SKAT Package

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1 Overview

SKAT package has functions to 1) test for associations between SNP sets and continuous/binary phenotypes with adjusting for covariates and kinships and 2) to compute power/sample size for future studies.

2 Association test

An example dataset (SKAT.example) has a genotype matrix (Z) of 2000 individuals and 67 SNPs, vectors of continuous (y.c) and binary (y.b) phenotypes, and a covariates matrix (X).

```
> library(SKAT)
> data(SKAT.example)
> names(SKAT.example)

[1] "Z" "X" "y.c" "y.b"
> attach(SKAT.example)
```

To test for associations, SKAT_Null_Model function should be used in prior to run SKAT to estimate parameters under the null model of no associations.

```
> # continuous trait
> obj<-SKAT_Null_Model(y.c ~ X, out_type="C")
> out.c<-SKAT(Z, obj)
> out.c$p.value

[1] 0.002877041

> # dichotomous trait
> obj<-SKAT_Null_Model(y.b ~ X, out_type="D")
> out.b<-SKAT(Z, obj)
> out.b$p.value

[1] 0.1401991
```

The returned object from SKAT has many information, such as number of markers in Z and number of markers to be used for the test. The version 2.1.0 has test.snp.mac which has MAC of each markers used in the test.

```
> out.c$param
$liu_pval
[1] 0.002938438
$Is_Converged
[1] 1
$n.marker
[1] 67
$n.marker.test
[1] 67
> out.c$test.snp.mac
 VAR1
       VAR2
              VAR3
                    VAR4
                           VAR5
                                  VAR6
                                        VAR7
                                               VAR8
                                                     VAR9 VAR10 VAR11 VAR12 VAR13
                 2
                        4
                            577
                                   432
                                                  4
                                                         2
                                                               3
                                                                      2
                                                                                  34
                                                                             1
VAR14 VAR15 VAR16 VAR17 VAR18 VAR19 VAR20 VAR21 VAR22 VAR23 VAR24 VAR25 VAR26
  657
           2
                82
                        1
                             25
                                   328
                                          465
                                                  2
                                                         4
                                                              85
                                                                    430
VAR27 VAR28 VAR29 VAR30 VAR31
                                VAR32 VAR33 VAR34 VAR35 VAR36 VAR37 VAR38 VAR39
          82
                 1
                        1
                               1
                                    15
                                           19
                                                  1
                                                       657
                                                               1
                                                                     35
VAR40 VAR41 VAR42 VAR43 VAR44 VAR45 VAR46 VAR47 VAR48 VAR49 VAR50 VAR51 VAR52
                      423
        913
                 1
                               2
                                     2
                                            1
                                                  1
                                                        29
                                                               2
                                                                          527
                                                                                  10
VAR53 VAR54 VAR55 VAR56 VAR57 VAR58 VAR59 VAR60 VAR61 VAR62 VAR63 VAR64 VAR65
  527
          8
                 3
                        2
                            200
                                     3
                                            1
                                                  1
                                                        15
                                                               1
                                                                      1
                                                                                   1
VAR66 VAR67
    2
>
```

When the trait is binary and the sample size is small, SKAT can produce conservative results. We developed a moment matching adjustment (MA) that adjusts the asymptotic null distribution by estimating empirical variance and kurtosis. By default, SKAT will conduct the MA adjustment when the sample size < 2000. In the following code, we use only 200 samples to run SKAT.

```
> IDX<-c(1:100,1001:1100)
> # With-adjustment
> obj.s<-SKAT_Null_Model(y.b[IDX] ~ X[IDX,],out_type="D")

Sample size (non-missing y and X) = 200, which is < 2000. The small sample adjustment is appl
> SKAT(Z[IDX,], obj.s, kernel = "linear.weighted")$p.value
```

```
[1] 0.1334122
```

