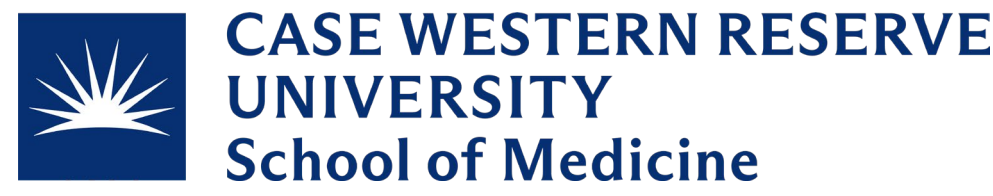


QUALITY CONTROL METRICS OF INDIVIDUAL GENETIC VARIANTS IN THE ALZHEIMER'S DISEASE SEQUENCING PROJECT ARE ASSOCIATED WITH FAVOR ANNOTATIONS.



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Introduction

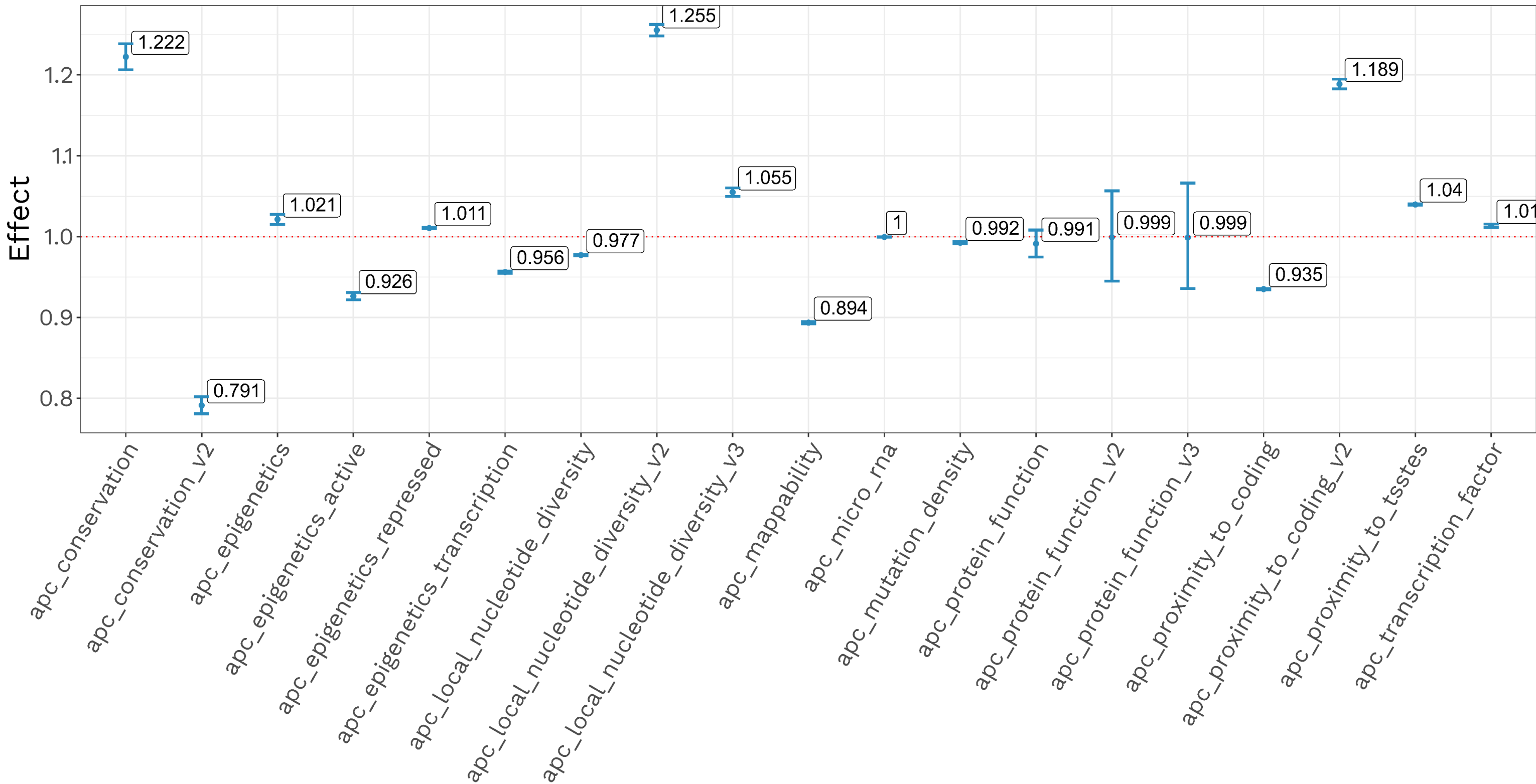
- The ADSP (Alzheimer's Disease Sequencing Project) released their 4th dataset consisting of **36,361 sequenced genomes, with 362 million variants**.
- The R4 release has 35,569 unique subjects, with **5,218** individuals of African Ancestry, **2,791** with Asian ancestry, **10,398** with Hispanic ancestry, **16,191** with Non-Hispanic White (NHW) ancestry, and **971** of Other/Unknown ancestry.

