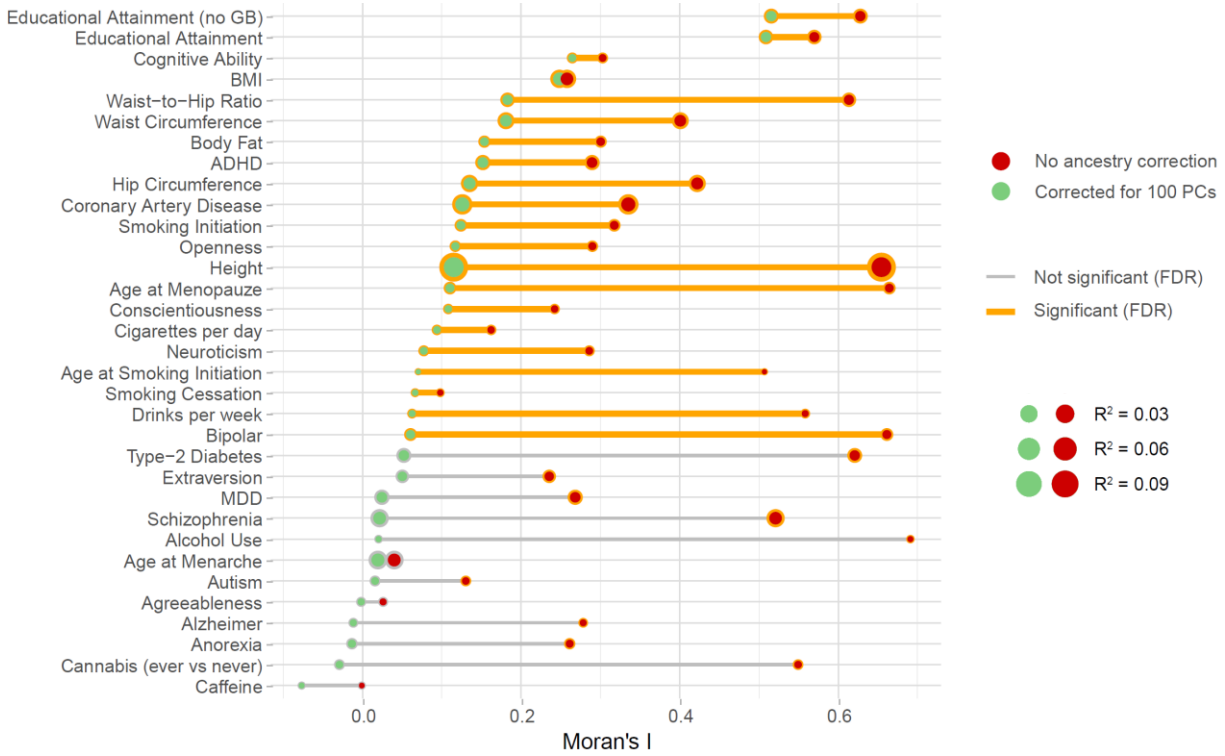
Gene-Environment Correlations - Geographic

Geography & Polygenic Scores

ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]



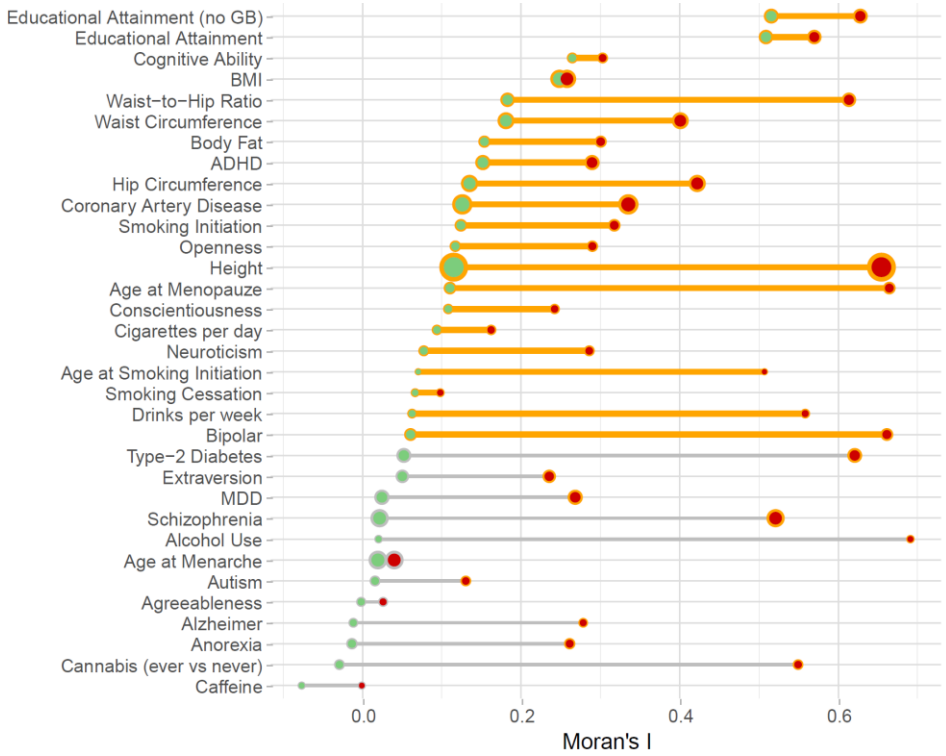
Moran's I = measure for geographic clustering

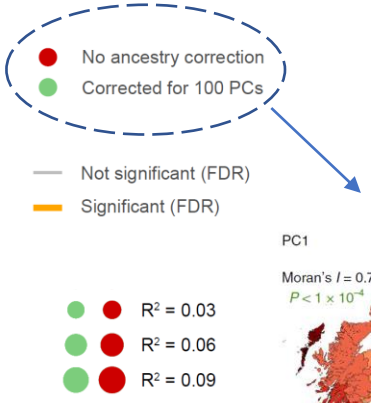
Geography & Polygenic Scores

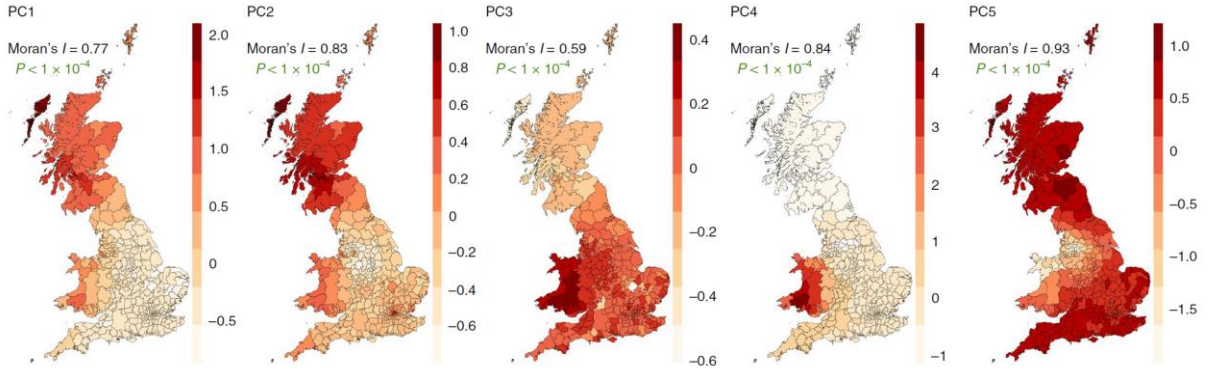
ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]







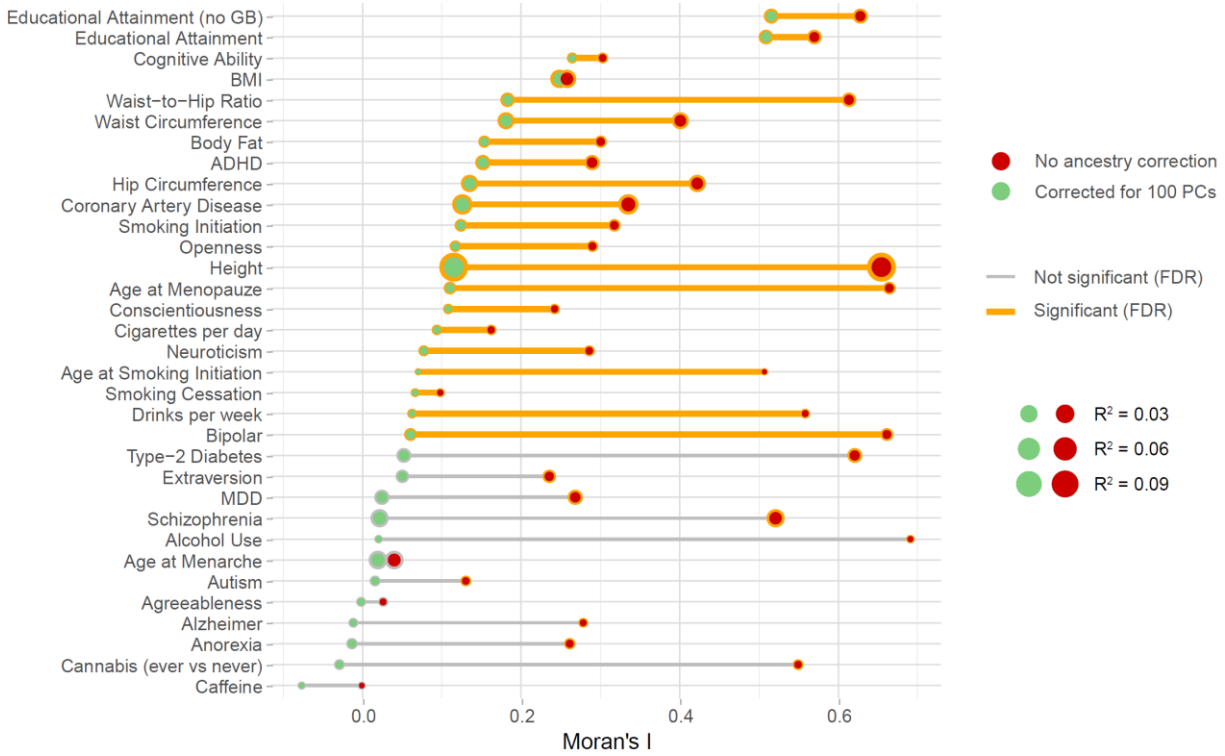
Moran's I = measure for geographic clustering

Geography & Polygenic Scores

ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

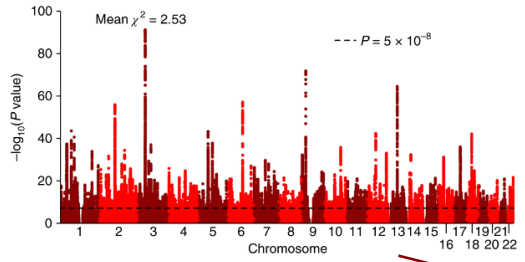
Genetic correlates of social stratification in Great Britain

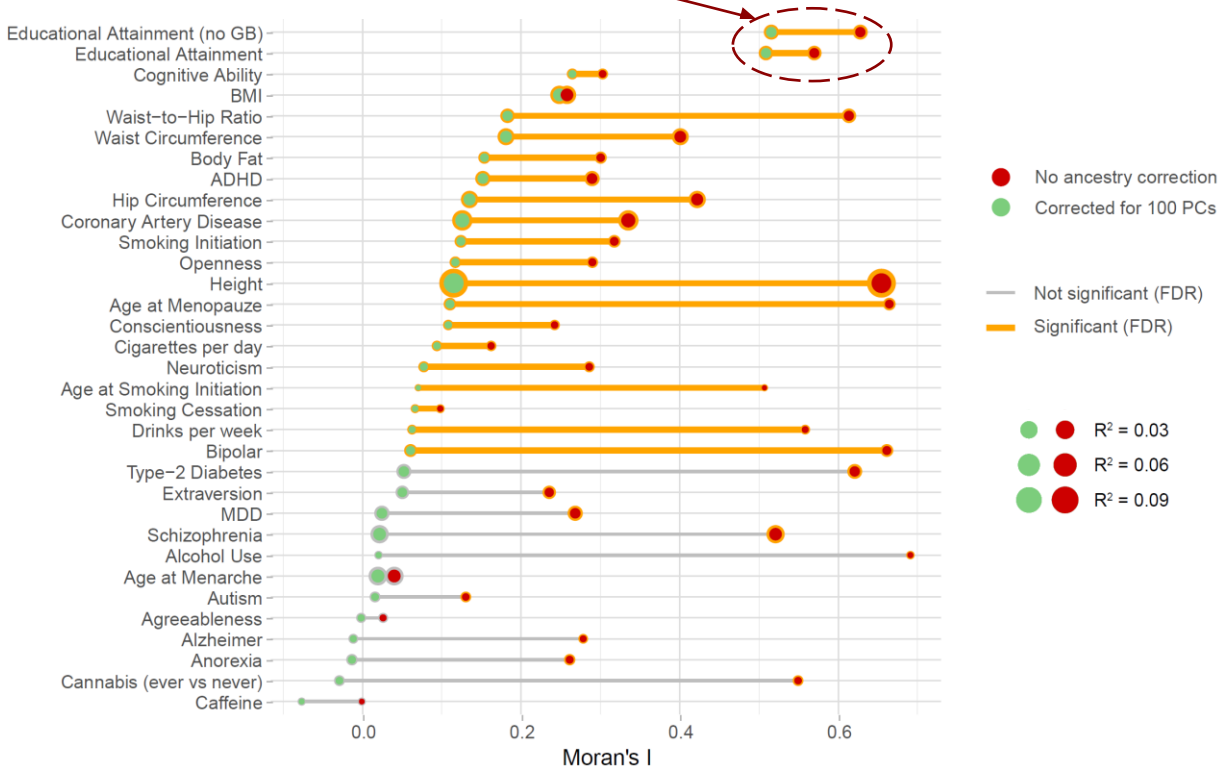
Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]



Moran's I = measure for geographic clustering

Geography & Polygenic Scores



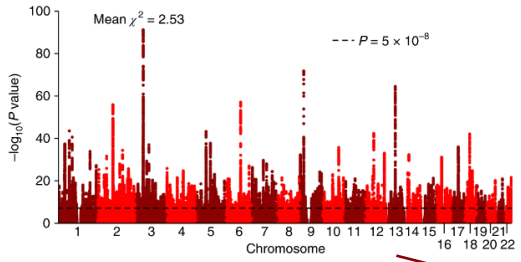


Moran's I = measure for geographic clustering

ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]

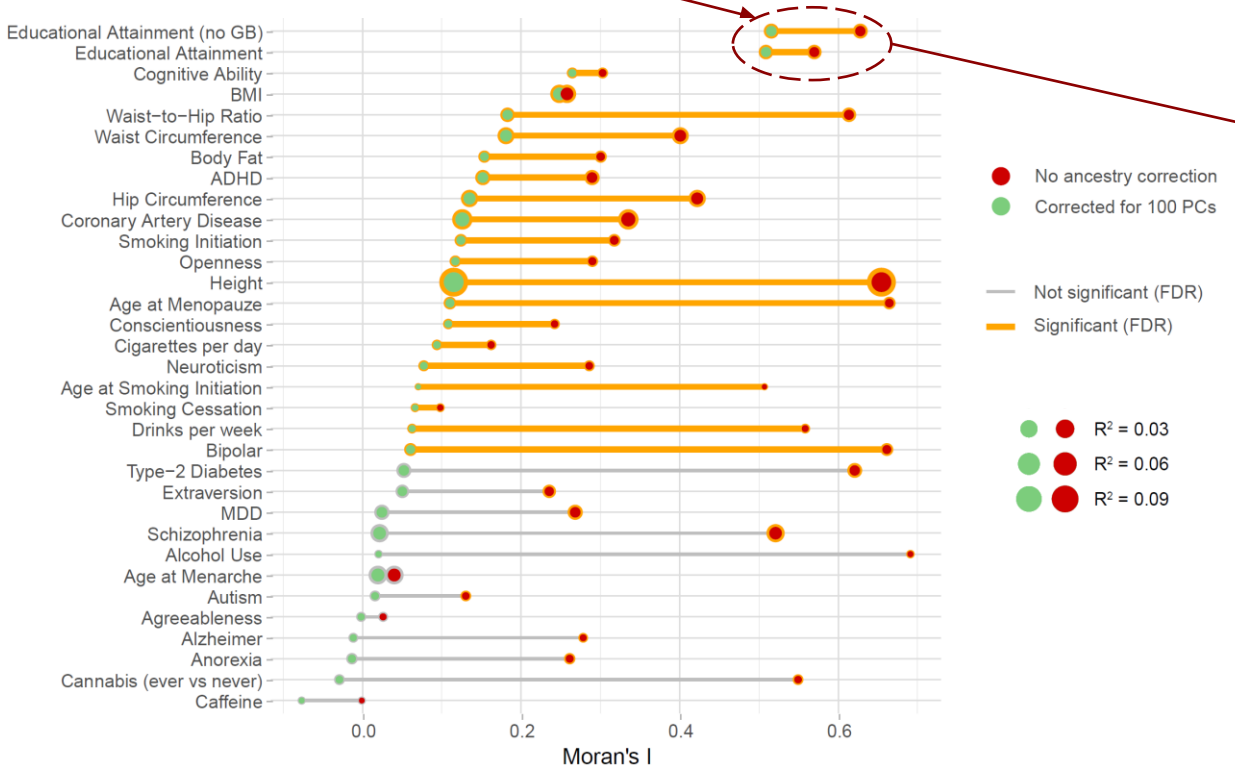


Geography & Polygenic Scores

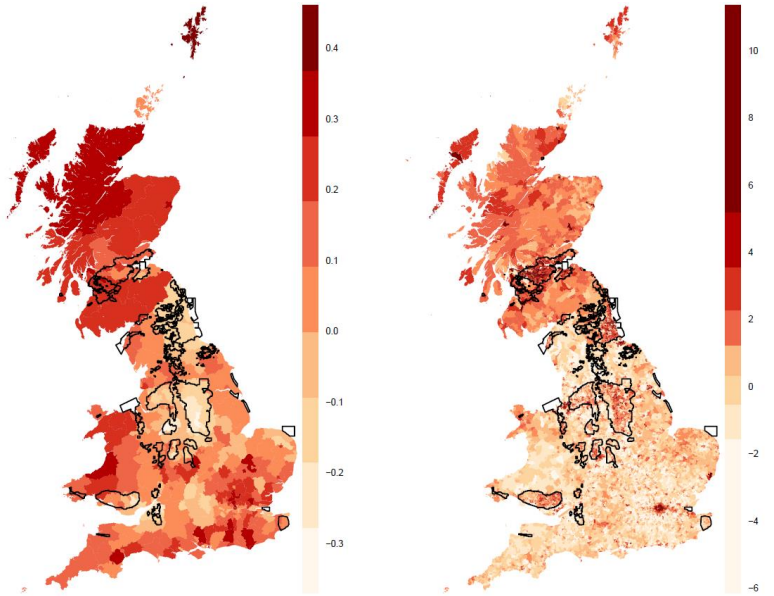
ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]



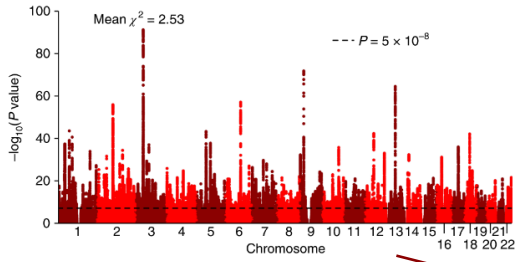
Moran's I = measure for geographic clustering



