A Genotype-First Approach to WES

What it means:

- All 20,000+ genes are fully sequenced
- Importantly, based on patient phenotype, genes are not filtered out of the analysis at this step
- All of the thousands of variants are carefully evaluated for properties that make them more likely to be disease-causing
- These variants are then compared to the patient's phenotype to see if they explain all, or part, of it

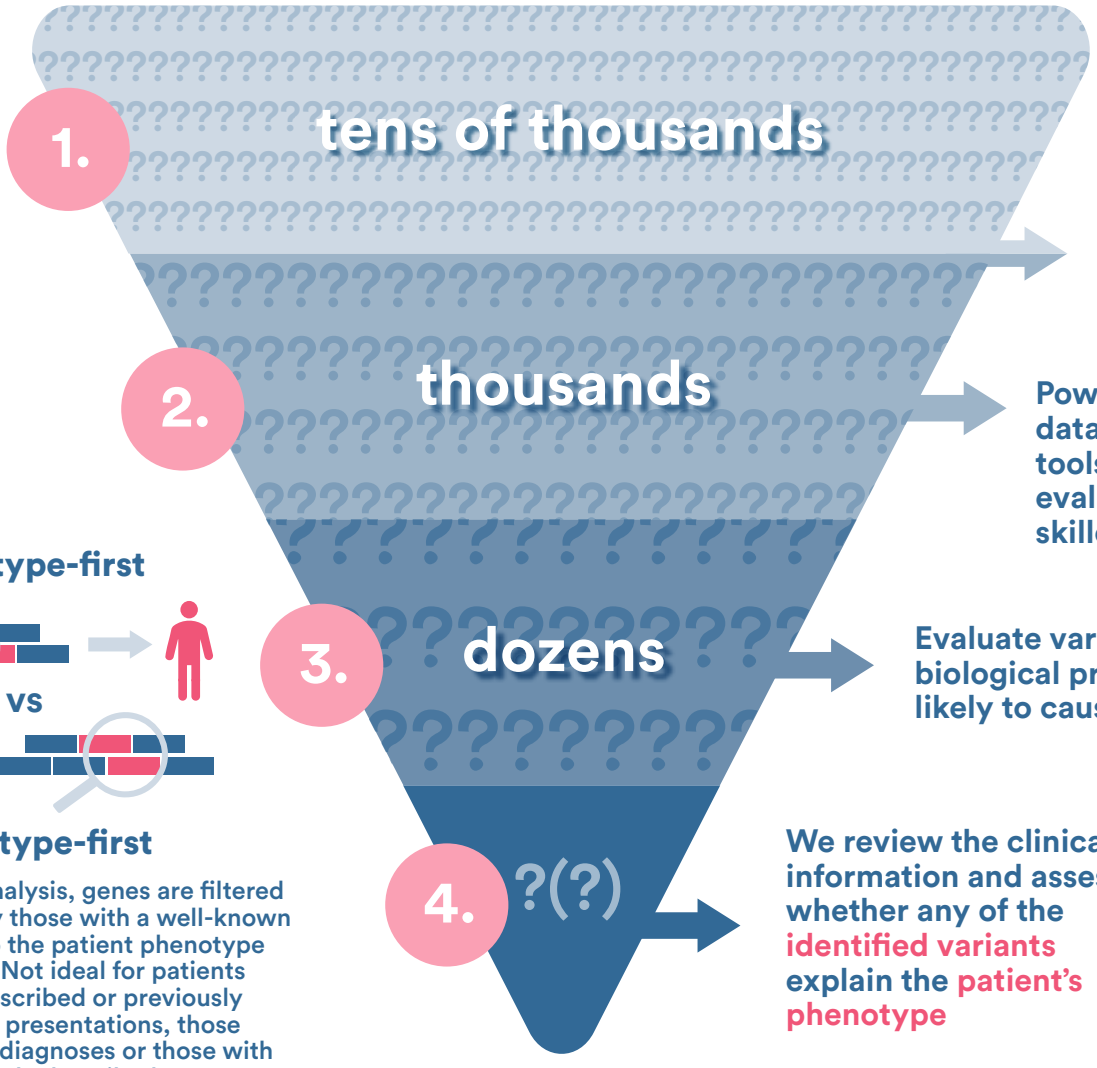
Why it matters:

- Allows for the identification of variants in patients with atypical or rarely reported presentations
- Has the potential to diagnose more than 1 condition
- Allows for the identification of suspicious variants in genes where a disease association is not yet established or only newly described

Our analysis is genotype first.
Our reporting is phenotype driven.
How it works?

! Genotype-first approach does not remove the need for providing good phenotypic information about the patient.

With each step we narrow the list of variants.



Genotype-first

vs

Phenotype-first

Early in the analysis, genes are filtered such that only those with a well-known association to the patient phenotype are analyzed. Not ideal for patients with rarely described or previously unrecognized presentations, those with multiple diagnoses or those with variants in newly described genes.