Australian Government
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National Health and Medical Research Council
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Old questions with new data: UKB as a disruptive data resource

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Program in Complex Trait Genomics

The University Of Queensland AUSTRALIA | IMB
Institute for Molecular Bioscience

The University Of Queensland AUSTRALIA | QBI
Queensland Brain Institute

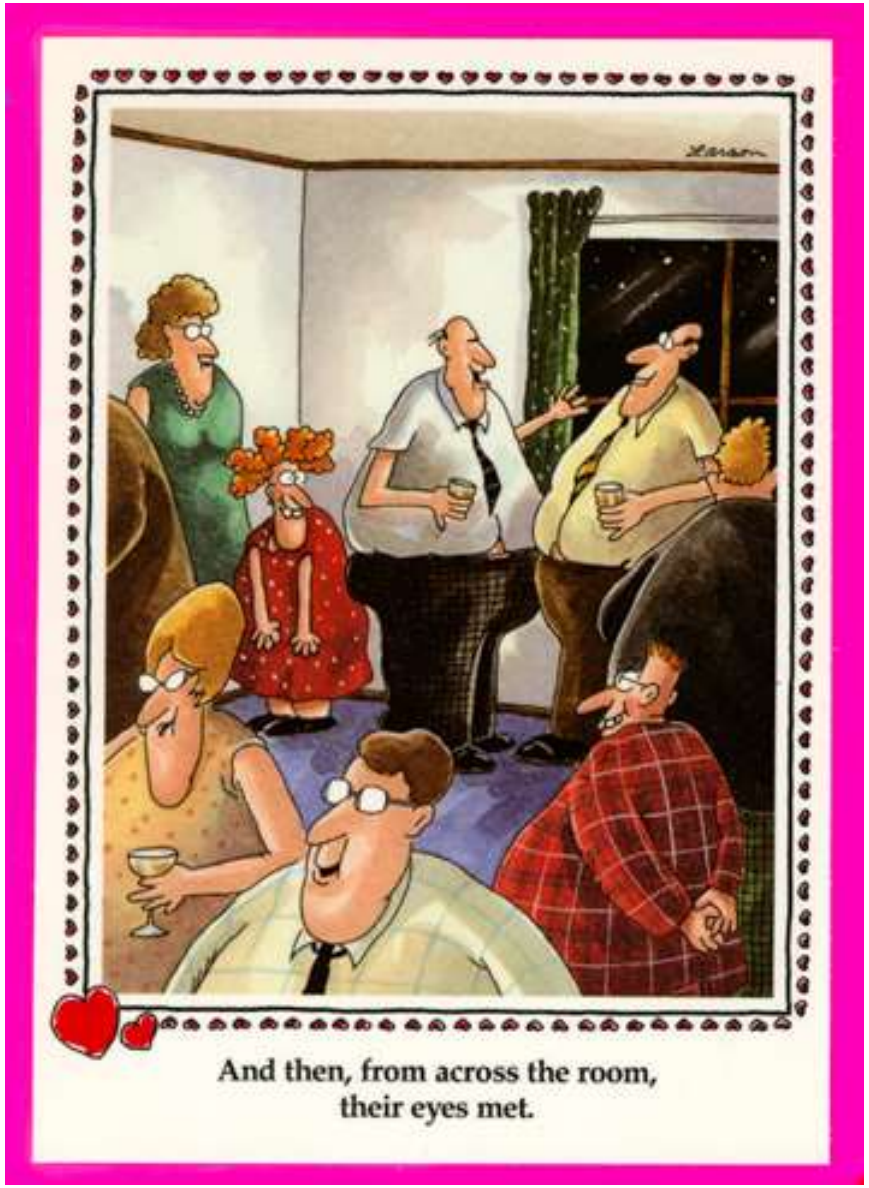
UKB and genetics research

- Disruptive in size
- Disruptive in data quality
- Disruptive in breadth
- Disruptive in model for research

UKB and complex trait genetics

- Discovery of gene variants and genes
- Discovery of putative causal epidemiological associations
- Estimation of genetic variation
- Estimation of genetic correlations between traits
- Genetic prediction of traits and disease
- **Addressing old questions with new data**

Assortative mating revisited



Partners may look/be alike because of

- Social homogamy
- Convergence in time because of similar environment (marital interaction)
- **Phenotype-driven mate choice**

Observation on similarity between spouses is not new

VOLUME II NOVEMBER, 1903 No. 4

ON THE LAWS OF INHERITANCE IN MAN*.

