university of groningen

Sex differences in genetic influences on childlessness

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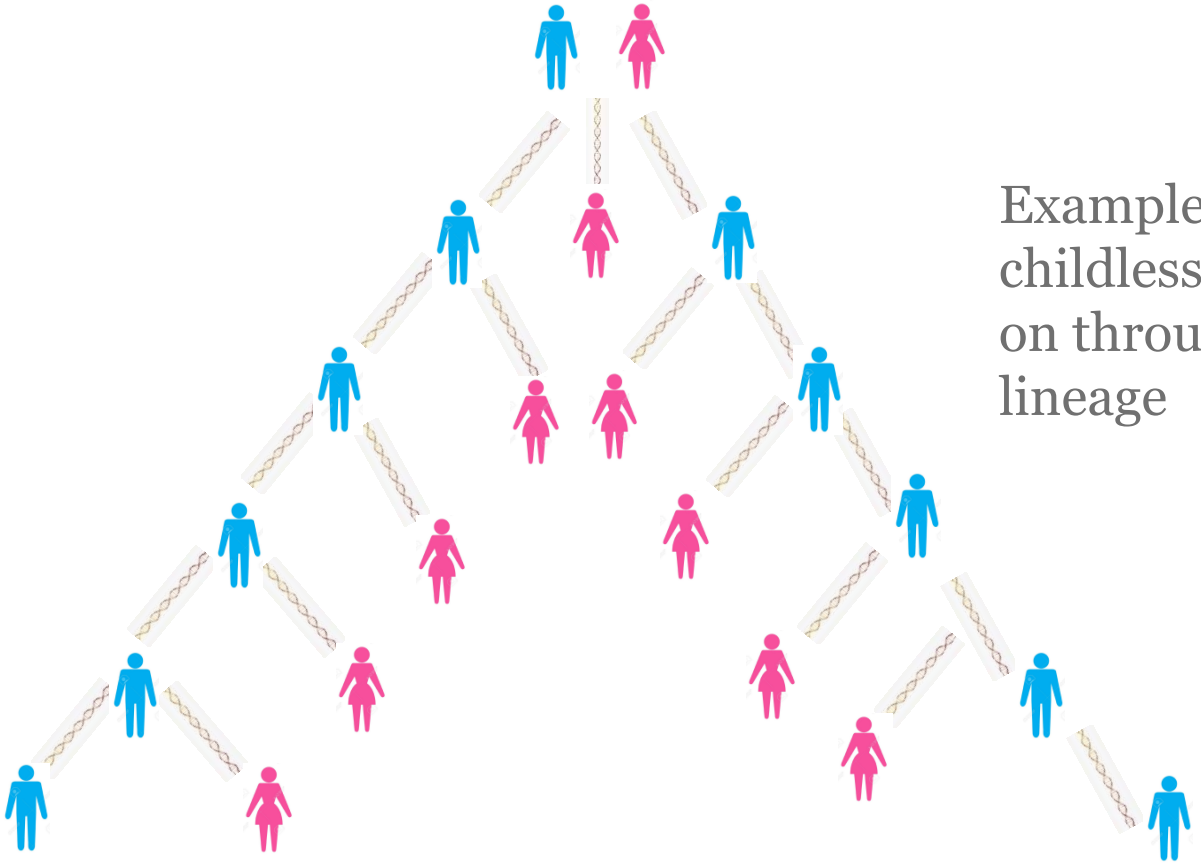
ICS
RUG/UU/RU

Background

- Previous research found:
  - Genetic influence on age at first birth (Nisen et al, 2013; Tropf et al, 2015)
  - Genetic influence on number ever born (Rodgers, Kohler, et al, 2001; Zietsch et al, 2014)
  - Genetic influence on childlessness (Kohler et al, 1999)
- Evolutionary unlikely (Fisher, 1930)
- However….
- Gene environment interactions (Rodgers, Hughes et al, 1999)
  - Fertility norms and genetic influences (Bras, Bavel & Mandemakers, 2013)
  - Genetic influence on early menopause and endometriosis (He et al, 2010)
- Sex differences (Hughes & Burleson, 2000; Gershoni & Pietrokovski, 2014)