Educational Attainment Polygenic Score

Townsend Index (measure of economic deprivation)

black lines = coal regions

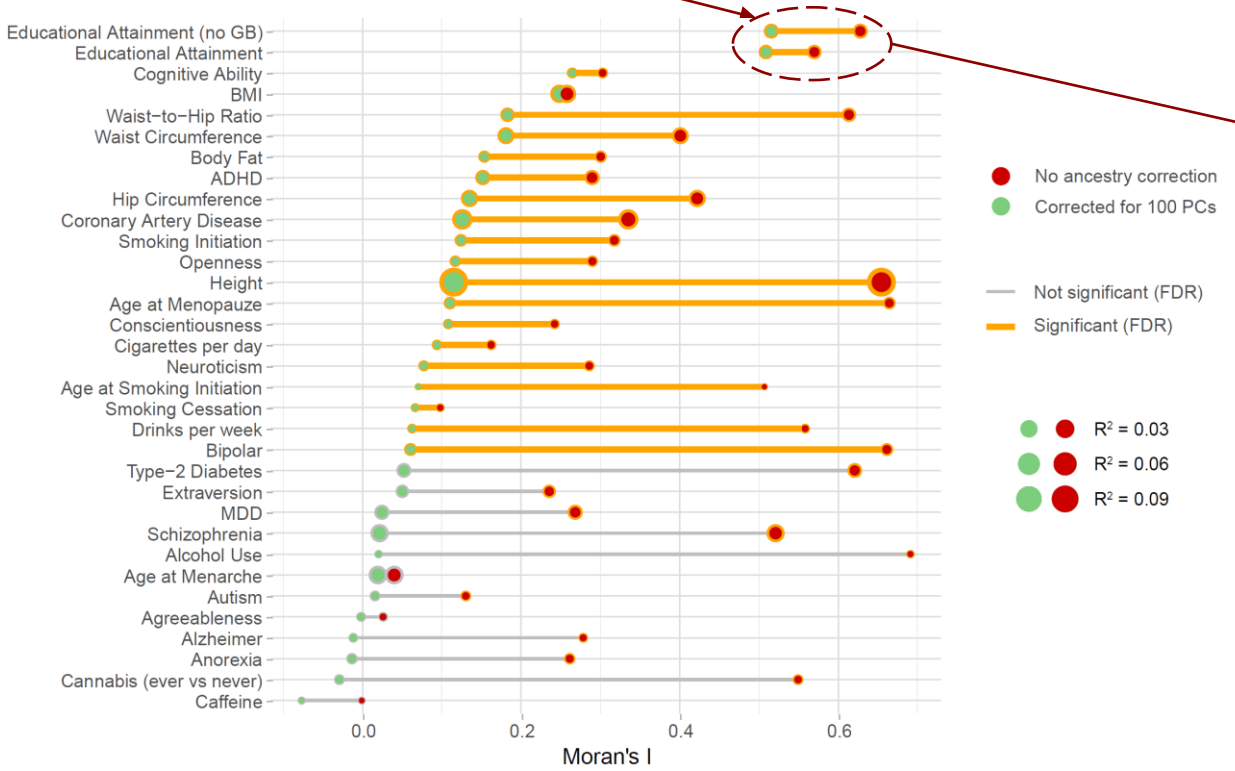


Geography & Polygenic Scores

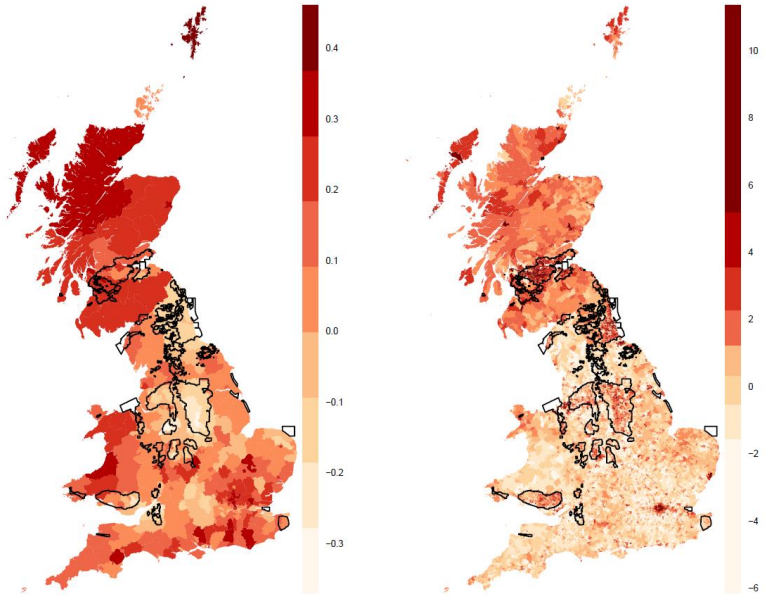
ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]



Moran's I = measure for geographic clustering

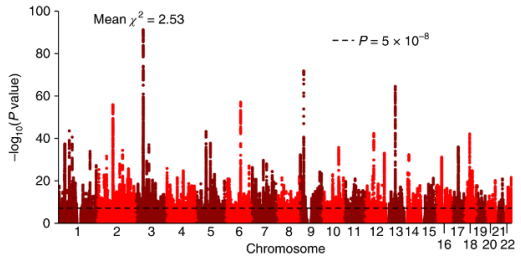


Educational Attainment Polygenic Score

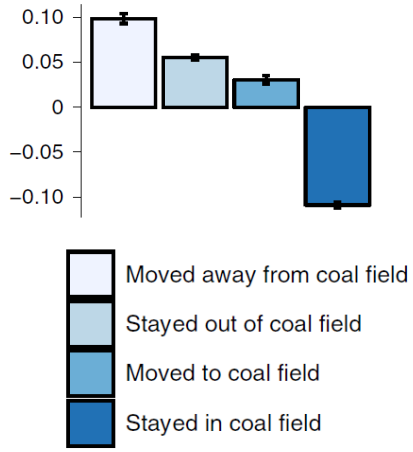
Townsend Index (measure of economic deprivation)

black lines = coal regions

Migration & SES



Educational Attainment Polygenic Score

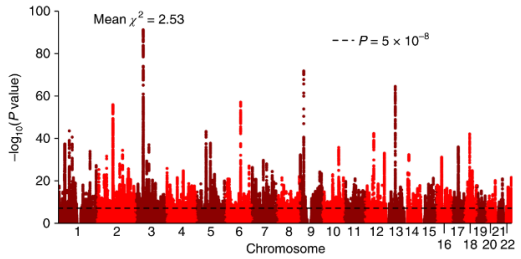


ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]

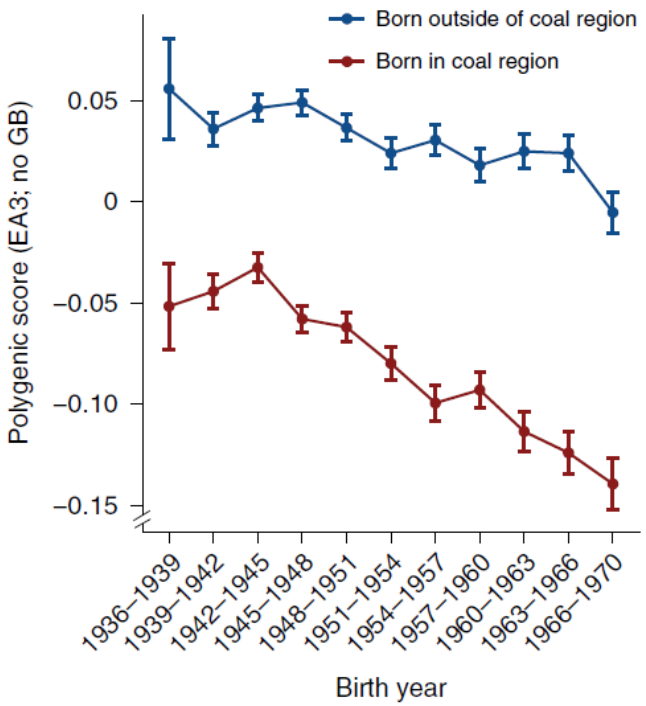
Migration & SES

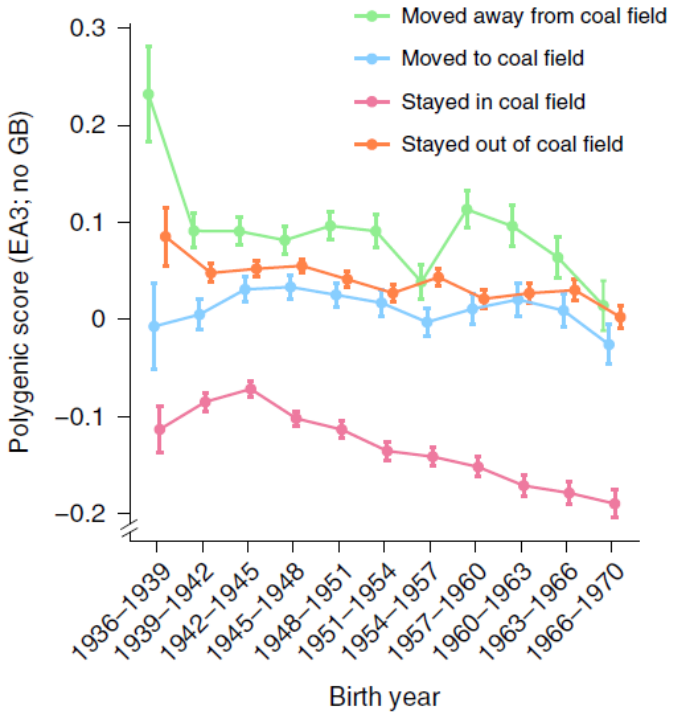


ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

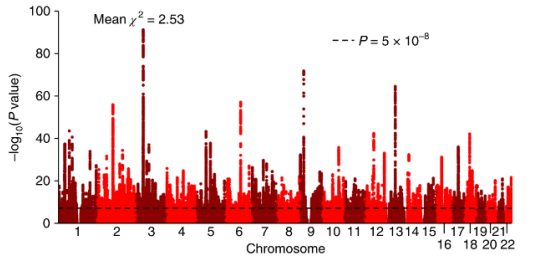
Genetic correlates of social stratification in Great Britain

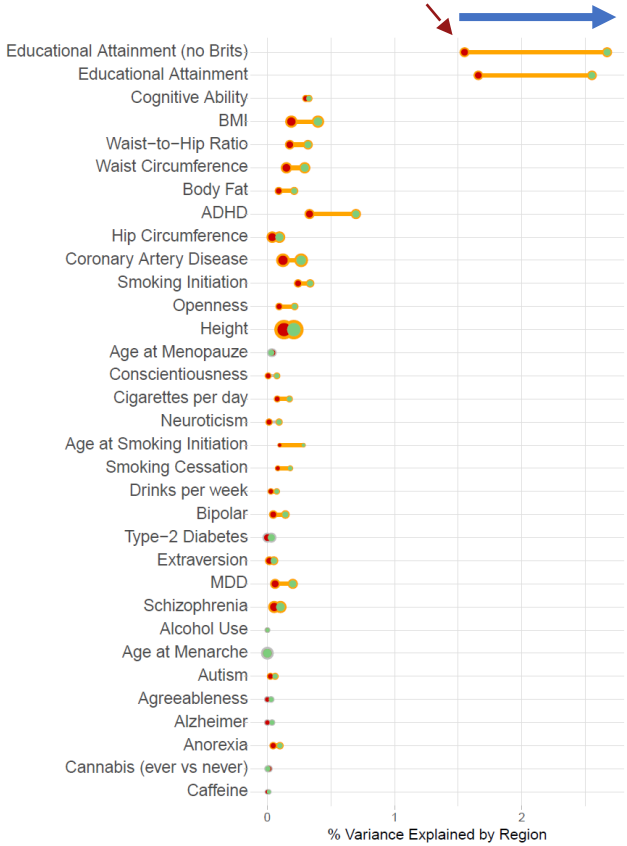
Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]





Migration & SES





← Polygenic Scores

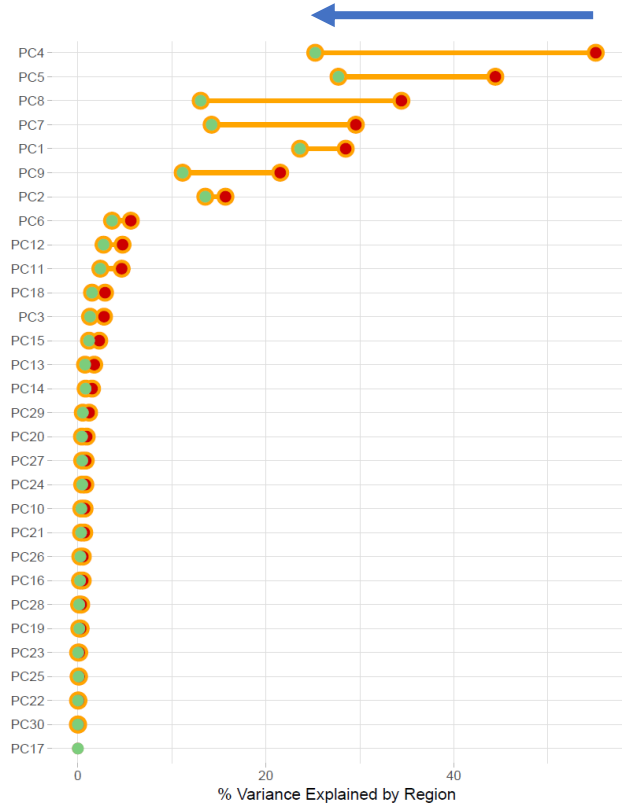
Birthplace

Current Address

Not significant (FDR)

Significant (FDR)

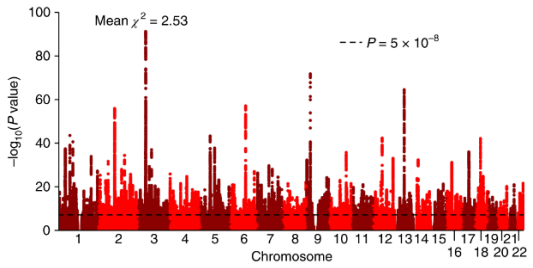
PCs →

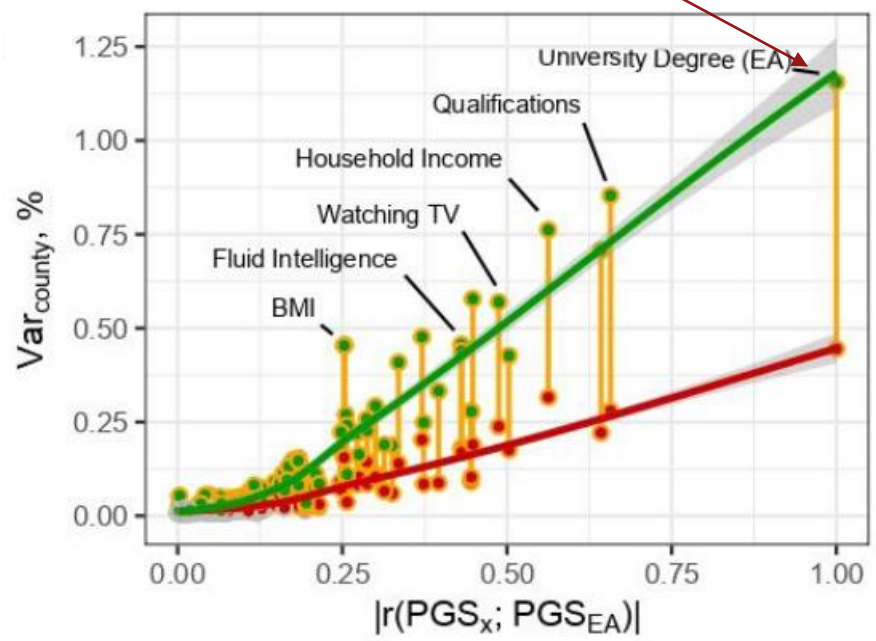


ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]





Birthplace

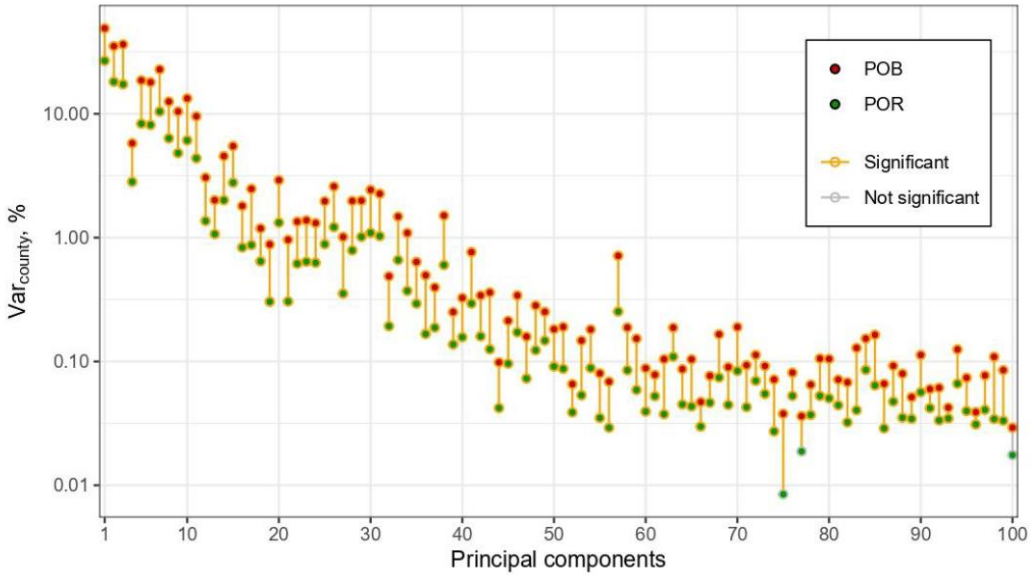
Current Address

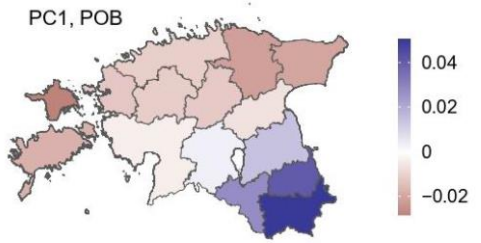
Not significant (FDR)

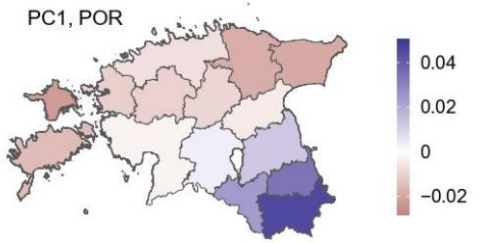
Significant (FDR)

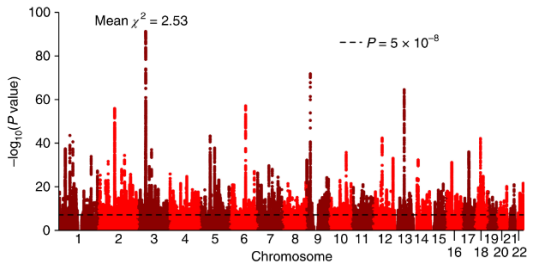
Assessing the impact of 20th century internal migrations on the genetic structure of Estonia

