




Follow-up on disease-gene-expression associations using DrugBank data






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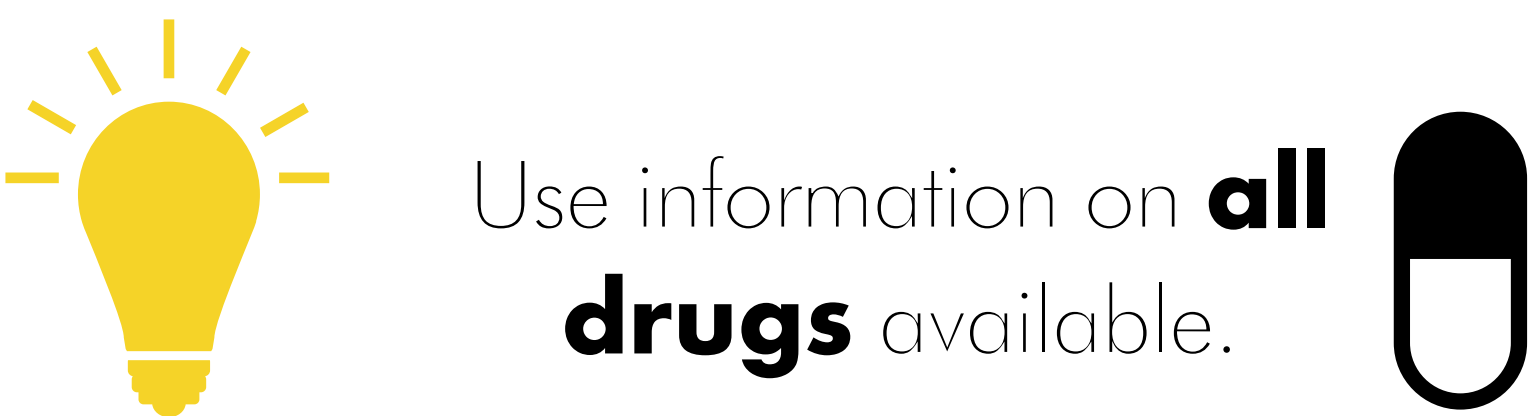
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1. Aim

1. **Verify** Mendelian randomisation (MR) results.
2. Use MR as a tool for repurposing/**repositioning** of drugs.



Use information on **all** drugs available.

2. Two Datasets



Trait - gene expression associations

Eleonora Porcu

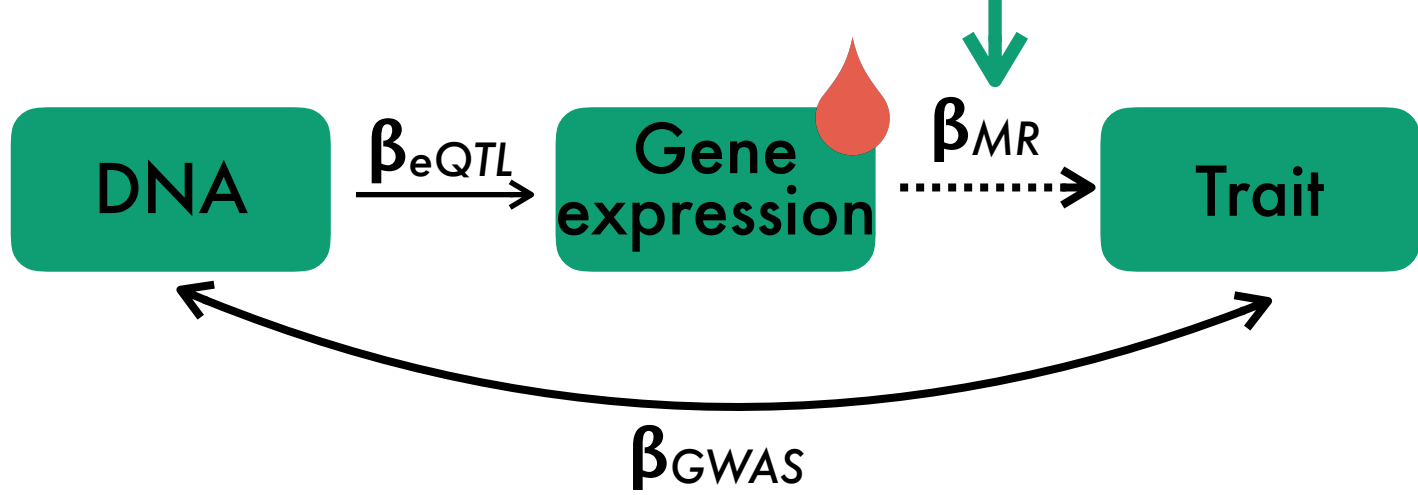
MR analysis of 42 traits and 15'978 genes

