

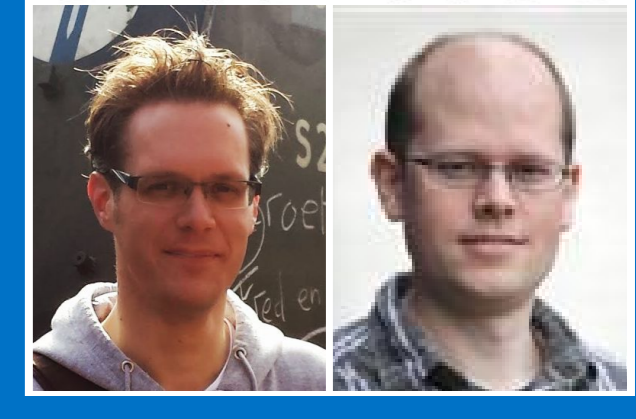
GAVIN: Gene-Aware Variant Interpretation for medical sequencing



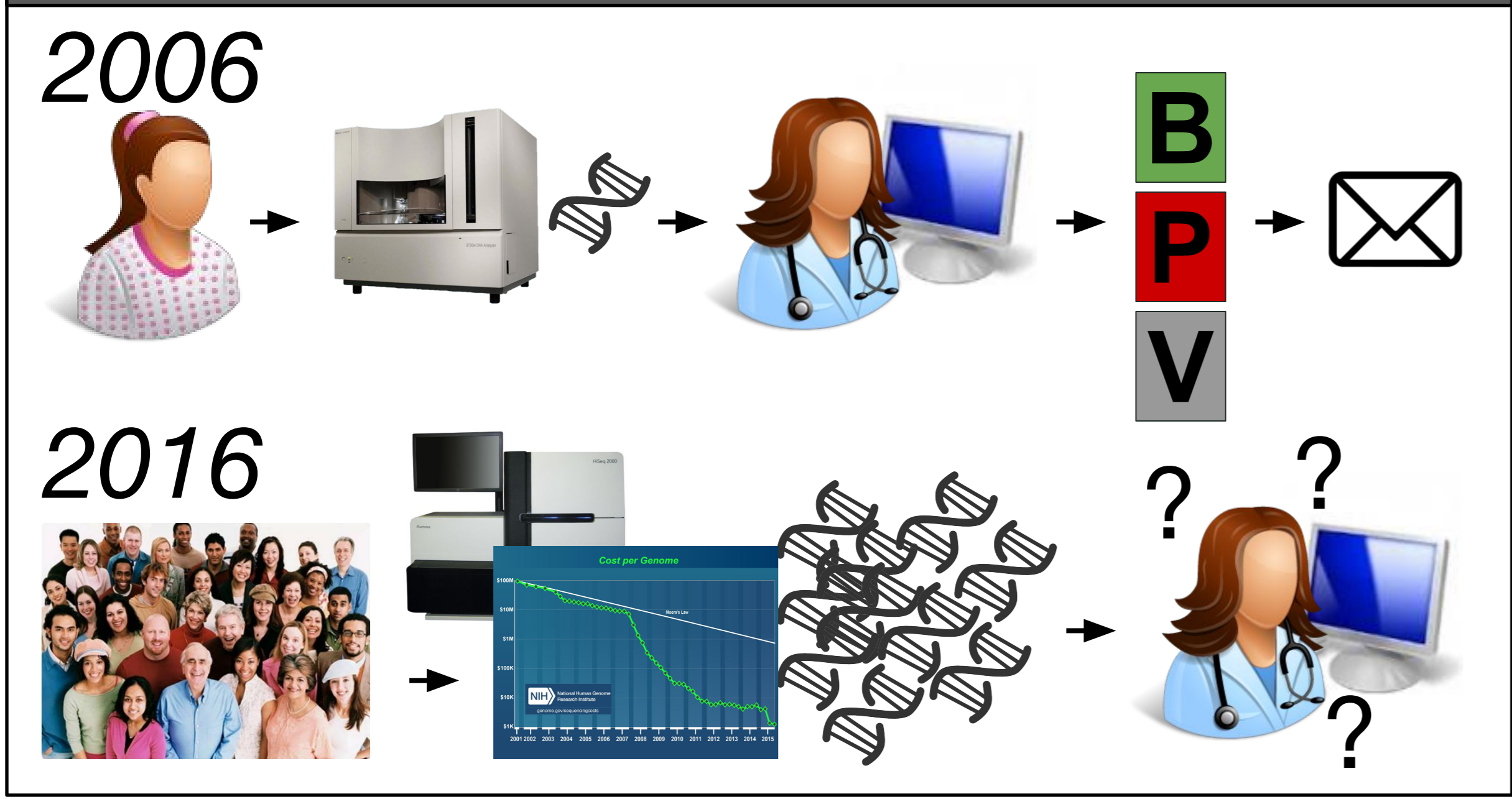