I. INHERITANCE OF PHYSICAL CHARACTERS.

By KARL PEARSON, F.R.S., assisted by ALICE LEE, D.Sc.
University College, London.

364 *On the Laws of Inheritance in Man*

DIAGRAM IV. *Distribution of Stature.*

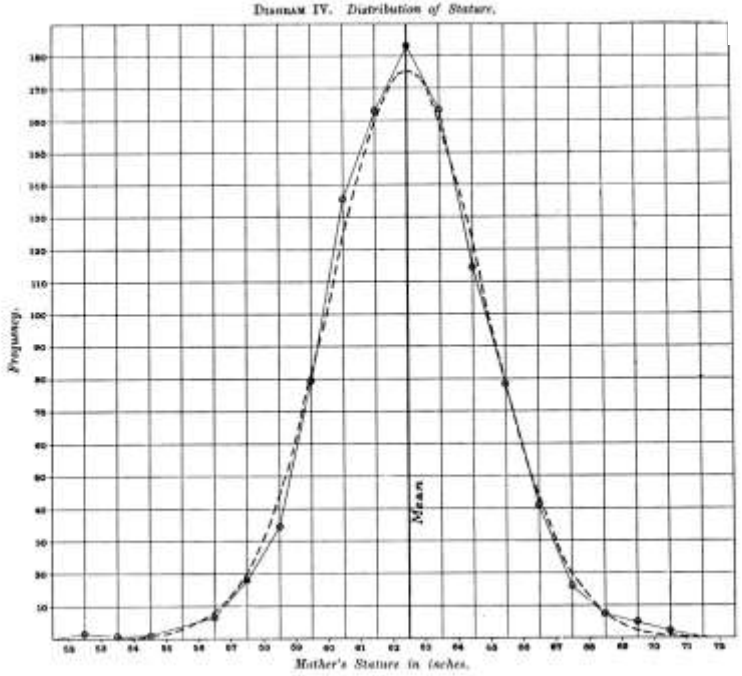
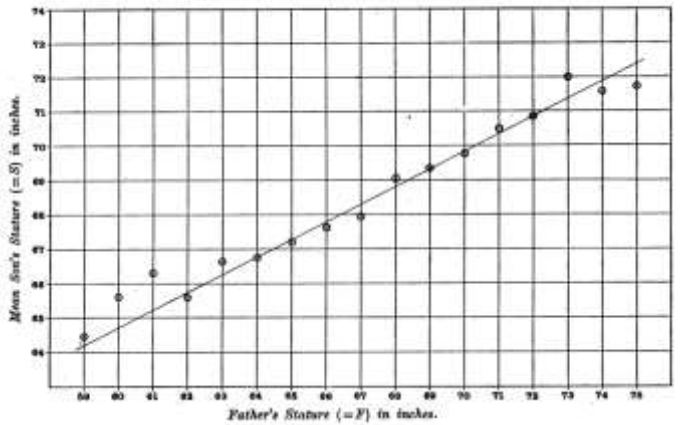


DIAGRAM I. *Probable Stature of Son for given Father's Stature.*
Regression Line: $S = 33{\cdot}73 + {\cdot}516\,F$. 1078 Cases.



PAIR	CORRELATION	SE
Spouse	0.28	0.02
Son-Father	0.51	0.02
Daughter-Father	0.51	0.01
Son-Mother	0.49	0.02
Daughter-Mother	0.51	0.01
Brother-brother	0.51	0.03
Sister-sister	0.54	0.02
Brother-sister	0.55	0.01

Observation on similarity between spouses is not new

Table. Approximation of Tetrachoric Partner Correlations in the Full Population From Case-Control Estimates

