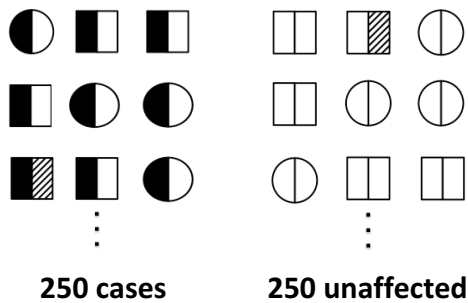


A protein-truncating variant (PTV) having the potential to destroy protein function has minor allele frequency 0.1%.

Is this PTV associated with T2D? Is the gene harboring this variant associated with T2D?

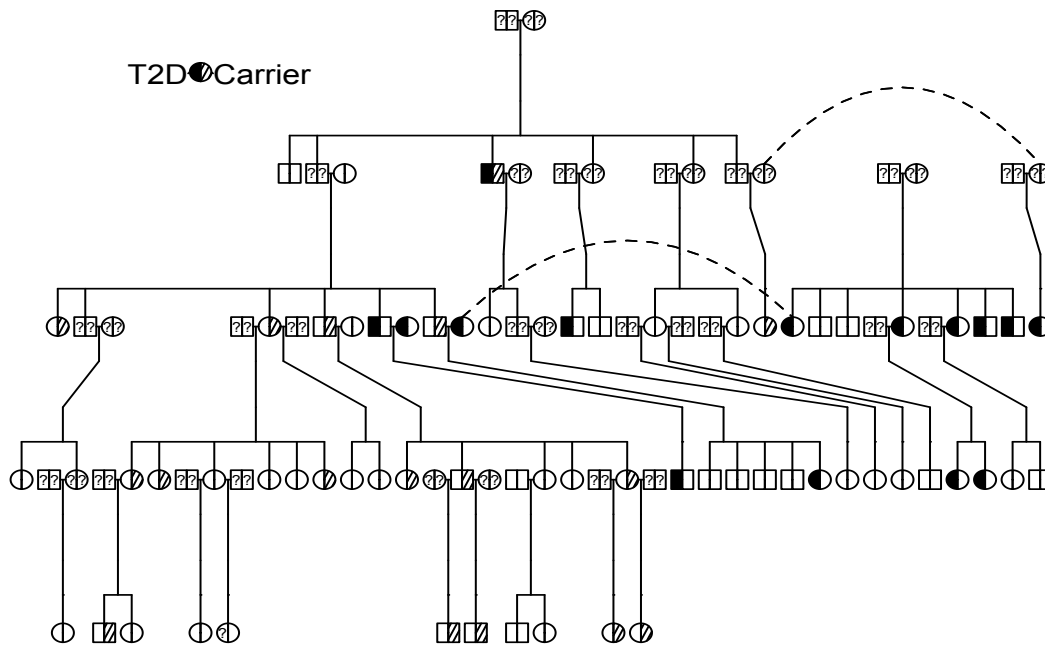
Population study



- A PTV with MAF 0.1% is observed on average once in **500 individuals**.
- Identifying 10 copies of the PTV in a population study requires sequencing **5,000 individuals**.
- Identifying 10 PTVs in the same gene requires sequencing **2,000 individuals**.*

*Assuming 100 PTV mutations per individual (30) and uniform probability for 20,000 genes.

Family-based study



In this study, this loss-of-function variant in *BBS12* is present in 17 related individuals, 1 of whom has diabetes – suggesting limited (if any) impact on T2D risk.