

ClinVar Report

James Diao

November 4, 2016

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
3.3	Empirical CDFs for All Penetrance Plots	7
3.4	Comparing Mean Penetrance between ExAC and 1000 Genomes	7

Sourcing ClinVar input from: clinvar_2016-08-02.vcf

Sending output to: Report_2016-08-02.pdf

1 Collect and Merge ClinVar Data

1.1 Import ClinVar VCF

Processed ClinVar data frame 115825 x 14 (selected rows/columns):

1.2 Merge ClinVar with 1000 Genomes and ExAC

Breakdown of ClinVar Variants

Subset_ClinVar	Number_of_Variants
Total ClinVar	115825
LP/P-ClinVar	32719
LP/P-ClinVar & ACMG	6424
LP/P-ClinVar & ACMG & ExAC	955
LP/P-ClinVar & ACMG & 1000 Genomes	147

Breakdown of ACMG-1000 Genomes Variants

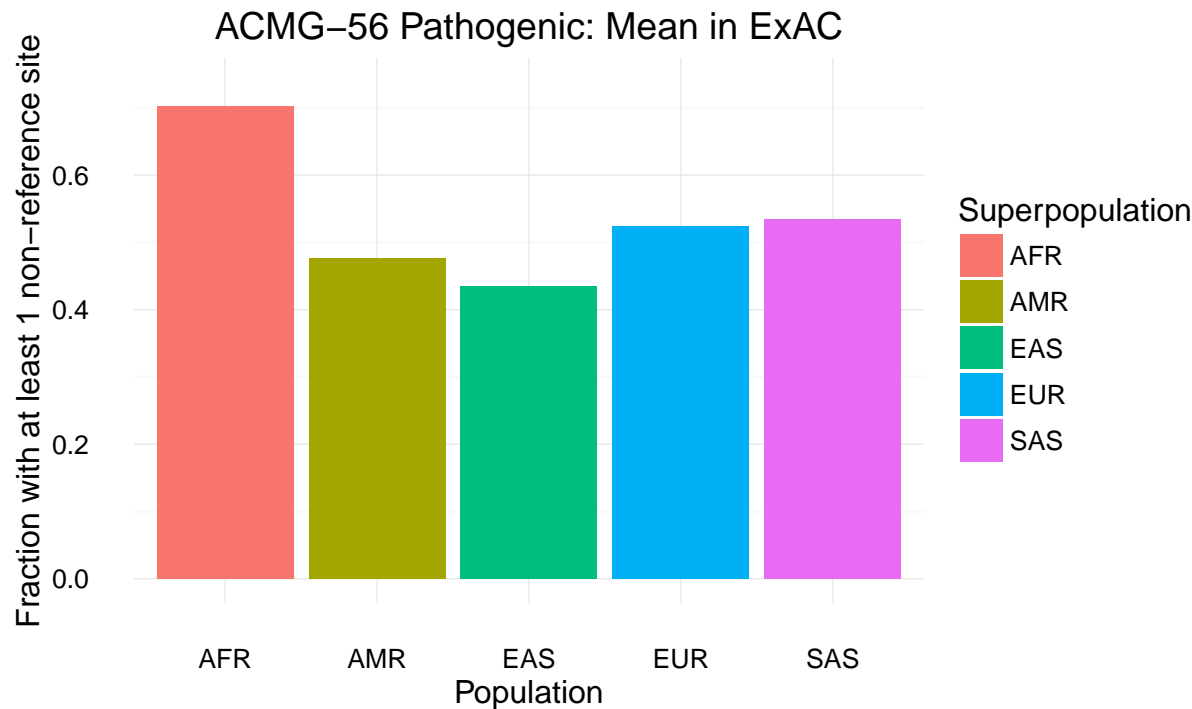
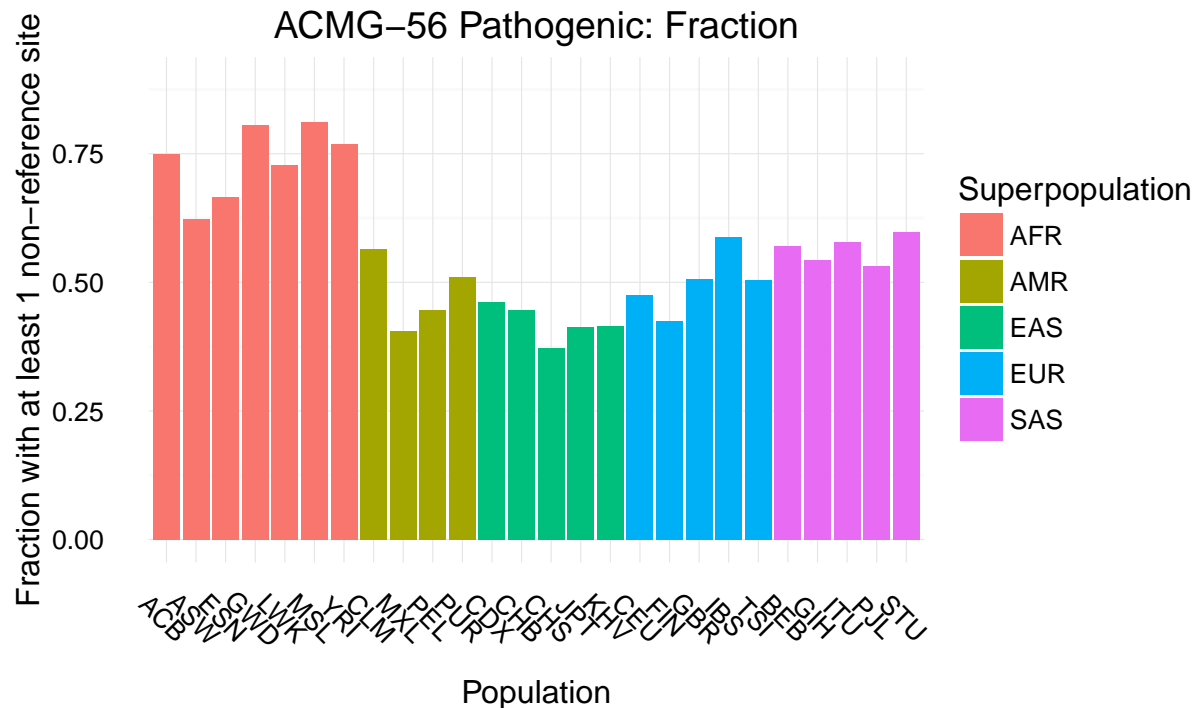
Subset_1000_Genomes	Number_of_Variants
Total 1000_Genomes & ACMG	139335
1000_Genomes & ACMG & ClinVar	4338
1000_Genomes & ACMG & LP/P-ClinVar	147