	Mean From Case-Control Data (Ratio 1:5)[a]		Approximation in Full Population	
Disorder	OR of Partner Being Affected	Tetrachoric Partner Correlation	Prevalence, *K* Value	Tetrachoric Partner Correlation[b]
Attention-deficit/hyperactivity disorder	7.20	0.45	7.2×10^{-3}	0.31
Autism spectrum disorder	10.80	0.47	1.5×10^{-3}	0.28
Schizophrenia	7.30	0.42	3.4×10^{-3}	0.26
Bipolar disorder	2.00	0.15	7.2×10^{-3}	0.10
Depression	1.84	0.16	3.6×10^{-2}	0.12
Generalized anxiety disorder	2.64	0.19	2.7×10^{-3}	0.11
Agoraphobia	3.56	0.24	1.8×10^{-3}	0.14
Social phobia	3.75	0.27	2.8×10^{-3}	0.16
Obsessive-compulsive disorder	2.42	0.17	2.3×10^{-3}	0.10
Substance abuse	3.87	0.37	3.9×10^{-2}	0.30
Anorexia nervosa	3.10	0.18	1.9×10^{-4}	0.08

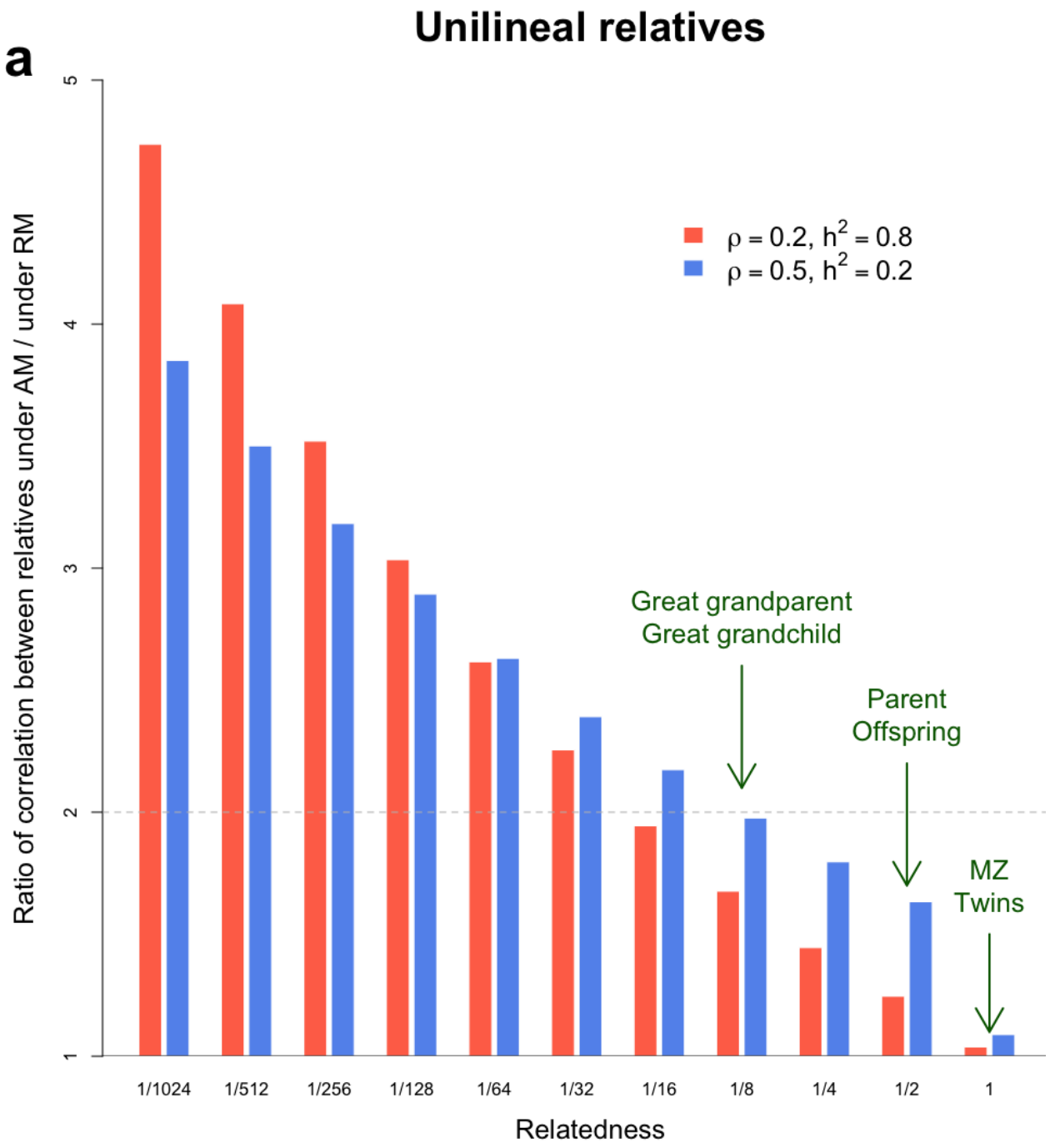
Peyrot 2016 JAMA Psychiatry

Genetic consequences of like-with-like AM

- Compared to a random mating population:
  (1) positive correlation in genetic values between mates
  (2) increase in genetic variance in the population
  (3) increased homozygosity at trait loci
  (4) increase in the correlation between relatives

→ Applies to disease and their risk factors

Increase in similarity between relatives

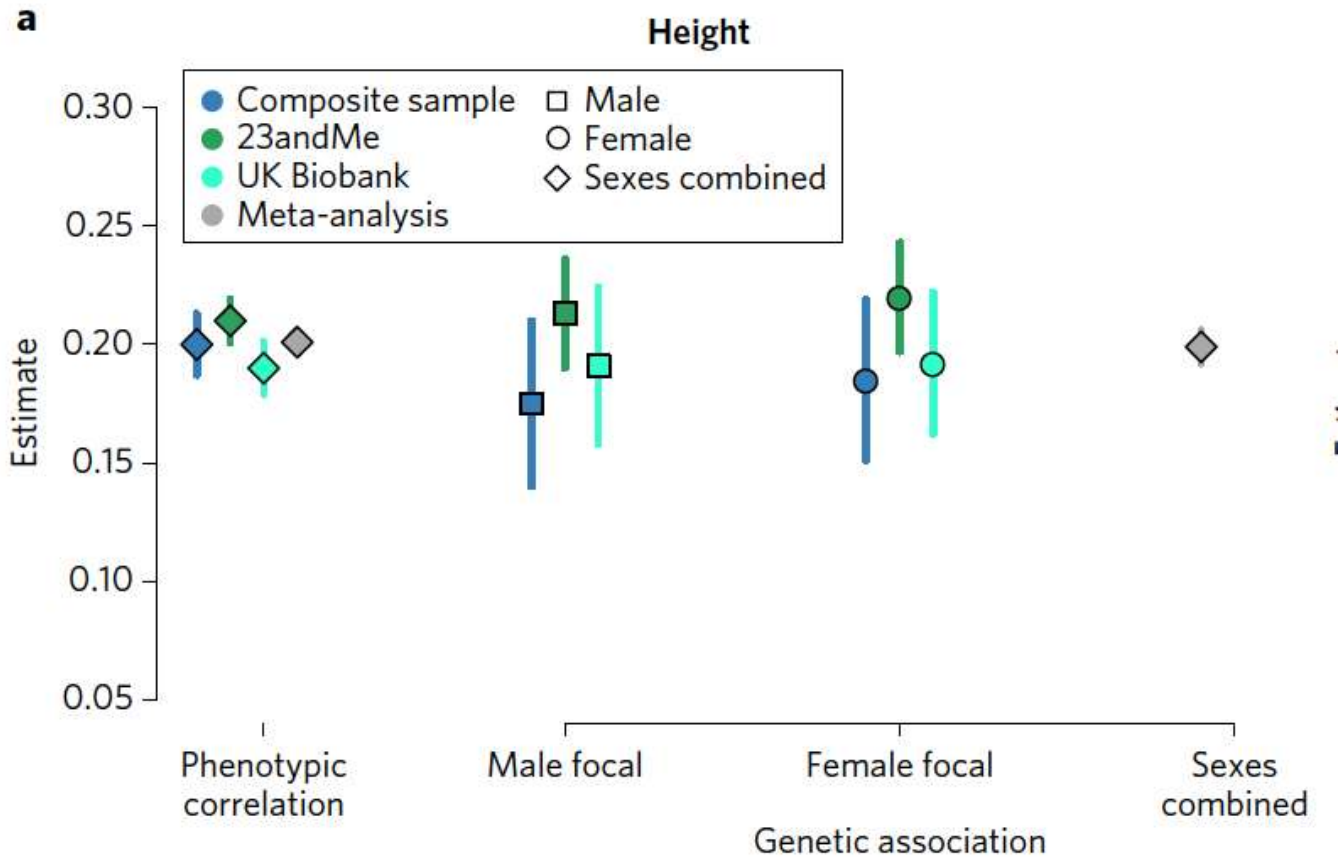


UK Biobank GWAS data

- Spouse pairs: Association between phenotype of one spouse with the genotype of their partner

