Genetic Confounding in Bullying Research

Causal Claims Revisited

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Background

Victimization → later internalizing problems
(Moore et al., 2017)

Perpetration → later externalizing problems
(Ttofi et al., 2012)

Bullying involvement and internalizing & externalizing problems are partly heritable
(Franić et al., 2014; Kendler et al., 2016; Nivard et al., 2015; Veldkamp et al., 2019)

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Are causal claims justified?

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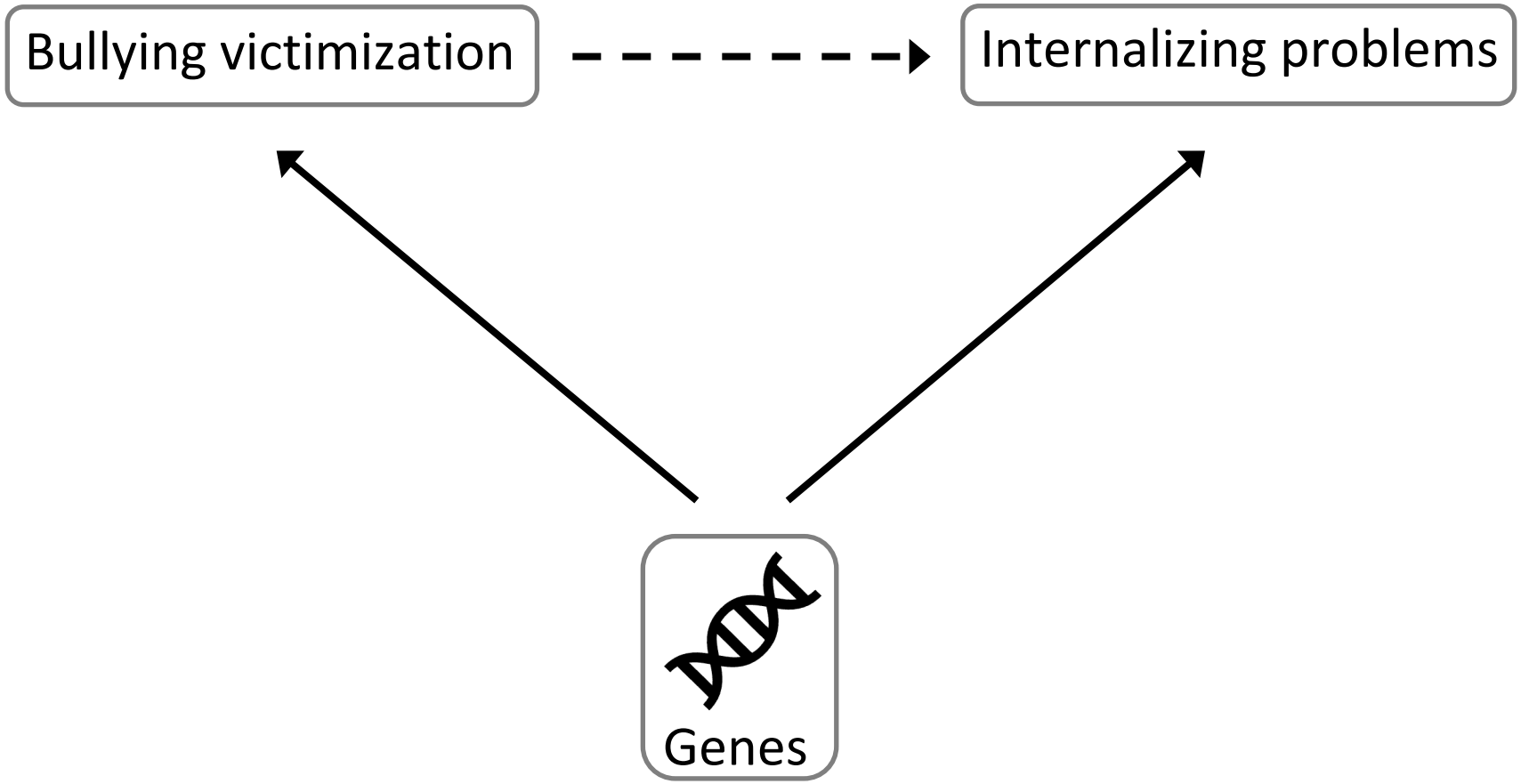
Genetic confounding



