ClinVar Report

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Contents

Sourcing ClinVar input from: clinvar_2016-03-02.vcf
Sending output to: Report_2016-03-02.pdf

1 Collect and Merge ClinVar Data

1.1 Import ClinVar VCF

```
## Processed ClinVar data frame 98880 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	98880
LP/P-ClinVar	30483
LP/P-ClinVar & ACMG	6078
LP/P-ClinVar & ACMG & ExAC	944
LP/P-ClinVar & ACMG & 1000 Genomes	165

```
## Breakdown of ACMG-1000 Genomes Variants
```

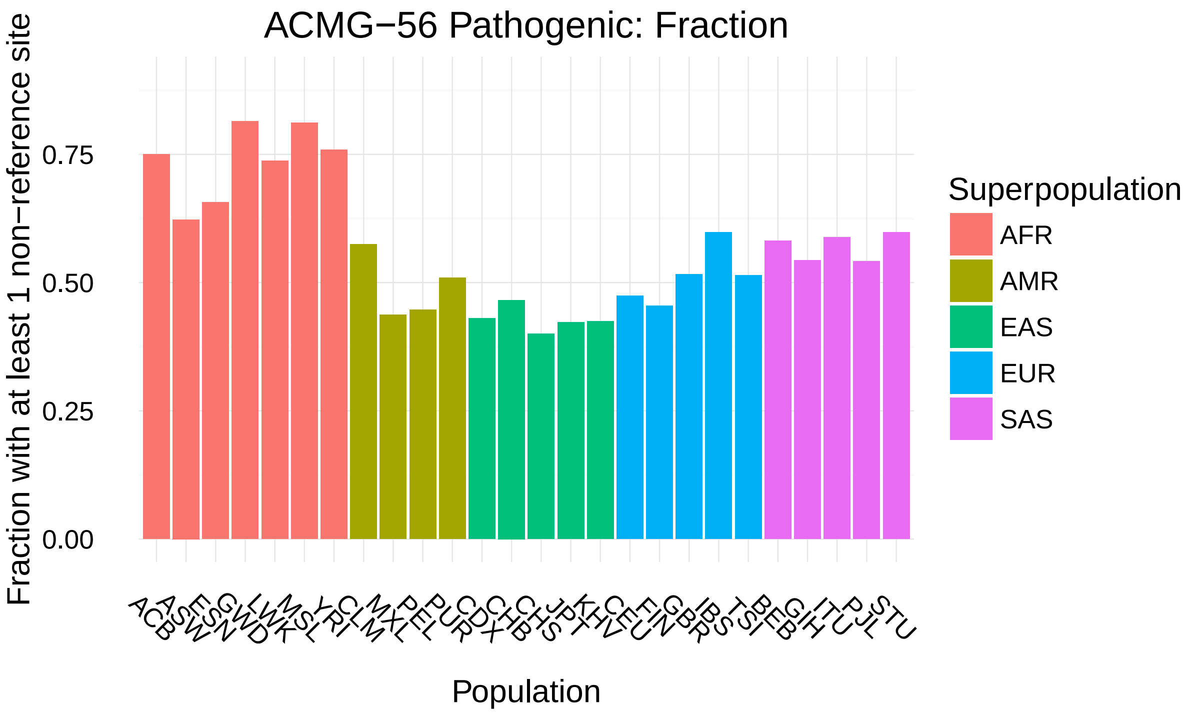
Subset_1000_Genomes	Number_of_Variants
Total 1000_Genomes & ACMG	139335
1000_Genomes & ACMG & ClinVar	3896
