

ClinVar Report

James Diao

January 8, 2017

Contents

1	Collect and Merge ClinVar Data	2
1.1	Import ClinVar VCF	2
1.2	Merge ClinVar with 1000 Genomes and ExAC	2
2	Summary Statistics	3
2.1	Fraction of Individuals with Pathogenic Non-Reference Sites	3
3	Penetrance Estimates	4
3.1	Max/Min Penetrance as a Function of $P(D)$ and $P(V D)$	4
3.2	Penetrance Estimates by Ancestry	5

Sourcing ClinVar input from: clinvar_2015-06-29.vcf

Sending output to: Report_2015-06-29.pdf

1 Collect and Merge ClinVar Data

1.1 Import ClinVar VCF

1.2 Merge ClinVar with 1000 Genomes and ExAC

Breakdown of ClinVar Variants

Subset_ClinVar	Number_of_Variants
Total ClinVar	110935
LP/P	25417
ACMG LP/P	5529
ACMG LP/P in gnomAD	1221
ACMG LP/P in ExAC	877
ACMG LP/P in 1000 Genomes	165

Breakdown of ACMG-gnomAD Variants

Subset_gnomAD	Number_of_Variants
ACMG in gnomAD	96742
ClinVar-ACMG in gnomAD	8400
LP/P-ACMG in gnomAD	1221