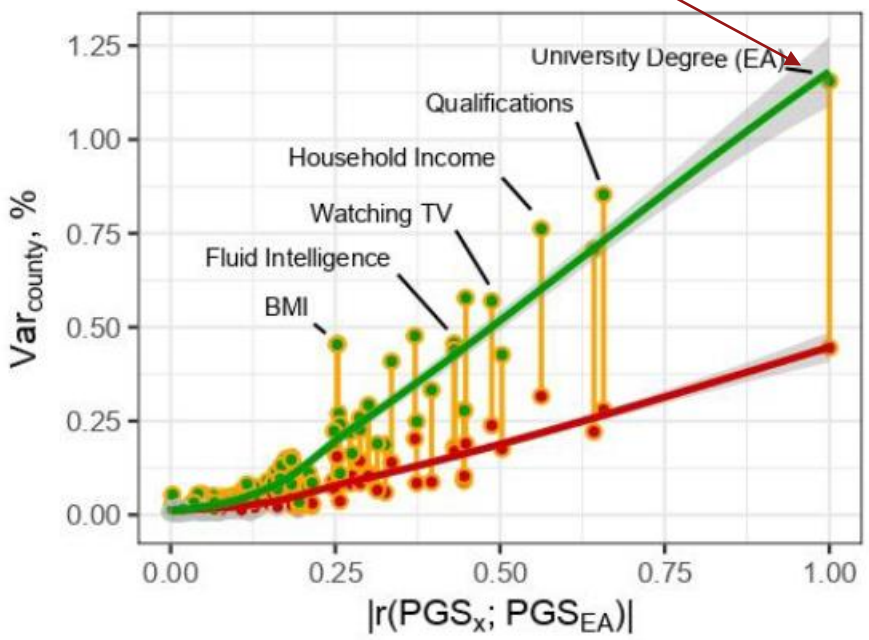
Ivan A. Kuznetsov[1,*], Estonian Biobank Research Team[1], Mait Metspalu[1], Uku Vainik[1,2,3], Luca Pagani[1,4], Francesco Montinaro[1,5], Vasili Pankratov[1,*]











Birthplace

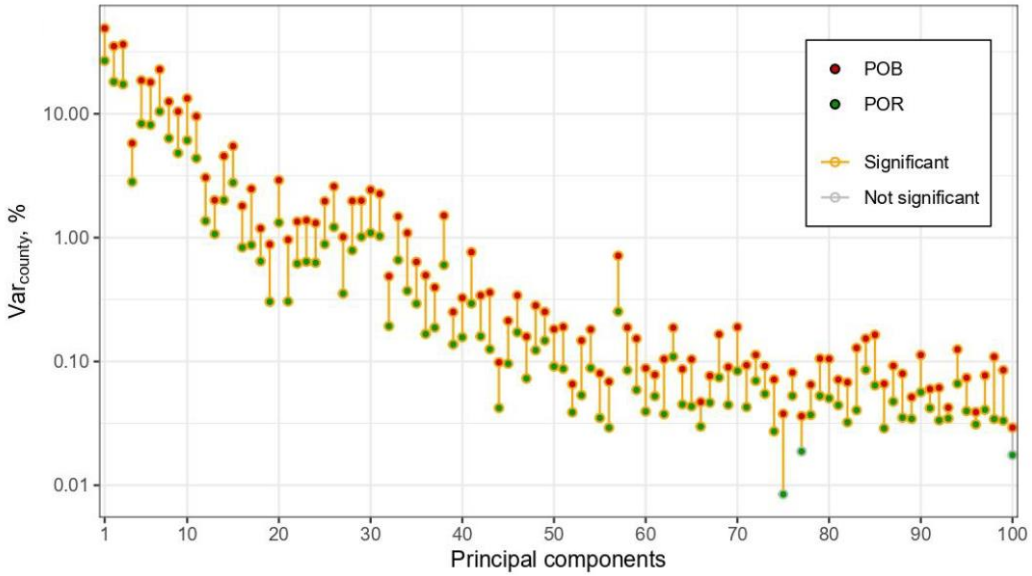
Current Address

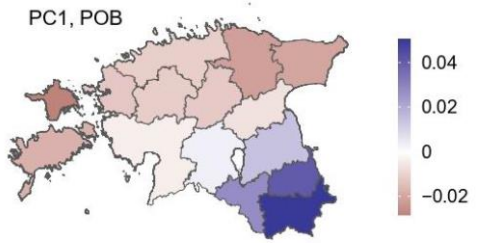
Not significant (FDR)

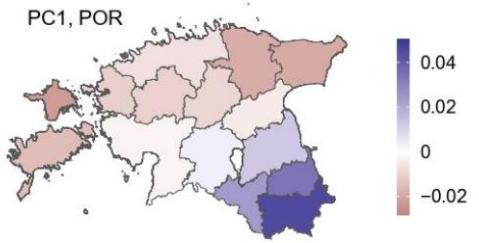
Significant (FDR)

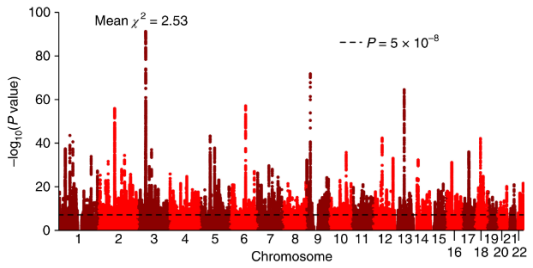
Assessing the impact of 20th century internal migrations on the genetic structure of Estonia

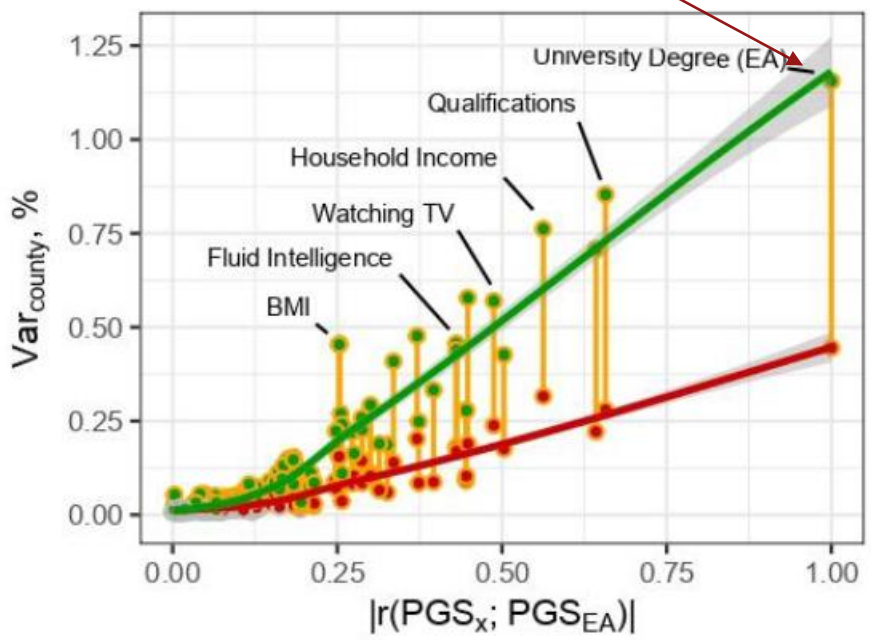
Ivan A. Kuznetsov[1,*], Estonian Biobank Research Team[1], Mait Metspalu[1], Uku Vainik[1,2,3], Luca Pagani[1,4], Francesco Montinaro[1,5], Vasili Pankratov[1,*]











Birthplace

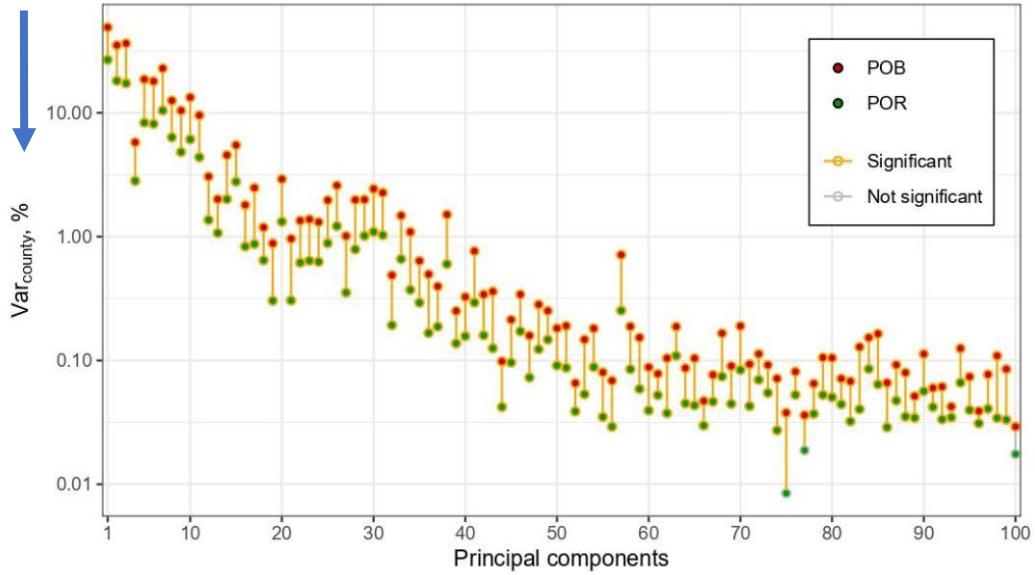
Current Address

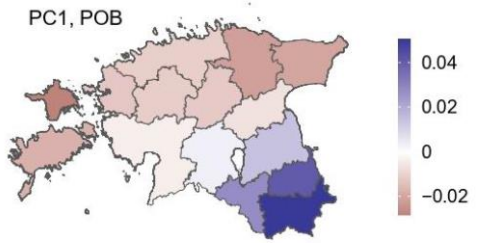
Not significant (FDR)

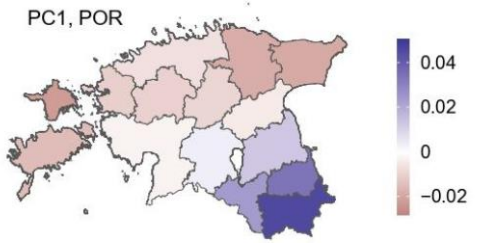
Significant (FDR)

Assessing the impact of 20th century internal migrations on the genetic structure of Estonia

Ivan A. Kuznetsov[1,*], Estonian Biobank Research Team[1], Mait Metspalu[1], Uku Vainik[1,2,3], Luca Pagani[1,4], Francesco Montinaro[1,5], Vasili Pankratov[1,*]

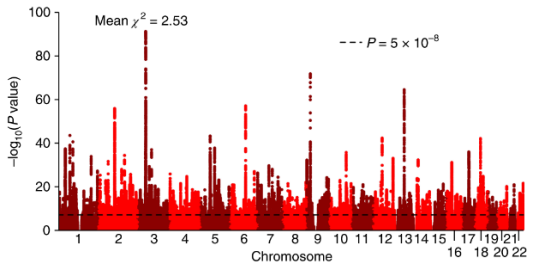


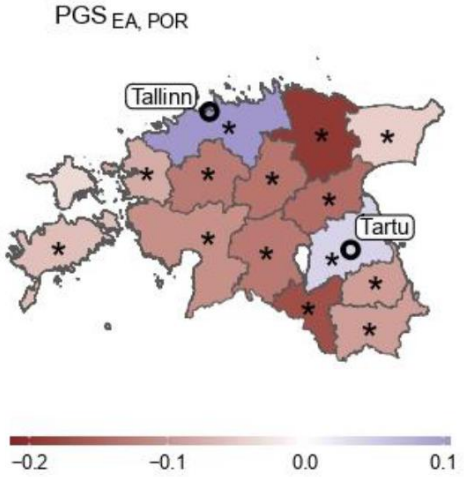


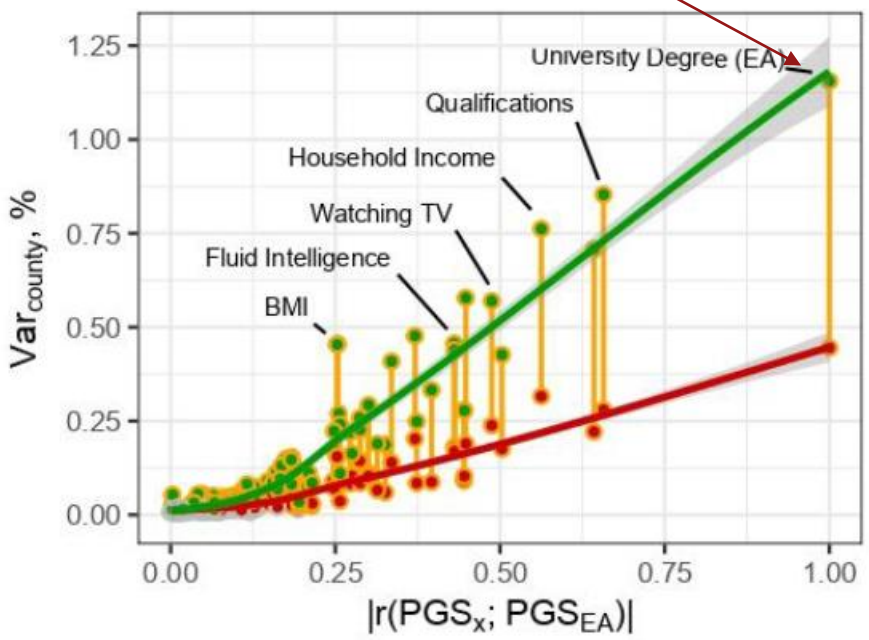


Assessing the impact of 20th century internal migrations on the genetic structure of Estonia

Ivan A. Kuznetsov[1,*], Estonian Biobank Research Team[1], Mait Metspalu[1], Uku Vainik[1,2,3], Luca Pagani[1,4], Francesco Montinaro[1,5], Vasili Pankratov[1,*]





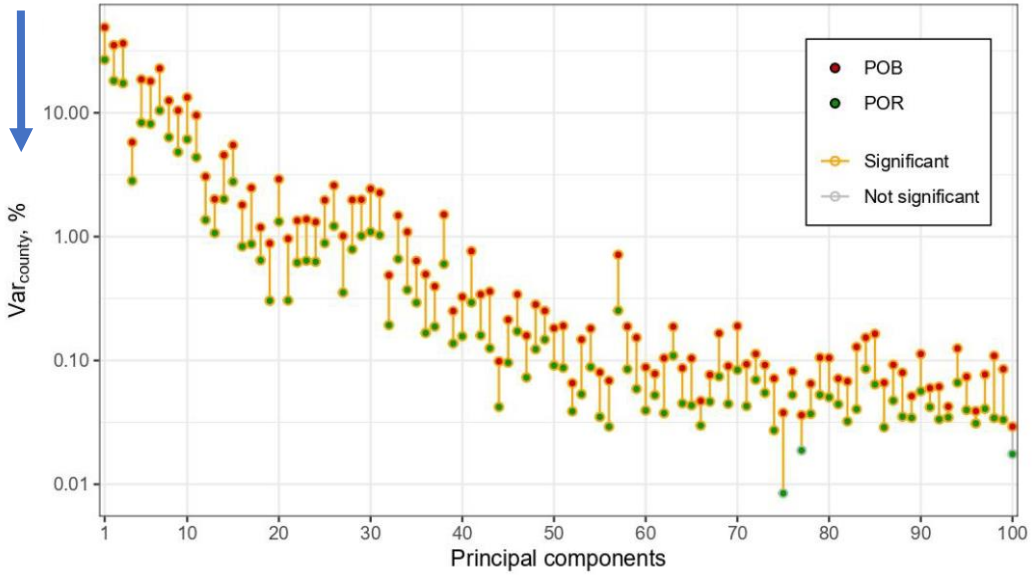


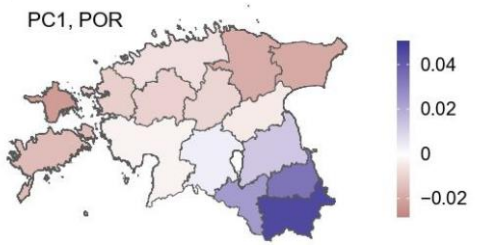
Birthplace

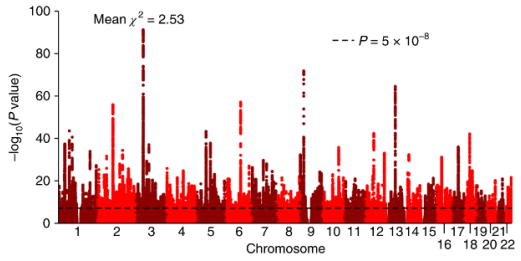
Current Address

Not significant (FDR)

Significant (FDR)





