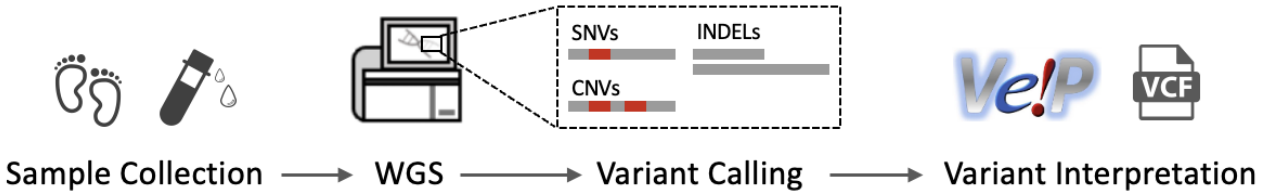
Sample Processing and Data Generation



Pharmacogenomics Risk Loci

Genotypes related to curated pediatric drugs in the PharmGKB.

Variants Filtration for Disease Panels

Global MAF < 1%.

Exclude common high-confidence LoF variants.

Proved pathogenicity (n=267,668):

• (Likely) Pathogenic variants from ClinVar.

Predicted Consequences:

• High confidence LoF variants (LOFTEE);

• Splice-variants (dbscSNV or Splice AI);

• Missense variants (REVEL, BayesDel or AlphaMissense).

Copy number variants (CNVs):

• SMA genotyping;

• (Likely) pathogenic CNVs (AnnotSV).

Variant Risk Stratification by

• In-house scoring system;

• Automated ACMG interpretation and classification.

Reviewing and returning positive results

Screened potential disease-causing variants

Manual review by clinicians with reference (ACMG guideline, medical records, family history)

Data archiving

Follow-up

Reporting

Childhood-onset diseases and Adulthood-onset diseases:
Dominant diseases and biallelic mutation in recessive diseases

Carrier status diseases:
Childhood-onset recessive diseases with heterozygous genotypes