ODISSEI Community Conference

22 October 2019 | Galgenwaard, Utrecht

ODISSEI

Open Data Infrastructure for Social Science and Economic Innovations

A genome-wide association study of health care costs

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NETHERLANDS TWIN REGISTER (NTR)

GENEN VAN ZOWEL MOEDER ALS BABY BEÏNVLOEDEN HET GEBOORTEGEWICHT

Een nieuwe publicatie in Nature Genetics

Lees meer

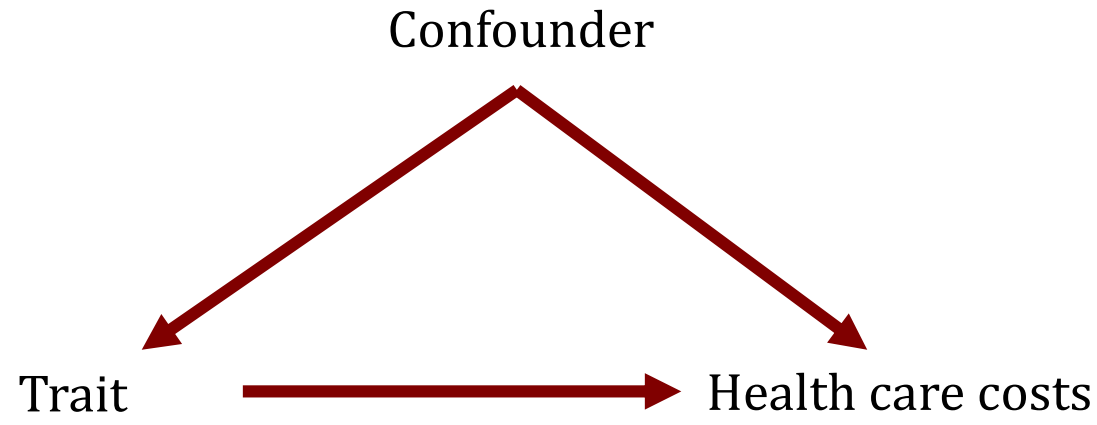
AANMELDEN, VERHUIZING OF WIJZIGING?

Neem contact op met het NTR

Lees meer

BACKGROUND

- Multiple physical and mental health and personality and cognitive traits have been associated with health care costs
  - Causal effect
  - Confounding
    - Socio-economic status, co-morbidity, genetic pleiotropy



GENETICS AS RESEARCH TOOL

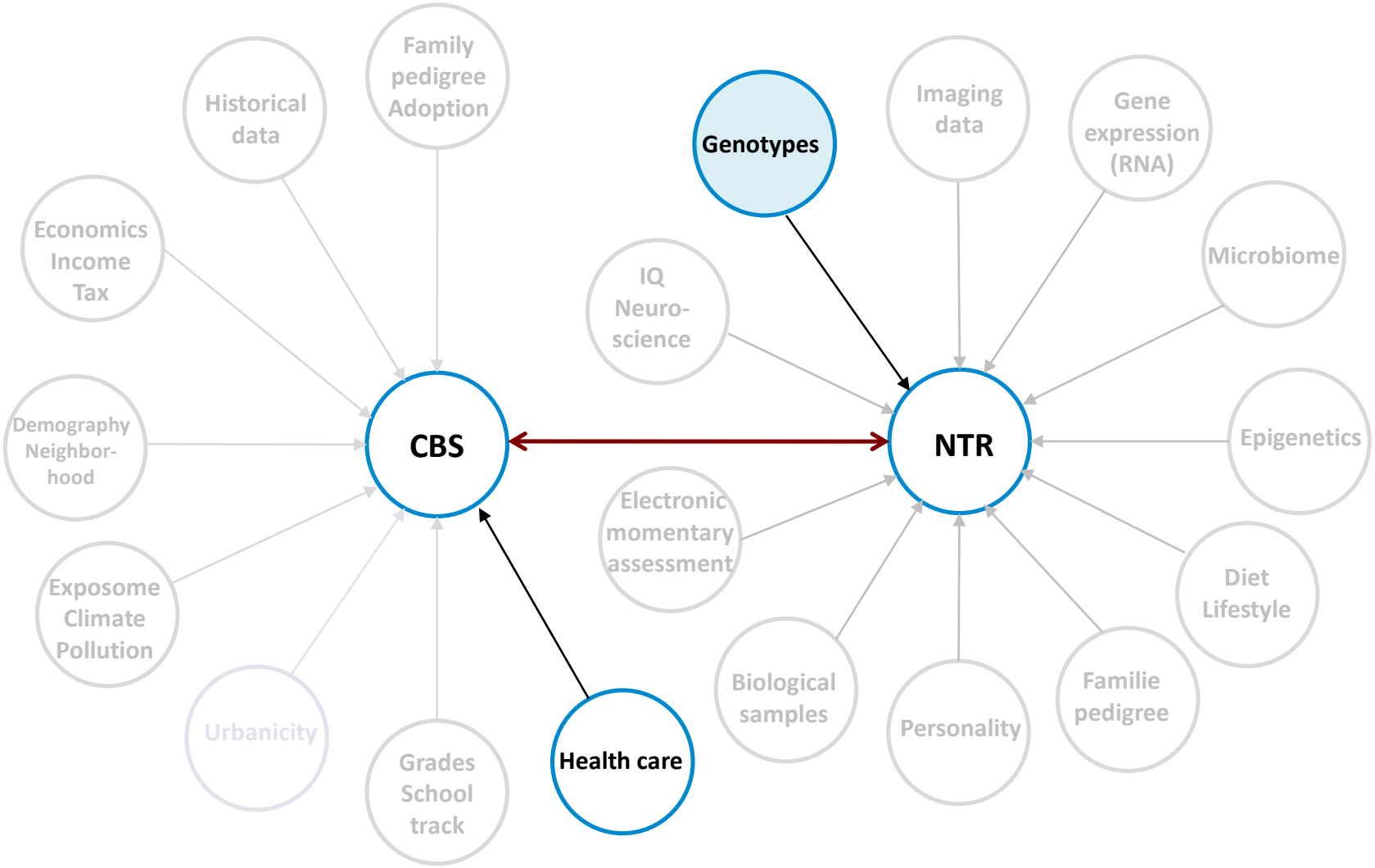
- Developments in molecular genetics allows the estimation of the causal impact of specific traits on health care costs