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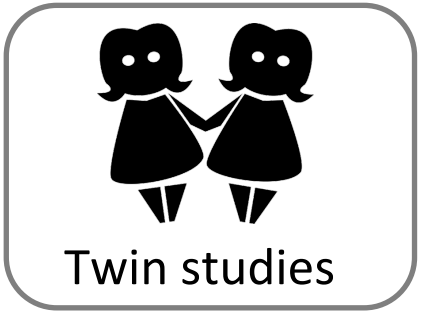
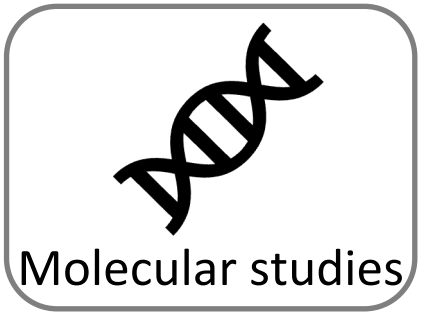
Heritability estimates



- Twin heritability



- SNP heritability
- R^2 polygenic scores

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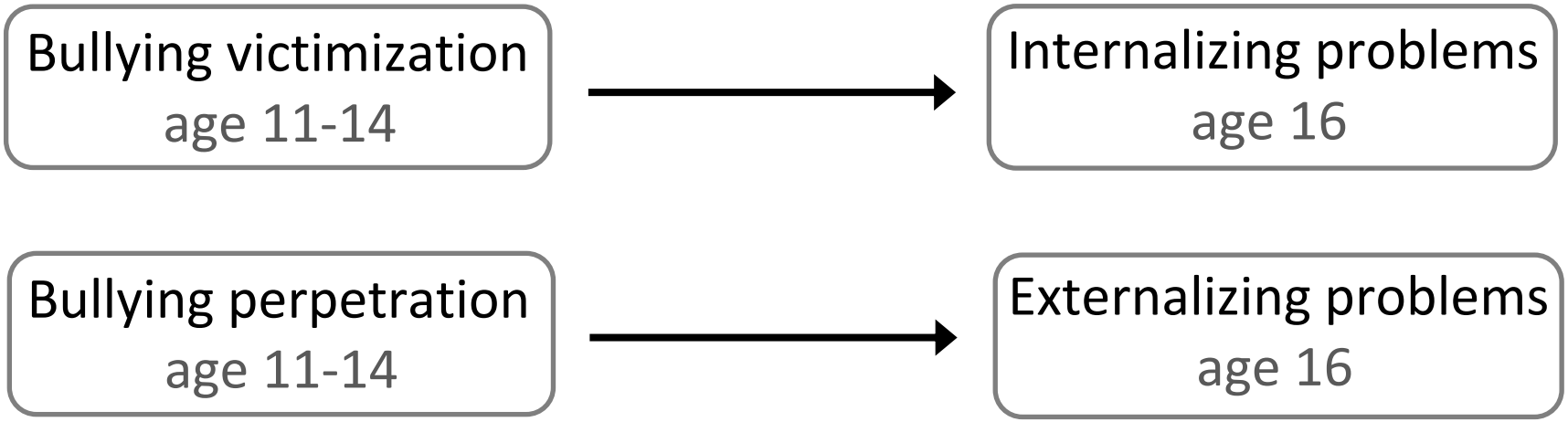
Aim

1. Investigate genetic confounding in the field of bullying research



2. Showcase *GsensY* (Pingault et al., 2021)

Pingault, J.-B., Rijsdijk, F., Schoeler, T., Choi, S. W., Selzam, S., Krapohl, E., O'Reilly, P. F., & Dudbridge, F. (2021). Genetic sensitivity analysis: Adjusting for genetic confounding in epidemiological associations. PLOS Genetics, 17(6), e1009590.