Breakdown of ACMG-ExAC Variants

Subset_ExAC	Number_of_Variants
Total ExAC & ACMG	58873
ExAC & ACMG & ClinVar	9344
ExAC & ACMG & LP/P-ClinVar	955

2 Summary Statistics

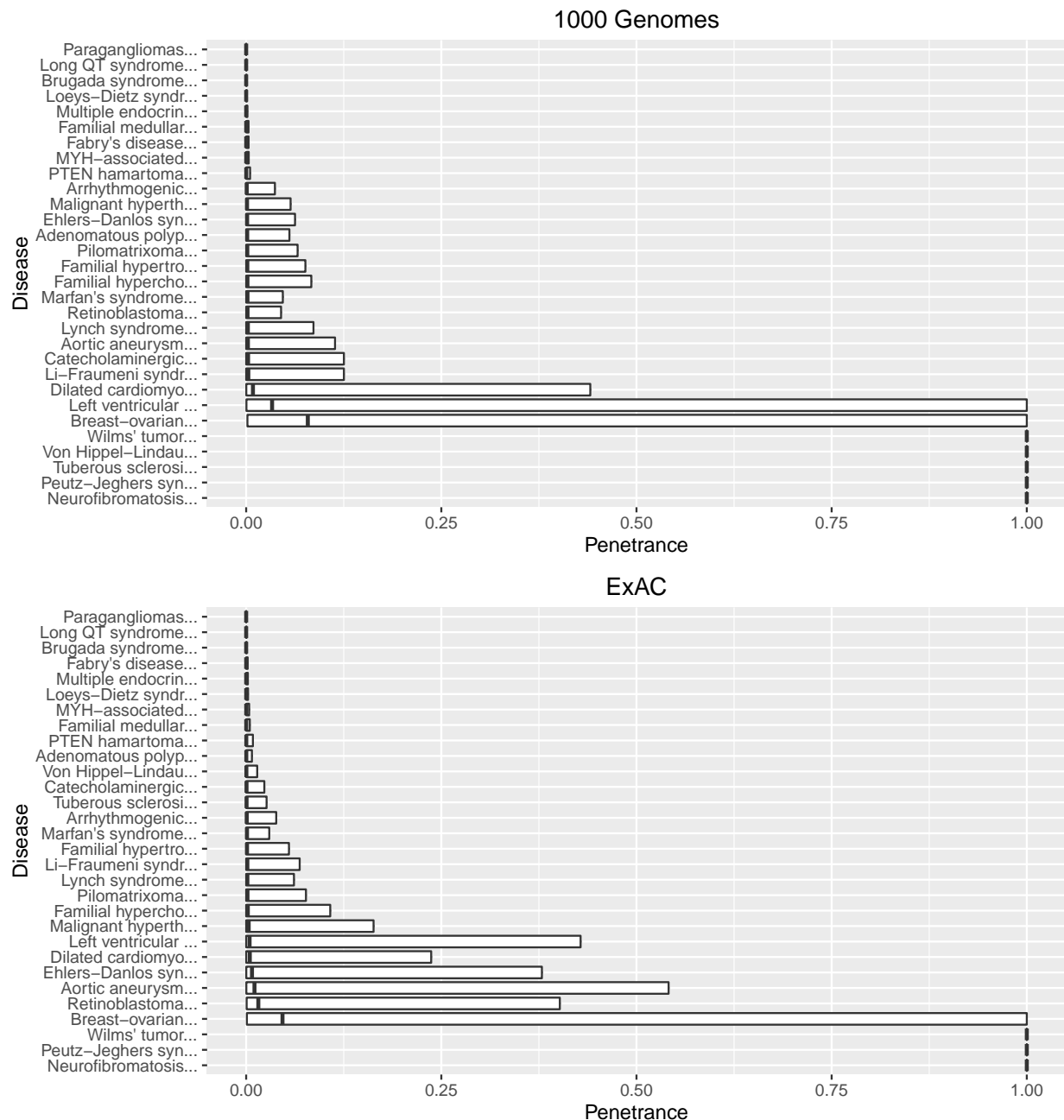
2.1 Fraction of Individuals with Pathogenic Non-Reference Sites