- A greater genetic predisposition to obesity was associated with higher health care costs (Wehby et al., 2017)
  - A 1 SD increase in BMI genetic risk score was associated with an increase of $805 in health care costs

RESEARCH QUESTIONS

- Which genetic variants are related to differences in health care costs?
  - A genome-wide association (GWA) analysis
- What are the genetic correlations between specific traits and health care costs?
  - Bivariate genome-based restricted maximum likelihood (GREML) analyses
- Which associations between specific traits and health care costs are due to a causal effect?
  - Genomic structural equation modelling (SEM) analyses

ODISSEI SECURE SUPERCOMPUTER (OSSC)



PARTICIPANTS

- ~21,000 NTR participants with genotype data
- ~16,500 NTR participants gave permission for linkage
- ~16,000 NTR participants with data on CBS health care costs

- After excluding ~1,000 NTR participants who are from non-European descent
  - Total sample size ~15,000
    - 40% males and 60% females

TOTAL HEALTH CARE COSTS

- Costs for 2009-2016
  - General practitioner care
  - Mental health care
  - Hospital care
  - Birth care
  - Geriatric care
  - Pharmacy
  - Physiotherapy
  - **No** dental care

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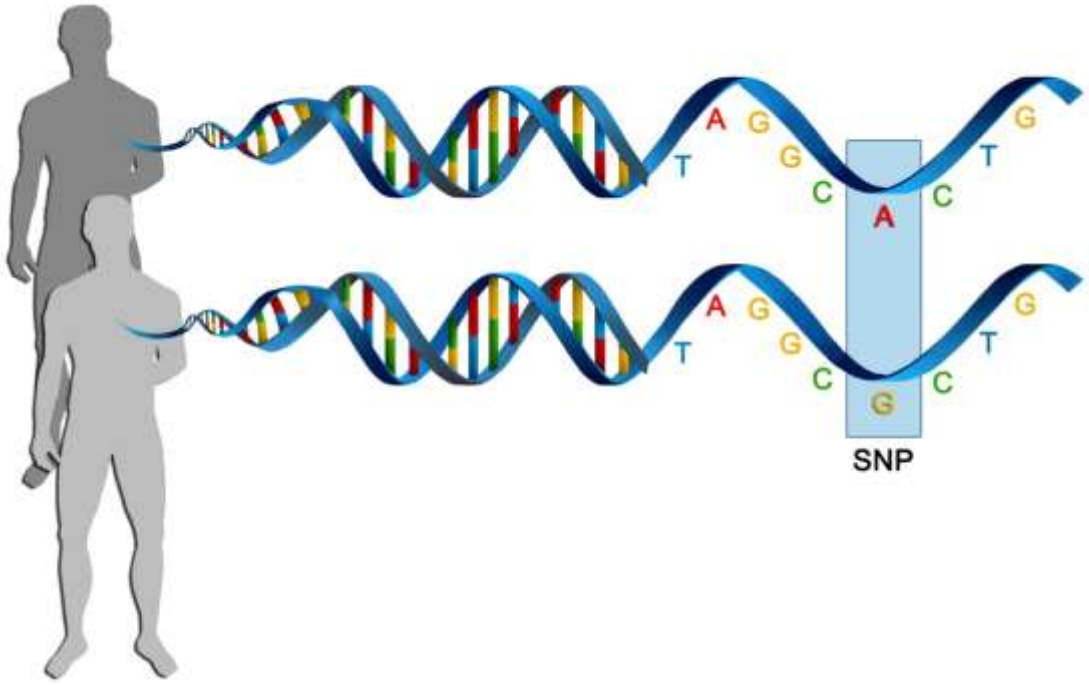
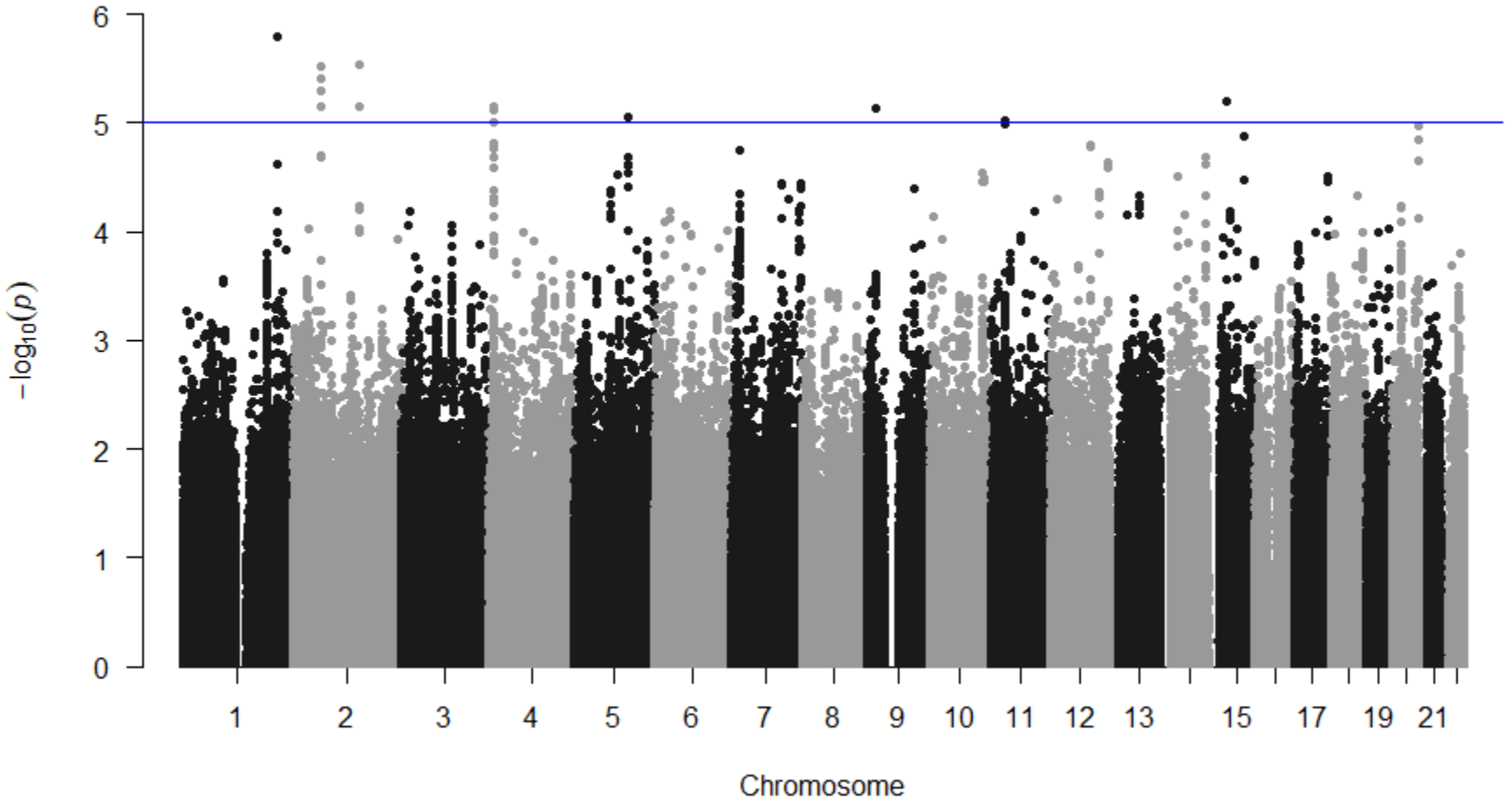
GENOME-WIDE ASSOCIATION STUDY (GWAS)