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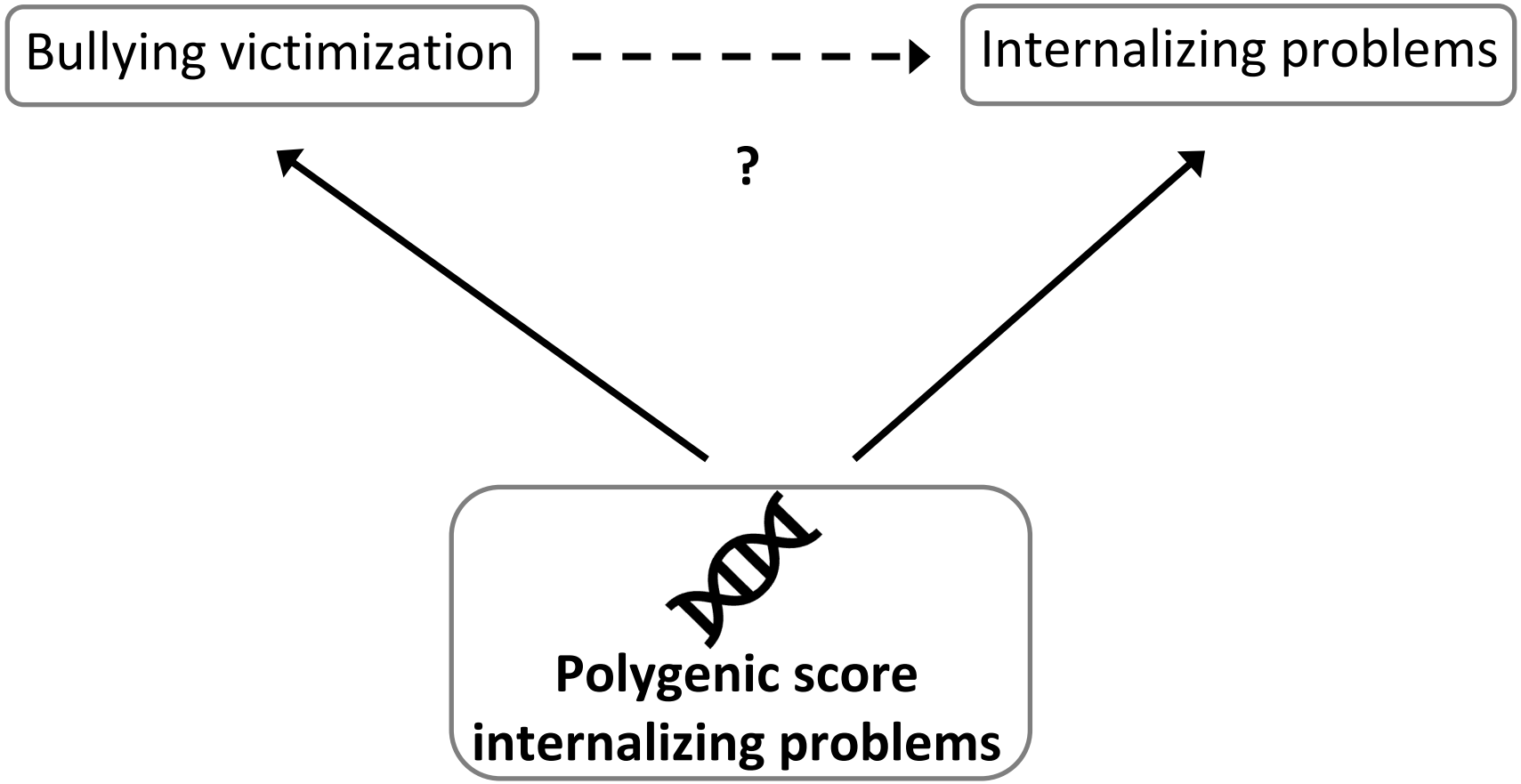
GsensY method