3 Penetrance Estimates

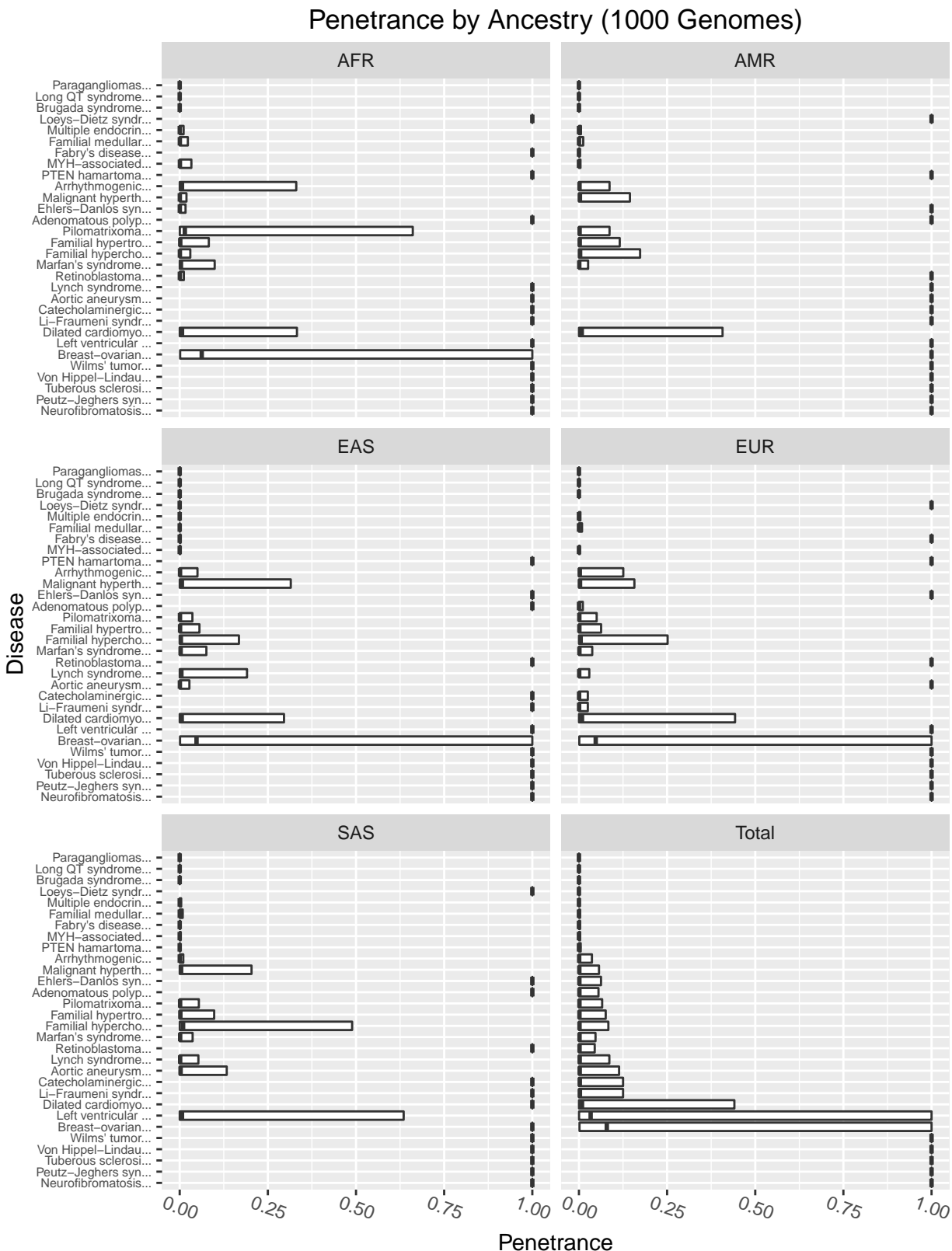
3.1 Max/Min Penetrance as a Function of $P(D)$ and $P(V|D)$

The left end of the boxplot indicates $P(D)$ AND $P(V|D)$ = lower value,
the bold line in the middle indicates $P(D)$ AND $P(V|D)$ = geometric_mean(values),
the right end of the boxplot indicates $P(D)$ AND $P(V|D)$ = upper value.

