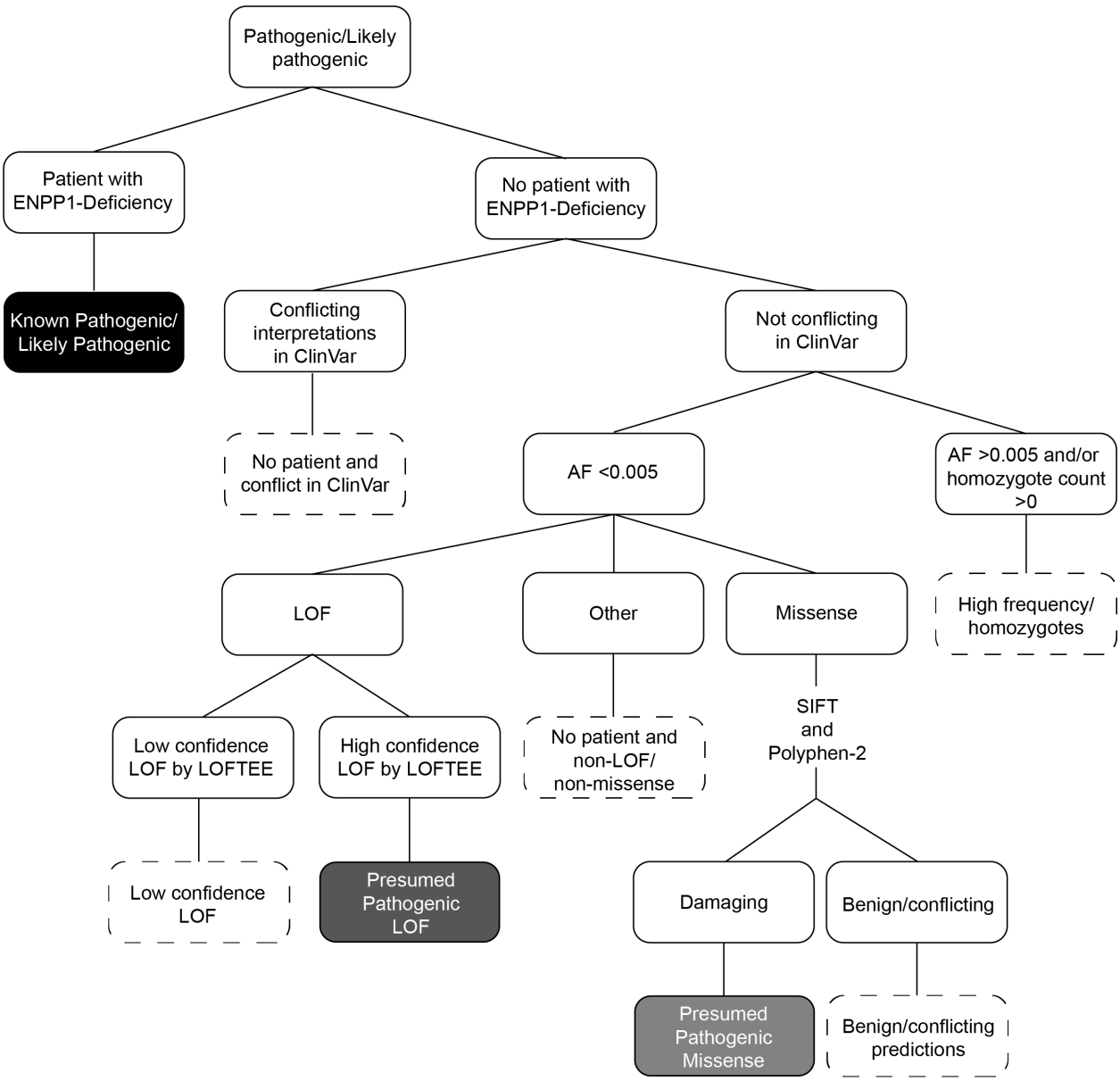
Supplemental Figures 1-3:
Selection Process for *ENPP1* Variants in Genetic Prevalence Estimates

