

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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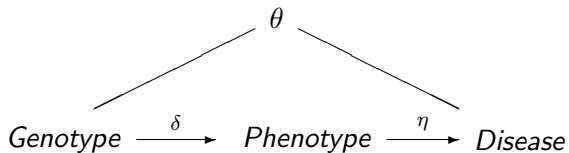
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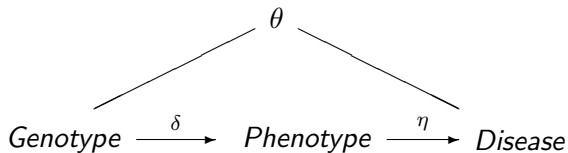
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 - Phenotype on pathway between gene and disease

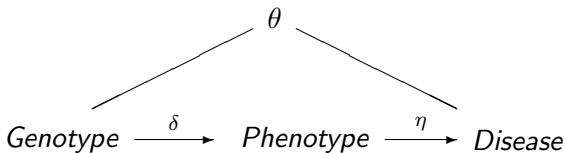


θ : Gene-Disease log odds-ratio, δ : difference in mean phenotypes,
 η : Phenotype-Disease log odds-ratio



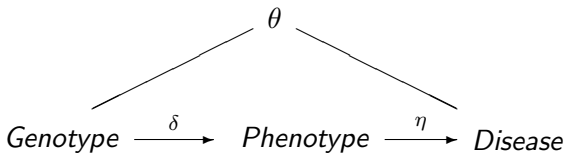
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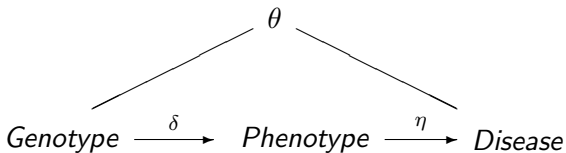
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$$\eta_{[k]} \approx \frac{k\theta}{\delta}$$

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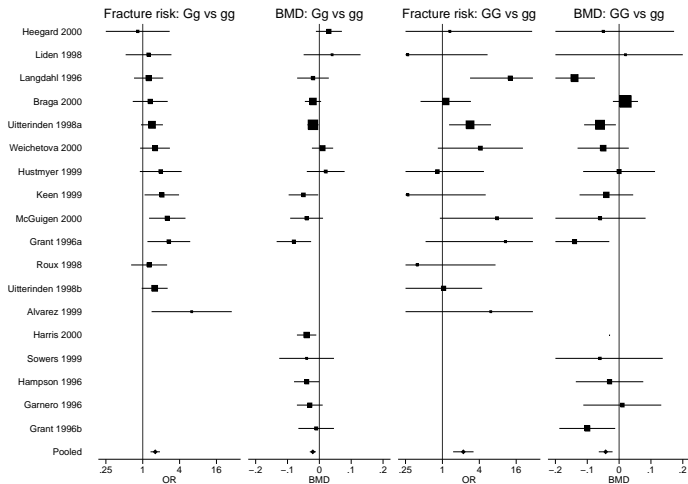
	gg	Gg	GG
Controls	y_{01}	y_{02}	y_{03}
Cases	y_{11}	y_{12}	y_{13}
log odds-ratios		θ_2	θ_3
Mean phenotype levels (controls)	μ_1	μ_2	μ_3
difference in mean phenotypes		δ_2	δ_3

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$$\begin{bmatrix} \theta_{2i} \\ \delta_{2i} \\ \theta_{3i} \\ \delta_{3i} \end{bmatrix} \sim \text{MVN} \left(\begin{bmatrix} \eta\delta_2 \\ \delta_2 \\ \eta\delta_3 \\ \delta_3 \end{bmatrix}, \mathbf{V}_i + \mathbf{B} \right)$$

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Combined	0.50	0.39	0.62

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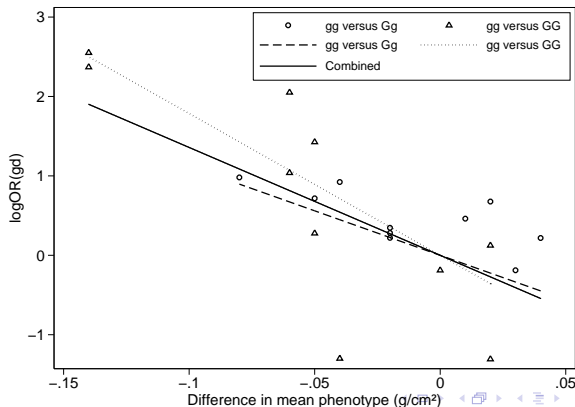
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$$\delta, \eta \sim N(0, 1 \times 10^6), \quad \lambda \sim \text{Beta}(0.5, 0.5)$$

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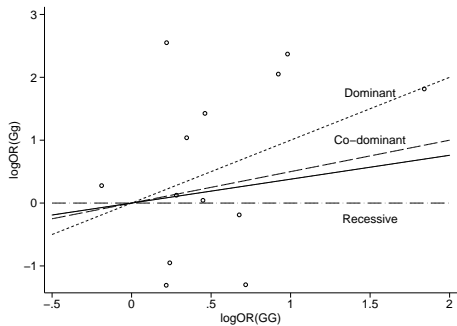
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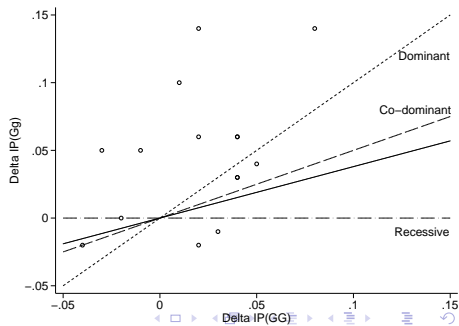
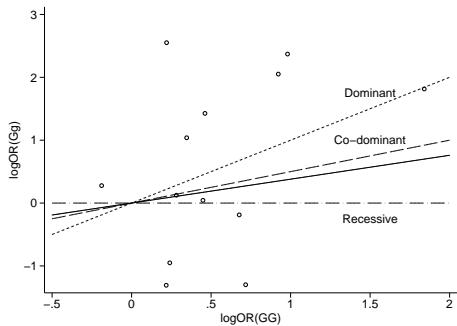
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Method of estimation	$OR_{pd,0.05}$	95% C.I./Cr.I.		λ	95% C.I./Cr.I.	
ML - MVN	0.42	0.28	0.61	0.33	0.19	0.47
Bayesian - PNF	0.46	0.32	0.61	0.30	0.17	0.45





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- Meta-analysis of genetic association studies using merged genotype comparisons [Salanti and Higgins, 2007]

Acknowledgements

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