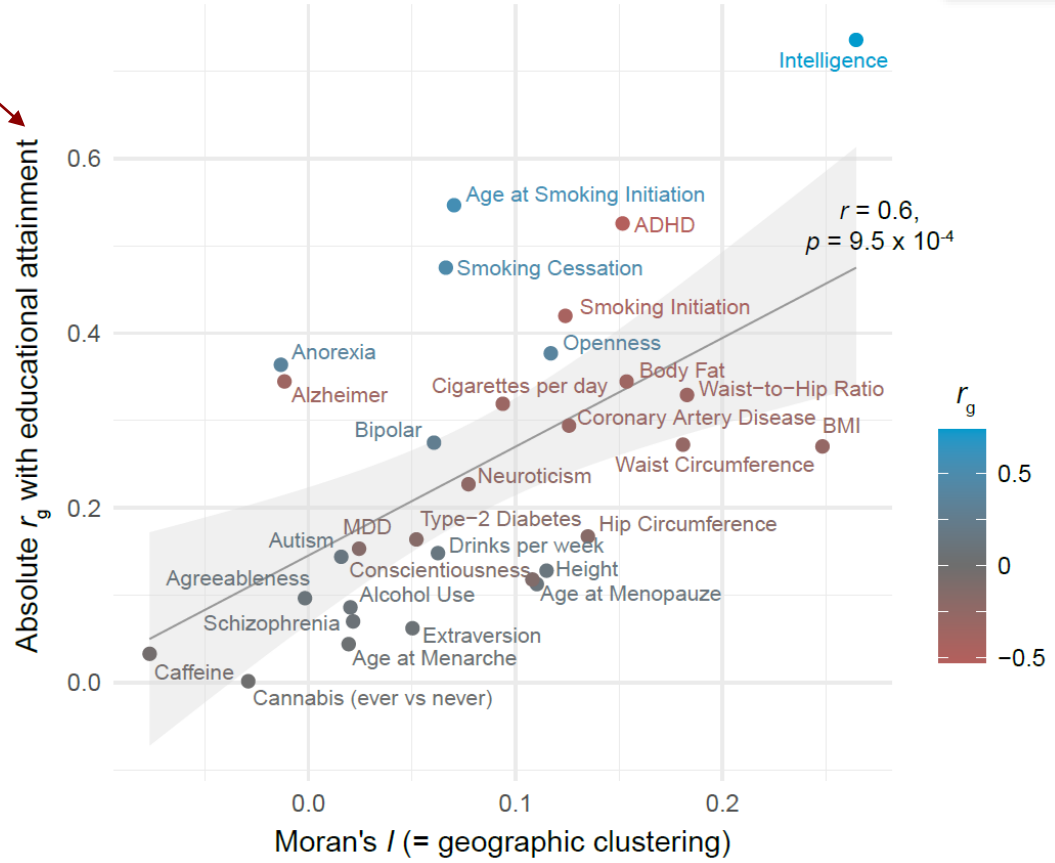


Sharing more genetic effects with EA = stronger geographic clustering

ARTICLES
https://doi.org/10.1038/s41562-019-0757-5
nature human behaviour

Genetic correlates of social stratification in Great Britain

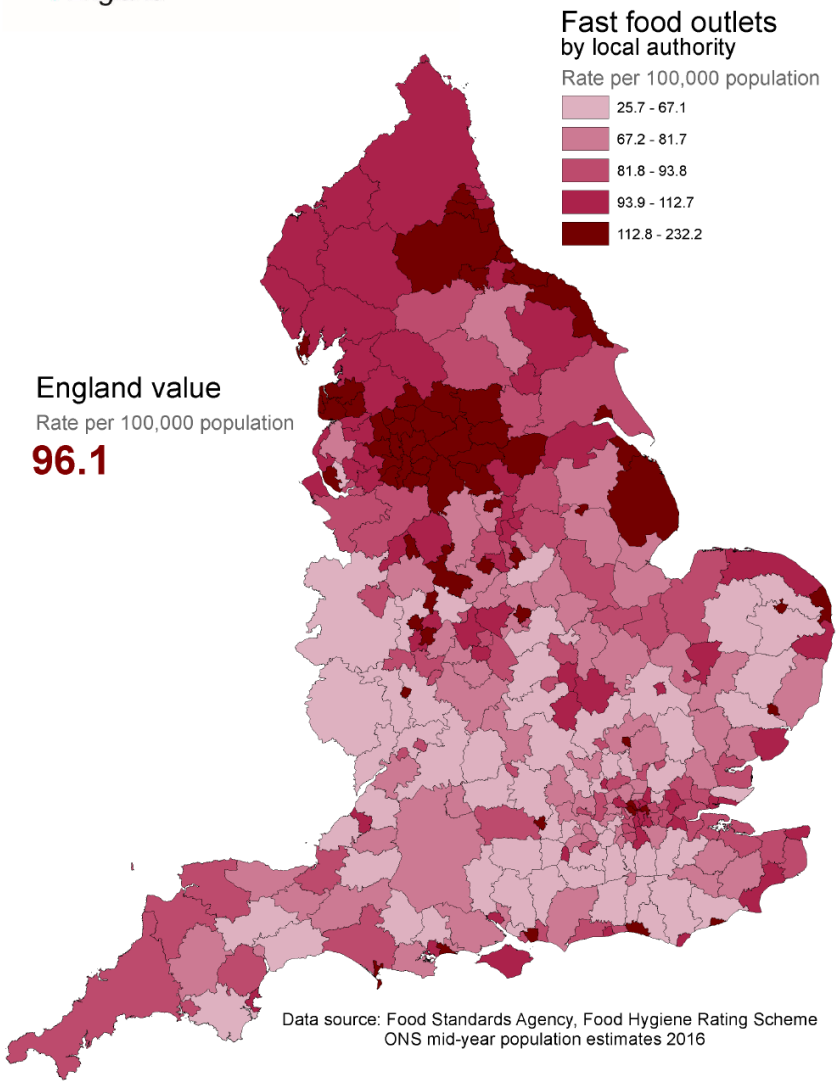
Abdel Abdellaoui[1*], David Hugh-Jones[2], Loic Yengo[3], Kathryn E. Kemper[3], Michel G. Nivard[4], Laura Veul[1], Yan Holtz[3], Brendan P. Zietsch[5], Timothy M. Frayling[6], Naomi R. Wray[3,7], Jian Yang[3,7], Karin J. H. Verweij[1] and Peter M. Visscher[3,7*]



Public Health England

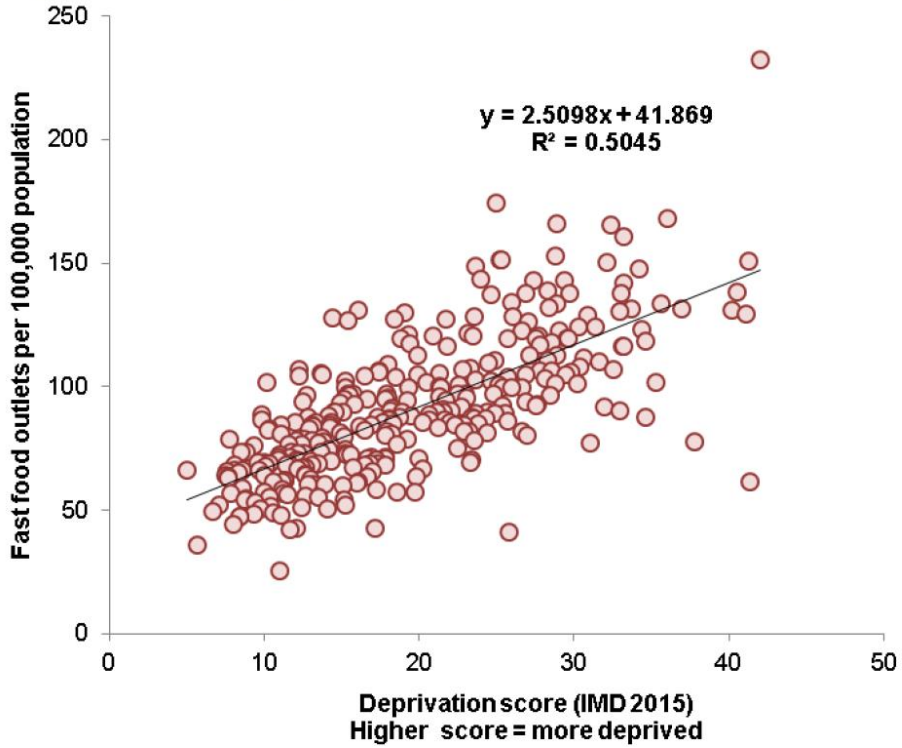
Obesity and the environment

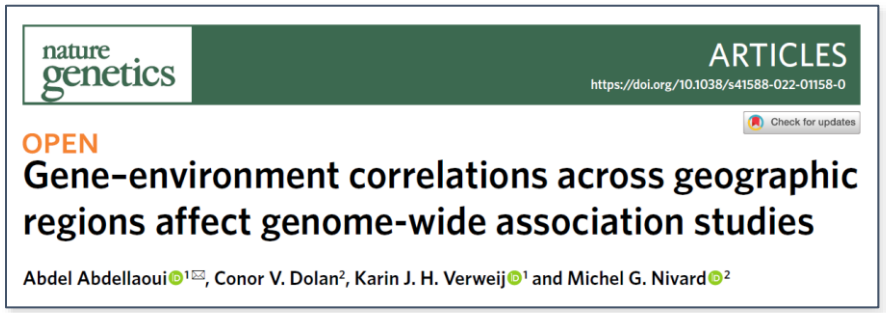
Density of fast food outlets at 31/12/2017



Public Health England

Relationship between density of fast food outlets and deprivation by local authority*



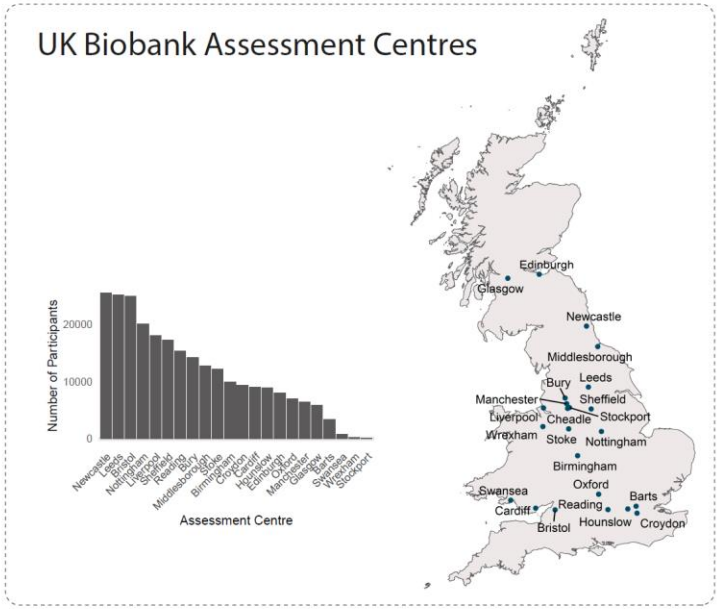


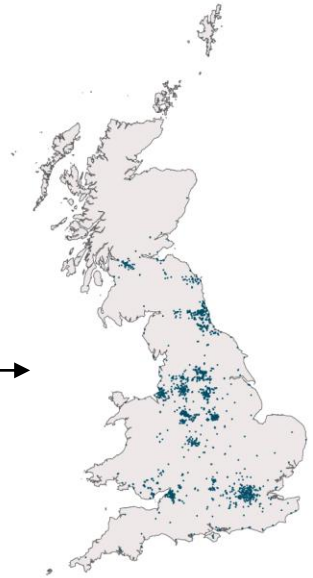
The paper consists of two parts:

- **Part 1**: detecting gene-environment correlations using polygenic scores in up to 43,516 siblings

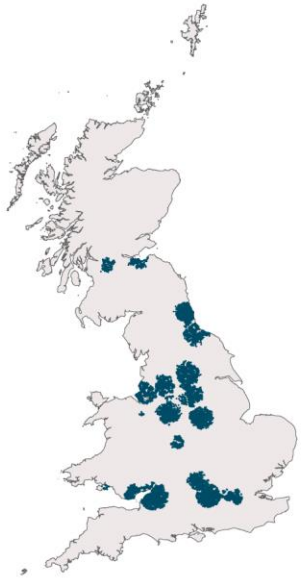
- **Part 2**: controlling for gene-environment correlations in GWASs in up to 254,387 participants

N = ~255k



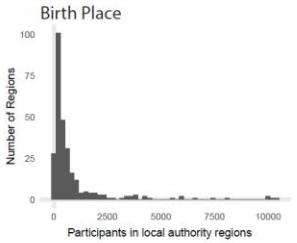


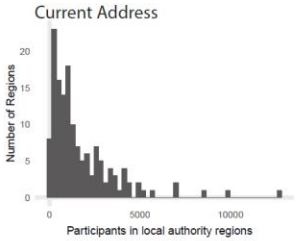
Birth Place



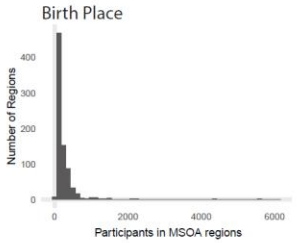
Current Address

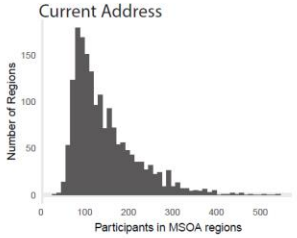
Local Authority



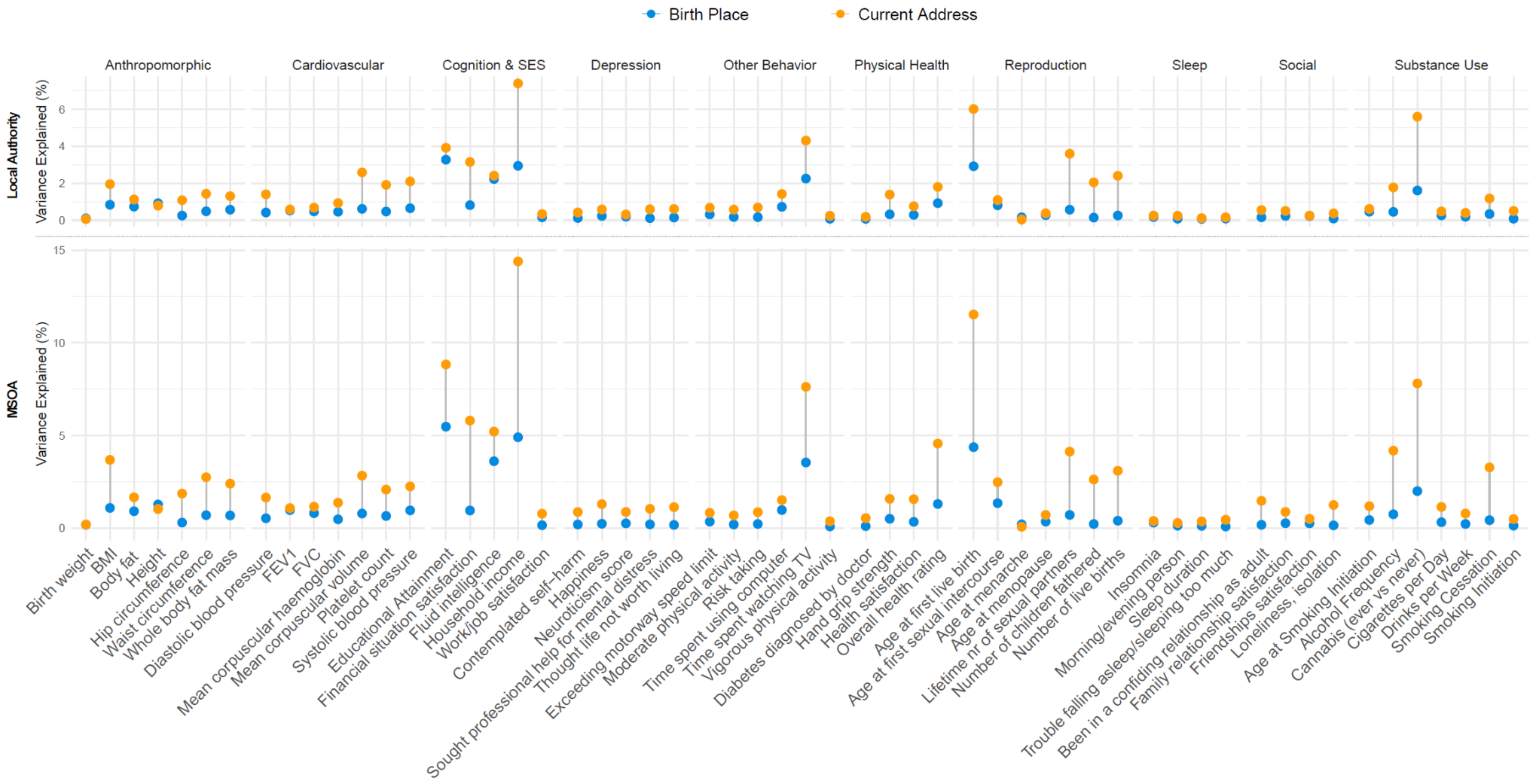


MSOA

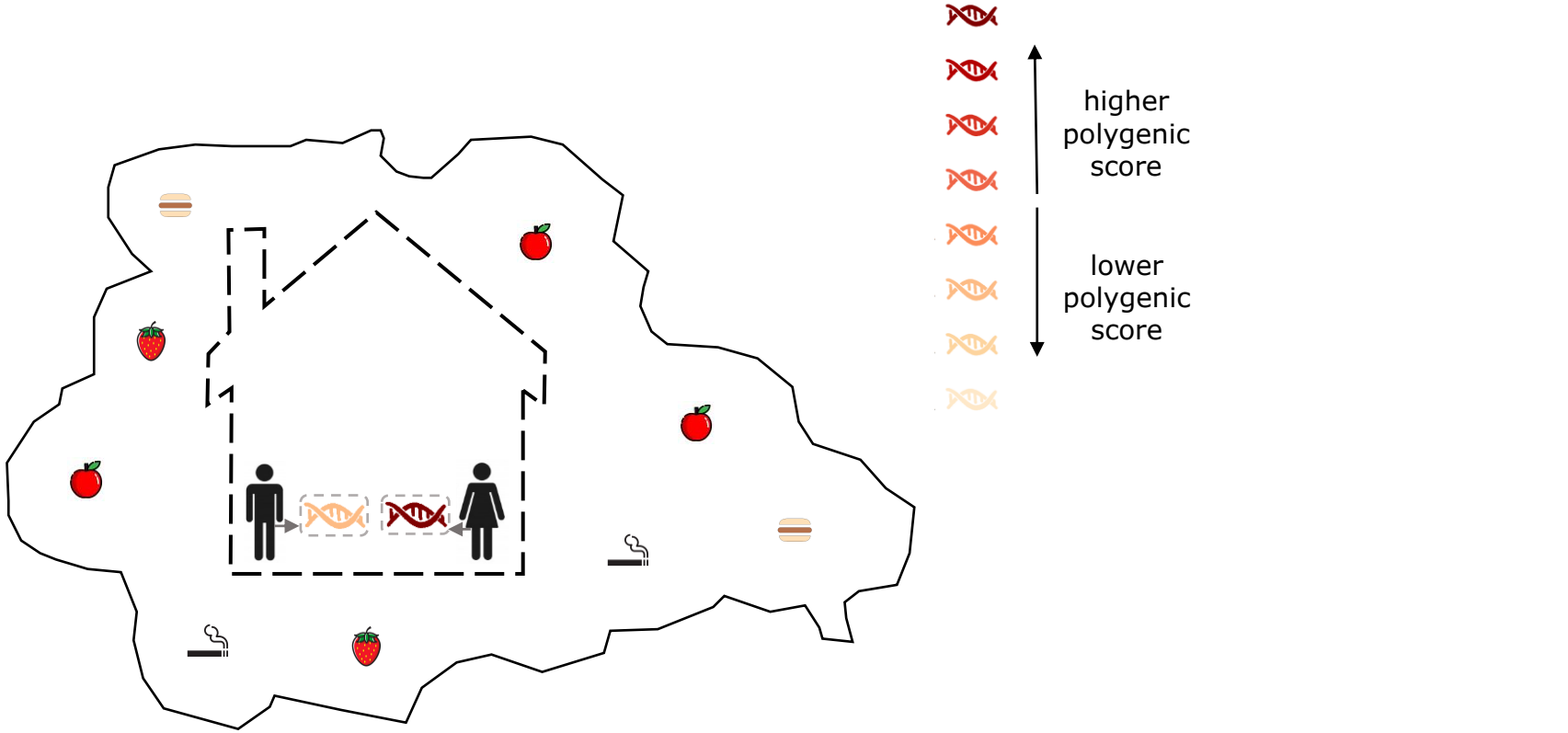




Variance explained by region:

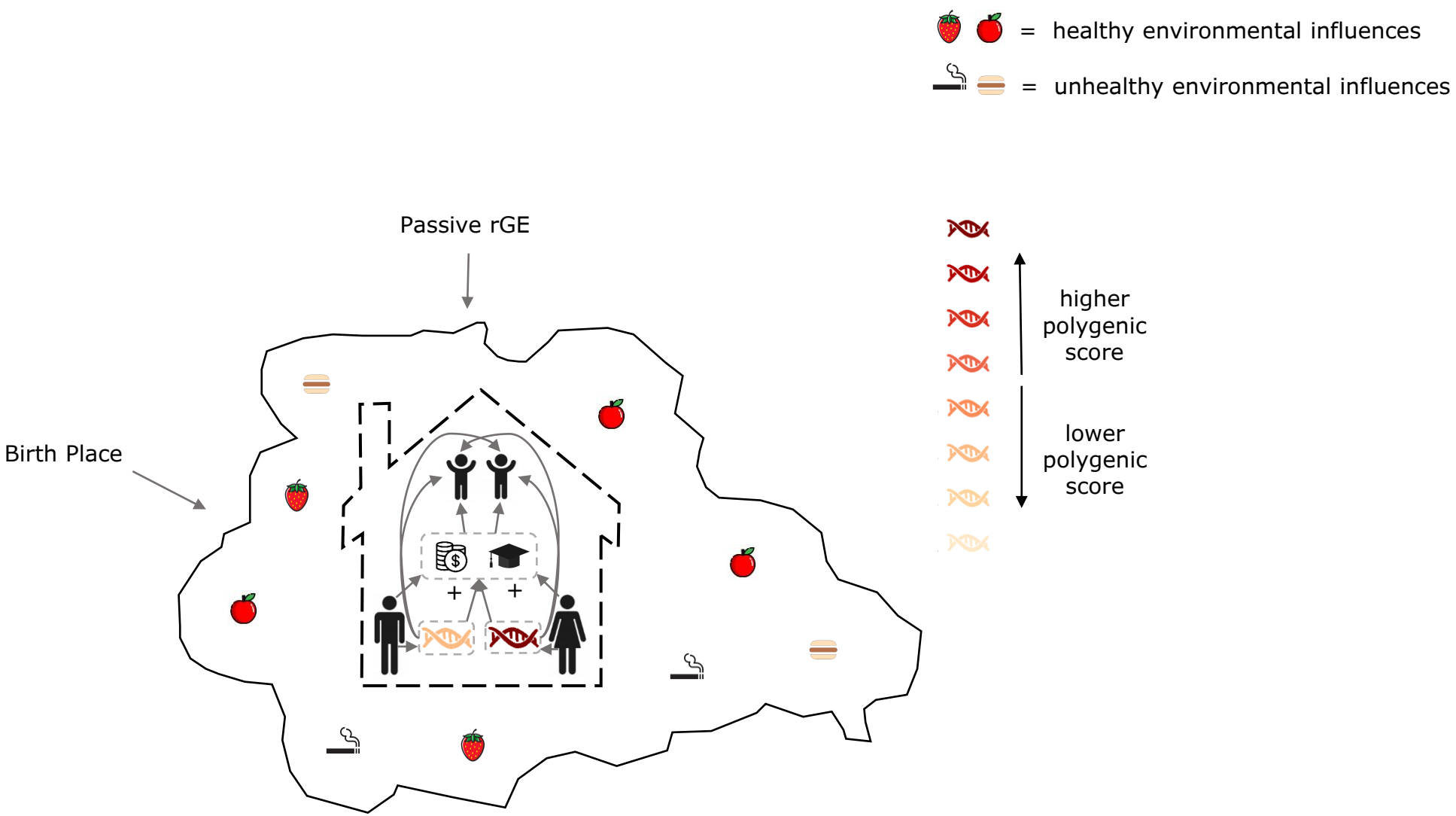


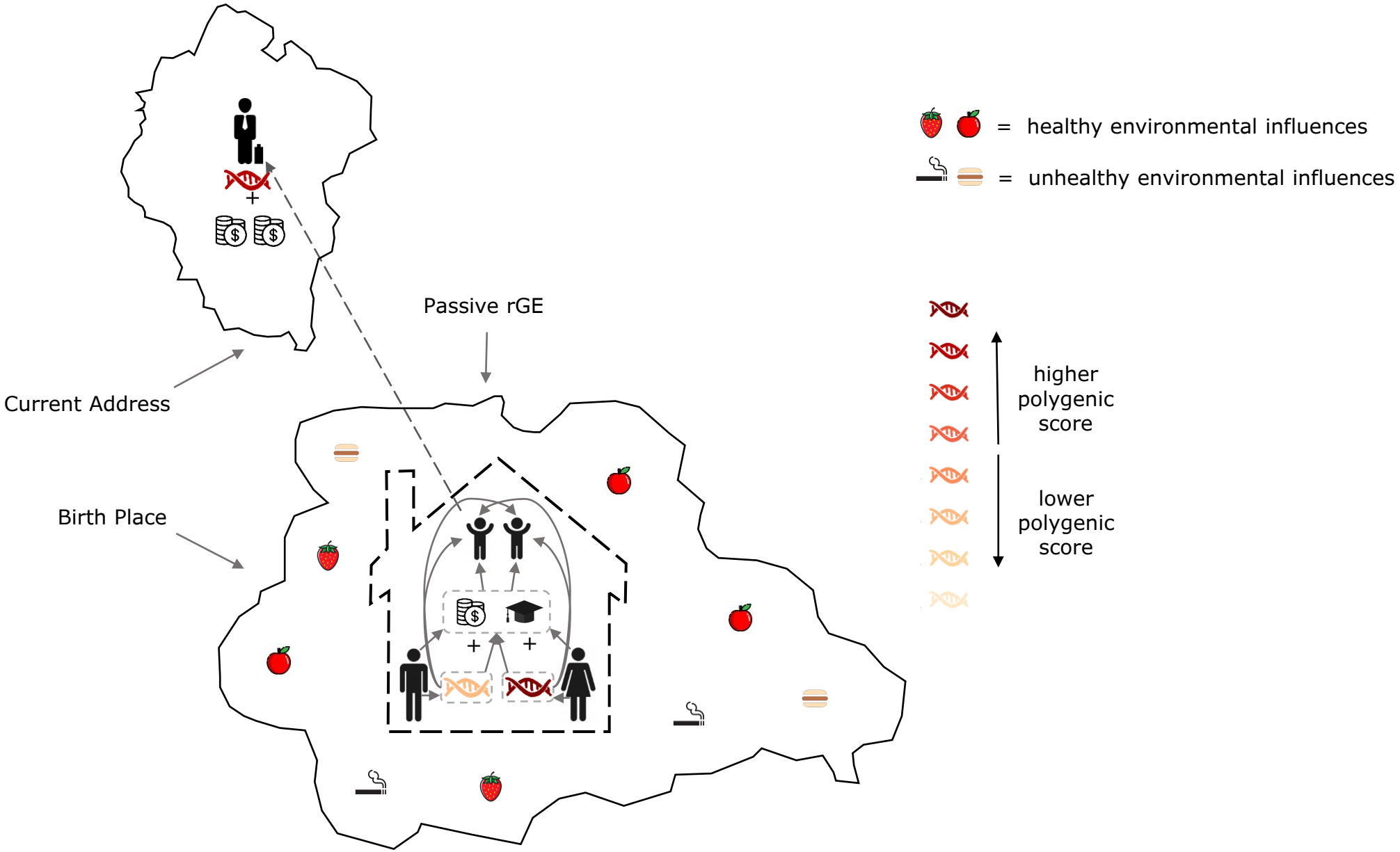
Polygenic Scores in Siblings

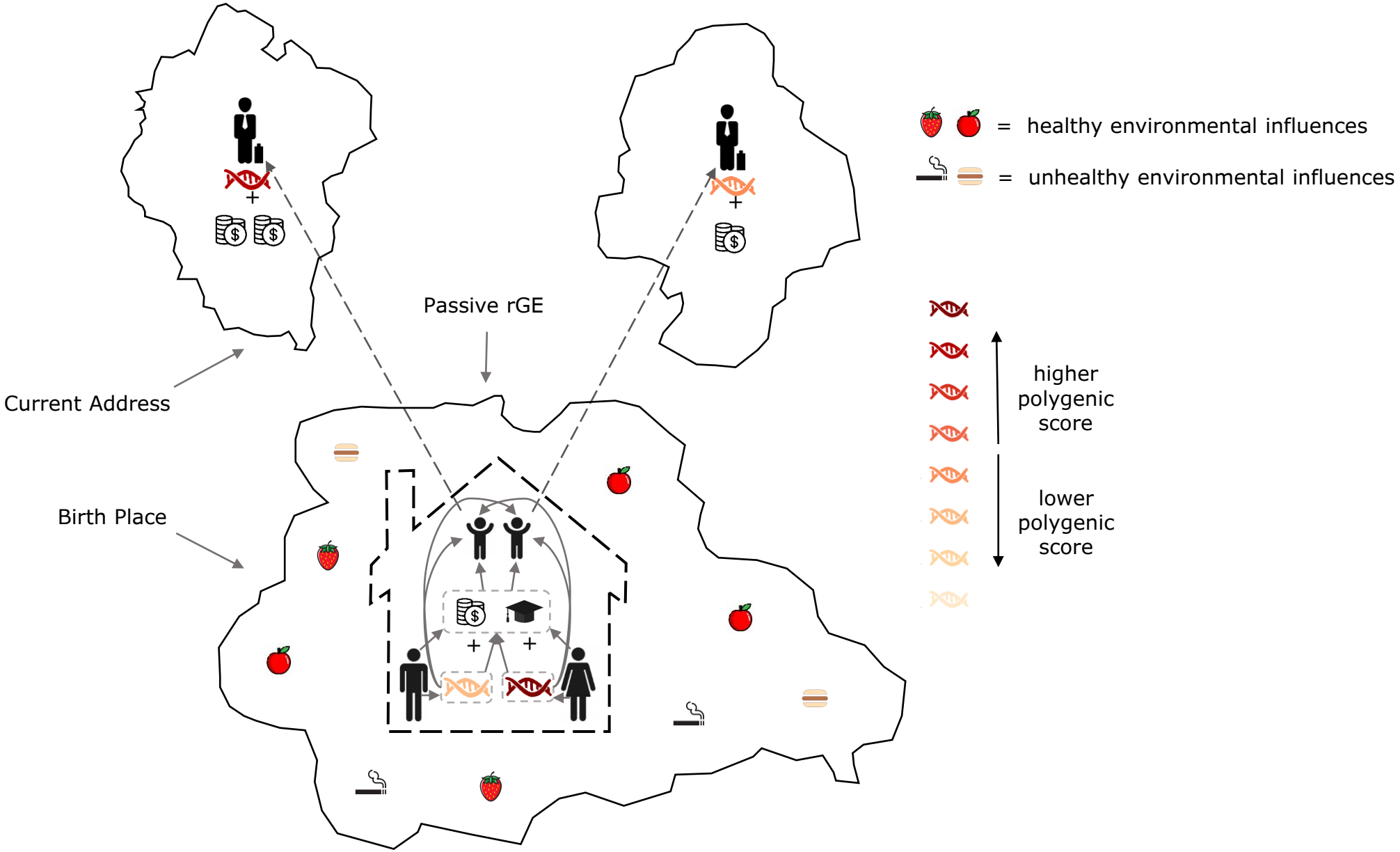

= healthy environmental influences
= unhealthy environmental influences
higher polygenic score
lower polygenic score

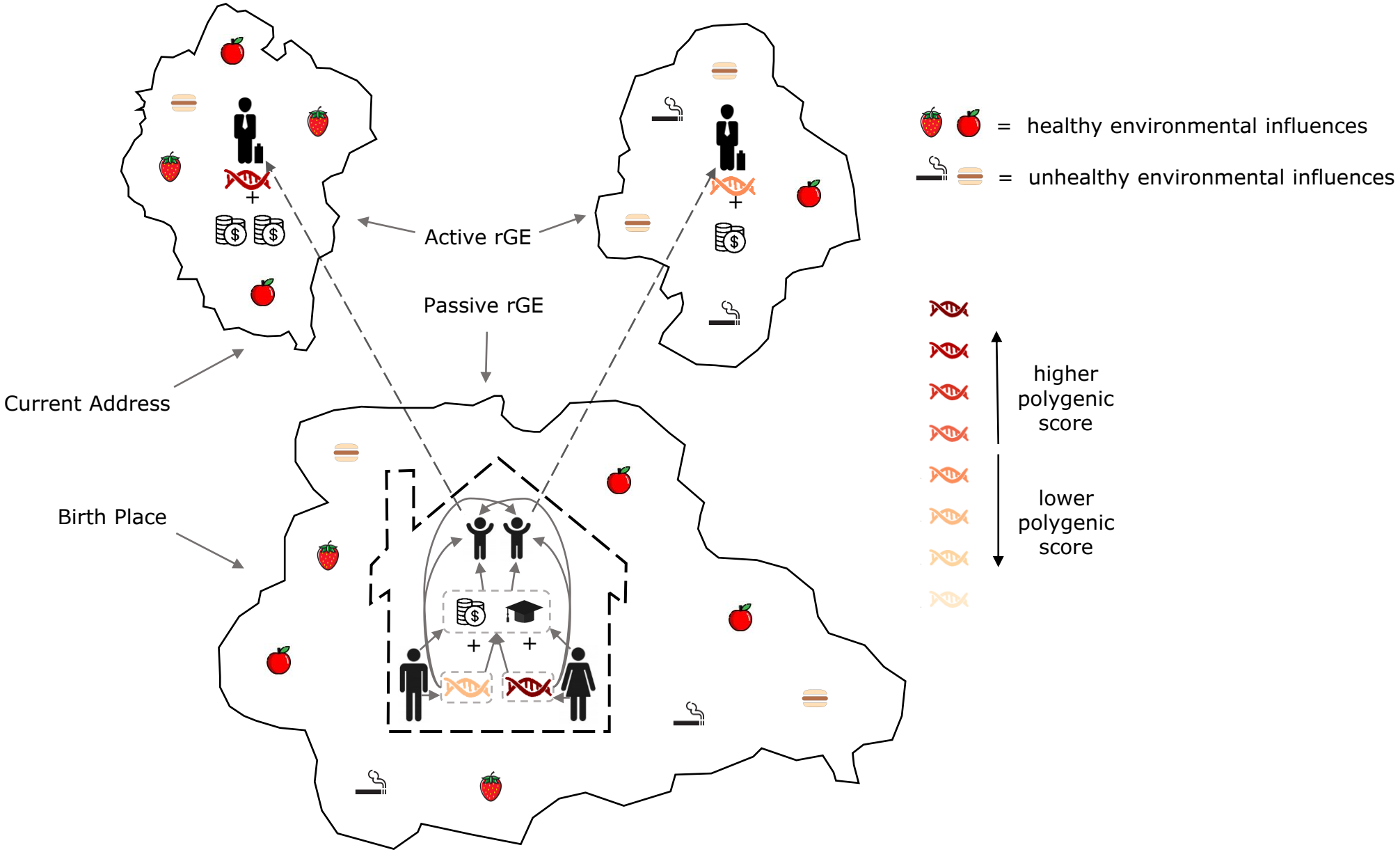

= healthy environmental influences
= unhealthy environmental influences
higher polygenic score
lower polygenic score
Birth Place


= healthy environmental influences
= unhealthy environmental influences
higher polygenic score
lower polygenic score
Birth Place


= healthy environmental influences
= unhealthy environmental influences
Passive rGE
Birth Place
higher polygenic score
lower polygenic score


= healthy environmental influences
= unhealthy environmental influences
Passive rGE
Current Address
Birth Place
higher polygenic score
lower polygenic score


Passive rGE
Current Address
Birth Place
= healthy environmental influences
= unhealthy environmental influences
higher polygenic score
lower polygenic score


= healthy environmental influences
= unhealthy environmental influences
Active rGE
Passive rGE
Current Address
Birth Place
higher polygenic score
lower polygenic score

The American Journal of Human Genetics *105*, 351–363, August 1, 2019

ARTICLE

Comparing Within- and Between-Family Polygenic Score Prediction

Saskia Selzam,[1,*] Stuart J. Ritchie,[1] Jean-Baptiste Pingault,[1,2] Chandra A. Reynolds,[3] Paul F. O'Reilly,[1,4] and Robert Plomin[1]

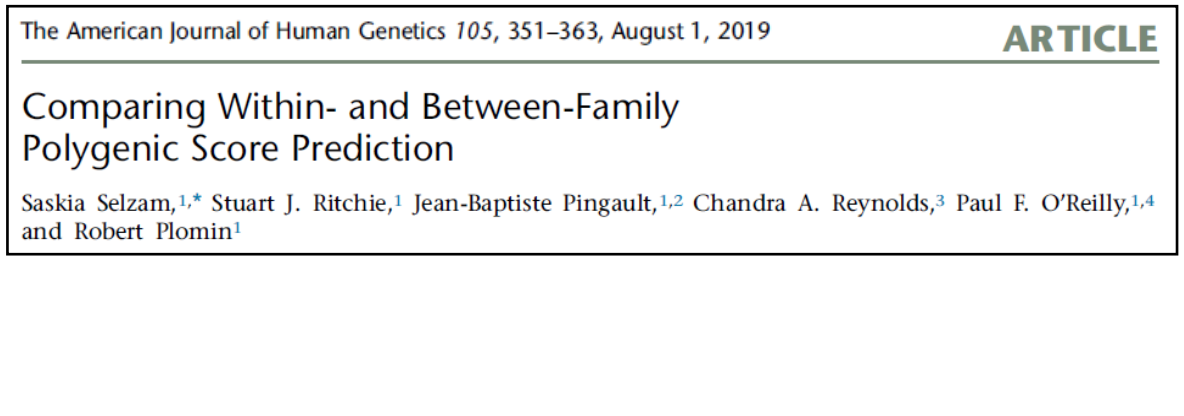
$$Y_{ij} = \alpha_0 + \beta PRS_{ij} + \gamma_j + \varepsilon_{ij},$$

The American Journal of Human Genetics *105*, 351–363, August 1, 2019 **ARTICLE**

Comparing Within- and Between-Family Polygenic Score Prediction

Saskia Selzam,[1,*] Stuart J. Ritchie,[1] Jean-Baptiste Pingault,[1,2] Chandra A. Reynolds,[3] Paul F. O'Reilly,[1,4] and Robert Plomin[1]

$$Y_{ij} = \alpha_0 + \beta PRS_{ij} + \gamma_j + \varepsilon_{ij},$$



$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

$$Y_{ij} = \alpha_0 + \underbrace{\beta PRS_{ij}}_{\text{Within-family effect}} + \gamma_j + \varepsilon_{ij},$$

$$Y_{ij} = \alpha_0 + \underbrace{\beta_W\left(PRS_{ij} - \overline{PRS_j}\right)}_{\text{Within-family effect}} + \underbrace{\beta_B\overline{PRS_j}}_{\text{Between-family effect}} + \gamma_j + \varepsilon_{ij}$$

The American Journal of Human Genetics *105*, 351–363, August 1, 2019 **ARTICLE**

Comparing Within- and Between-Family Polygenic Score Prediction

Saskia Selzam,[1,*] Stuart J. Ritchie,[1] Jean-Baptiste Pingault,[1,2] Chandra A. Reynolds,[3] Paul F. O'Reilly,[1,4] and Robert Plomin[1]

$$Y_{ij} = \alpha_0 + \underbrace{\beta PRS_{ij}}_{\text{Within-family effect}} + \gamma_j + \varepsilon_{ij},$$

$$Y_{ij} = \alpha_0 + \underbrace{\beta_W\left(PRS_{ij} - \overline{PRS_j}\right)}_{\text{Within-family effect}} + \underbrace{\beta_B \overline{PRS_j}}_{\text{Between-family effect}} + \gamma_j + \varepsilon_{ij}$$

The American Journal of Human Genetics *105*, 351–363, August 1, 2019 **ARTICLE**

Comparing Within- and Between-Family Polygenic Score Prediction

Saskia Selzam,[1,*] Stuart J. Ritchie,[1] Jean-Baptiste Pingault,[1,2] Chandra A. Reynolds,[3] Paul F. O'Reilly,[1,4] and Robert Plomin[1]

In children (N ~2,300 pairs), predictive power of polygenic scores of cognitive traits (intelligence & education) was 60% greater between families than within families.

$$Y_{ij} = \alpha_0 + \beta PRS_{ij} + \gamma_j + \varepsilon_{ij},$$

Within-family effect

$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

Between-family effect

We looked at adult siblings (N ~26k pairs) in UK Biobank.

PRS = Educational Attainment Polygenic Score (based on GWAS excluding all British)

$$Y_{ij} = \alpha_0 + \beta PRS_{ij} + \gamma_j + \varepsilon_{ij},$$

Within-family effect

$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

Between-family effect

We looked at adult siblings (N ~26k pairs) in UK Biobank.

PRS = Educational Attainment Polygenic Score (based on GWAS excluding all British)

Are there any additional gene-environment correlations at the regional level not captured by family?

$$Y_{ij} = \alpha_0 + \beta PRS_{ij} + \gamma_j + \varepsilon_{ij},$$

Within-family effect ← *Decreases when adding between-family effect*

$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

Between-family effect

We looked at adult siblings (N ~26k pairs) in UK Biobank.