- Genome-wide association study = a study that tests the effect of a genetic variant (SNP) on a trait across the whole human genome



MANHATTAN PLOT



GENES

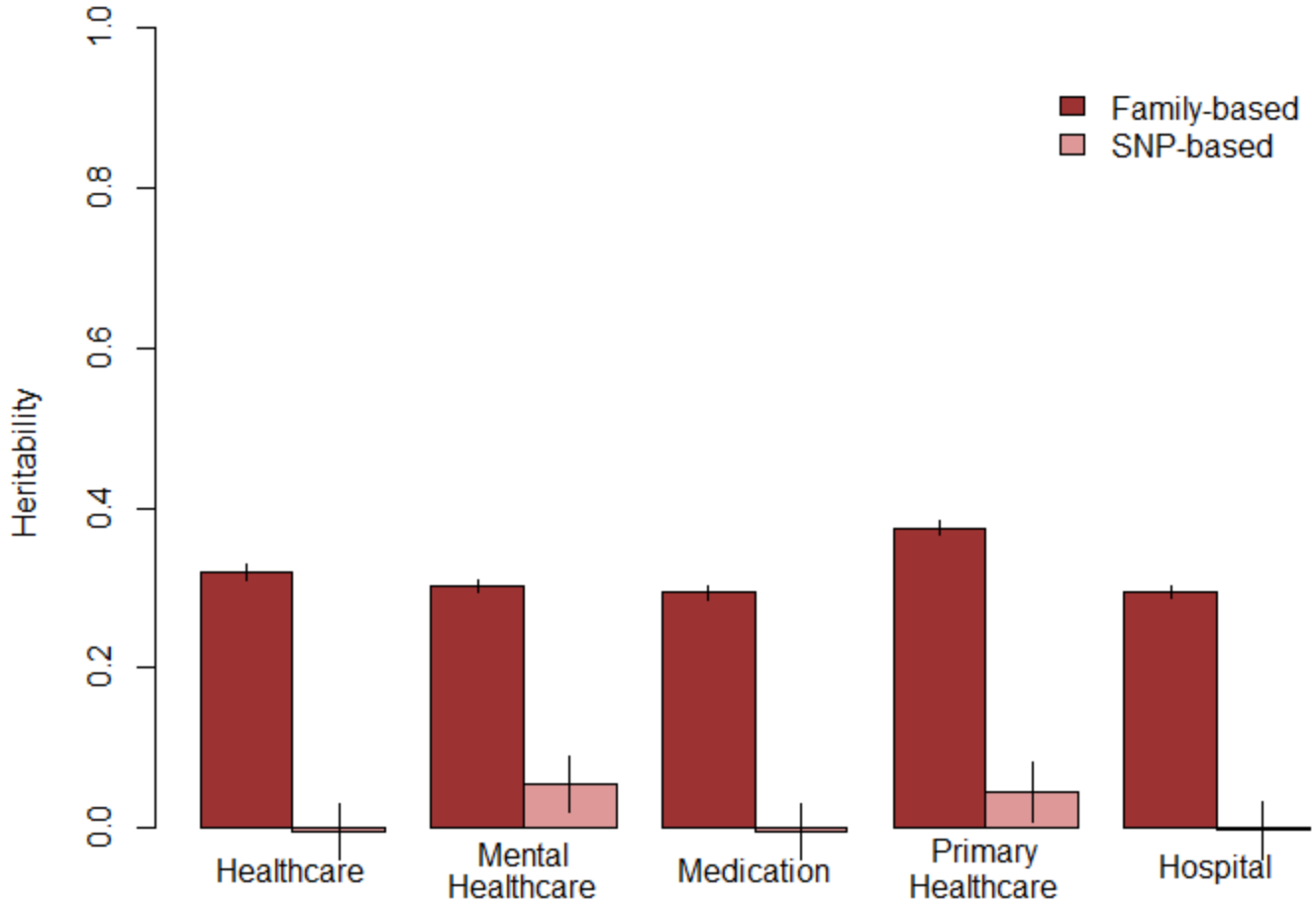
Chr	BP	Beta	SE	p	gene	function
1	213985718	-.091	.019	$2x10^{-6}$	PROX1-AS1	
2	64641736	.058	.012	$3x10^{-6}$	AC008074.3	
2	150252104	-.055	.012	$3x10^{-6}$	LYPD6	Acts as a modulator of nicotinic acetylcholine receptors (nAChRs) function in the brain
4	10845207	.062	.014	$7x10^{-6}$	WDR1	Involved in myocardium sarcomere organization. Required for cardiomyocyte growth and maintenance.
5	122000212	.057	.013	$9x10^{-6}$	RP11-166A12.1	