FAVOR annotations

- Each of the **362 million genetic variants** were processed to generate **functional annotations** using the **FAVOR database**.
- FAVOR integrates data from multiple databases, including **CADD v1.5, GENCODE v31, Annovar, WGSa, ClinVar, ENCODE, SnpEff, 1000 Genome, TOPMed Bravo Freeze 8 and gnomAD v3**.
- FAVOR functional scores are divided into **17 groups**, along with **annotation Principal Components (aPCs)**, which are the first variant-specific PC calculated from each standardized individual annotation score within these 17 groups.

Predicted Effects of a change of one unit in the FAVOR aPCs on the odds of failing VFlag 1.

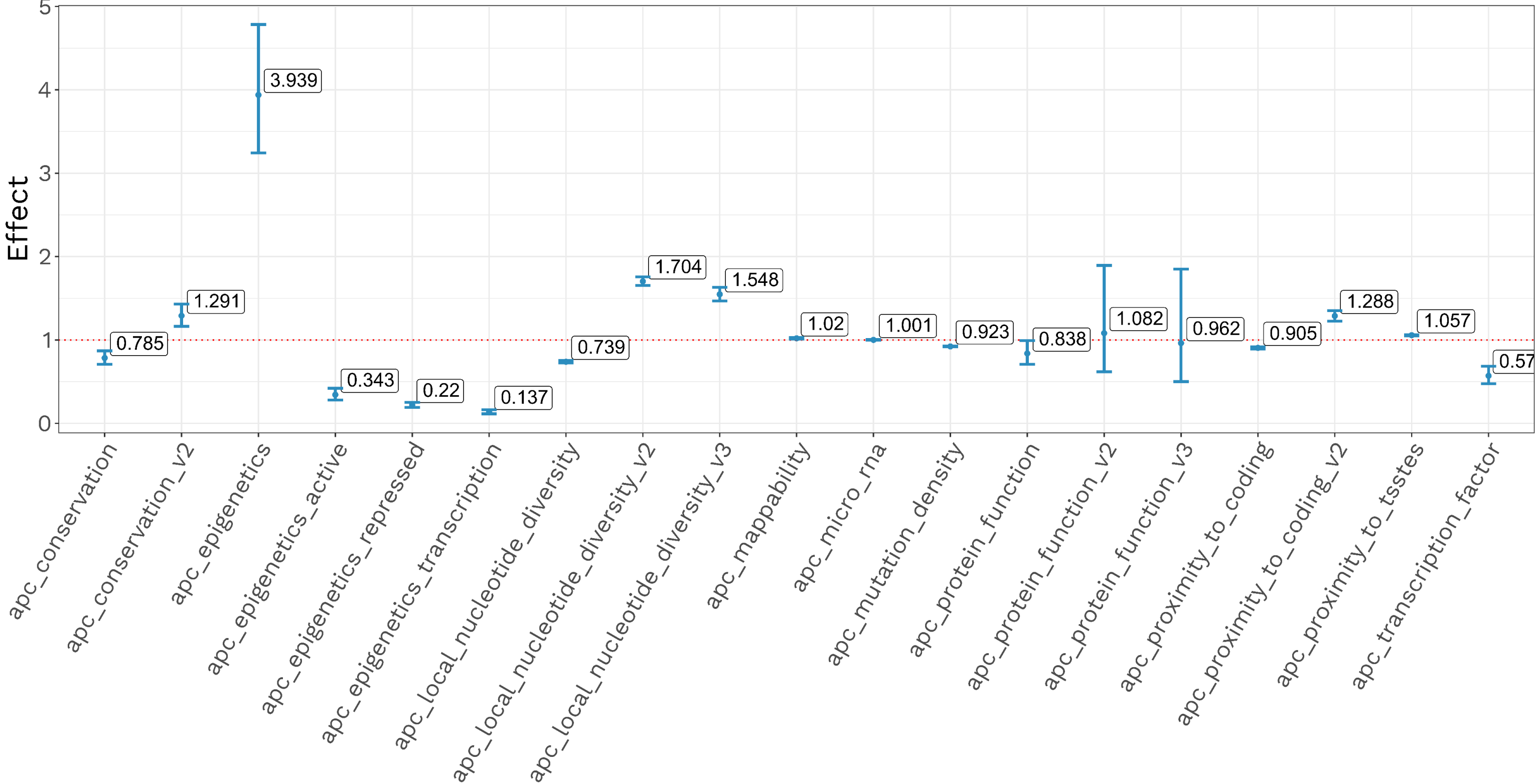
A variant fails VFlag 1 if GATK 'FILTER'!= 'PASS' or is in tranche >=99.7%.