- Population: Within-person association between trait increasing alleles at different loci

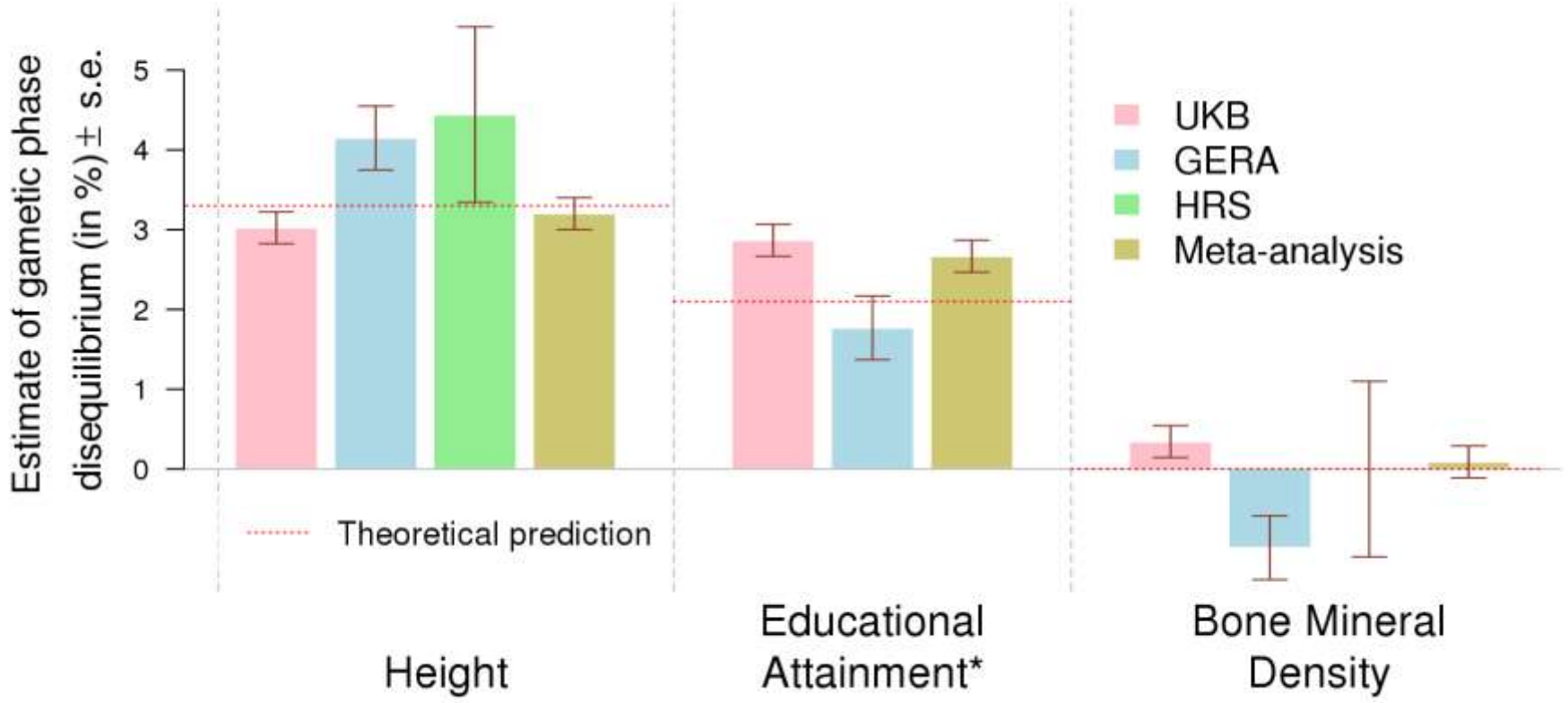
Spouse genetic correlation consistent with mate choice on height