Trait	Gene	-log(P) MR
T1	A	1
	B	8
	C	20
	D	3
	E	2

594'834 causal
effect estimates

Causal effect of gene
expression on traits
estimated through
Mendelian randomisation
(MR)

$$\beta_{MR} = \frac{\beta_{GWAS}}{\beta_{eQTL}}$$

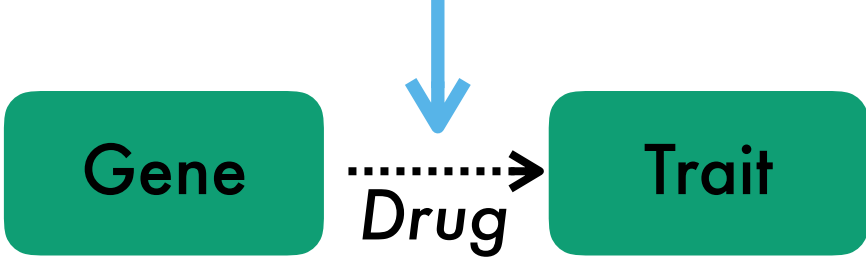


Trait examples: Total cholesterol,
schizophrenia, Crohn's disease.

DrugBank.ca

Publicly available drug encyclopedia

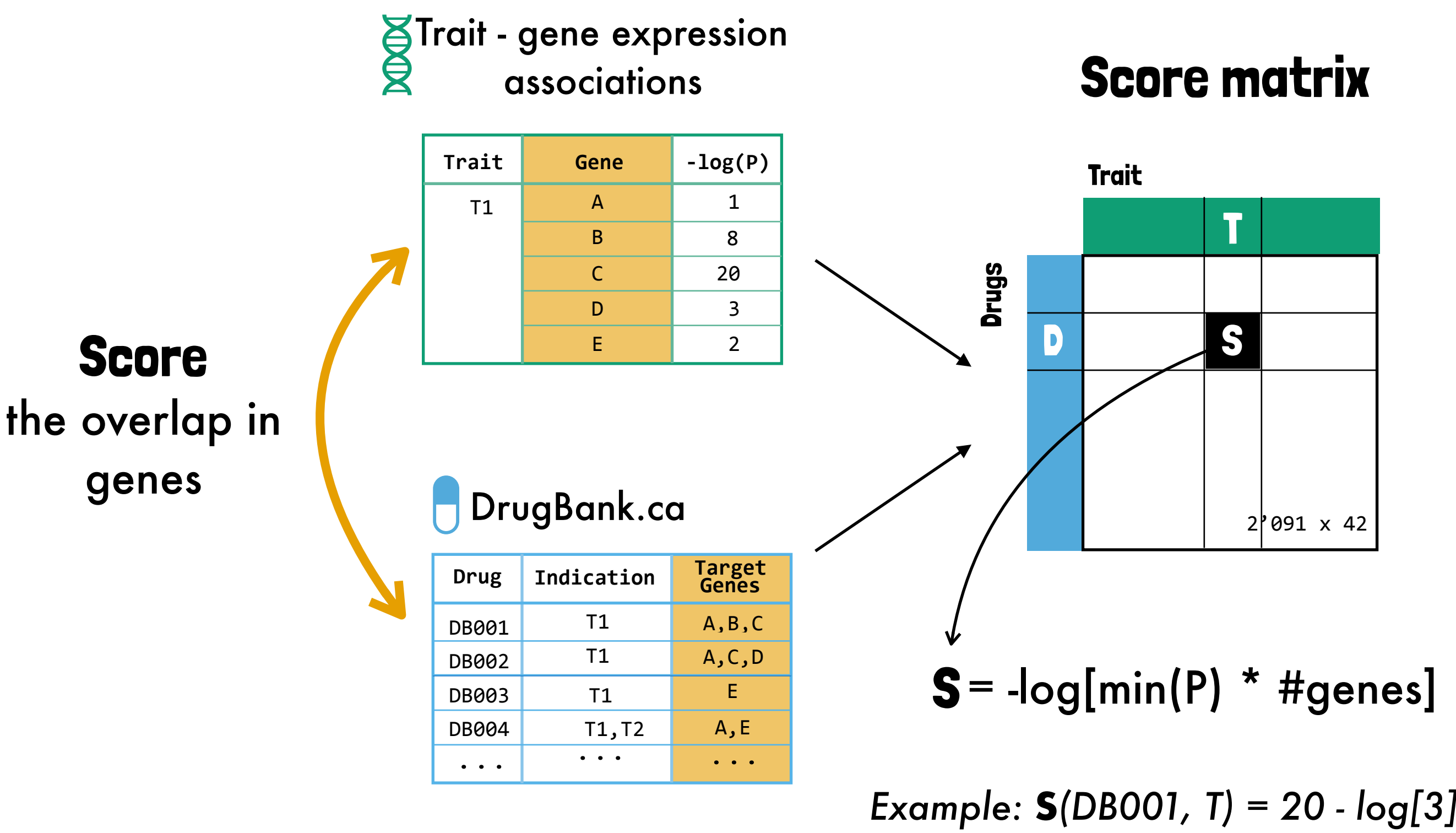
Drug	Indication	Target Genes
DB001	T1	A, B, C
DB002	T1	A, C, D
DB003	T1	Q
DB004	T1, T2	A, C, P
...