Breakdown of ACMG-ExAC Variants

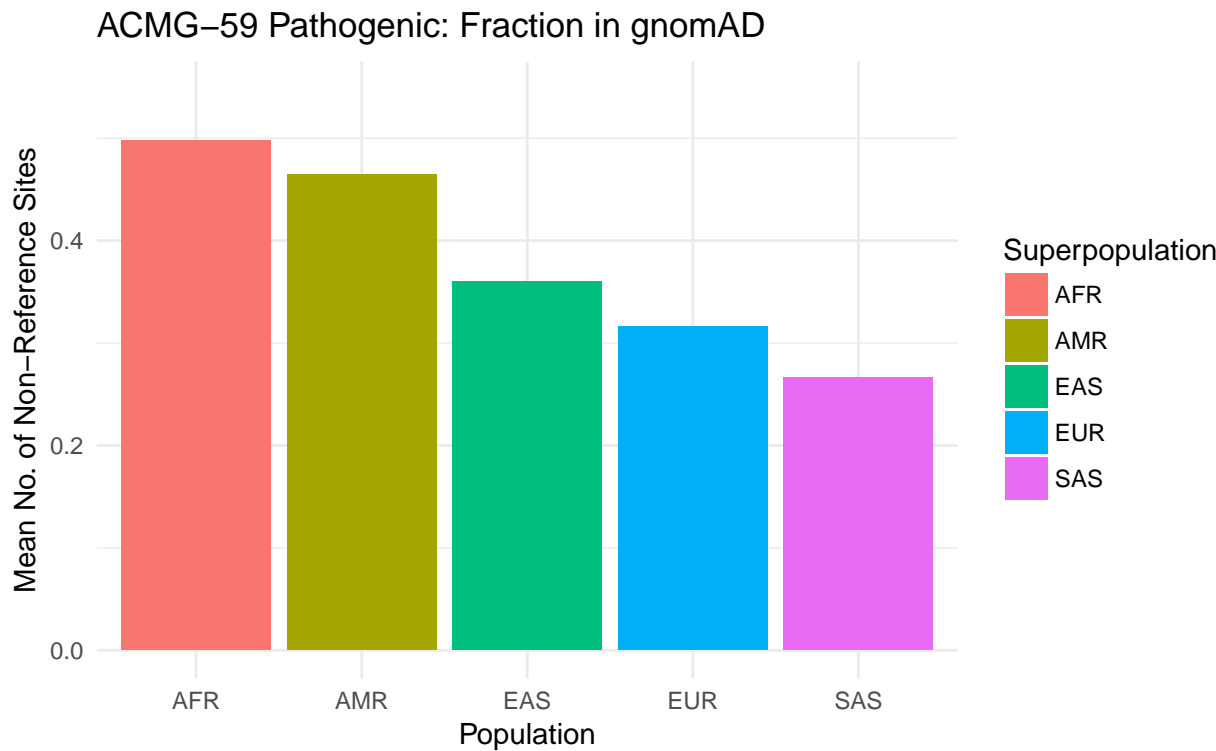
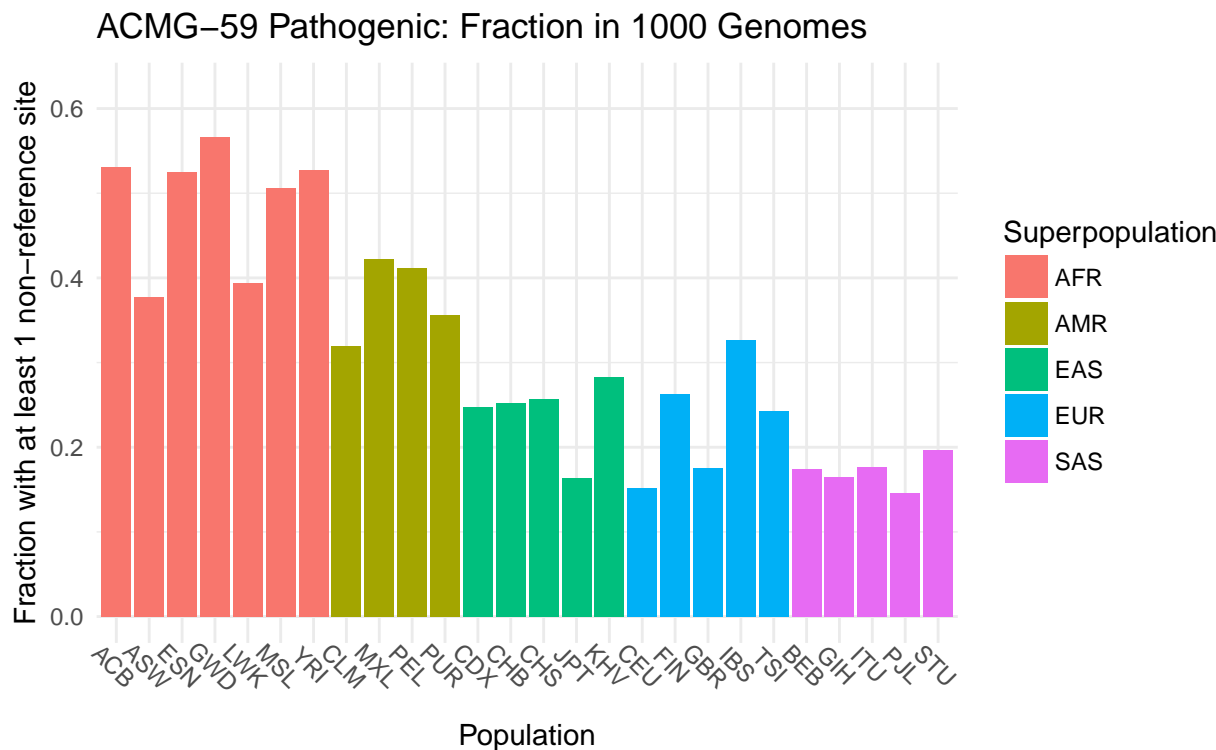
Subset_gnomAD	Number_of_Variants
ACMG in ExAC	59883
ClinVar-ACMG in ExAC	6836
LP/P-ACMG in ExAC	877

Breakdown of ACMG-1000G Variants

Subset_gnomAD	Number_of_Variants
ACMG in 1000G	141466
ClinVar-ACMG in 1000G	2911
LP/P-ACMG in 1000G	165