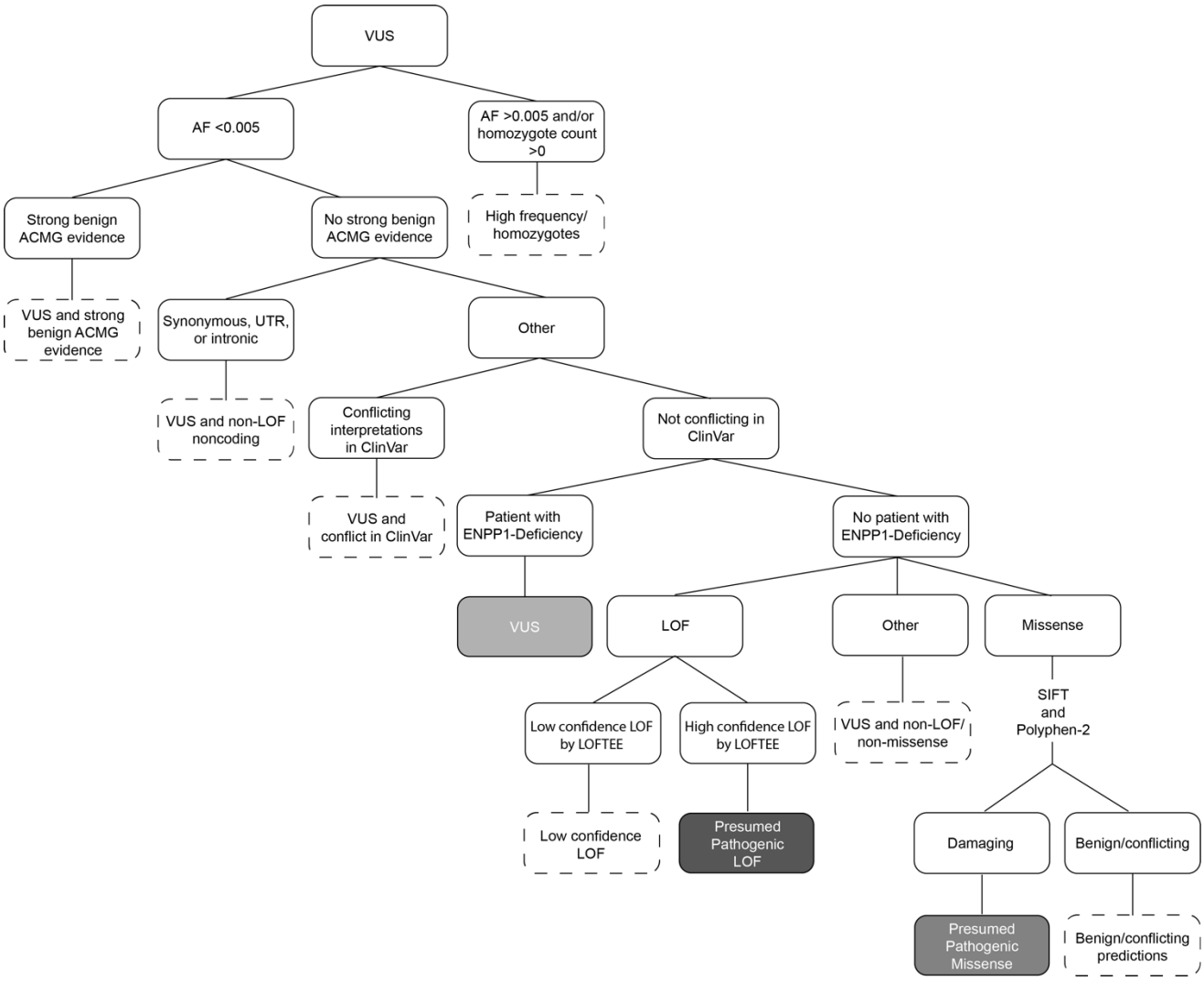


Supplemental Figure 1. Selection Process for Published *ENPP1* Variants Classified as Pathogenic/Likely Pathogenic

Variants must have a non-zero allele frequency in the Genome Aggregation Database (gnomAD) to be included.

Grey/black nodes are variants that will be included in the calculation. Nodes with dashed lines are variants that will be excluded from the calculation. Loss of Function (LOF) variants include nonsense, frameshift, splicing, and start-loss variants.