>

If you don't want to use the adjustment, please set Adjustment=FALSE in the SKAT_Null_Model function.

```
> # Without-adjustment
> obj.s<-SKAT_Null_Model(y.b[IDX] ~ X[IDX,],out_type="D", Adjustment=FALSE)
> SKAT(Z[IDX,], obj.s, kernel = "linear.weighted")$p.value
[1] 0.147093
```

Resampling based approaches to adjust for binary traits have been developed and implemented in SKATBinary function. When you use the SKATBinary function, Adjustment=TRUE in SKAT_Null_Model is not necessary. Implemented methods are 1) Efficient resampling (ER); 2) ER with adaptive resampling (ER.A); 3) Quantile adjusted moment matching (QA); 4) Moment matching adjustment (MA); 5) No adjustment (UA); and 6) Hybrid. "Hybrid" (default method) selects a method based on the total minor allele count (MAC), the number of individuals with minor alleles (m), and the degree of case-control imbalance. Detailed description of these methods can be found in the following reference:

Lee, S., Fuchsberger, C., Kim, S., Scott, L. (2016) An efficient resampling method for calibrating single and gene-based rare variant association analysis in case–control studies. *Biostatistics* (2016) 17 (1): 1-15.

```
> # default hybrid approach
> out<-SKATBinary(Z[IDX,], obj.s, kernel = "linear.weighted")
> out$p.value
[1] 0.147093
>
```

We have recently developed more scalable and accurate method for binary traits, which is implemented in SKATBinary_Robust function. Detailed description of these methods can be found in the following reference:

Zhao, Z., Bi, W., Zhou, W., VanderHaar, P., Fritsche, L.G., Lee, S. (2020) UK Biobank Whole-Exome Sequence Binary Phenome Analysis with Robust Region-based Rare-Variant Test. *AJHG*, 106: 3-12, doi:https://doi.org/10.1016/j.ajhg.2019.11.012

```
> # Robust approach
> out<-SKATBinary_Robust(Z[IDX,], obj.s, kernel = "linear.weighted")
> out$p.value
[1] 0.1511284
```

2.1 Assign weights for each SNP

It is assumed that rarer variants are more likely to be causal variants with large effect sizes. To incorporate this assumption, the linear weighted kernel uses a weighting scheme and is formulated as ZWWZ', where Z is a genotype matrix, and $W = diag\{w_1, \ldots, w_m\}$ is a weight matrix. In the previous examples, we used the default beta(1,25) weight, $w_i = dbeta(p_i, 1, 25)$, where dbeta is a beta density function, and p_i is a minor allele frequency (MAF) of SNP i. Different parameters for the beta weight can be used by changing weights beta. For example, weight beta=c(0.5,0.5) will use the Madsen and Browning weight.

```
> SKAT(Z, obj, kernel = "linear.weighted", weights.beta=c(0.5,0.5))$p.value [1] 0.4931639
```

You can use your own weight vector by using the weights parameter. For the logistic weight, we provide a function to generate the weight.

```
> # Shape of the logistic weight
>
> MAF<-1:1000/1000
> W<-Get_Logistic_Weights_MAF(MAF, par1=0.07, par2=150)
> par(mfrow=c(1,2))
> plot(MAF,W,xlab="MAF",ylab="Weights",type="1")
> plot(MAF[1:100],W[1:100],xlab="MAF",ylab="Weights",type="1")
> par(mfrow=c(1,2))
> # Use logistic weight
> weights<-Get_Logistic_Weights(Z, par1=0.07, par2=150)
> SKAT(Z, obj, kernel = "linear.weighted", weights=weights)$p.value
[1] 0.3293643
```

2.2 SKAT-O: Combined Test of burden test and SKAT

A test statistic of the combined test is

$$Q_{\rho} = (1 - \rho)Q_S + \rho Q_B,$$

where Q_S is a test statistic of SKAT, and Q_B is a score test statistic of the burden test. The ρ value can be specified by using the r.corr parameter (default: r.corr=0).

```
> #rho=0, SKAT
> SKAT(Z, obj, r.corr=0)$p.value
[1] 0.1401991
> #rho=0.9
> SKAT(Z, obj, r.corr=0.9)$p.value
[1] 0.06031026
```

```
> #rho=1, Burden test
> SKAT(Z, obj, r.corr=1)$p.value
[1] 0.06095529
```