1000_Genomes & ACMG & LP/P-ClinVar	165

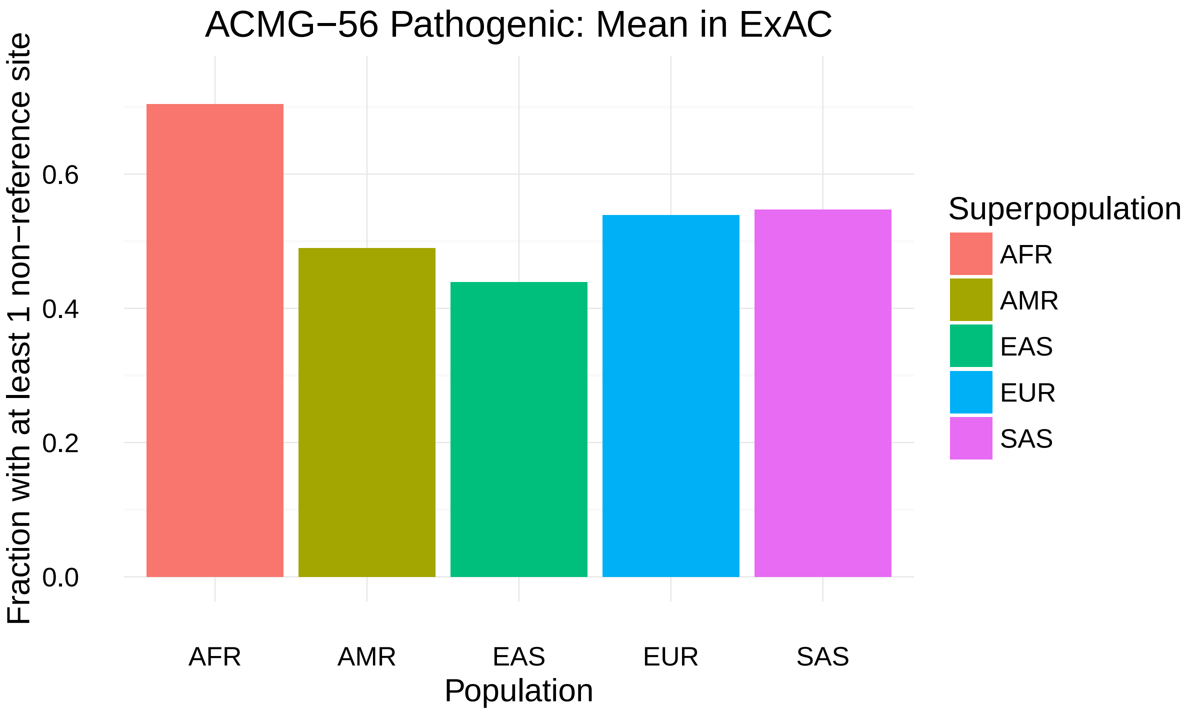
```
## Breakdown of ACMG-ExAC Variants
```

Subset_ExAC	Number_of_Variants
Total ExAC & ACMG	58873
ExAC & ACMG & ClinVar	8010
ExAC & ACMG & LP/P-ClinVar	944

2 Summary Statistics

2.1 Fraction of Individuals with Pathogenic Non-Reference Sites

