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.