2 Summary Statistics

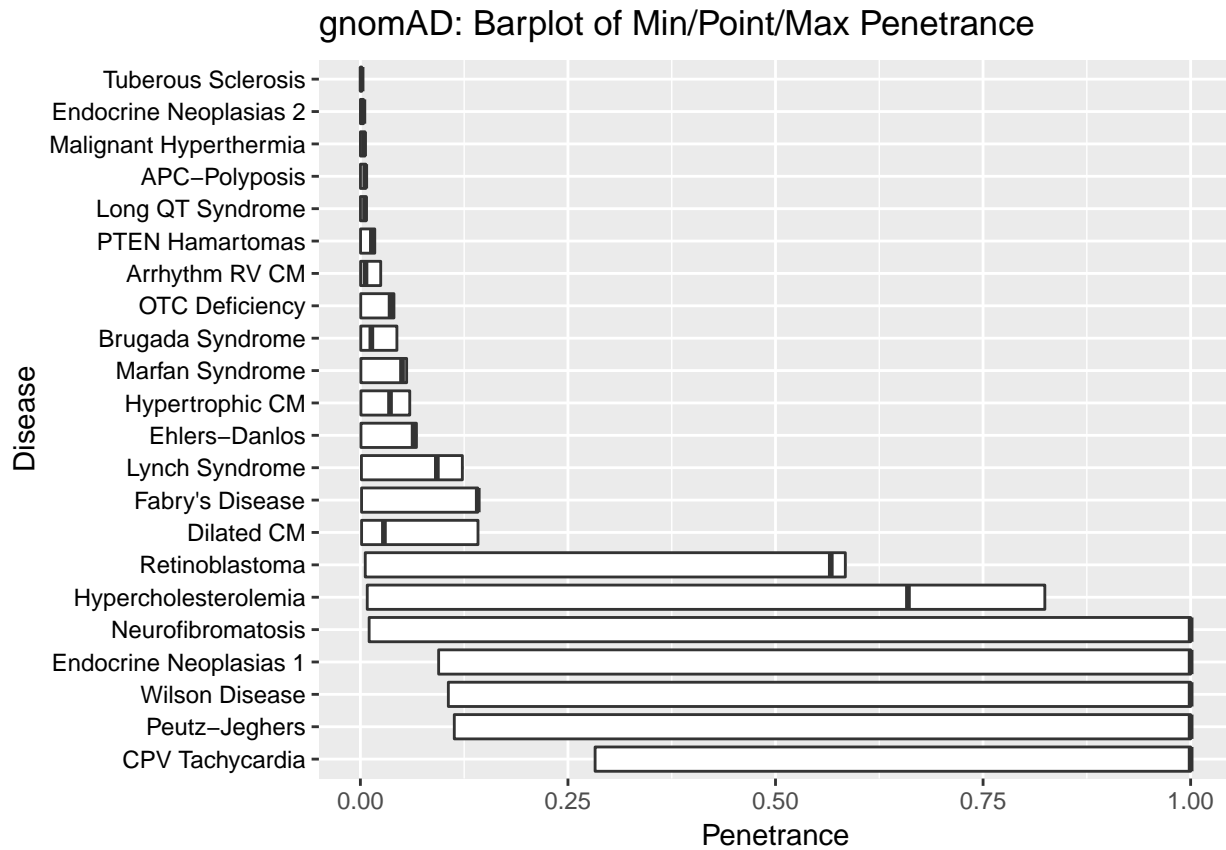
2.1 Fraction of Individuals with Pathogenic Non-Reference Sites