Variants taken from Chromosomes 21 and 22 from the ADSP R4 data release.

Predicted Effects of a change of one unit in the FAVOR aPCs on the odds of failing VFlag 2.

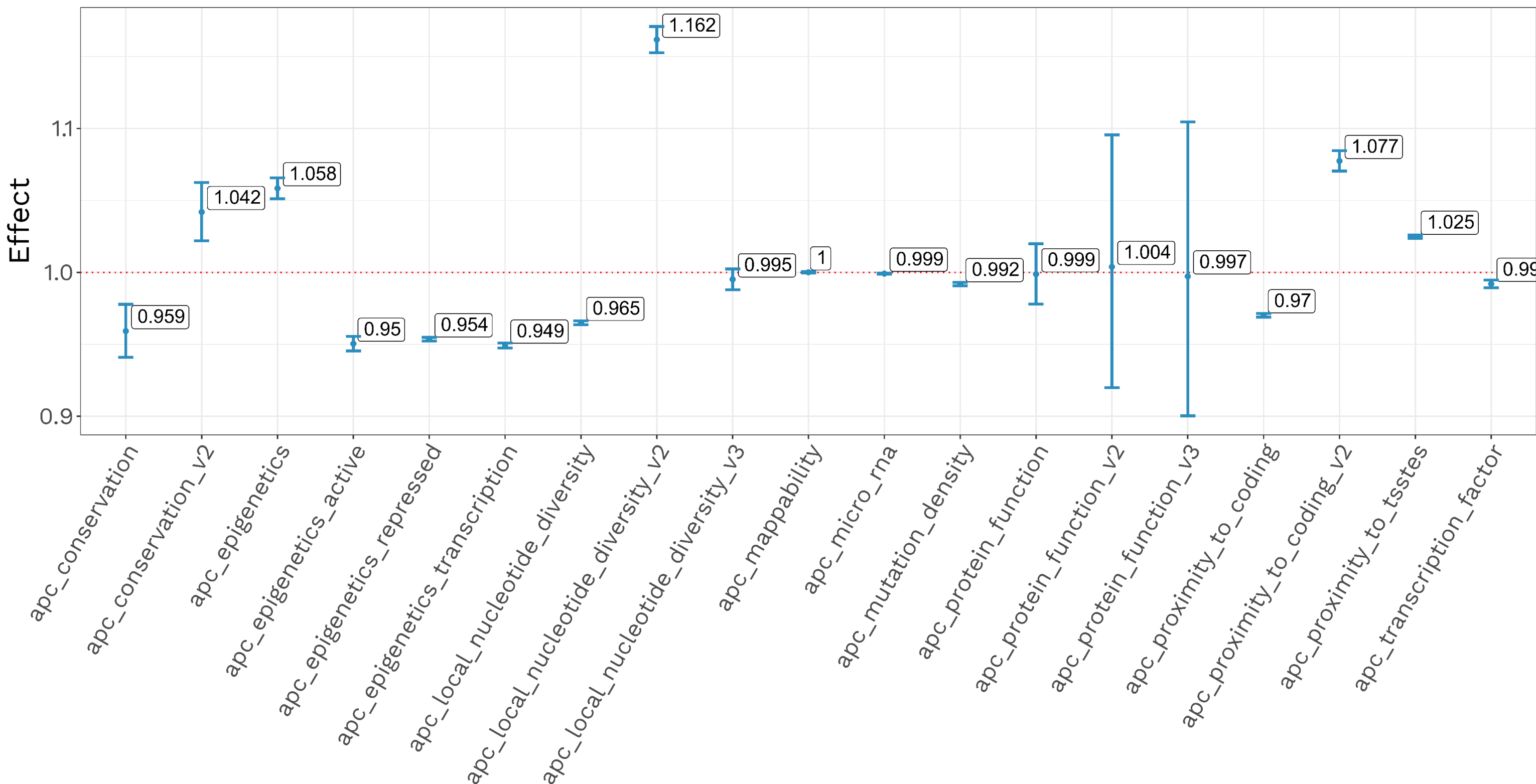
A variant fails VFlag 2 if all genotypes have DP<10 and/or GQ<20.