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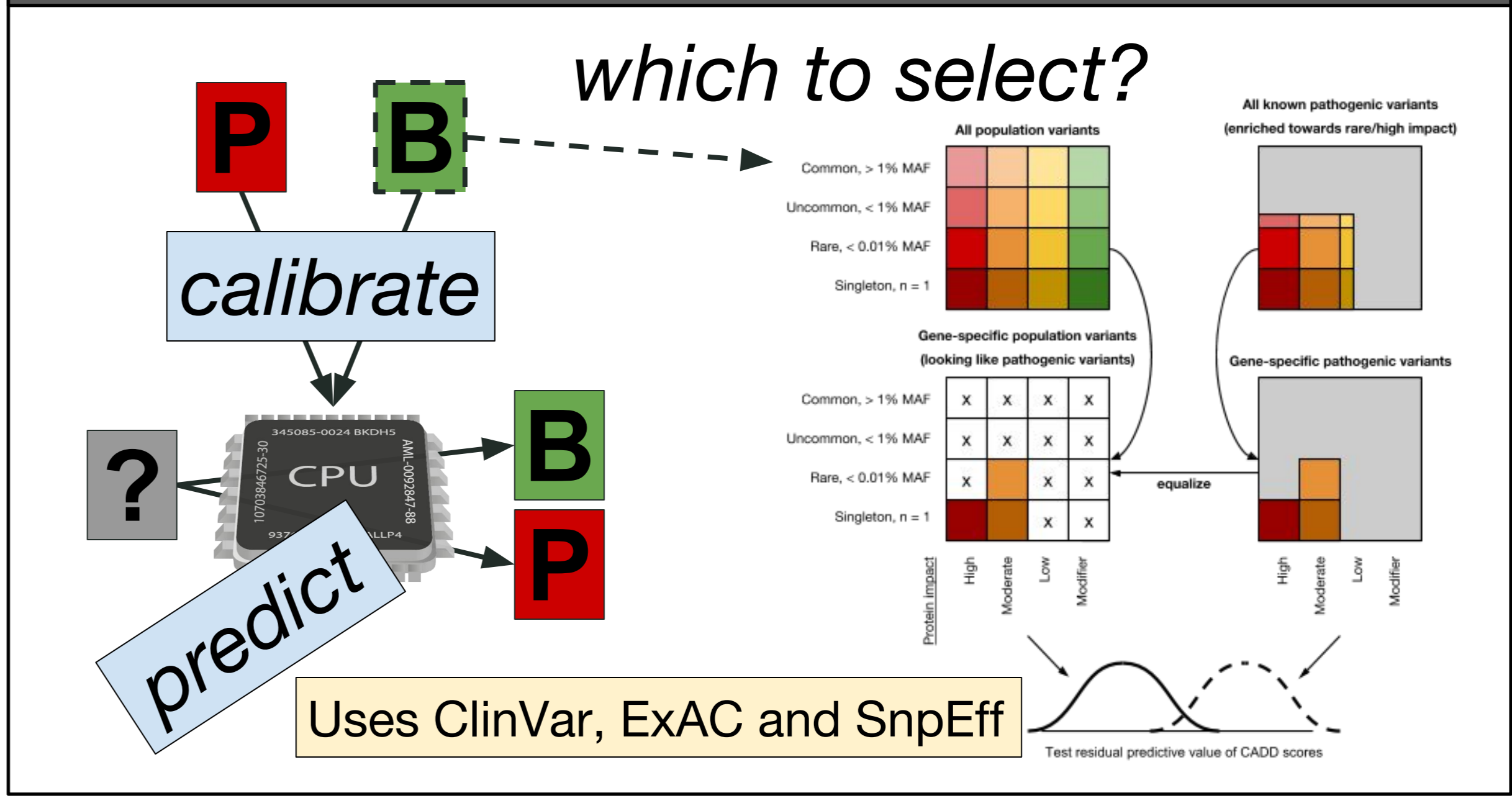
SYSTEMS GENETICS