Robinson 2017 Nature Human Behaviour

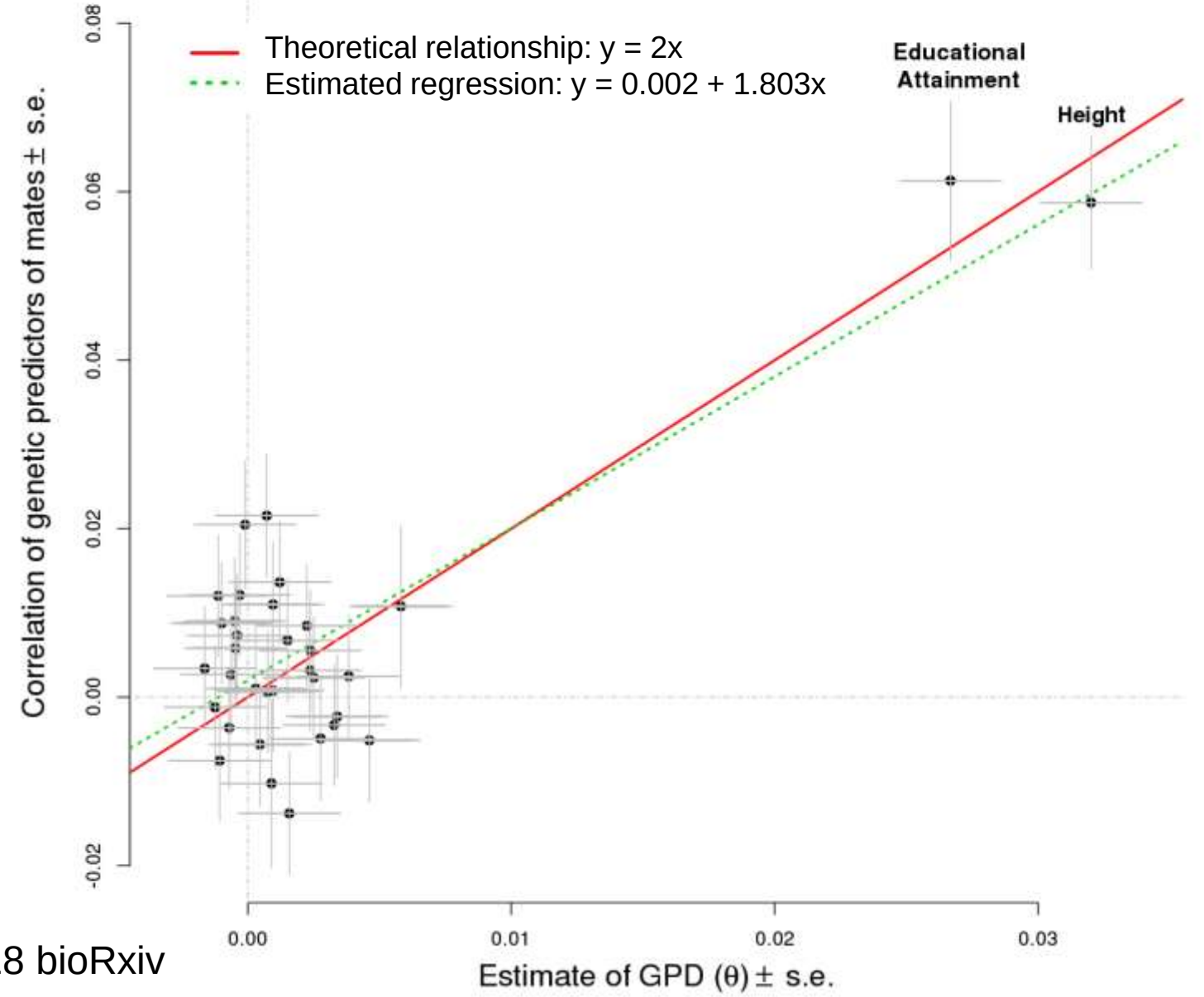
Effect of assortative mating on the genome

metric: correlation of trait-increasing alleles between odd and even chromosomes



Yengo 2018 bioRxiv

Verification using spouse pairs



Yengo 2018 bioRxiv

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N H M R C

Loic Yengo

Matt Robinson