- DrugBank.ca [1] contains **detailed drug data** (i.e. chemical, pharmacological and pharmaceutical).
- ~10K drugs, of which we use 7'127 drugs that have at least one gene target.

[1] Wishart DS, Feunang YD, Guo AC, Li EJ, Marcu A, Grant JR, Siu J, Johnson D, Li C, Sayeedo Z, Assempour N, Iynkkaran I, Liu Y, Maciejewski A, Gale N, Wilson A, Chiu L, Cummings R, Li D, Pon A, Knox C, Wilson M. DrugBank 5.0: a major update to the DrugBank database for 2018. Nucleic Acids Res. 2017 Nov 8. doi: 10.1093/nar/glx1037.

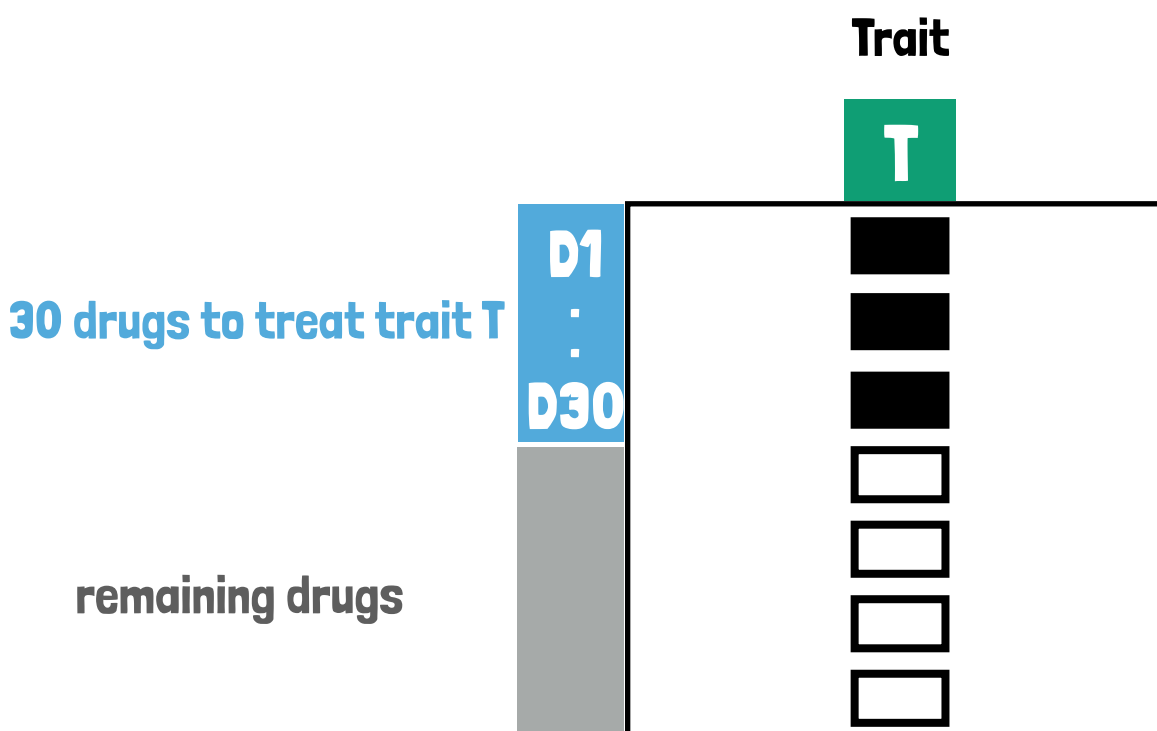
3. Method



4. Analyses

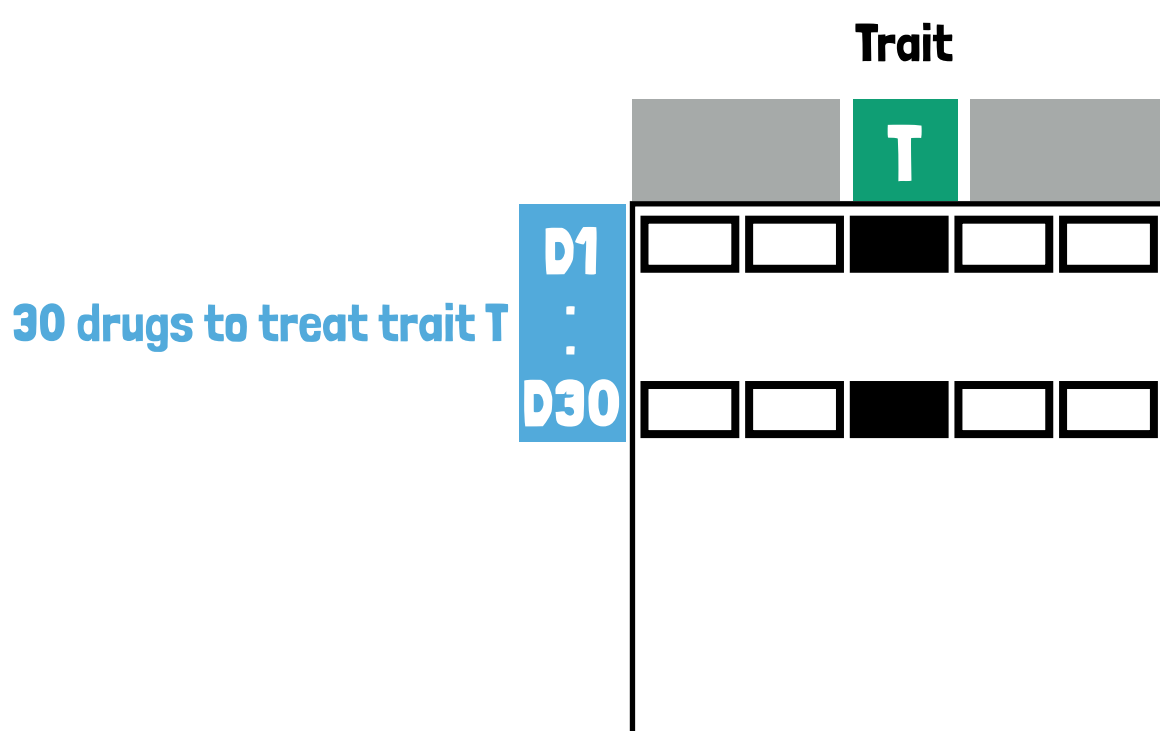
Approach A: comparing drugs

Are the scores of trait-specific drugs enriched in MR results compared to trait-unspecific drugs scores?