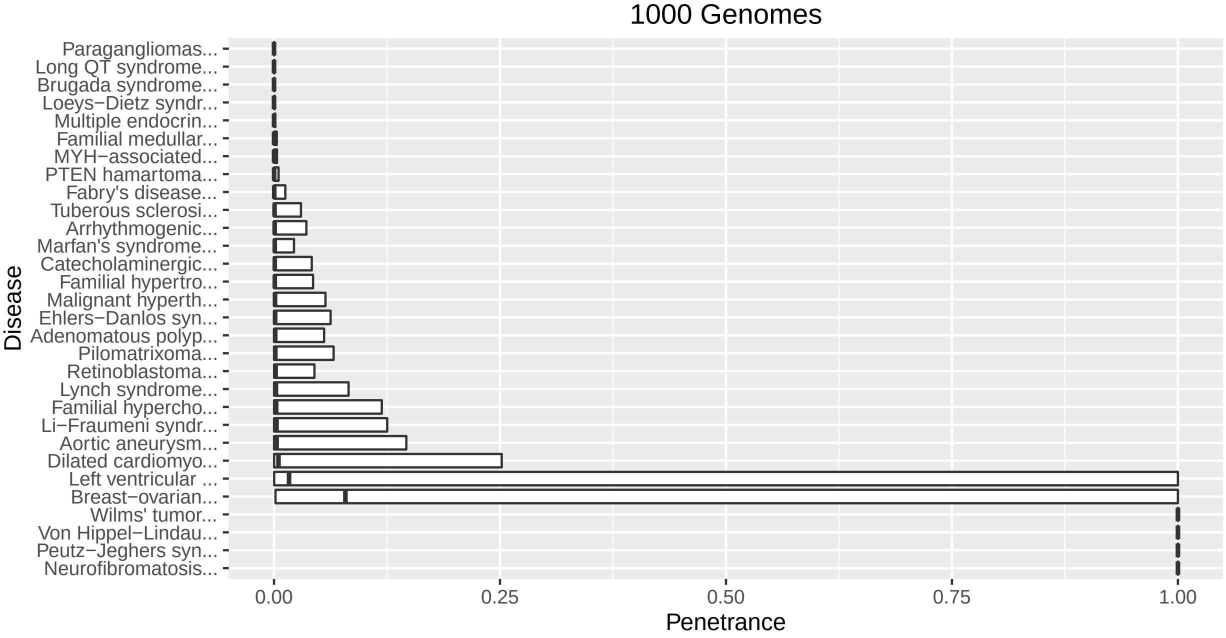


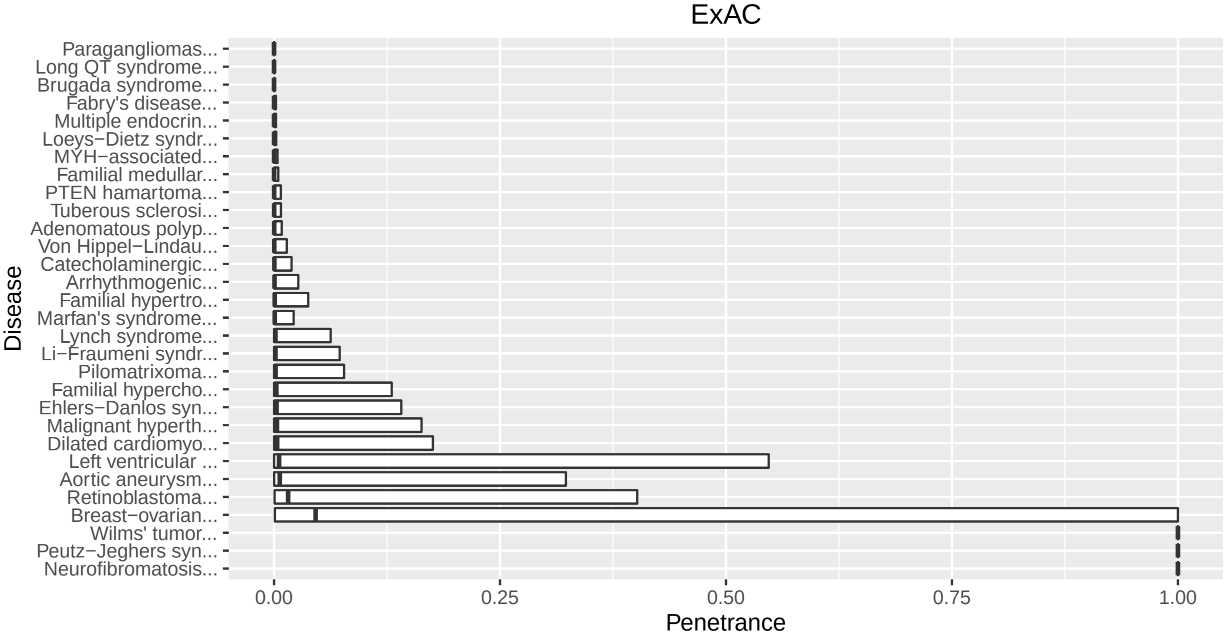


3 Penetrance Estimates

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

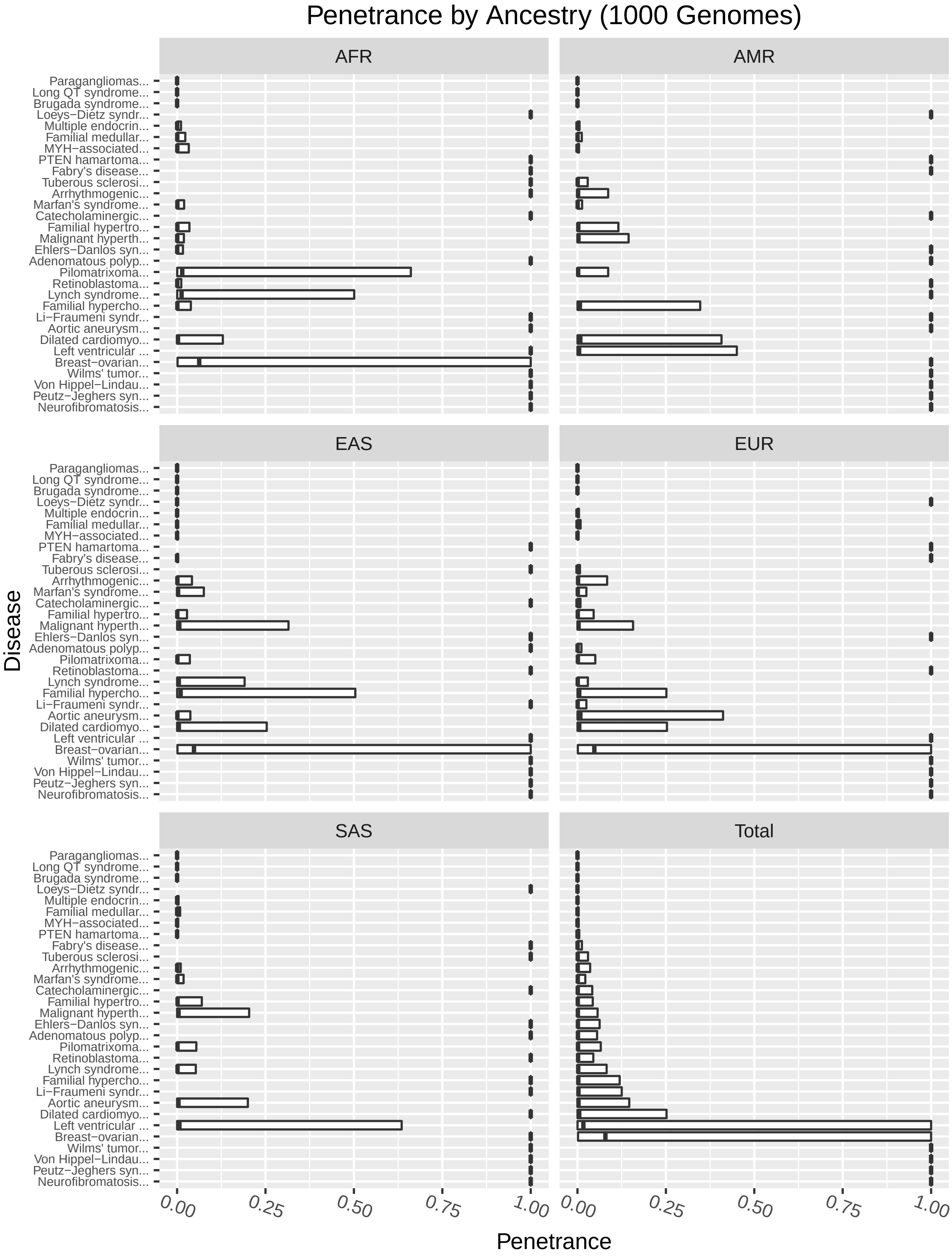
The left end of the boxplot indicates P(D) AND P(V|D) = lower value,
the bold line in the middle indicates P(D) AND P(V|D) = geometric_mean(values),