PRS = Educational Attainment Polygenic Score (based on GWAS excluding all British)

Are there any additional gene-environment correlations at the regional level not captured by family?

$$Y_{ij} = \alpha_0 + \underbrace{\beta PRS_{ij}}_{\text{Within-family effect}} + \gamma_j + \varepsilon_{ij},$$

$$Y_{ij} = \alpha_0 + \overbrace{\beta_W\left(PRS_{ij} - \overline{PRS_j}\right)}^{\text{Within-family effect}} + \underbrace{\beta_B \overline{PRS_j}}_{\text{Between-family effect}} + \gamma_j + \varepsilon_{ij}$$

We looked at adult siblings (N ~26k pairs) in UK Biobank.

PRS = Educational Attainment Polygenic Score (based on GWAS excluding all British)

Are there any additional gene-environment correlations at the regional level not captured by family? ⟶

$$Y_{ijk} = \alpha_0 + \overbrace{\beta_W\left(PRS_{ijk} - \overline{PRS_j} - \overline{PRS_k}\right)}^{\text{Within-family effect}} + \underbrace{\beta_{BF}(\overline{PRS_j} - \overline{PRS_k})}_{\text{Between-family effect}} + \overbrace{\beta_{BR}(\overline{PRS_k})}^{\text{Between-region effect}} + \gamma_j + \gamma_k + \varepsilon_{ijk}$$

?

Within-family effect

$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

Between-family effect

PRS = Educational Attainment Polygenic Score (based on GWAS excluding all British)

Are there any additional gene-environment correlations at the regional level not captured by family?

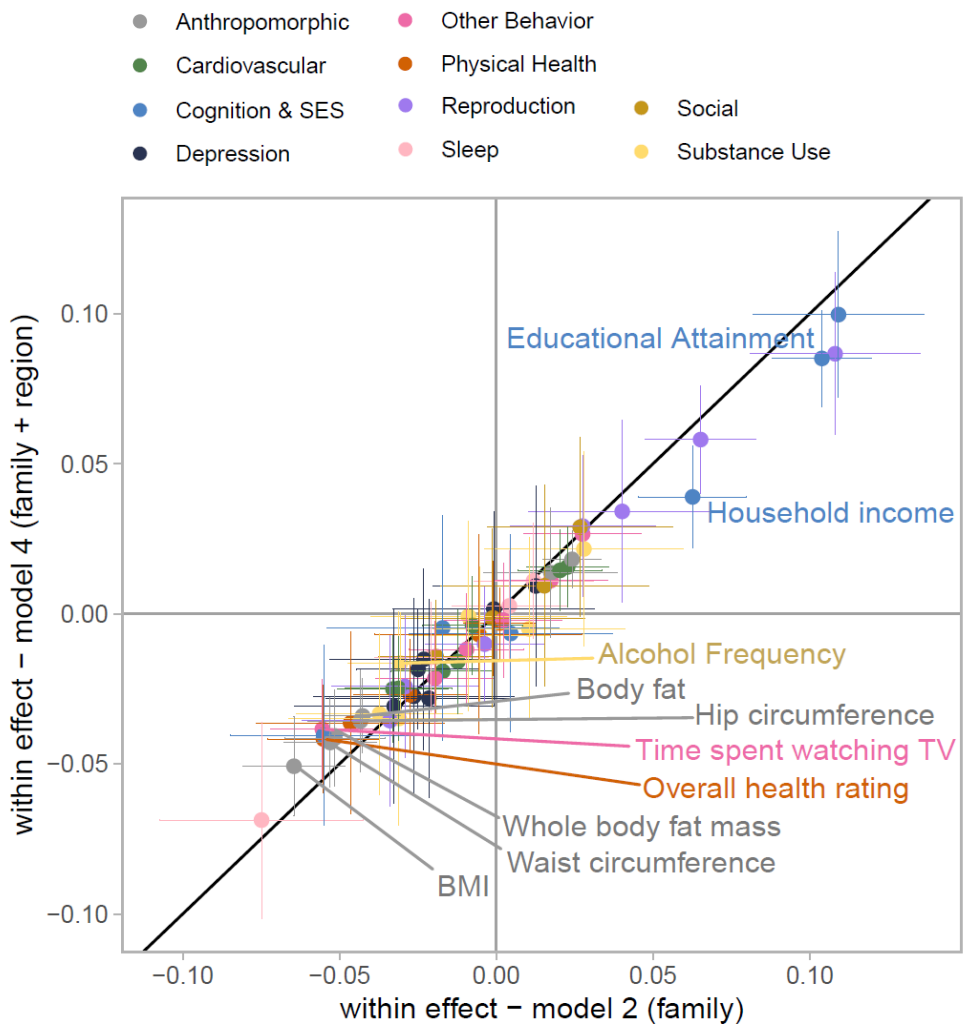
?

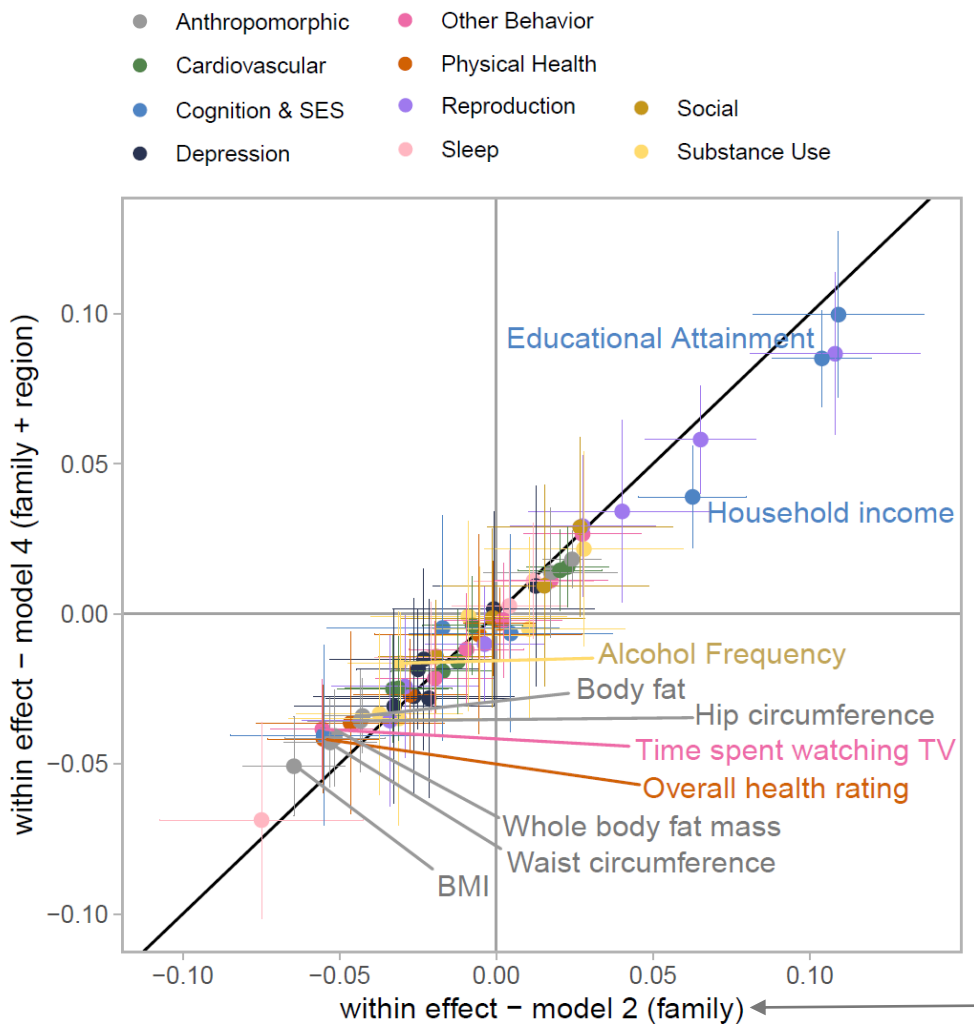
Within-family effect

Between-region effect

$$Y_{ijk} = \alpha_0 + \beta_W\left(PRS_{ijk} - \overline{PRS_j} - \overline{PRS_k}\right) + \beta_{BF}\left(\overline{PRS_j} - \overline{PRS_k}\right) + \beta_{BR}\left(\overline{PRS_k}\right) + \gamma_j + \gamma_k + \varepsilon_{ijk}$$

Between-family effect


Anthropomorphic
Cardiovascular
Cognition & SES
Depression
Other Behavior
Physical Health
Reproduction
Sleep
Social
Substance Use
Educational Attainment
Household income
Alcohol Frequency
Body fat
Hip circumference
Time spent watching TV
Overall health rating
Whole body fat mass
Waist circumference
BMI
0.10
0.05
0.00
−0.05
−0.10
−0.10
−0.05
0.00
0.05
0.10
within effect − model 4 (family + region)
within effect − model 2 (family)



Between-family effect

$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

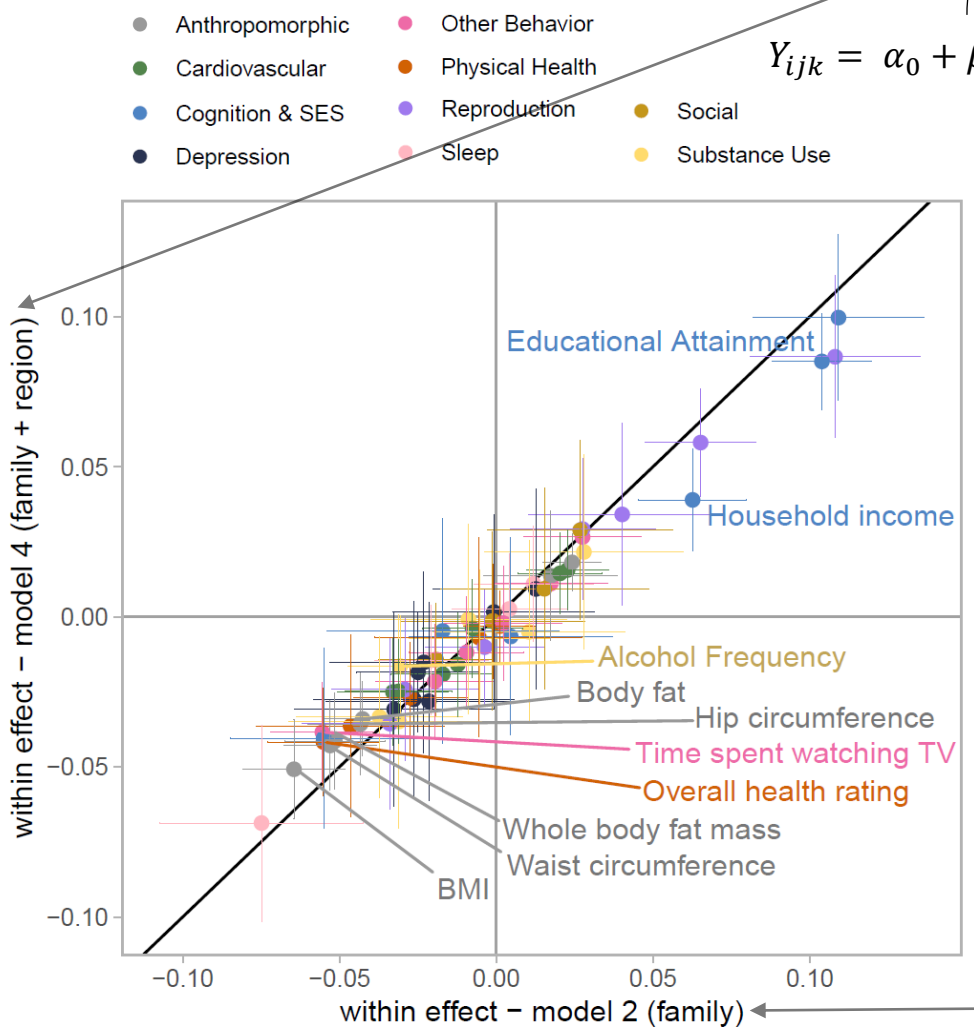
Within-family effect

Within-family effect

Between-region effect

$$Y_{ijk} = \alpha_0 + \beta_W\left(PRS_{ijk} - \overline{PRS_j} - \overline{PRS_k}\right) + \beta_{BF}\left(\overline{PRS_j} - \overline{PRS_k}\right) + \beta_{BR}\left(\overline{PRS_k}\right) + \gamma_j + \gamma_k + \varepsilon_{ijk}$$

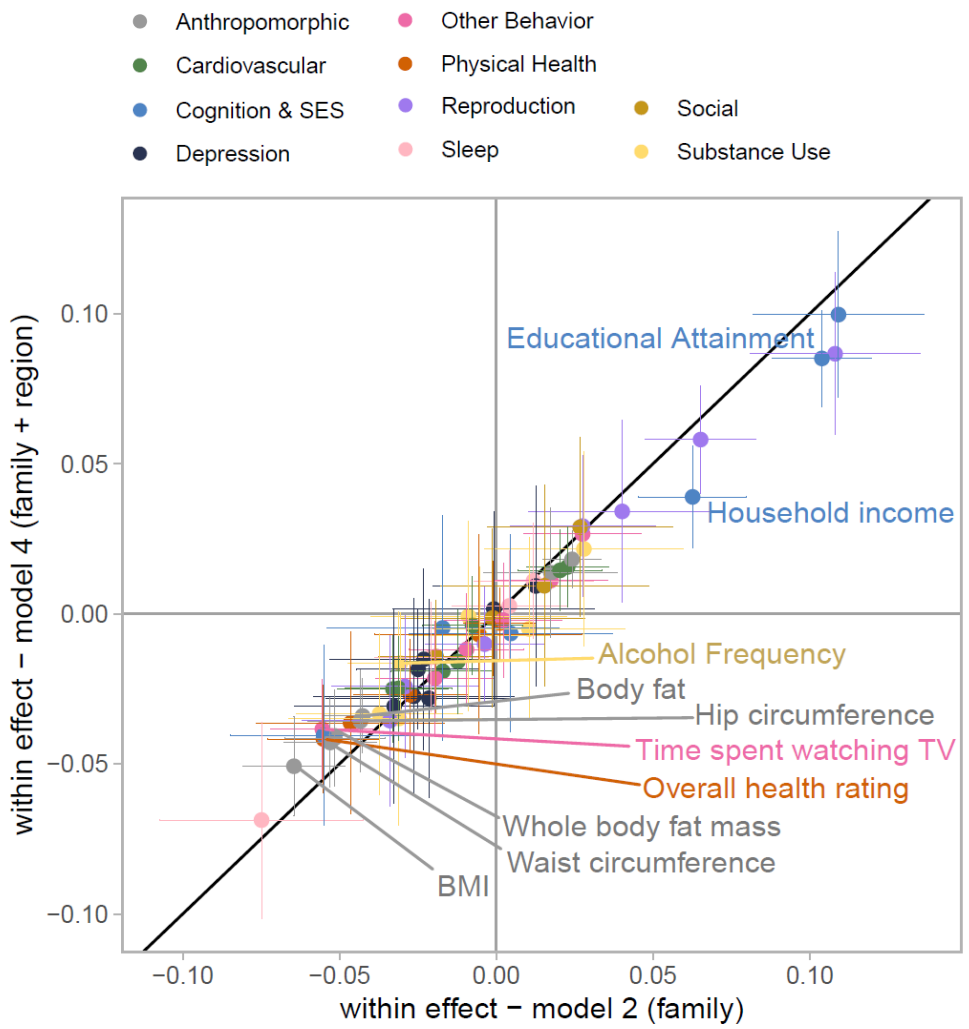
Between-family effect



Between-family effect

$$Y_{ij} = \alpha_0 + \beta_W\left(PRS_{ij} - \overline{PRS_j}\right) + \beta_B\overline{PRS_j} + \gamma_j + \varepsilon_{ij}$$

Within-family effect



Adding geography significantly decreased within-family effect for 10 traits. The most significant 5:

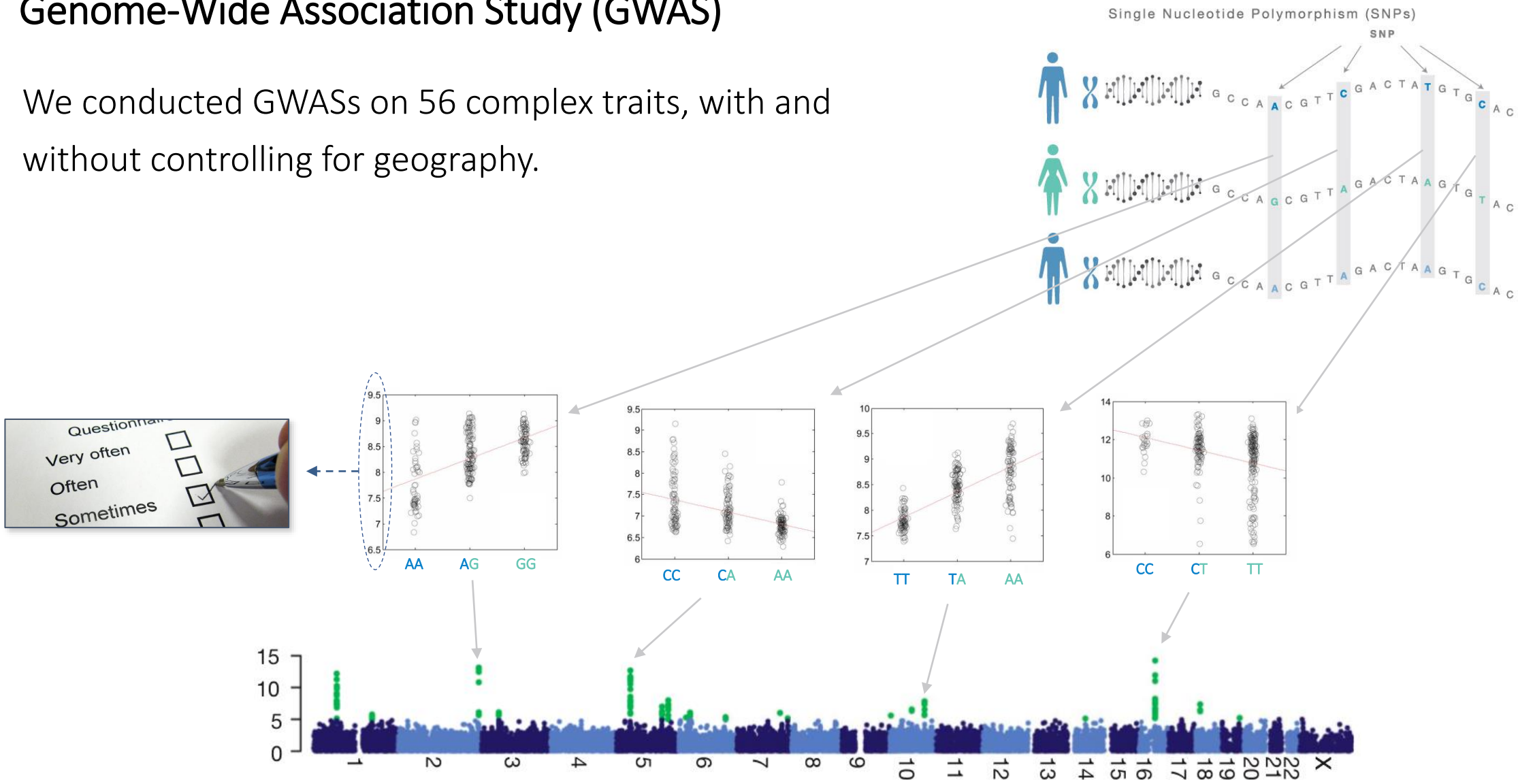
- BMI ($p = 1 \times 10^{-5}$)
- Waist circumference ($p = 1 \times 10^{-4}$)
- Household income ($p = 1 \times 10^{-4}$)
- Time spent watching TV ($p = 3 \times 10^{-4}$)
- Whole body fat mass ($p = 6 \times 10^{-4}$)

These are traits that are more subject to change after siblings migrated out of the parental residence.