3 Penetrance Estimates

3.1 Max/Min Penetrance as a Function of $P(D)$ and $P(V|D)$

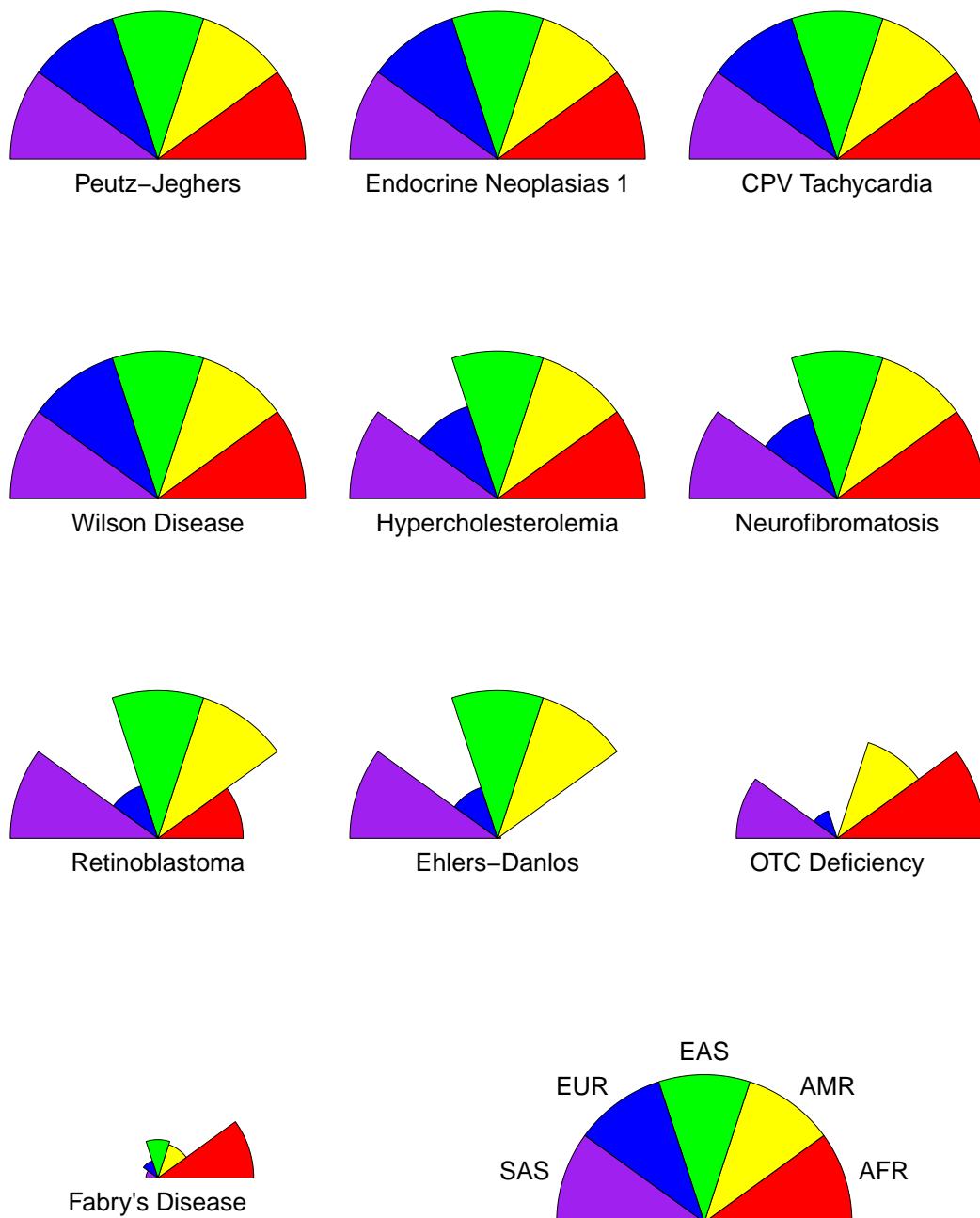
The left end of the boxplot indicates $P(V|D) = 0.01$,
the bold line in the middle indicates $P(V|D) = \text{point value}$,
the right end of the boxplot indicates $P(V|D) = 1$.



Note: Some diseases have mean theoretical penetrance = 1 because the assumed allelic heterogeneity is greater than is possible, given the observed prevalence and allele frequencies.