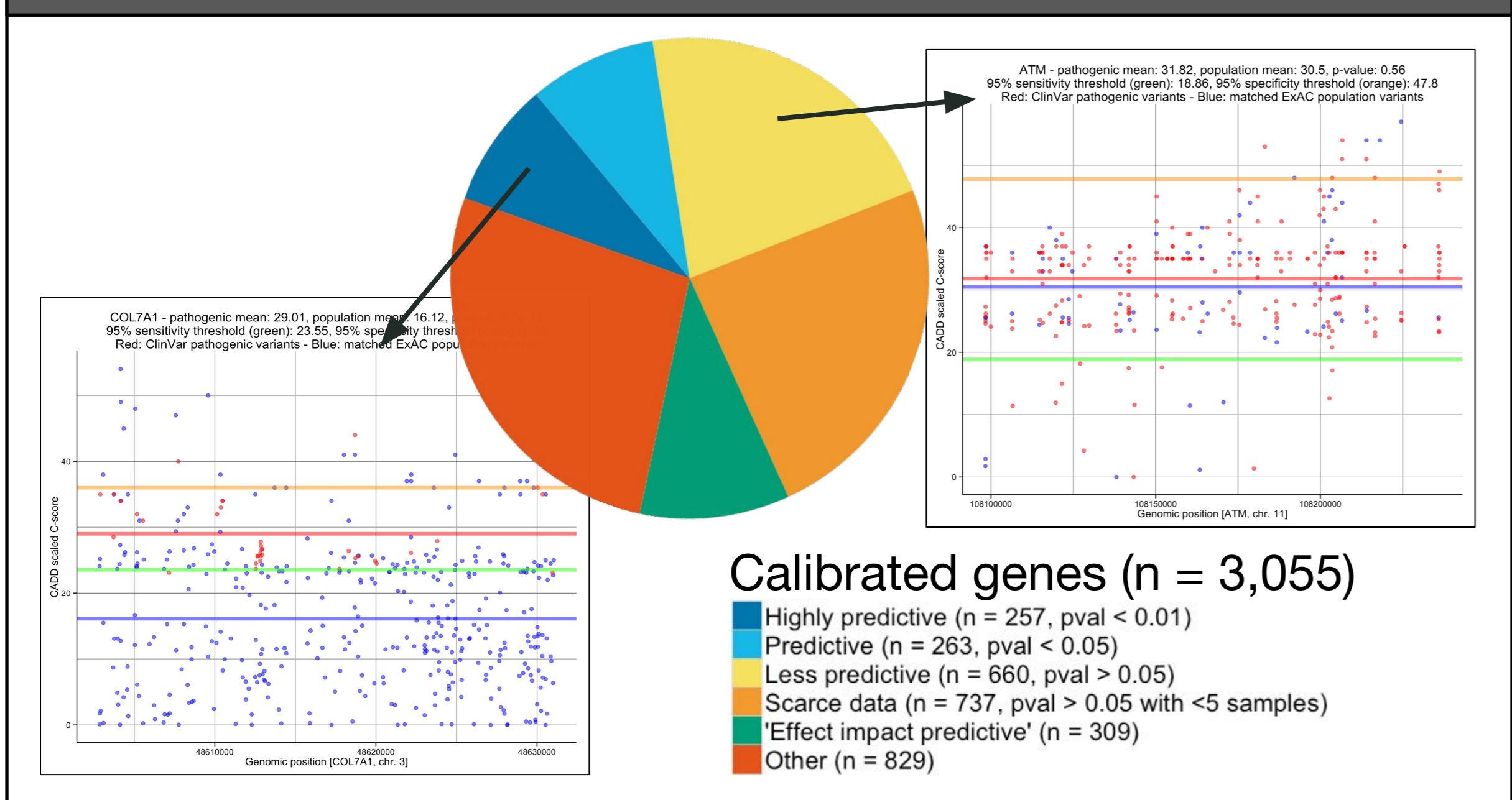
The challenge of medical sequencing
 More individuals & more DNA sequenced
 Need smart tools to assist classification