Sexual antagonism



Example: female childlessness passed on through male lineage

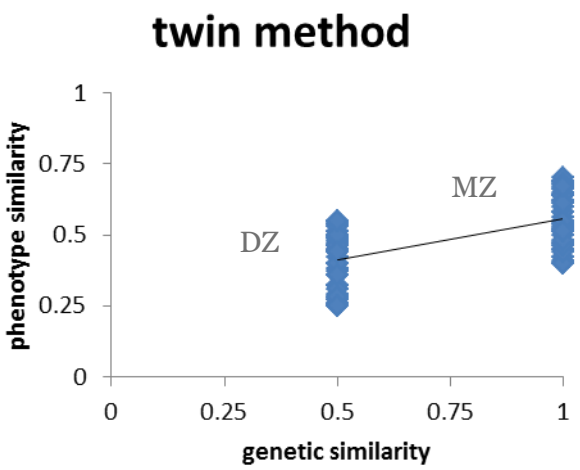
Research questions

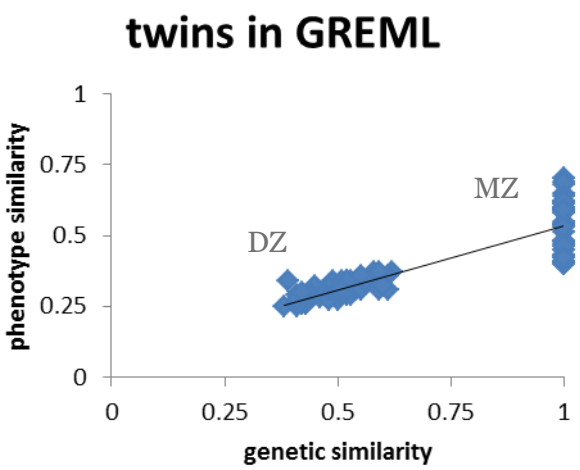
- Is there is a genetic influence on childlessness?
- Do different genes influence childlessness in men and women?

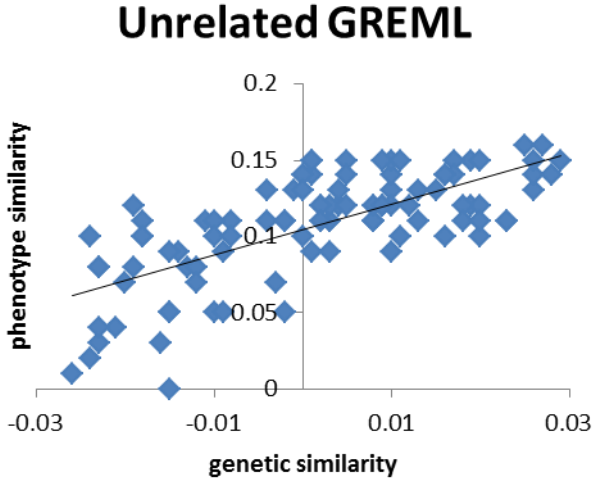
Data

- Swedish Twin Register (n=9,942)
- Same sex and opposite sex twin pairs
- Individuals with measured genetic information
- Women over 45 and men over 50 years of age

