Meta-analysis of Mendelian randomization studies

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Outline

1. Brief introduction to Mendelian randomization

2. Concepts in the meta-analysis model

3. Description of the example and the meta-analysis model

4. An extension to the meta-analysis model

5. Summary and discussion

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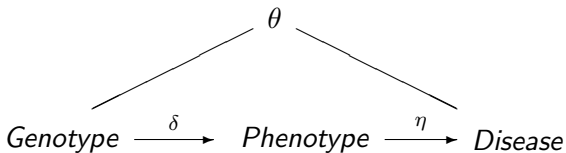# Brief introduction to Mendelian randomization

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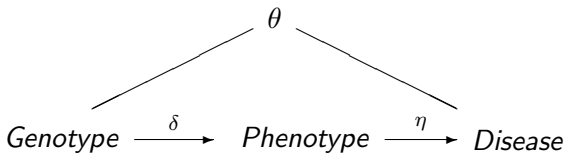- Mendel's 2nd law: individual randomized to a genotype at conception

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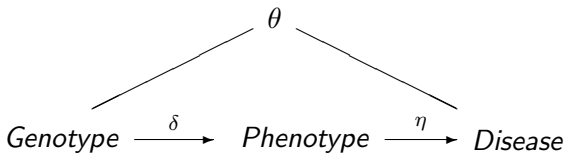 - Phenotype on pathway between gene and disease

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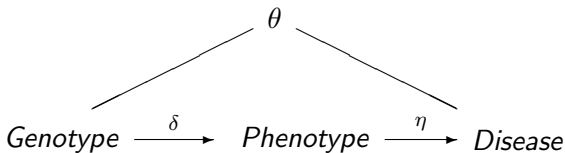$$Genotype \xrightarrow{\delta} Phenotype \xrightarrow{\eta} Disease$$

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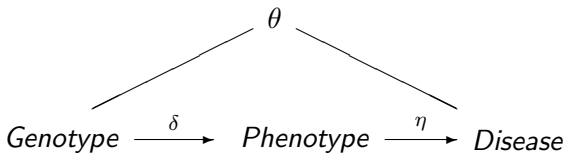- Instrumental-variable (IV) methods for continuous outcome measures

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$$\eta_{[k]} \approx \frac{k\theta}{\delta}$$

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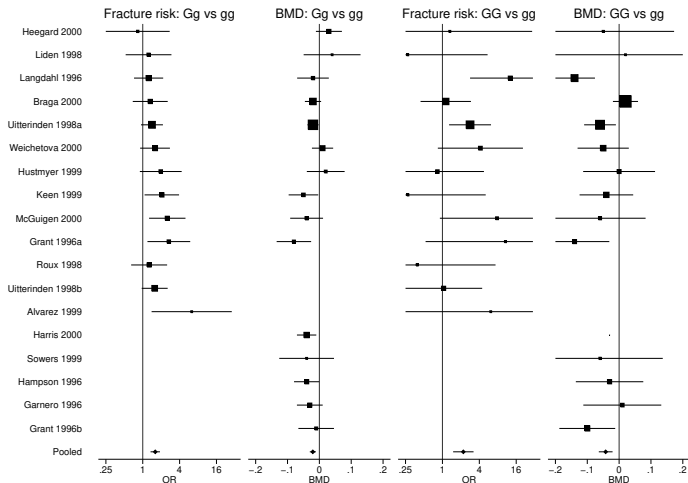|	gg	Gg	GG
Controls	y_{01}	y_{02}	y_{03}
Cases	y_{11}	y_{12}	y_{13}
log odds-ratios		θ_2	θ_3
Mean phenotype levels (controls)	μ_1	μ_2	μ_3
difference in mean phenotypes		δ_2	δ_3

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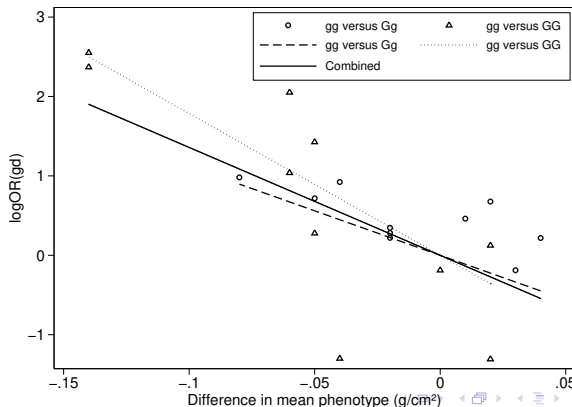
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$$\delta, \eta \sim N(0, 1 \times 10^6), \quad \lambda \sim Beta(0.5, 0.5)$$

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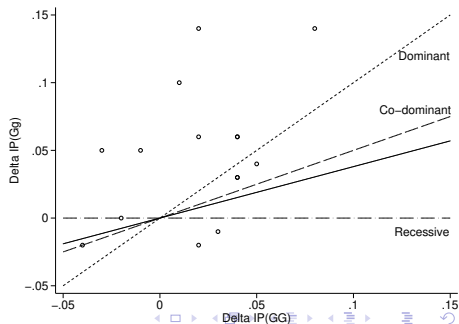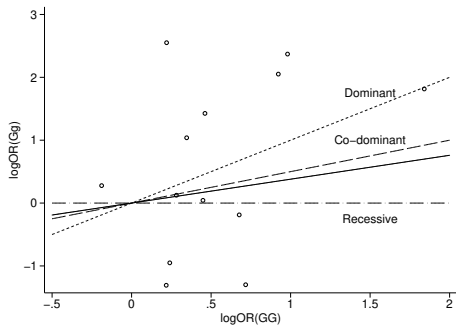$$\theta_{3i} \sim N(\eta\delta, var(\theta_{3i})), \quad \delta_{3i} \sim N(\delta, var(\delta_{3i}))$$

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ML - MVN	0.42	0.28	0.61	0.33	0.19	0.47
Bayesian - PNF	0.46	0.32	0.61	0.30	0.17	0.45
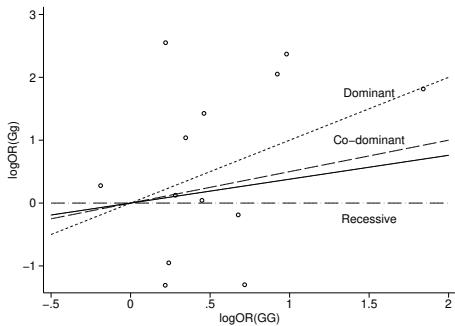
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- Meta-analysis of genetic association studies using merged genotype comparisons [Salanti and Higgins, 2007]

Acknowledgements

- Student conference award

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