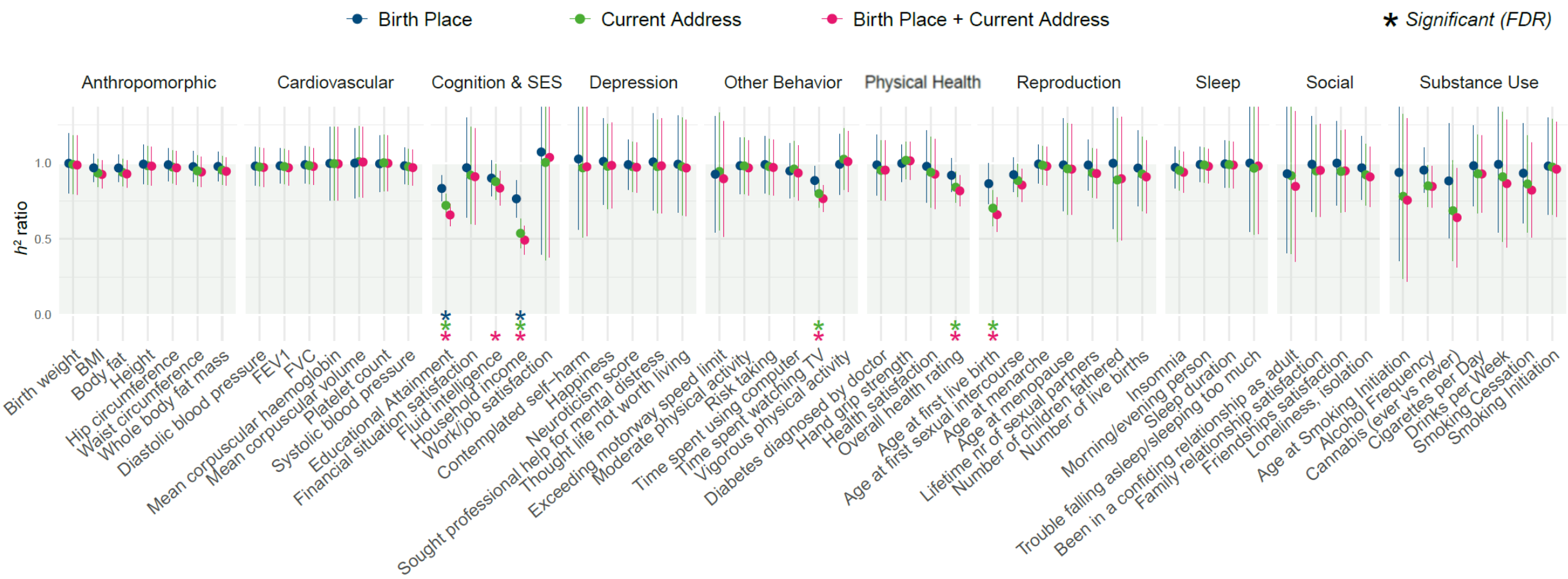
GWASs Controlled for Geography

Genome-Wide Association Study (GWAS)

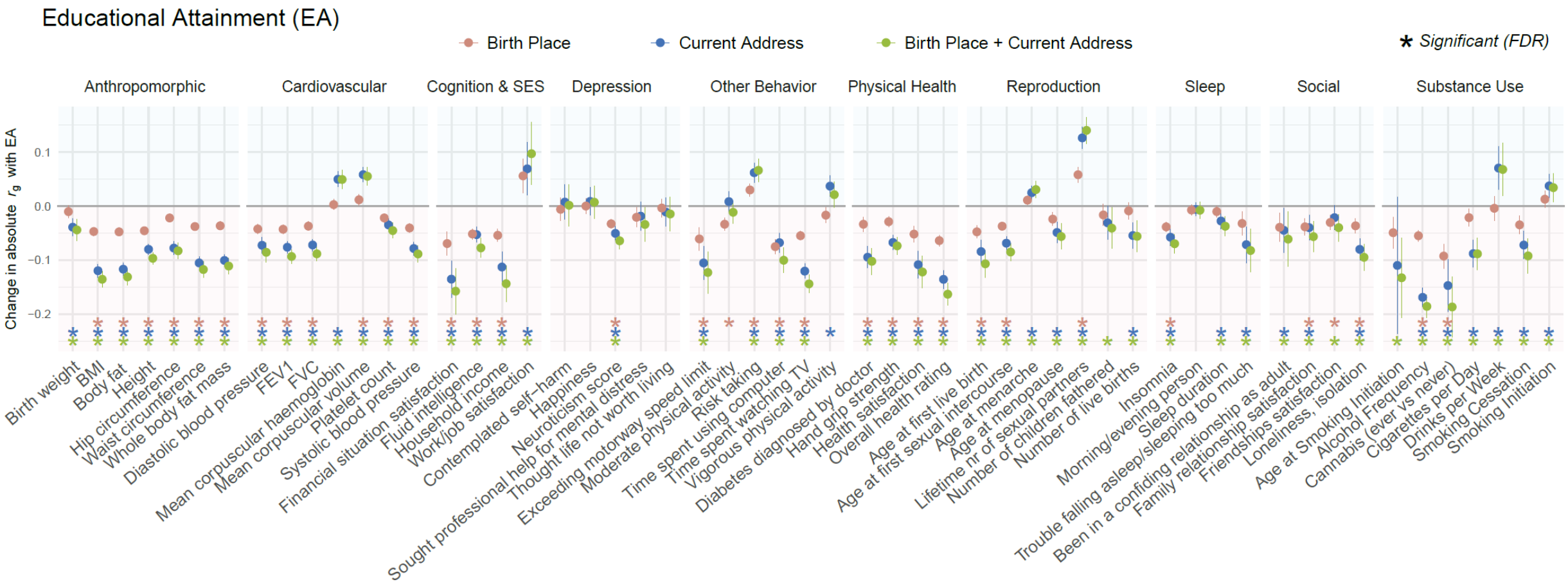
- We conducted GWASs on 56 complex traits, with and without controlling for geography.



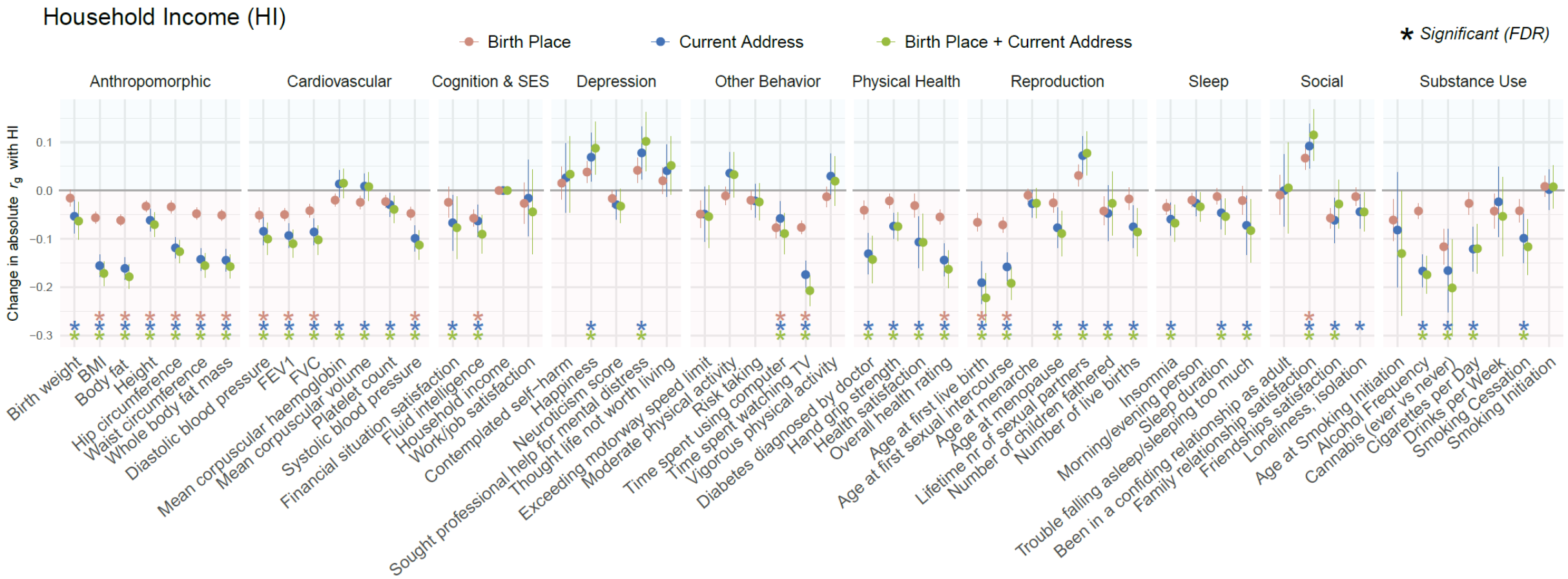
Changes in SNP-based heritability



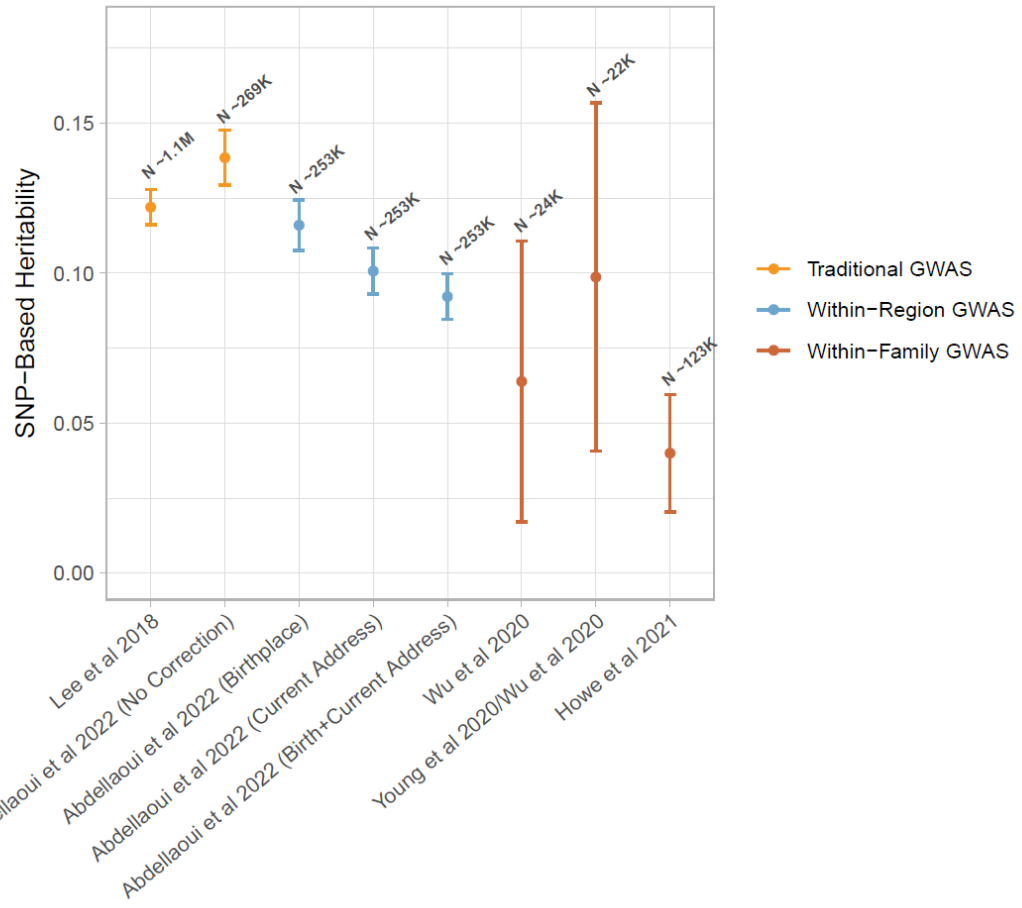
Changes in genetic correlation with SES - Educational Attainment



Changes in genetic correlation with SES - Household Income

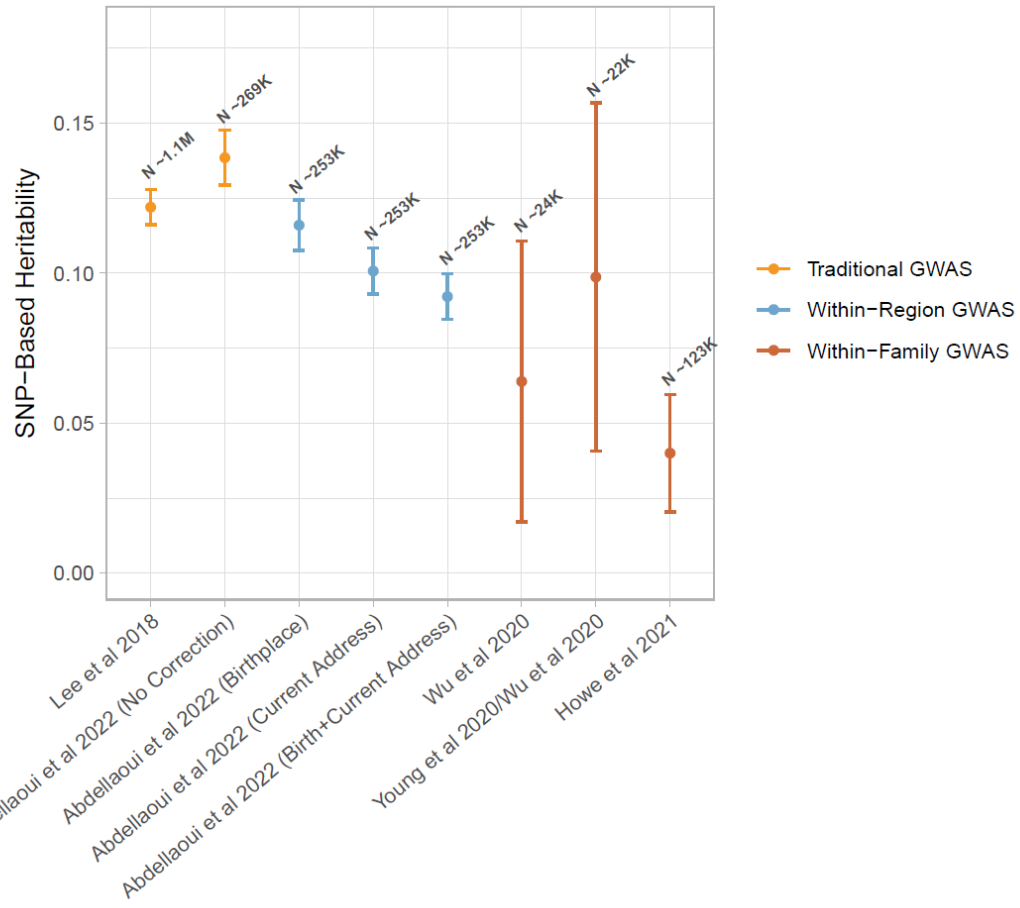


- Controlling for geographic region decreases the heritability for SES (education/income)



- Controlling for geographic region decreases the heritability for SES (education/income)

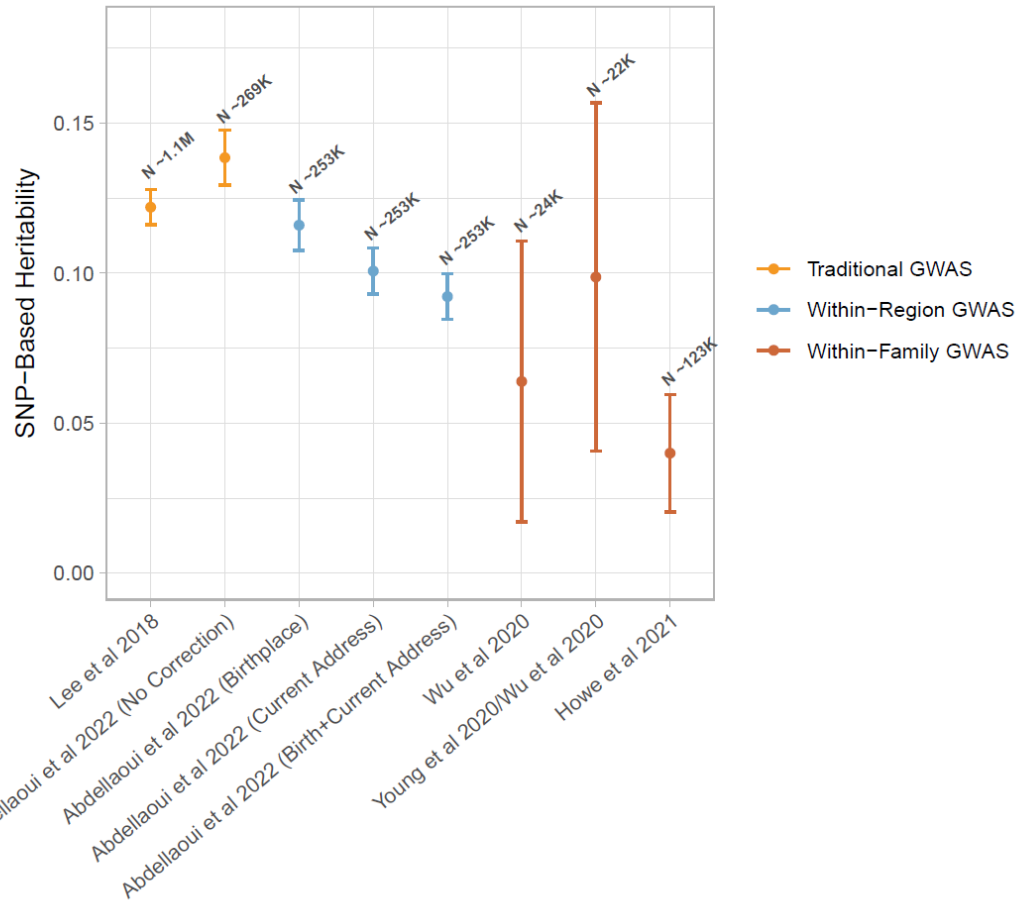
- Controlling for region reduces genetic correlations with SES (EA/income), most significantly for BMI, sedentary behavior, and substance use



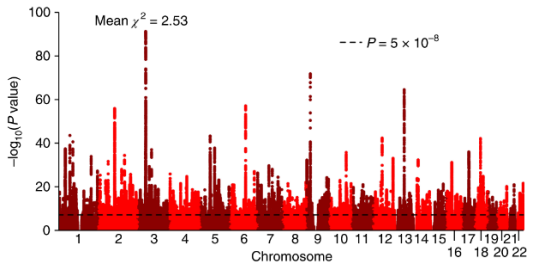
- Controlling for geographic region decreases the heritability for SES (education/income)

- Controlling for region reduces genetic correlations with SES (EA/income), most significantly for BMI, sedentary behavior, and substance use

- Our findings can be explained driven by both passive and active gene-environment correlations