If method="optimal.adj" or "SKATO" (both are equivalent), SKAT-O method will be performed, which computes p-values with eight different values of $\rho = (0, 0.1^2, 0.2^2, 0.3^2, 0.4^2, 0.5^2, 0.5, 1)$ and then uses the minimum p-value as a test statistic. If you want to use the original implementation of SKAT-O, use method="optimal", which uses eleven equally spaced ρ values from 0 to 1 as a grid of ρ s. We recommend to use "SKATO" or "optimal.adj", since it has a better type I error control.

```
> #Optimal Test
> SKAT(Z, obj, method="SKATO")$p.value
[1] 0.1008976
>
```

2.3 Combined test of common and rare variants

It is possible that both common and rare variants are associated with phenotypes. To test for combined effects of common and rare variants, SKAT_CommonRare function can be used. The detailed description of the combined test can be found in the following reference:

Ionita-Laza, I., Lee, S., Makarov, V., Buxbaum, J. Lin, X. (2013). Sequence kernel association tests for the combined effect of rare and common variants. *AJHG*, 92(6):841-53.

```
> # Combined sum test (SKAT-C and Burden-C)
>
> SKAT_CommonRare(Z, obj)$p.value

[1] 0.2238025
> SKAT_CommonRare(Z, obj, r.corr.rare=1, r.corr.common=1)$p.value

[1] 0.1546374
> # Adaptive test (SKAT-A and Burden-A)
>
> SKAT_CommonRare(Z, obj, method="A")$p.value

[1] 0.4372293
> SKAT_CommonRare(Z, obj, r.corr.rare=1, r.corr.common=1, method="A")$p.value

[1] 0.1548059
```

2.4 Impute missing genotypes.

If there are missing genotypes, SKAT automatically imputes them based on Hardy-Weinberg equilibrium. You can choose from "bestguess", "fixed" or "random". The "bestguess" imputes missing genotypes as most likely values (0,1,2), the "fixed" imputes missing genotypes by assigning the mean genotype value (2p, p) is the MAF) and the "random" imputes missing genotypes by generating binomial (2,p) random variables. The default imputation method for the SKAT function is "fixed" and for the SKATBinary function is "bestguess".

```
> # Assign missing
> Z1<-Z
> Z1[1,1:3]<-NA
> # bestguess imputation
> SKAT(Z1,obj,impute.method = "bestguess")$p.value
[1] 0.1401991
> # fixed imputation
> SKAT(Z1,obj,impute.method = "fixed")$p.value
[1] 0.1401982
> # random imputation
> SKAT(Z1,obj,impute.method = "random")$p.value
[1] 0.1401991
>
```

2.5 Resampling

SKAT package provides functions to carry out resampling method to compute empirical p-values and to control for family wise error rate. Two different resampling methods are implemented. "bootstrap" conducts a parametric bootstrap to resample residuals from H_0 with adjusting for covariates. When there is no covariate, "bootstrap" is equivalent to the permutation. "perturbation" perturbs the residuals by multiplying standard normal random variables. The default method is "bootstrap". From ver 0.7, we do not provide the "perturbation" method.

```
> Get_Resampling_Pvalue(re) # get resampling p-value
$p.value
[1] 0.1463707

$is_smaller
[1] FALSE
> detach(SKAT.example)
```

When there are many genes/SNP sets to test, resampling methods can be used to control family-wise error rate. Examples are provided in the next section.