AF = allele frequency in gnomAD

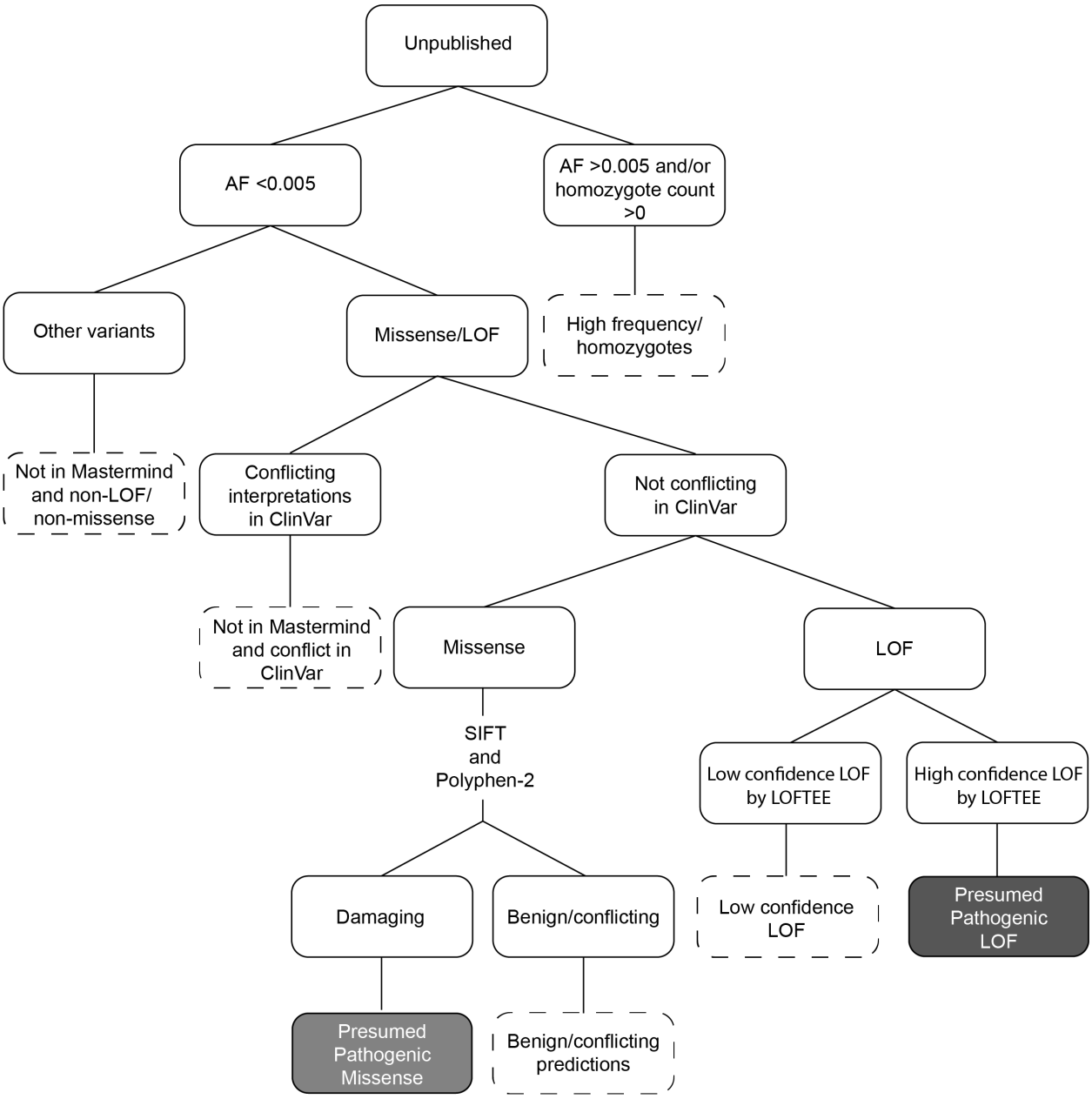


Supplemental Figure 2. Selection Process for Published *ENPP1* Variants Classified as Variants of Undetermined Significance (VUS)

Variants must have a non-zero allele frequency in the Genome Aggregation Database (gnomAD) to be included.

Grey/black nodes are variants that will be included in the calculation. Nodes with dashed lines are variants that will be excluded from the calculation. Loss of Function (LOF) variants include nonsense, frameshift, splicing, and start-loss variants.

AF = allele frequency in gnomAD



Supplemental Figure 3. Selection Process for Unpublished *ENPP1* Variants

Variants must have a non-zero allele frequency in the Genome Aggregation Database (gnomAD) to be included.

Grey/black nodes are variants that will be included in the calculation. Nodes with dashed lines are variants that will be excluded from the calculation. Loss of Function (LOF) variants include nonsense, frameshift, splicing, and start-loss variants.

AF = allele frequency in gnomAD