Twin and GREML method

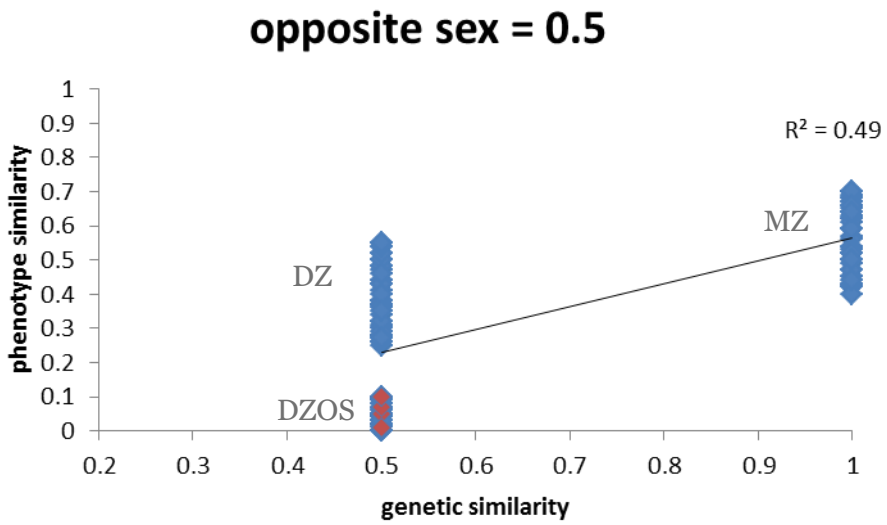


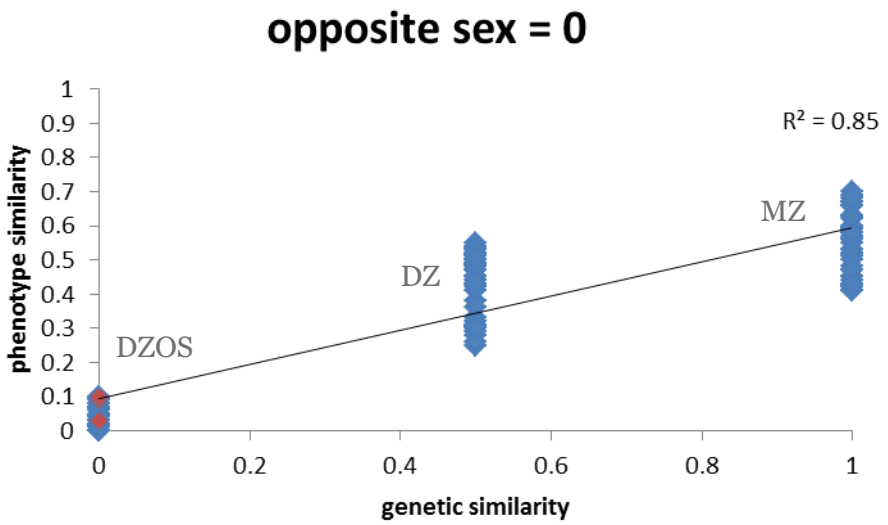




Sex differences

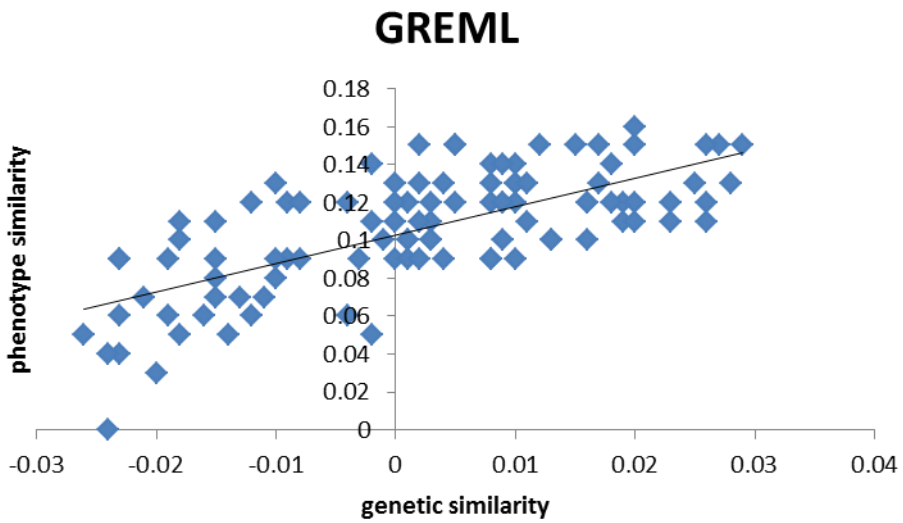
Sex-limitation model

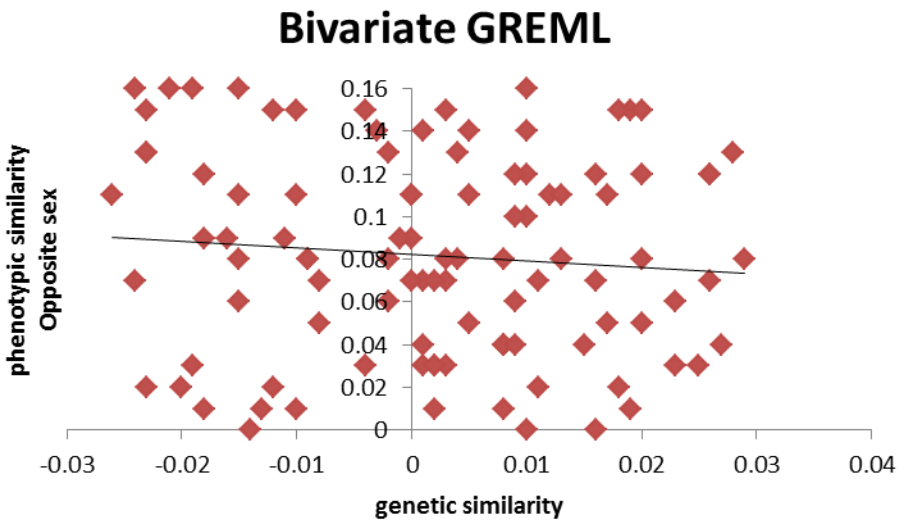