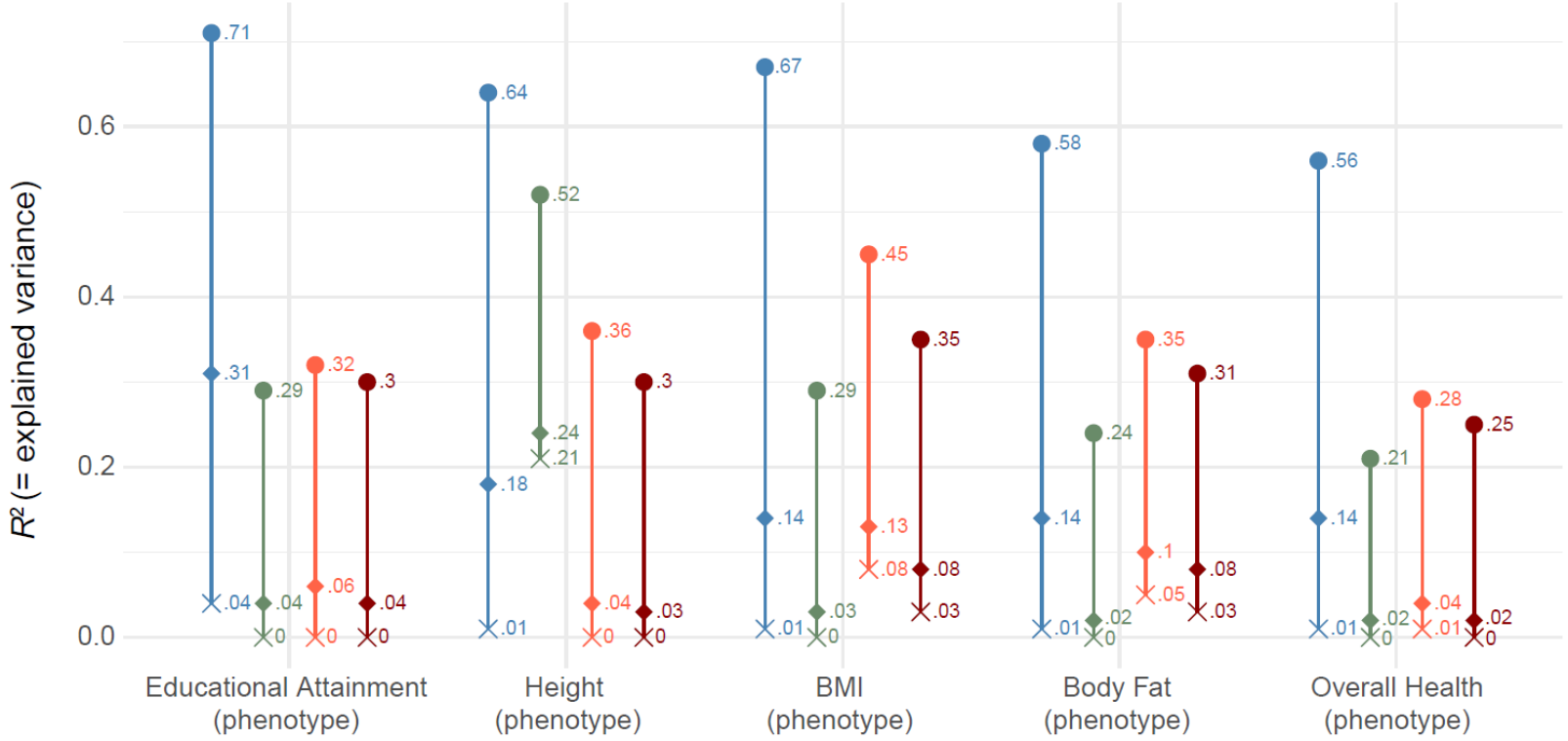


Genes associated with educational attainment are also associated with environmental exposures (rich vs poor neighborhoods)



Educational Attainment (polygenic score)
Height (polygenic score)
BMI (polygenic score)
Body Fat (polygenic score)

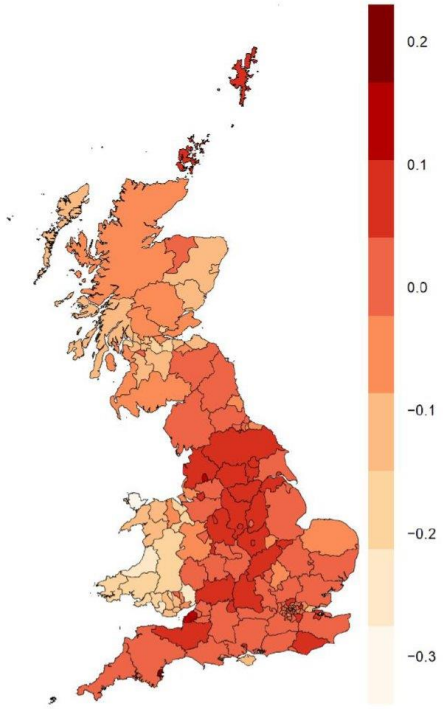
Individual−Level
Regional Averages: MSOA Regions
Regional Averages: Local Authority Regions



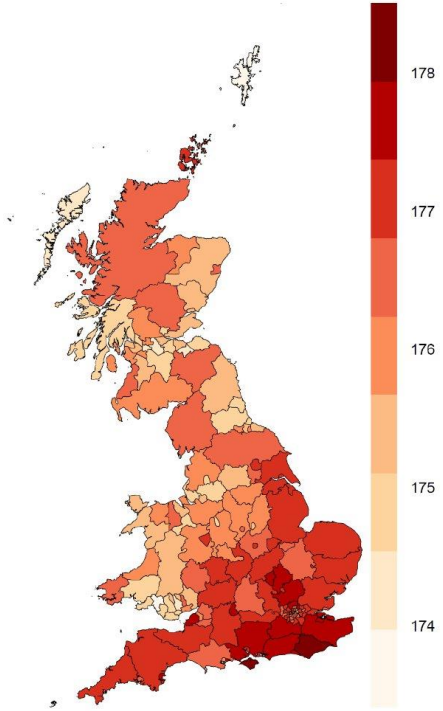
◆ MSOA Regions

● Local Authority Regions

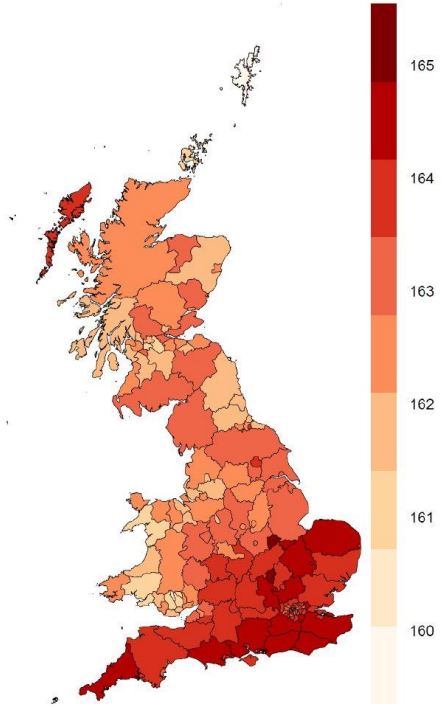
Unpublished results



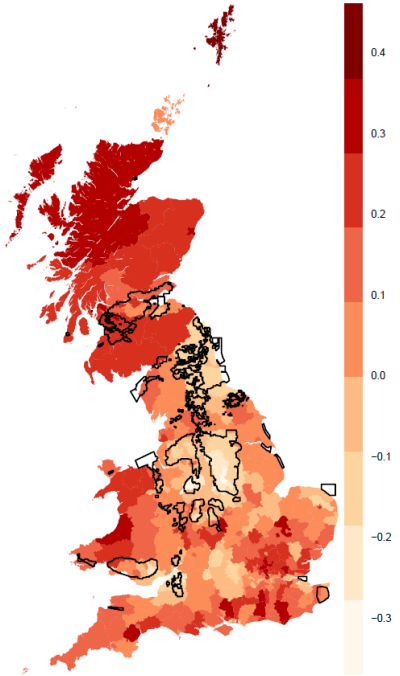
Height Polygenic Score



Phenotypic Height (males)



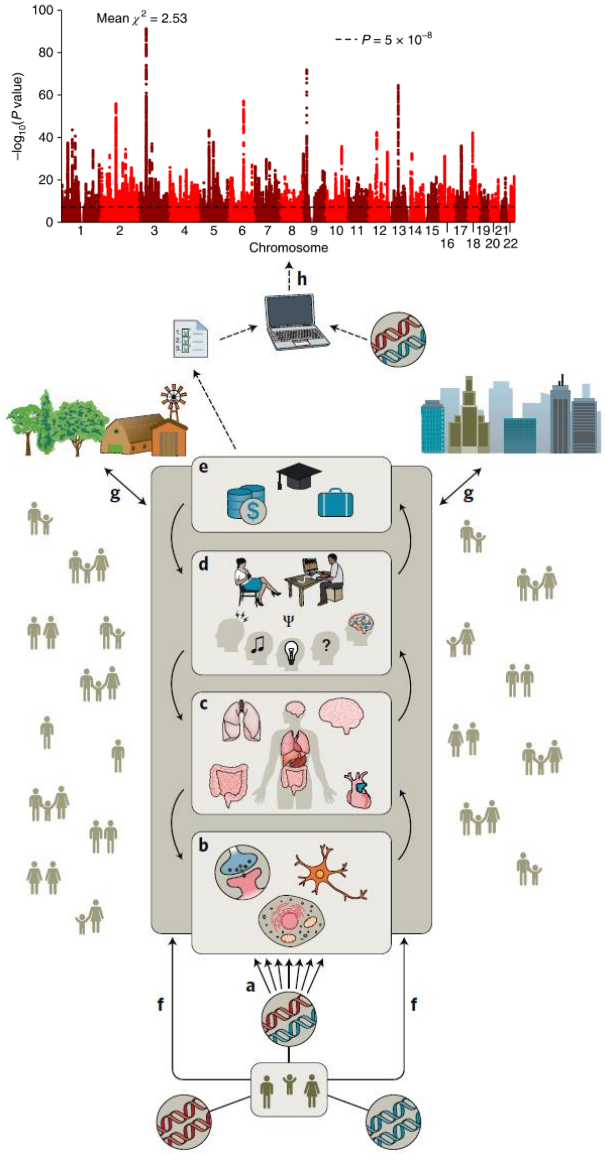
Phenotypic Height (females)



Educational Attainment Polygenic Score

Key points

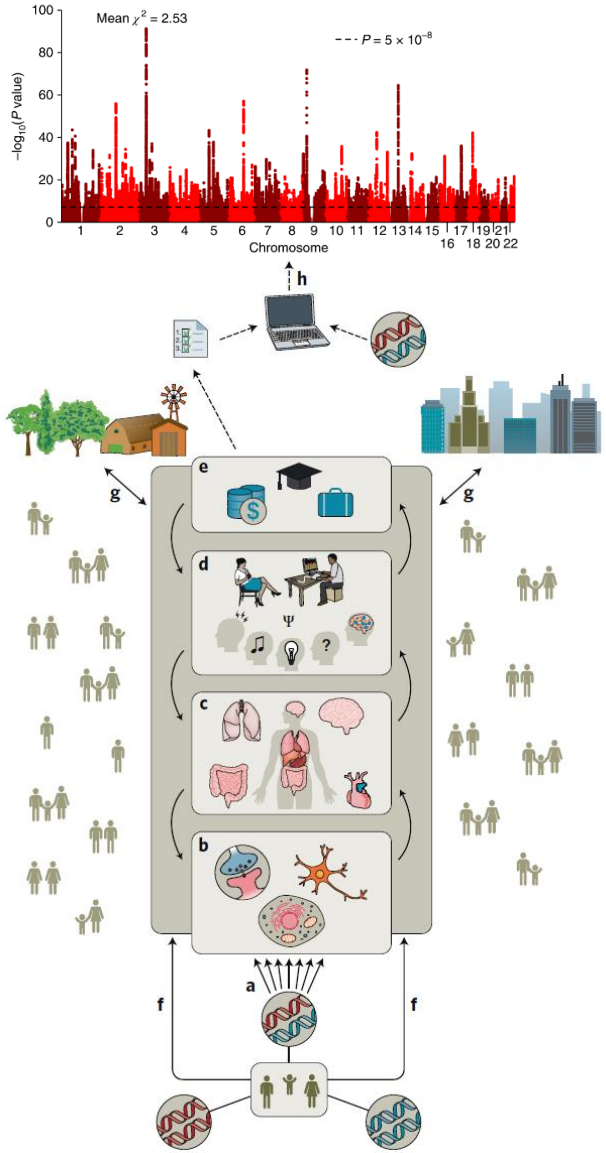
Society makes genetic effects stronger.



Key points

Society makes genetic effects stronger.

We reward certain genetic propensities with a better environment, and “punish” the lack of those propensities with a worse environment.



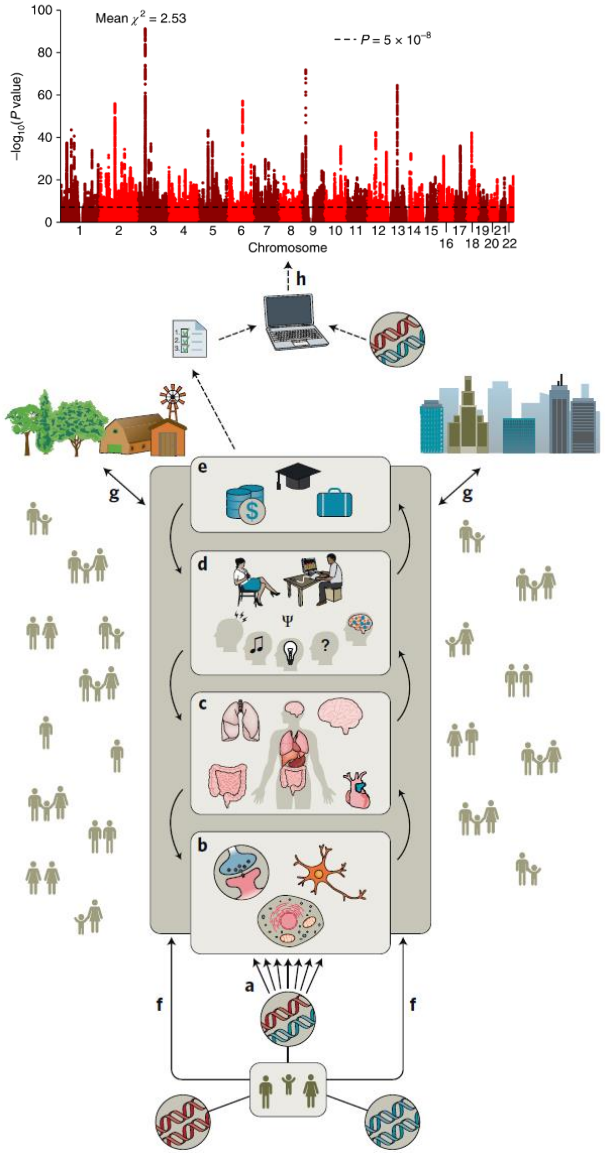
Key points

Society makes genetic effects stronger.

We reward certain genetic propensities with a better environment, and “punish” the lack of those propensities with a worse environment.

This makes society more unequal.

This makes studying genetics more difficult.



WIRED **Genetic Screening Now Lets Parents Pick the Healthiest Embryos**

AT 18 MONTHS old, Aurea Yenmai Smigrodzki is inquisitive like any other toddler. She likes peanut butter, the beach, and mobile phones—or any toys that look like phones. She likes to copy her mum and dad, Thuy and Rafal, when they are using theirs. Aurea doesn't know it yet, but her birth was very special: She is the world's first PGT-P baby, meaning she is statistically less likely than the rest of us to develop a genetic disease or disorder throughout her life.

LifeView™
Powered by Genomic Prediction

Why Choose Us | Our Tests | Clinicians | The Science | Company | contact

*Working with **173** Clinics in **37** countries and **6** continents ... and growing.*

Contact us to find a clinic near you

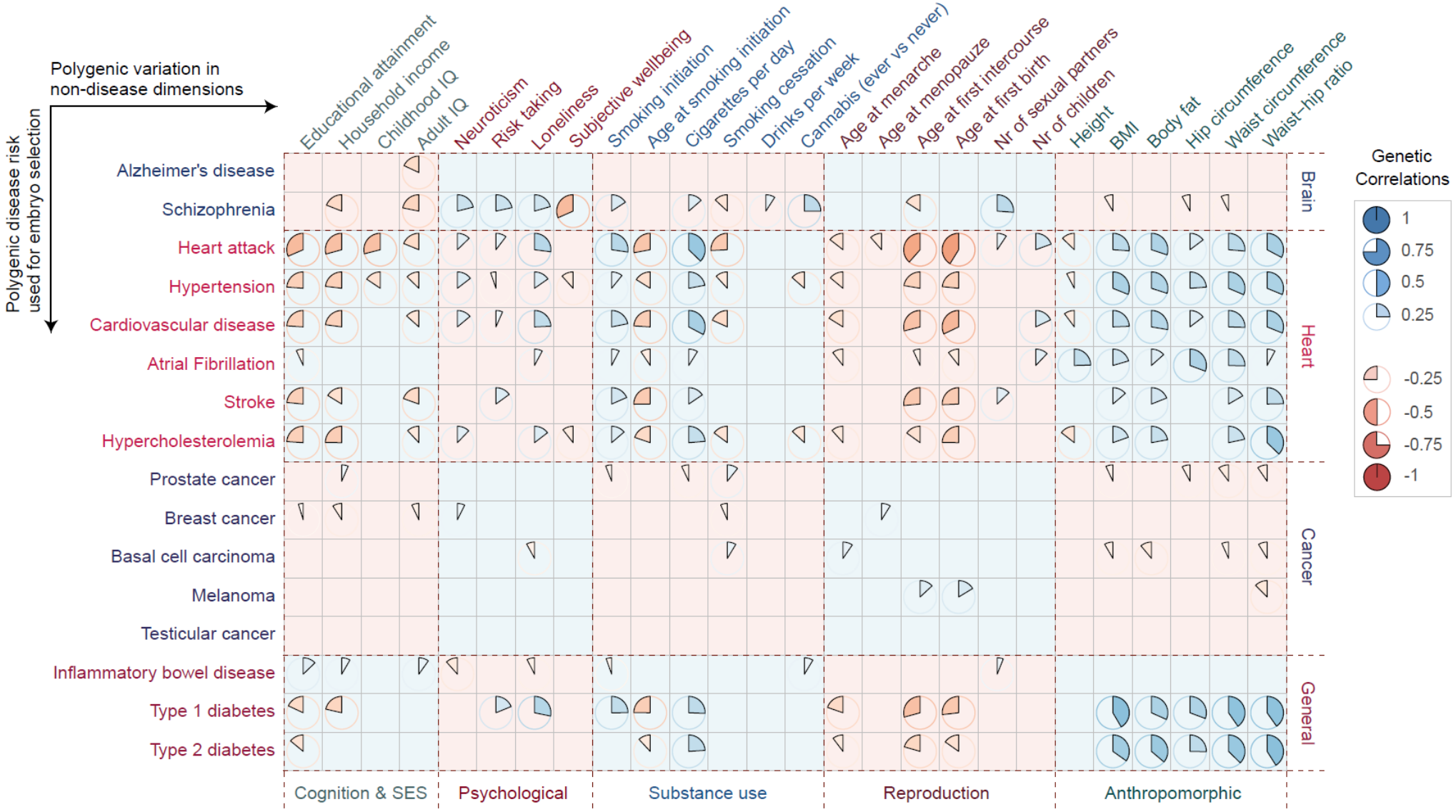
LifeView Patients Providers Resources About Us

4.2 Does Genomic Prediction screen purely cosmetic traits?

No, we only provide risk scores for polygenic traits related to diseases, not for purely cosmetic traits such as hair color and eye color. Our goal is to provide improved health to IVF families.

4.3 Does Genomic Prediction Clinical Laboratory screen embryos for increased intelligence i.e. high IQ?

No.



Unpublished results