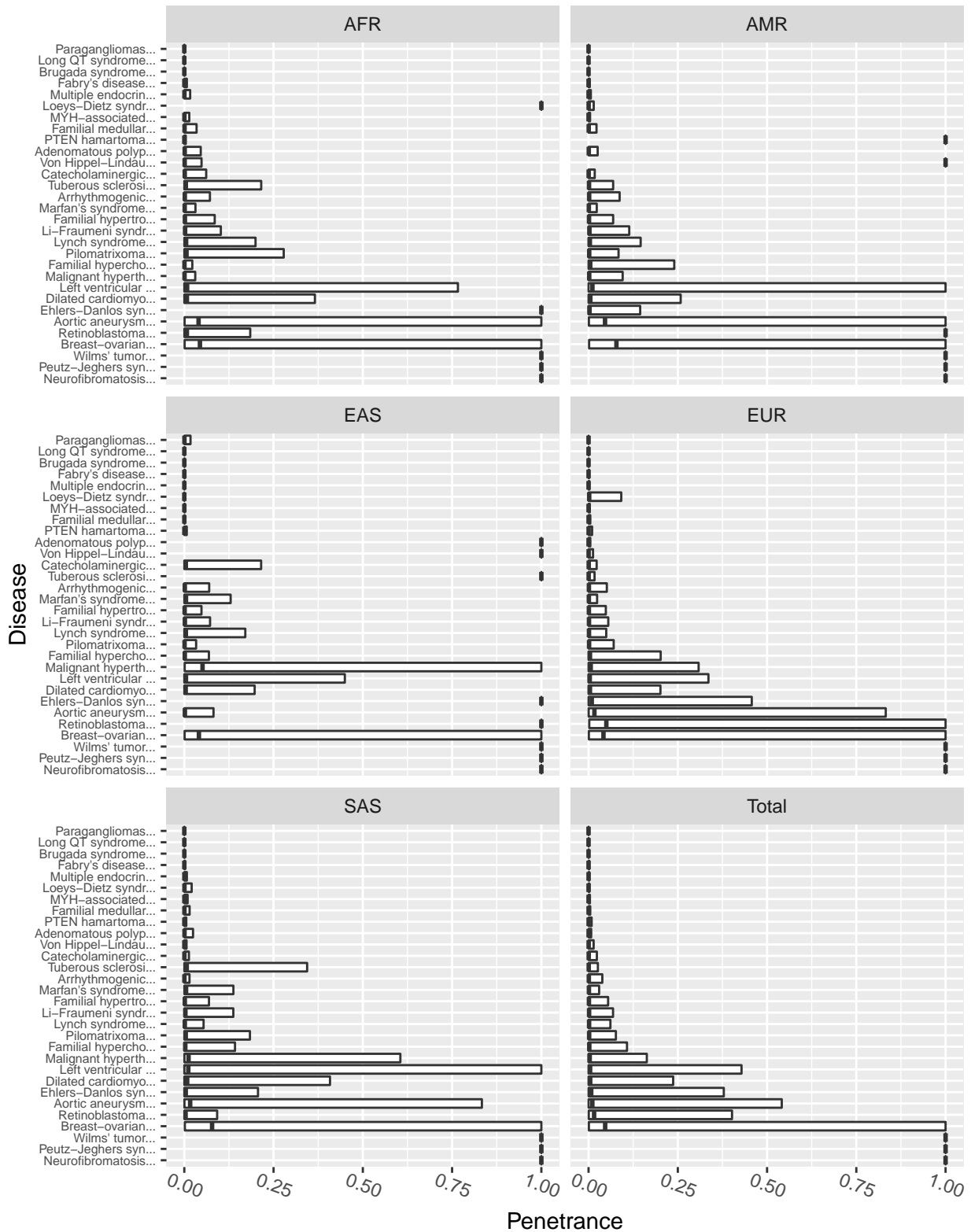


Note: Prevalence ranges of 5x were assumed for all point estimates of prevalence.
For example: a point estimate of 0.022 would be given the range 0.01-0.05.