3.2 Penetrance Estimates by Ancestry

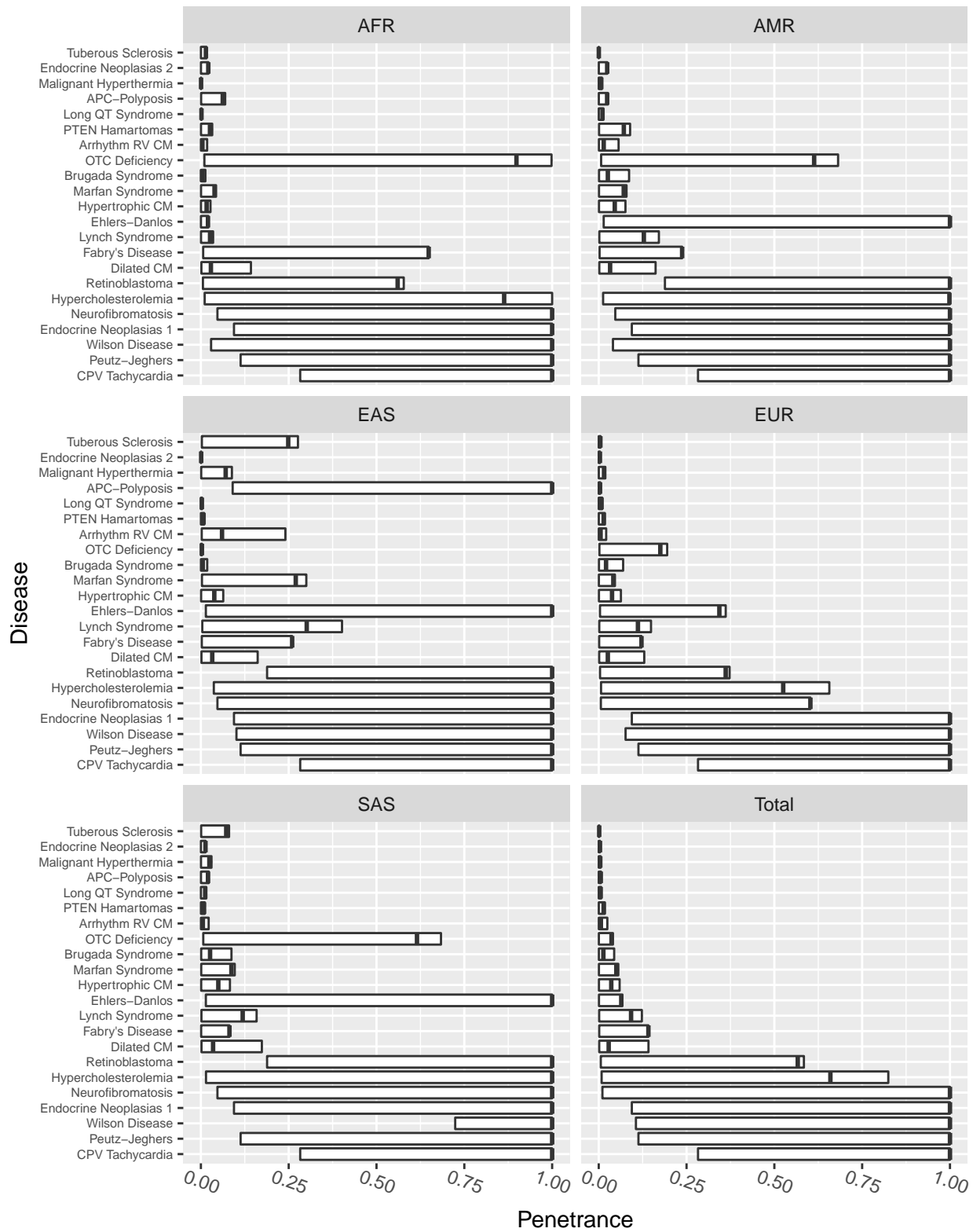
Radar Plot: Max Penetrance by Ancestry (gnomAD)