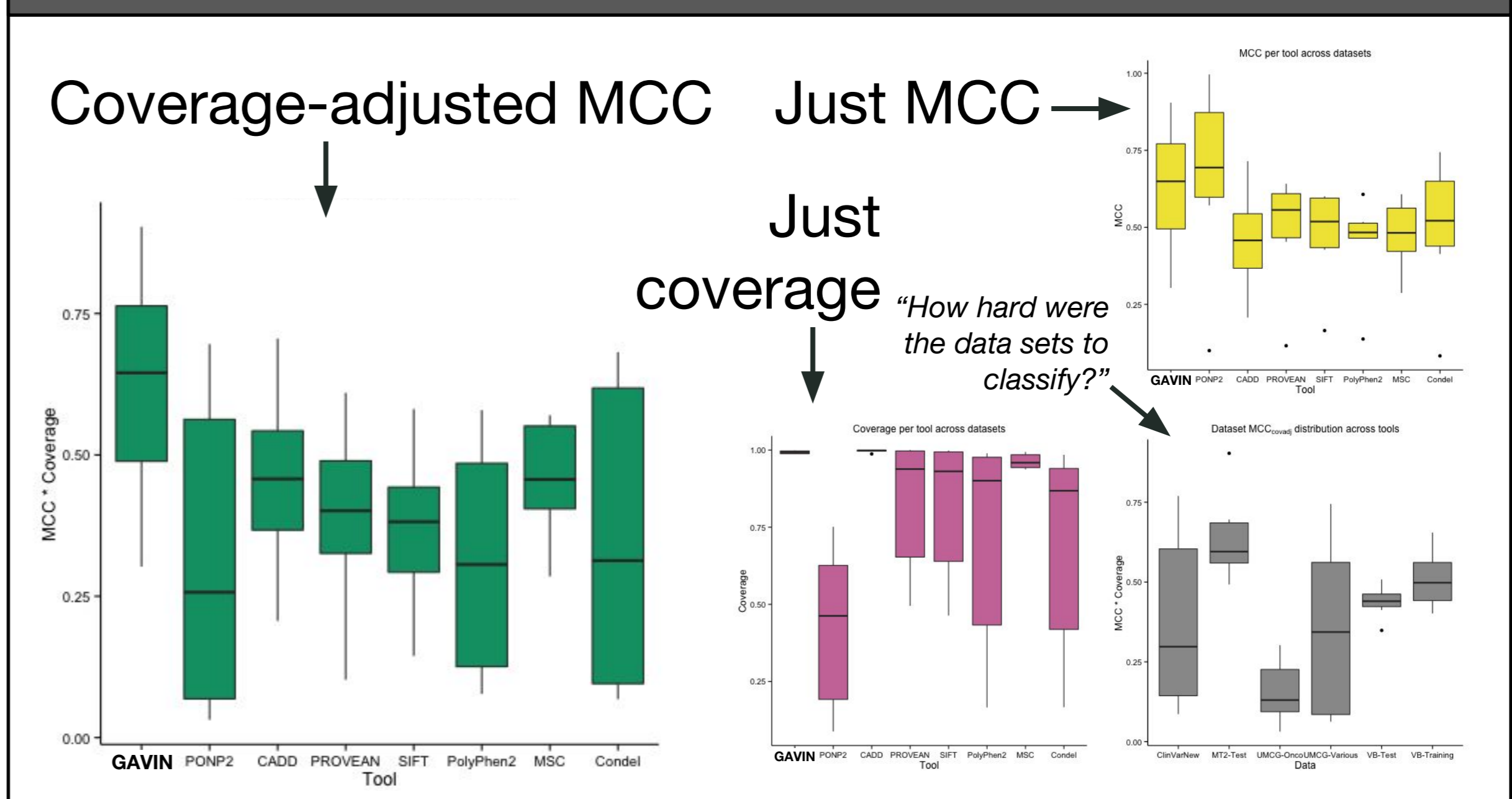
GAVIN gene-based calibration of CADD scores
 Avoid bias by selecting benign variants similar to pathogenic variants instead of distant ones



Finding 'true' predictiveness of CADD scores
 For some genes it works better than for others
 For many genes, we don't have enough data yet