the right end of the boxplot indicates P(D) AND P(V|D) = upper value.

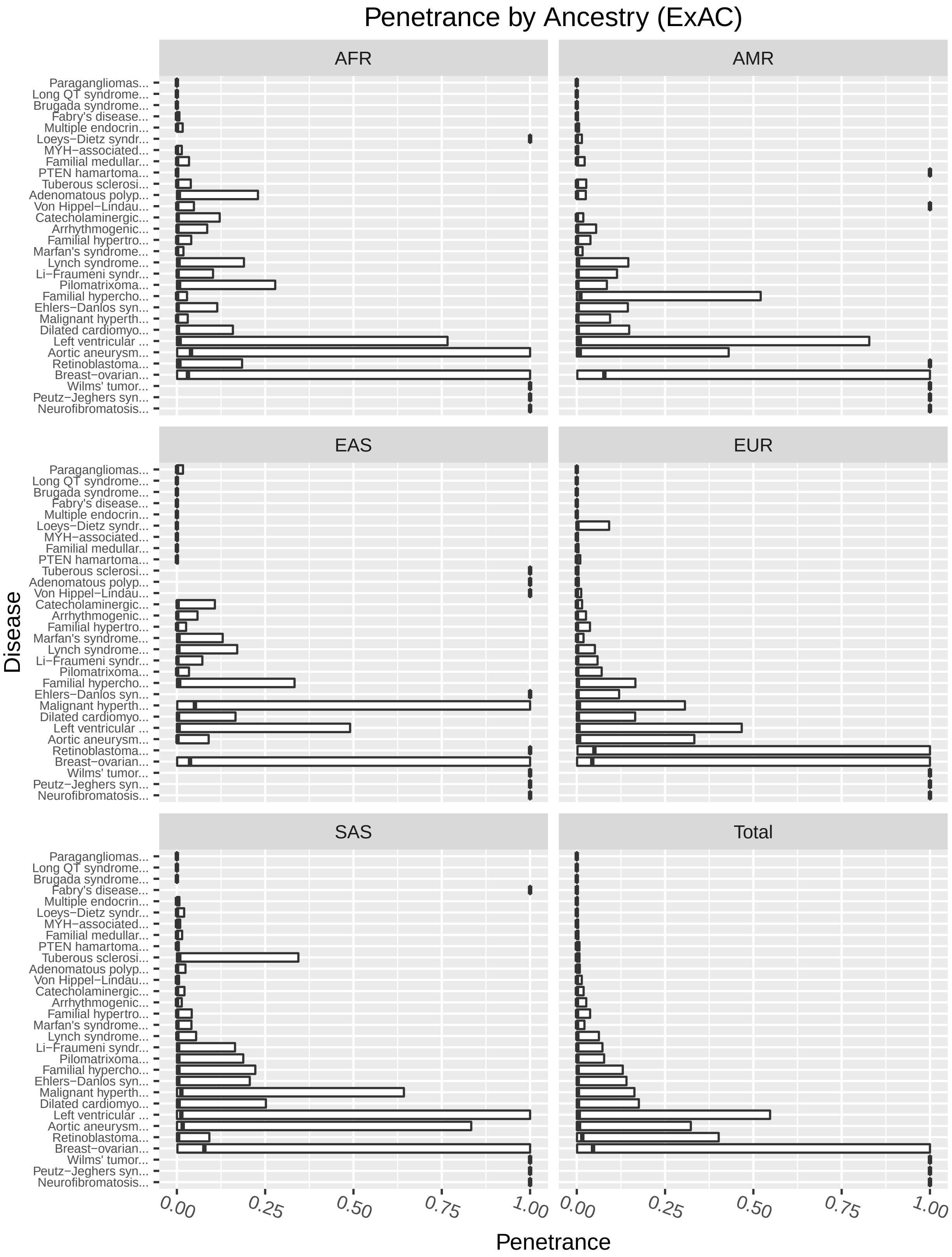




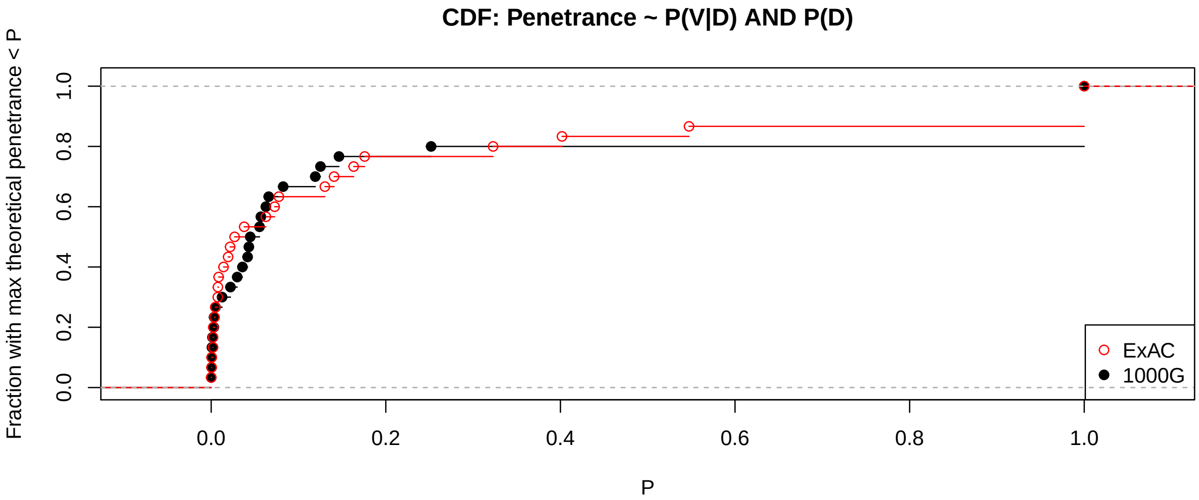
Note: Prevalence ranges of 5x were assumed for all point estimates of prevalence.
For example: a point estimate of 0.022 would be given the range 0.01-0.05.