Sex differences

Bivariate GREML

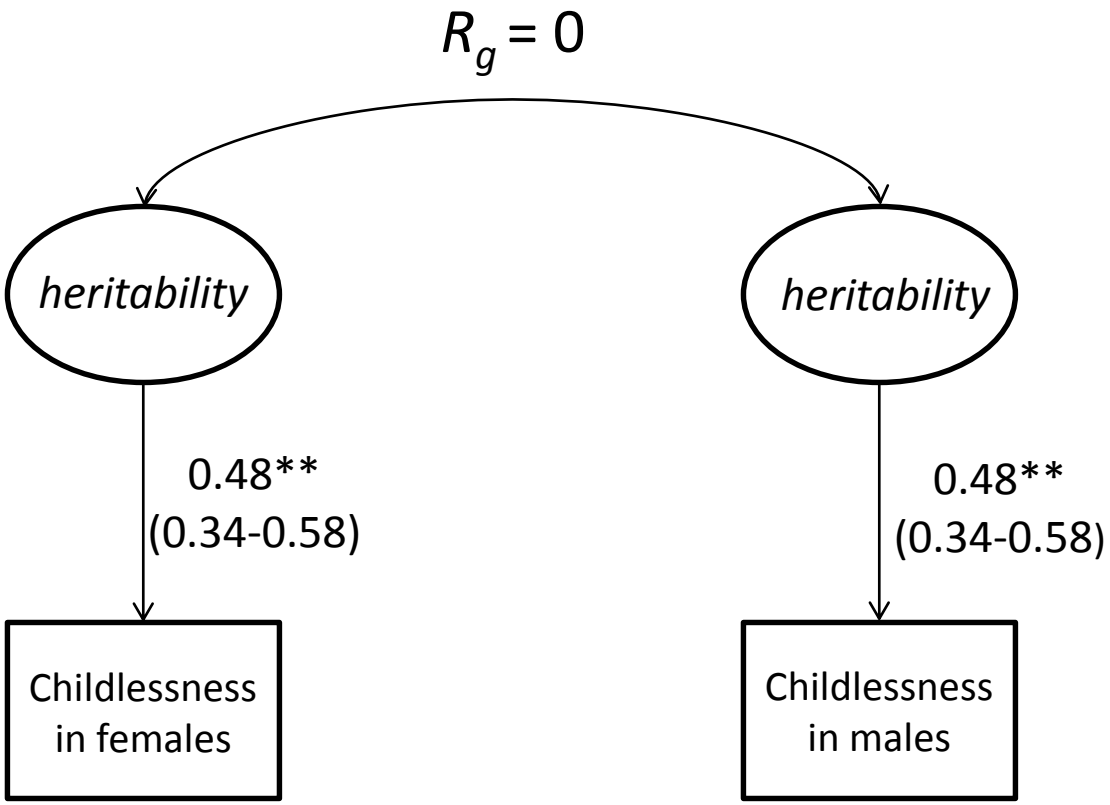




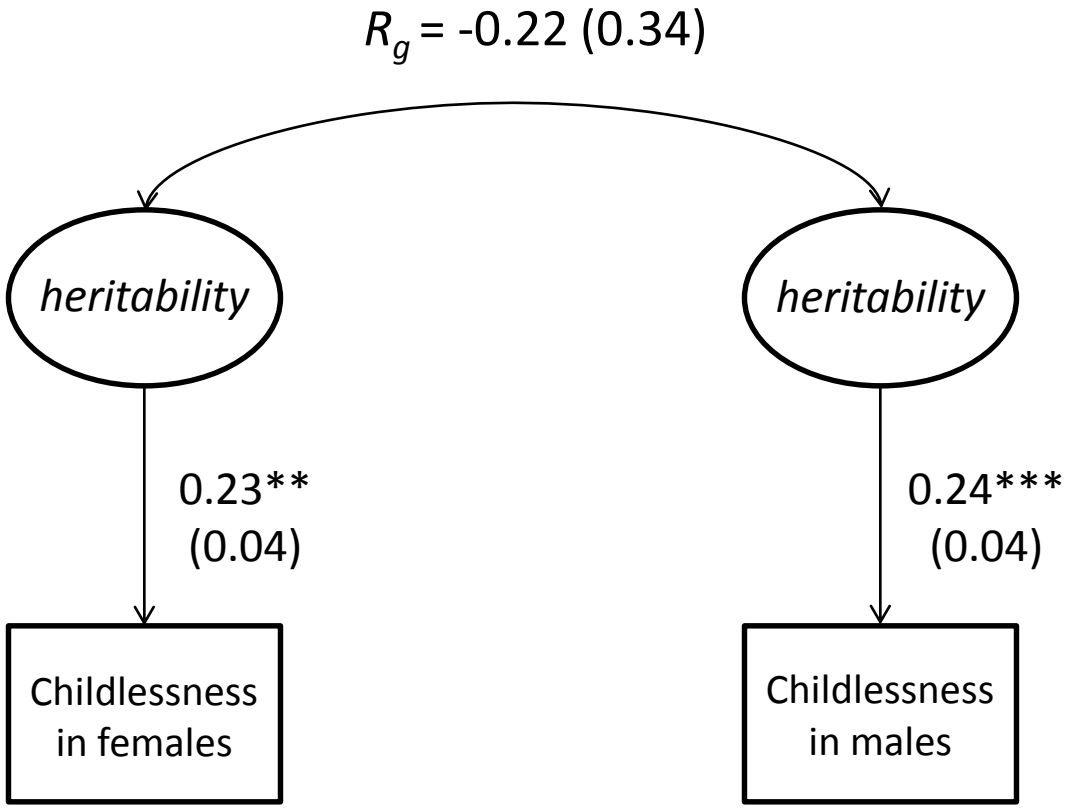
Same sex pairs

Opposite sex pairs

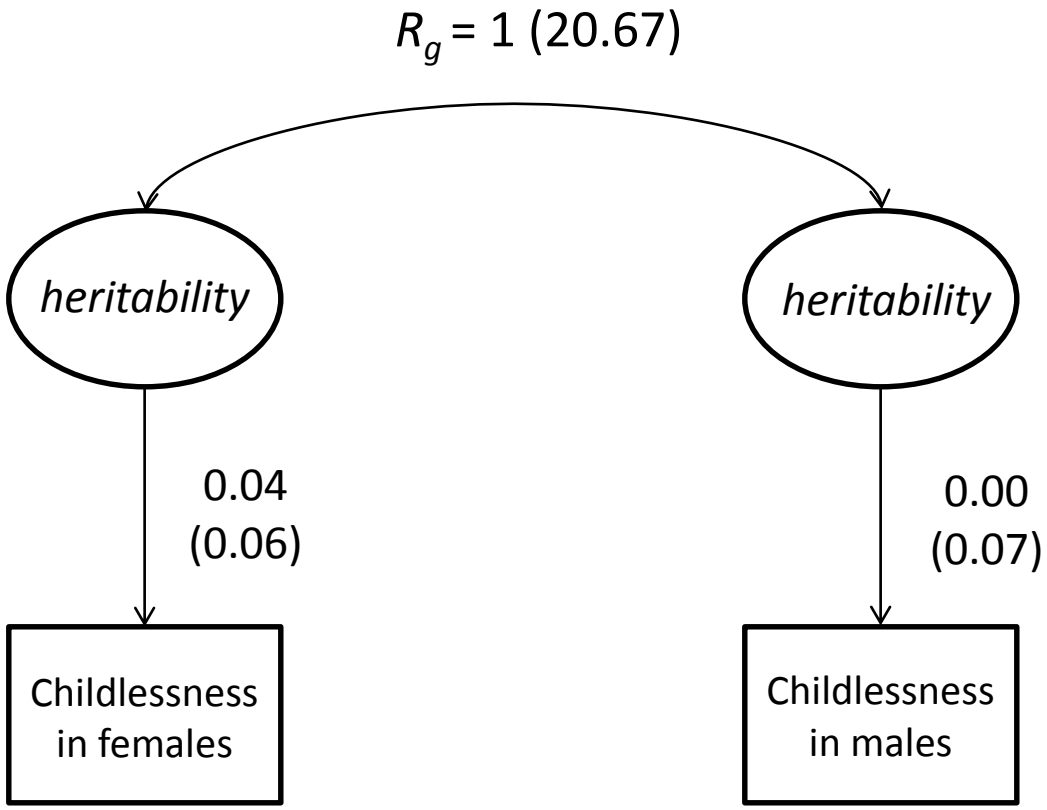
Results twin method



Results twins in GREML



Results GREML method on unrelated individuals



Conclusions

- Moderate levels of heritability of childlessness
- Different genes involved in childlessness in men and women
- Higher heritability from the twin study than from the GREML method