Step 1: Genetic confounding – polygenic scores



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GsensY analysis

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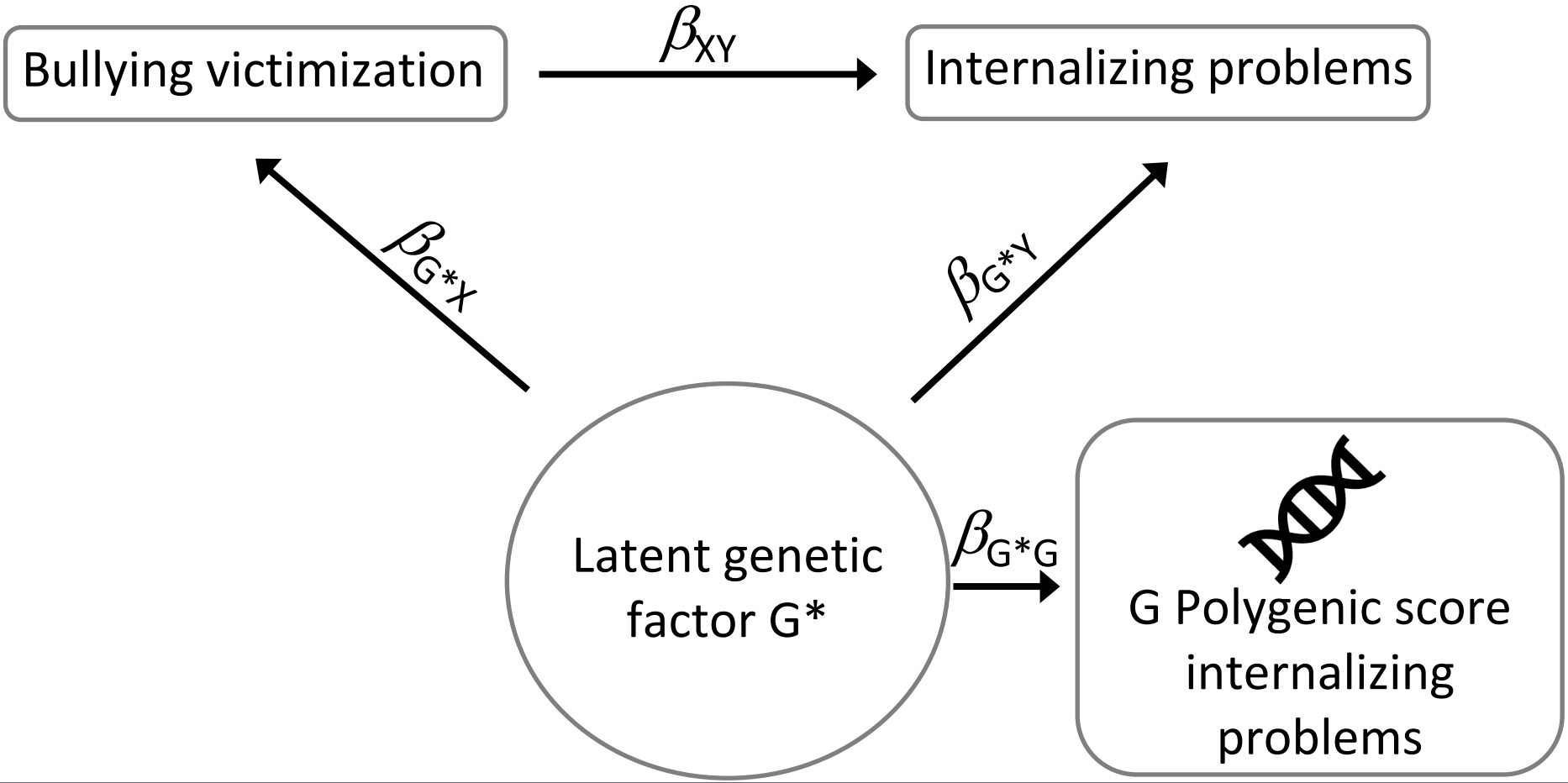
Step 2: Genetic confounding – hypothetical models: what if polygenic scores explained a proportion of variance in internalizing problems similar to SNP and twin heritability



When can this method be used?