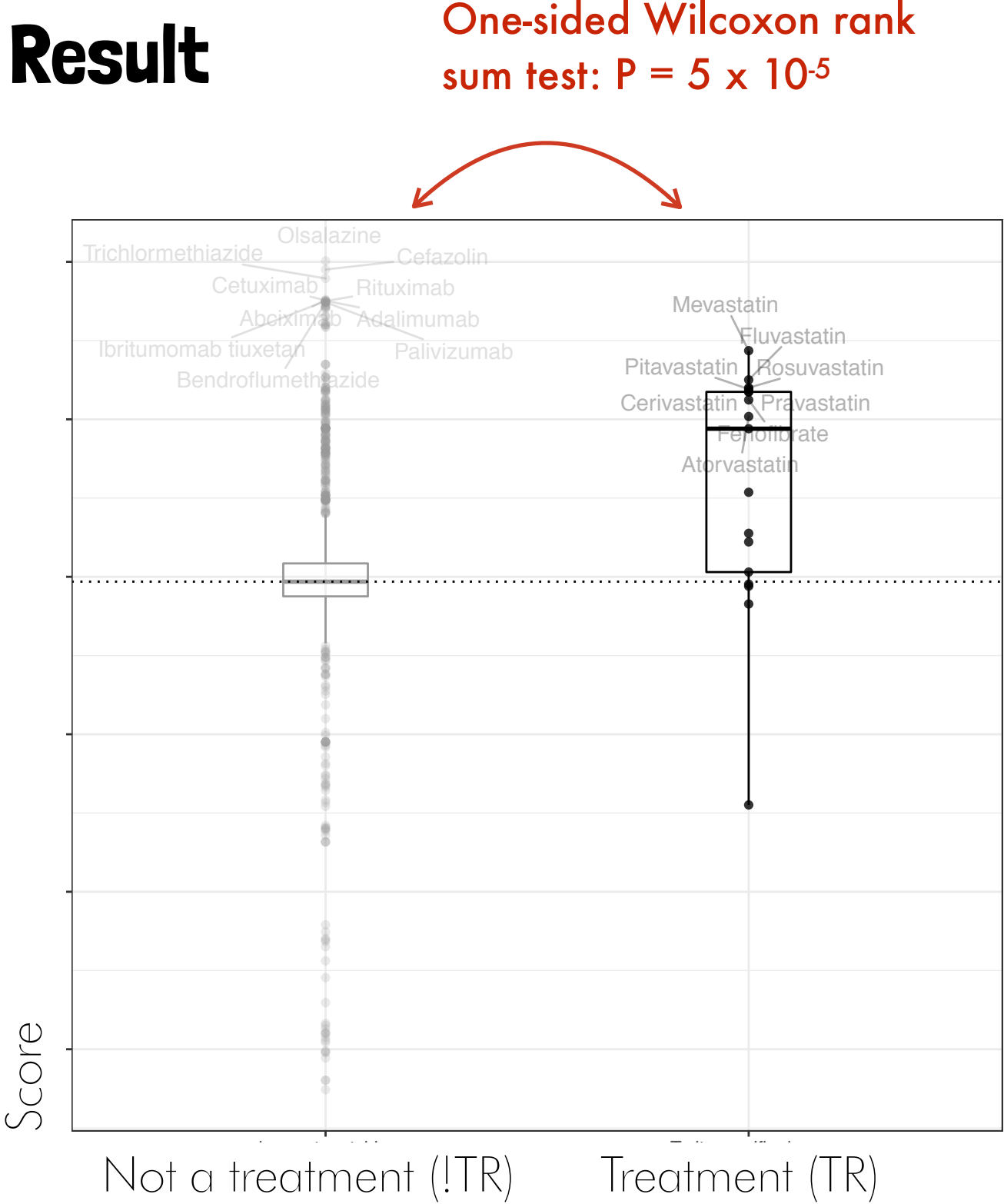
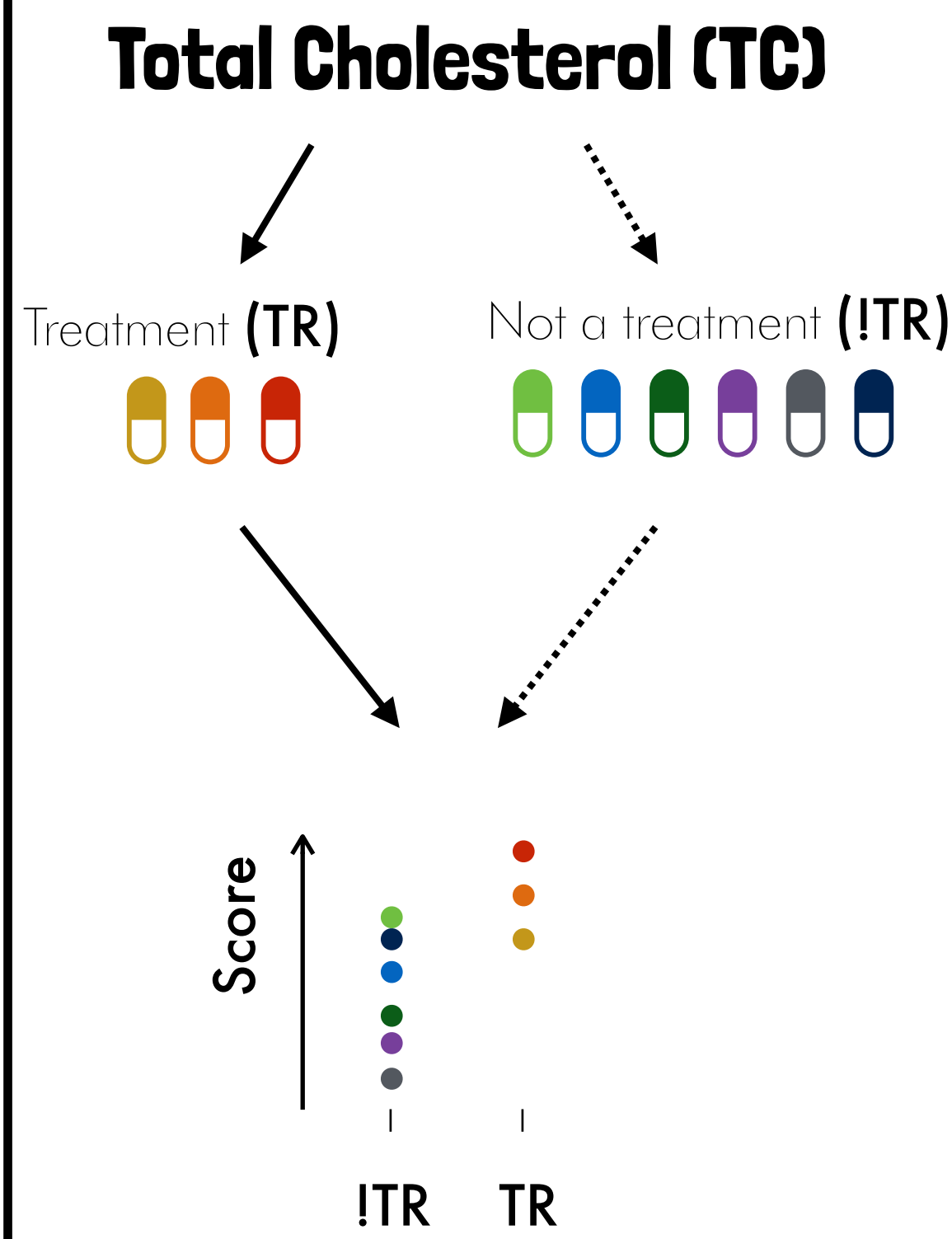
Approach B: comparing traits

Are trait-specific drugs enriched in MR results for that trait T, compared to other traits?



5a. Approach A: comparing drugs

Example



5b. Approach B: comparing traits

Example