Limitations

- Heritability estimates and sex differences based on related individuals
- Inflation due to environmental influences

Thank you for your attention

References

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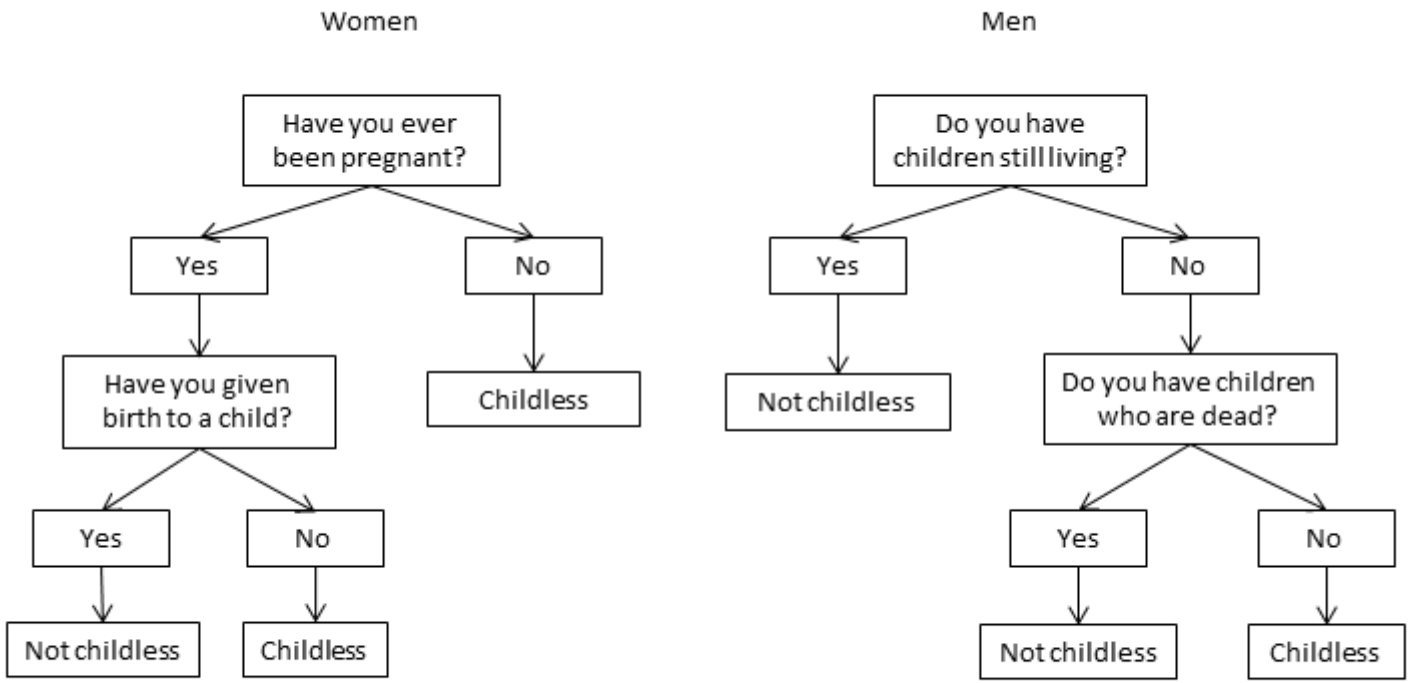
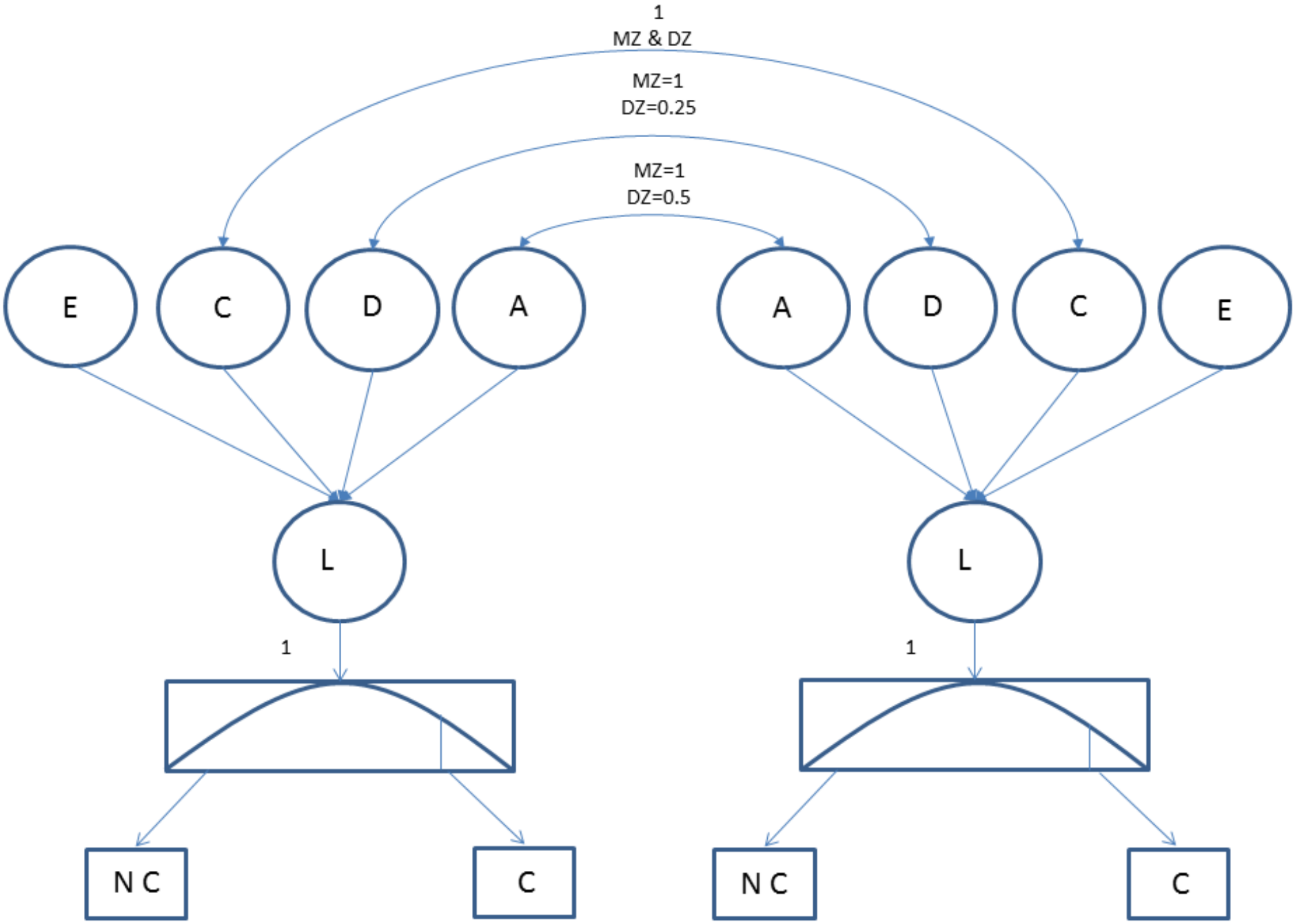
Extra information


Women
Have you ever been pregnant?
Yes
No
Have you given birth to a child?
Childless
Yes
No
Not childless
Childless
Men
Do you have children still living?
Yes
No
Not childless
Do you have children who are dead?
Yes
No
Not childless
Childless


1
MZ & DZ
MZ=1
DZ=0.25
MZ=1
DZ=0.5
E
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D
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Genotyping

- Genotyping with Illumina OmniExpress 700K chip
- Imputed according to the 1000 genome imputation panel
- Selected SNPs from the HapMap3 panel
- SNPs with MAF 1%, missing rate 3% and who failed the Hardy-Weinberg equilibrium for a threshold of 10^{-6} are removed

Sample sizes

Sample		N	N complete pairs
Female	MZ	1158	513
	DZ	2254	814
Male	MZ	1167	513
	DZ	1612	549
Opposite sex		3751	1223
Total		9942	3612