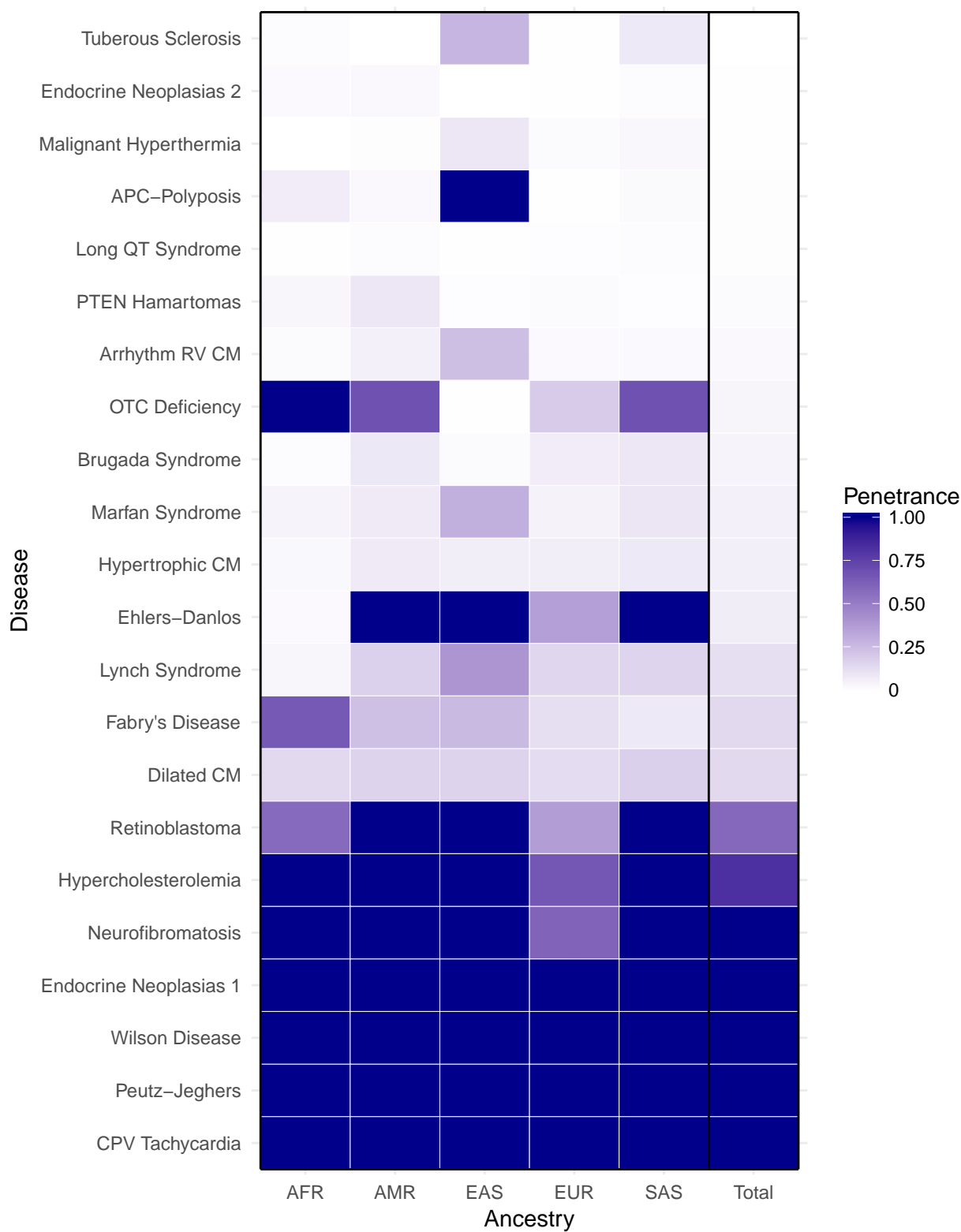
[1] These are the top 10 diseases by summed allele frequencies. NULL values are not plotted.

[1] Each radius is proportional to the penetrance of the disease in the given population.

Barplot: Penetrance by Ancestry (gnomAD)



Heatmap: Max Penetrance by Ancestry (gnomAD)



Dark gray boxes are NA: no associated variants discovered in that ancestral population.