HERITABILITY

- SNP-based heritability = variance explained by genetic variants that are shared between unrelateds (between families)

- Family-based heritability = variance explained by the genetic resemblance between family members (within families)

HERITABILITY



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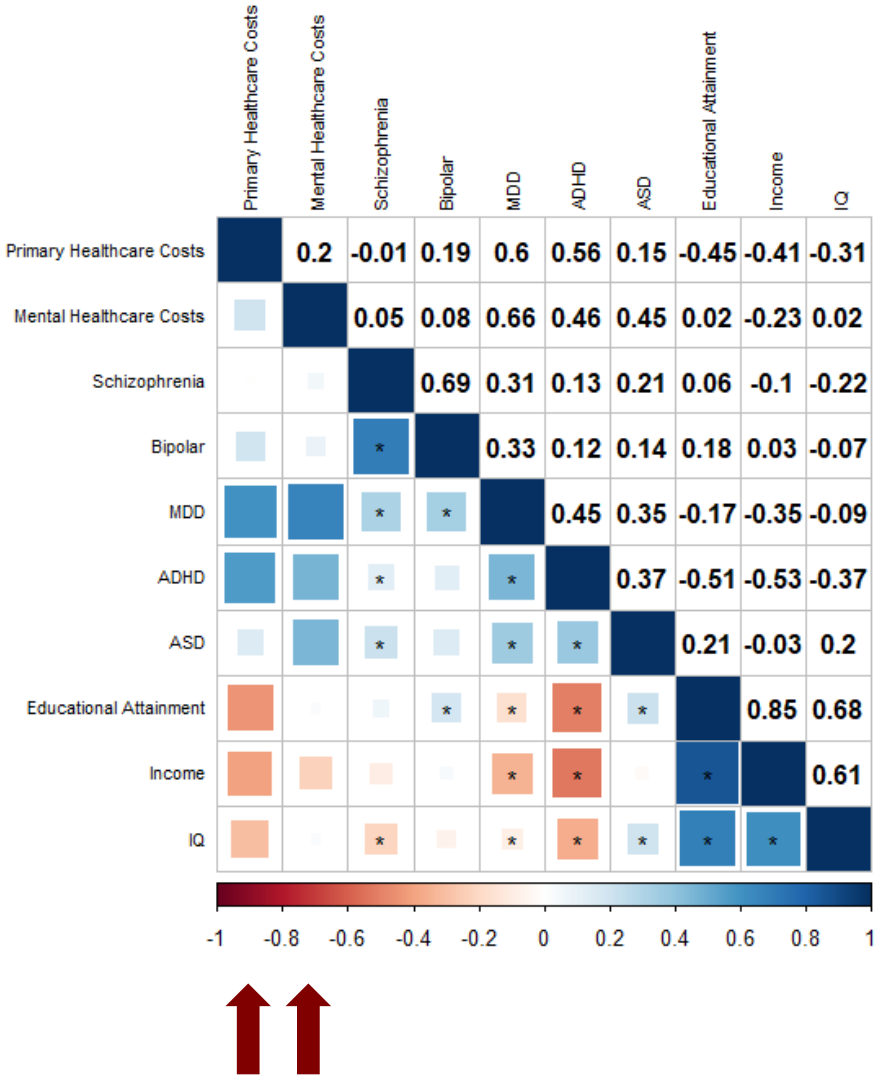
GENETIC CORRELATIONS



GENETIC ASSOCIATIONS

- Genetic associations can be estimated by using the results of the GWAS on health care costs and another trait
  - Can be due to a (reversed) causal effect
  - Can be due to genetic pleiotropy
- A genetic association between a trait and health care costs is a prerequisite for the existence of a causal effect

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OSSC POSSIBILITIES

- Other ODISSEI cohorts also have genotype data of their participants
- Multiple sociological outcomes available
  - Education, longevity, psychiatric disorders, entrepreneurship, neighbourhood characteristics
- Genomics is only one of the research areas within biology
  - Epigenomics, transcriptomics, proteomics, metabolomics

VRAGEN?

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