Variants taken from Chromosomes 21 and 22 from the ADSP R4 data release.

Predicted Effects of a change of one unit in the FAVOR aPCs on the odds of failing VFlag 3.

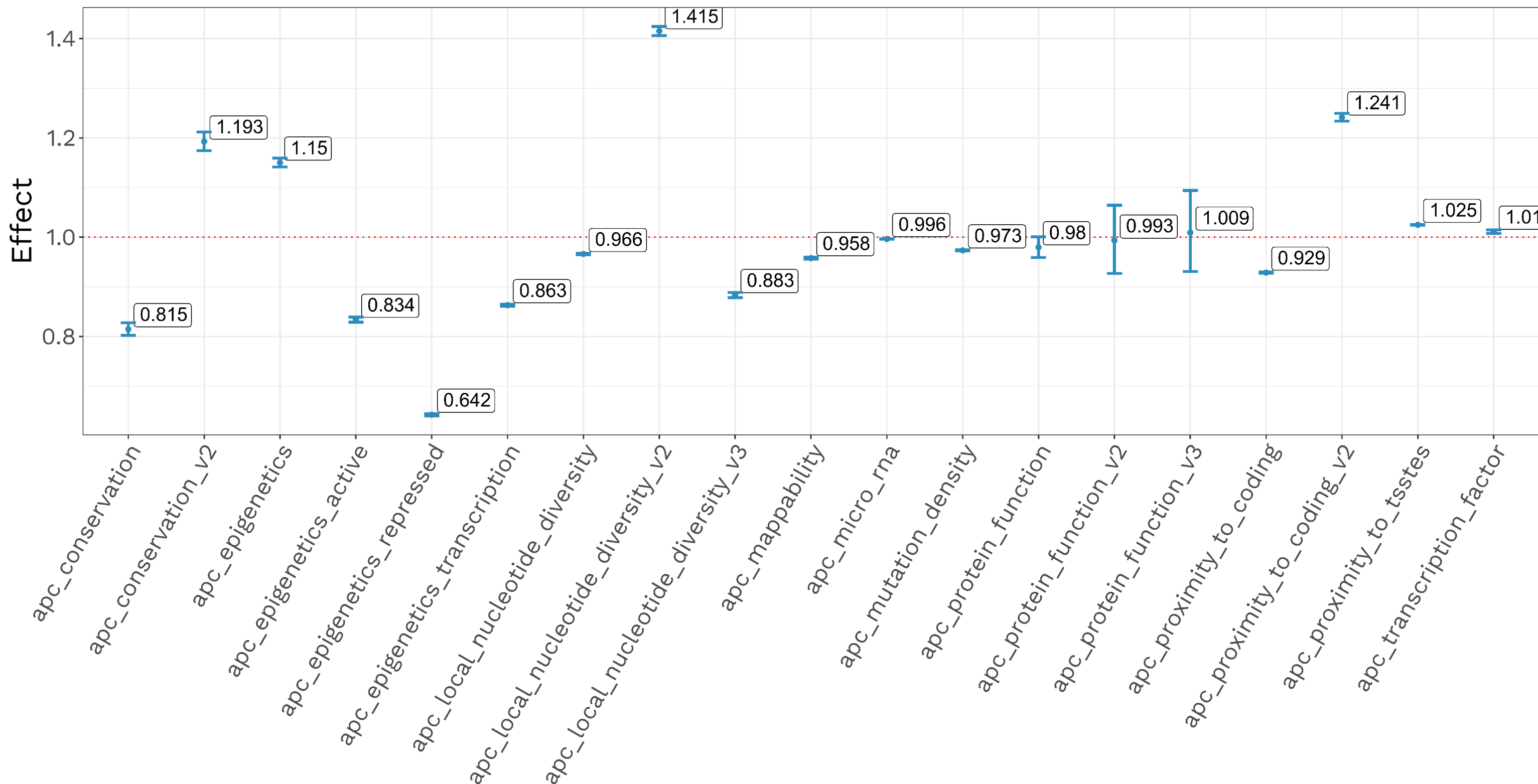
A variant fails VFlag 3 if MAF = 0.



Variants taken from Chromosomes 21 and 22 from the ADSP R4 data release.

Predicted Effects of a change of one unit in the FAVOR aPCs on the odds of failing VFlag 4.

A variant fails VFlag 4 if Call Rate <= 80%.



Variants taken from Chromosomes 21 and 22 from the ADSP R4 data release.