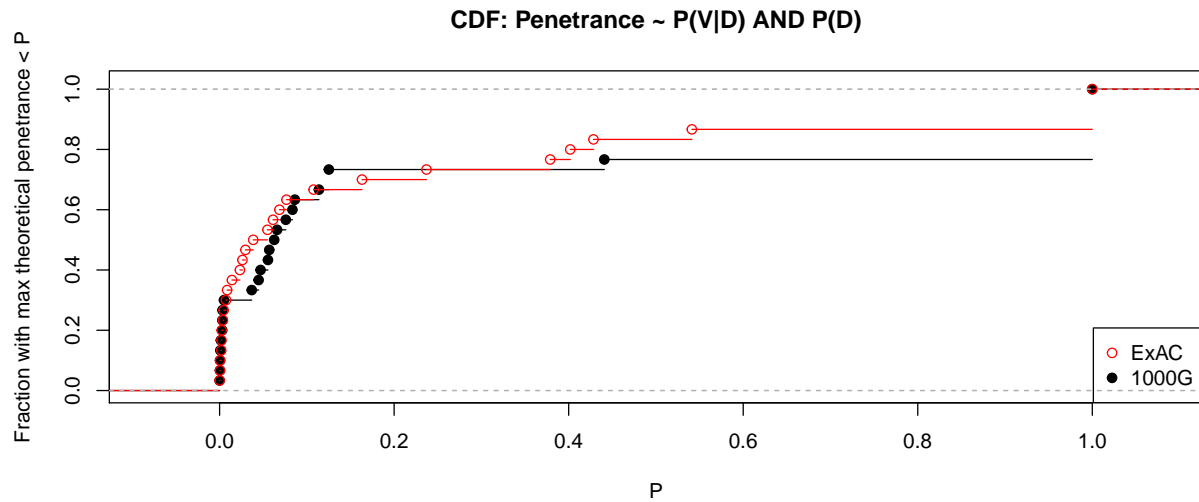
3.2 Penetrance Estimates by Ancestry



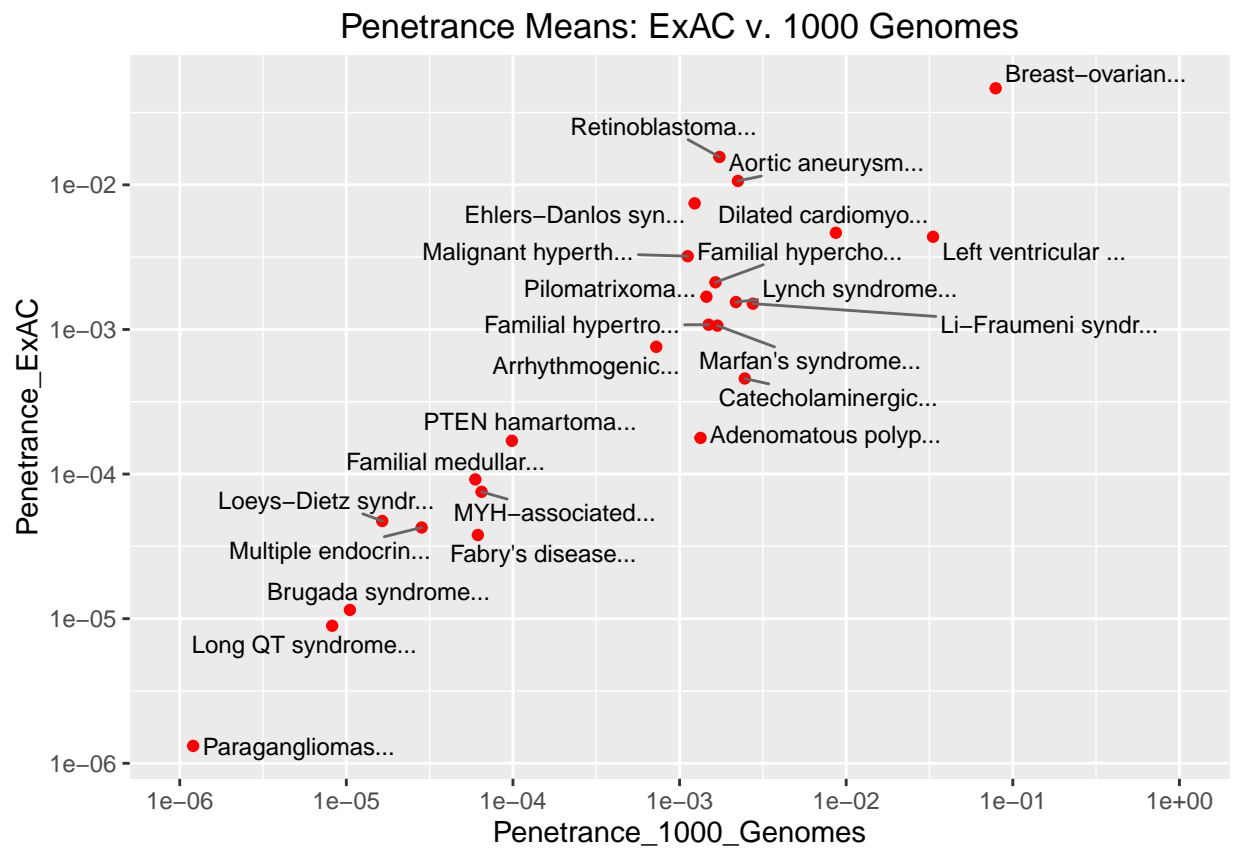
Penetrance by Ancestry (ExAC)



3.3 Empirical CDFs for All Penetrance Plots



3.4 Comparing Mean Penetrance between ExAC and 1000 Genomes



The Pearson correlation is 0.87.

Max penetrance values computed using 1000 Genomes are 1.5-fold larger than those computed using ExAC.