1. **Genome-wide association study available on the outcome trait (internalizing/externalizing problems)**

✓ Internalizing: Howard et al. (2018), *N* = 322,580

✓ Externalizing: Karlsson Linnér et al. (2021), *N* ~ 1.5 million (incl. 23andMe)

2. **Genome-wide genetic data and data on bullying involvement and later maladjustment available for the target sample**

✓ TRacking Adolescents' Individual Lives Survey (TRAILS)
(Oldehinkel et al., 2015)

3. **SNP and twin heritability estimates available from other study**

✓ Internalizing: SNP heritability 10.2%; twin heritability ~50%

✓ Externalizing: SNP heritability 10%-44%; twin heritability 61%-80%
(Franić et al., 2014; Howard et al., 2018; Karlsson Linnér et al., 2021; Kendler et al., 2016; Nivard et al., 2015; Pappa et al., 2015)

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Sample and measures

Sample: population and high-risk cohort study TRacking Adolecents' Individual Lives Survey (TRAILS)

Inclusion: All participants with genome-wide genetic data, self-report data on bullying involvement between age 11 and 14, and self-report data on internalizing and externalizing problems at age 16 (*n* = 1604)

Measures: Youth and Adult Self-Report (YSR and ASR): 1 item for bullying victimization, 1 item for bullying perpetration and scales for internalizing (21 items) and externalizing problems (32 items)

Trait measures were skwewed → log-transformation

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Analyses

1. Polygenic scores: LDPRED (Vilhjálmsson et al., 2015)
   PGS_{INT} R^2 ~1.5%
   PGS_{EXT} R^2 ~3%

2. Exposure (bullying involvement), outcome (internalizing and externalizing problems), and polygenic scores residualized for sex and 10 principal components

3. Correlations between residualized exposure, outcome, and polygenic scores

4. Input for R package *GsensY:* correlations, and SNP and twin heritability estimates

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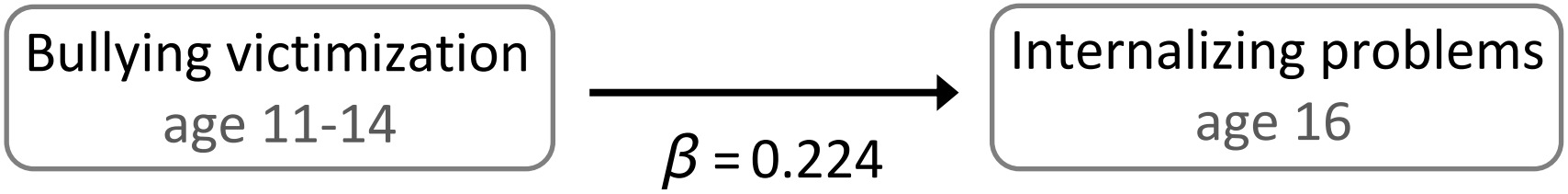
Results



Polygenic score model: ↓ 3%

SNP heritability model: ↓ 17%

Twin heritability model: ↓ 90%

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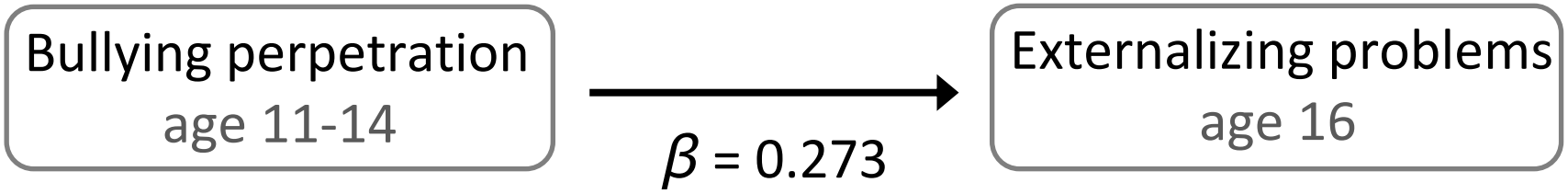
Results



Polygenic score model: ↓ 4%

SNP heritability model: ↓ 14%-63%

Twin heritability model: ↓ 91%-100%

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Discussion

- Important to consider genetic confounding in bullying research

- Showcased method can be broadly used to assess the magnitude of genetic confounding

Limitations

- Models used to inflate effects of polygenic scores to more fully capture the genetic effect should be interpreted with caution

- *GsensY* less reliable when polygenic score explains only a small proportion of trait variance (~1%) with $n < 3{,}000$

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trails

Conflicts of interest and Acknowledgements

Conflict of Interest Disclosures: None of the authors have conflicts of interest to report.

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