Example Data

We have 3 variants and 6 samples with their genotypes noted here. Samples 1-3 are "cases" and samples 4-6 are "controls".

Variant	Sample1	Sample2	Sample3	Sample4	Sample5	Sample6
PDGFRB:p.Arg685His	1/0	0/0	1/1	1/1	1/1	0/0
PDGFRB:p.Arg695Cys	0/0	0/0	0/0	0/0	0/0	0/0
PDGFRB:p.Arg709His	1/0	0/0	1/0	1/0	0/0	0/0

Using this data, each method will be described below

Method = "sample"

Using the method = "sample" argument, odds ratios will be calculated using counts of cases and controls if they have an alternative allele that meets "dominant" or "recessive" model conditions.

Model = "dominant"; level = "variant"

Under these parameters, we will calculate odds ratios according to the dominant model (one copy or heterozygotes are sufficient to cause the phenotype) at the variant level. For PDGFRB:p.Arg685His, Case samples 1 and 3 have at least one qualifying variant, while Sample 2 does not. Control samples 4 and 5 have at least one qualifying variant, while Sample 6 does not. Therefore, the contingency table will be represented as:

	Case	Control
Homozygous Alt or Heterozygous	2 (Sample 1,3)	2 (Sample 4, 5)
Homozygous Ref	1 (Sample 2)	1 (Sample 6)

Model = "recessive"; level = "variant"

Under these parameters, we will calculate odds ratios according to the recessive model (two copies, or homozygotes, are sufficient to cause the phenotype) at the variant level. For PDGFRB:p.Arg685His, Case Sample 3 is homozygous, while Samples 1 and 2 are not. Control Samples 4 and 5 are homozygous, while Sample 6 is not. Therefore, the contingency table will be represented as:

	Case	Control
Homozygous Alt	1 (Sample 3)	2 (Sample 4, 5)
Heterozygous or Homozygous Ref	2 (Sample 1,2)	1 (Sample 6)

Model = "dominant"; level = "gene"

Under these parameters, we will calculate odds ratios according to the dominant model (one copy, or heterozygotes are sufficient to cause the phenotype) by collapsing variants across a gene. For PDGFRB, we have 3 variants with varying genotypes across the samples. According to the dominant model, having at least one variant in the gene will be sufficient to cause the phenotype. Therefore, the contingency table will be represented as:

	Case	Control
Homozygous Alt or Heterozygous	2 (Sample 1,3)	2 (Sample 4, 5)
Homozygous Ref	1 (Sample 2)	1 (Sample 6)

Model = "recessive"; level = "gene"

Under these parameters, we will calculate odds ratios according to the recessive model (two copies, or homozygotes, are sufficient to cause the phenotype) at the variant level. For PDGFRB, we have 3 variants with varying genotypes across the samples. According to the recessive model, we will require that samples be homozygous Alt to be counted here. Therefore, the contingency table will be represented as:

	Case	Control
Homozygous Alt	1 (Sample 3)	2 (Sample 4, 5)
Heterozygous or Homozygous Ref	2 (Sample 1,2)	1 (Sample 6)

Model = "dominant"; level = "domain"

Since the 3 example variants here lie in the same domain, the contingency table will follow the model = "dominant"; level = "gene" example.

Model = "recessive": level = "domain"

Since the 3 example variants here lie in the same domain, the contingency table will follow the model = "recessive"; level = "gene" example.

Method = "allelic"

Level = "variant"

Under these parameters, we will calculate odds ratios by counting the number of alternative alleles present in each case/control group. For PDGFRB:p.Arg685His, Sample 1 is heterozygous, Sample 2 is homozygous Ref, and Sample 3 is homozygous Alt, resulting in a total of 3 ref alleles out of a possible 6 (two copies per sample). For controls, Sample 4 and 5 are homozygous alt, while Sample 6 is homozygous Ref, resulting in 4 alternative alleles out of a possible 6. Therefore, the contingency table will be represented as:

	Case	Control

Total number of alt alleles	3	4
Total number of ref alleles	3	2

Level = “gene” or Level = “domain”

Under these paramaters, we will calculate odds ratios by counting the number of alternative alleles present in each gene in each case/control group. For PDGFRB, Sample 1 has 2 alt alleles; Sample 2 has 0 alt alleles; Sample 3 has 3 alt alleles, resulting in 5 total alleles. Control Sample 4 has 3 alt alleles; Sample 5 has 2 alt alleles; Sample 6 has 0 alt allele, resulting in 5 total alt alleles. For the background, we assume that each person will contribute at most 2 alleles, since we commonly run this for variants with allele frequency < 0.01 (1%), therefore, the total number of possible alleles for each case control group is 6 (2 * n_samples). Therefore the contingency table will be represented as:

	Case	Control
Total number of alt alleles	5	5
Total number of ref alleles	1	1