3.2 Penetrance Estimates by Ancestry

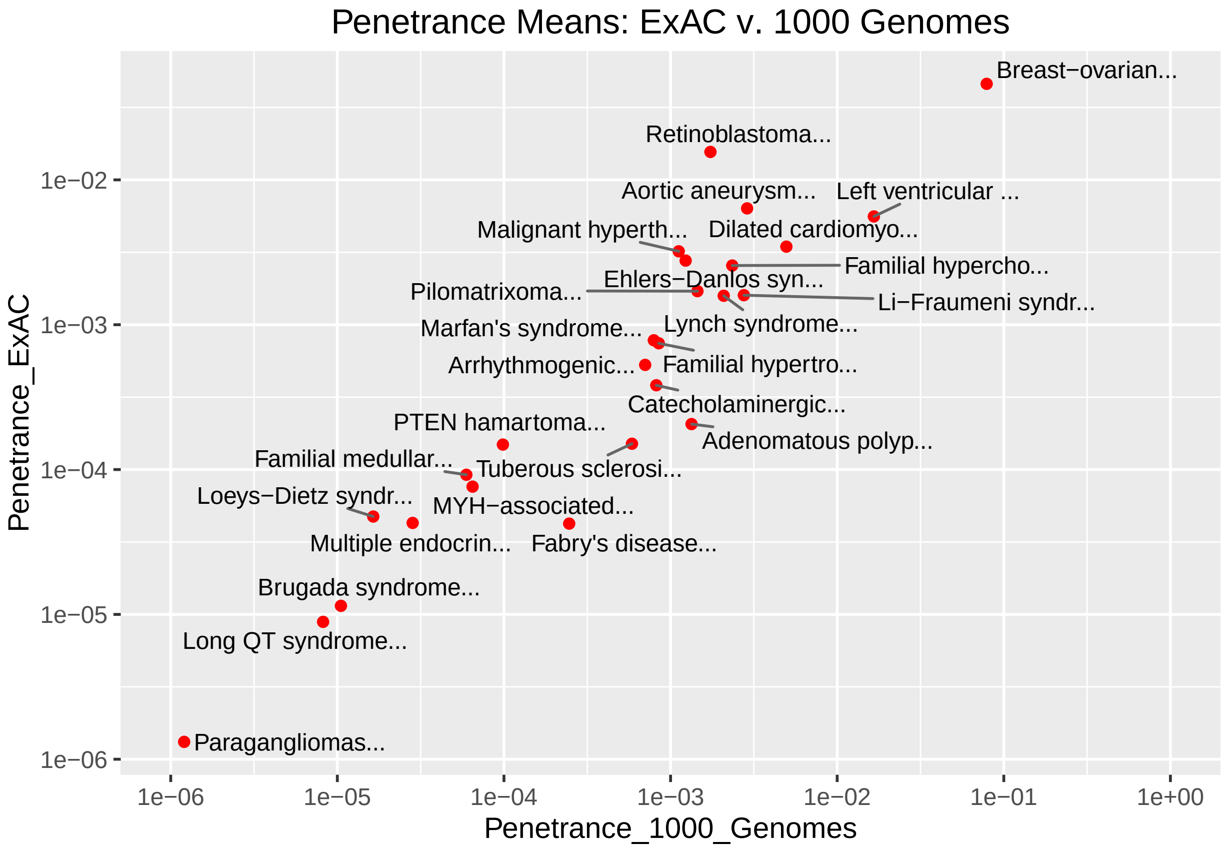



Penetrance by Ancestry (ExAC)
AFR
AMR
EAS
EUR
SAS
Total
Disease
Paragangliomas...
Long QT syndrome...
Brugada syndrome...
Fabry's disease...
Multiple endocrin...
Loeys−Dietz syndr...
MYH−associated...
Familial medullar...
PTEN hamartoma...
Tuberous sclerosi...
Adenomatous polyp...
Von Hippel−Lindau...
Catecholaminergic...
Arrhythmogenic...
Familial hypertro...
Marfan's syndrome...
Lynch syndrome...
Li−Fraumeni syndr...
Pilomatrixoma...
Familial hypercho...
Ehlers−Danlos syn...
Malignant hyperth...
Dilated cardiomyo...
Left ventricular ...
Aortic aneurysm...
Retinoblastoma...
Breast−ovarian...
Wilms' tumor...
Peutz−Jeghers syn...
Neurofibromatosis...
0.00
0.25
0.50
0.75
1.00
Penetrance

3.3 Empirical CDFs for All Penetrance Plots



3.4 Comparing Mean Penetrance between ExAC and 1000 Genomes



The Pearson correlation is 0.94.
Max penetrance values computed using 1000 Genomes are 1.6-fold larger than those computed using ExAC.