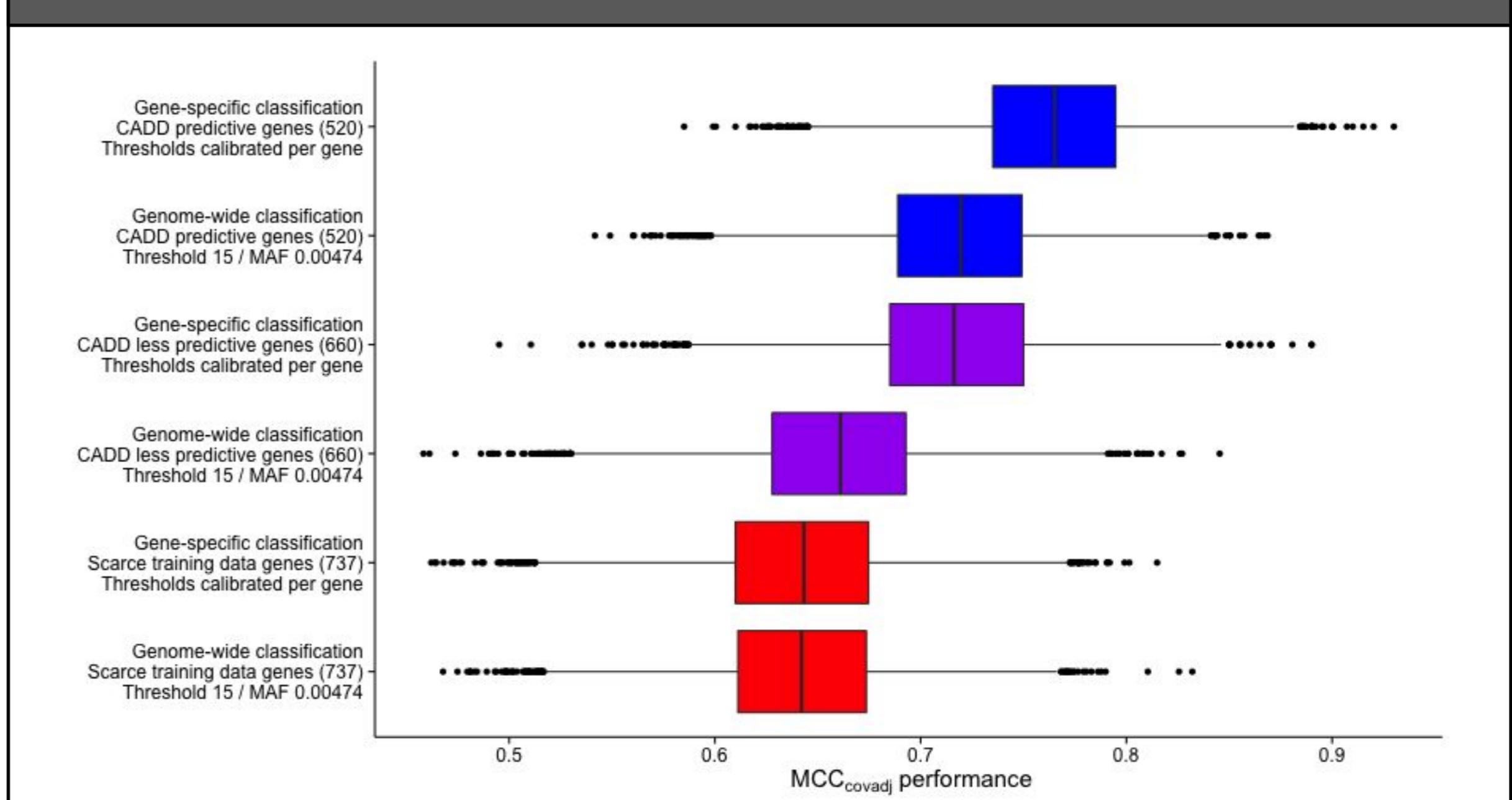
GAVIN performance benchmark
 Matthews Correlation Coefficient (MCC)
 Tools don't always classify, correct for coverage



GAVIN performance benchmark details
 6 data sets (VarBench DS7 2x, ClinVarNew, MutationTaster2, UMCG clinical 2x)
 and 8 tools (GAVIN, CADD, MSC, PONP2, SIFT, PolyPhen2, PROVEAN, Condel)



The power of gene-based calibration
 Gene-specific thresholds have better performance than genome-wide thresholds



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