2.6 Adjust for kinship

If related individuals exist in your data, you need to adjust for kinship. SKAT_NULL_emmaX function uses linear mixed model (EMMAX) to estimate the variance component, which will be subsequently used to adjust for kinship. For the kinship adjustment, SKAT_NULL_emmaX function should be used instead of SKAT_Null_Model.

```
> data(SKAT.fam.example)
> attach(SKAT.fam.example)
> # K: kinship matrix
> obj<-SKAT_NULL_emmaX(y ~ X, K=K)
> SKAT(Z, obj)$p.value

[1] 0.2123192
> # SKAT-0
> SKAT(Z, obj, method="SKATO")$p.value

[1] 0.352943
> detach(SKAT.fam.example)
```

2.7 X chromosome test

Since male has only one copy of X-chromosome, special care is needed to test for associations in X-chromosome. We have developed a method to test for X-chromosome in region based rare variant test with and without X-inactivation. To use it, you need to use SKAT_Null_Model_ChrX to fit the null model and SKAT_ChrX for association tests. Detailed description of association tests in X-chromosome can be found in the following reference:

Ma, C., Boehnke, M., Lee, S., the GoT2D Investigators (2015) Evaluating the Calibration and Power of Three Gene-based Association Tests of Rare Variants for the X Chromosome, *Genetic Epidemiology*, 39 (7): 499-508.

For Y chromosome, you can use the same null model function for X with Model.Y=TRUE. The p-value can be calculated with SKAT_ChrY function. The following example use the same genotype matrix previously used to show how these functions can be used.

3 Plink Binary format files

>

For the genome-wide data analysis, plink binary format files can be used in SKAT. To use plink files, plink bed, bim and fam files, and your own setid file that contains information of SNP sets are needed. Example files can be found on the SKAT/MetaSKAT google group page.

```
> # Create the MW File
> File.Bed<-"./Example1.bed"
> File.Bim<-"./Example1.bim"</pre>
> File.Fam<-"./Example1.fam"</pre>
> File.SetID<-"./Example1.SetID"
> File.SSD<-"./Example1.SSD"
> File.Info<-"./Example1.SSD.info"
> # To use binary ped files, you have to generate SSD file first.
> # If you already have a SSD file, you do not need to call this function.
> Generate_SSD_SetID(File.Bed, File.Bim, File.Fam, File.SetID, File.SSD, File.Info)
Check duplicated SNPs in each SNP set
No duplicate
1000 Samples, 10 Sets, 984 Total SNPs
[1] "SSD and Info files are created!"
  Now you can open SSD and Info file and run SKAT.
> FAM<-Read_Plink_FAM(File.Fam, Is.binary=FALSE)
> y<-FAM$Phenotype
> # To use a SSD file, please open it first. After finishing using it, you must close it.
> SSD.INFO<-Open_SSD(File.SSD, File.Info)
1000 Samples, 10 Sets, 984 Total SNPs
Open the SSD file
> # Number of samples
> SSD.INFO$nSample
[1] 1000
> # Number of Sets
> SSD.INFO$nSets
[1] 10
> obj<-SKAT_Null_Model(y ~ 1, out_type="C")</pre>
> out<-SKAT.SSD.All(SSD.INFO, obj)
> out
$results
     SetID
              P.value N.Marker.All N.Marker.Test
1 GENE_01 0.77747880
                                94
                                               94
2 GENE_02 0.06245208
                                84
                                               84
```

108

108

3 GENE_03 0.38416582

4	GENE_04	0.46179268	101	101
5	GENE_05	0.18548863	103	103
6	GENE_06	0.93255760	94	94
7	GENE_07	0.18897220	104	104
8	GENE_08	0.73081683	96	96
9	GENE_09	0.67366458	100	100
10	GENE_10	0.40310682	100	100

\$P.value.Resampling
NULL

\$OUT.snp.mac

\$OUT.snp.mac\$GENE_01

SNP0056	SNP0083	SNP0035	SNP0027	SNP0037	SNP0011	SNP0071	SNP0033	SNP0025	SNP0088
217	219	188	214	192	183	193	186	195	214
SNP0014	SNP0036	SNP0074	SNP0017	SNP0016	SNP0022	SNP0087	SNP0094	SNP0057	SNP0028
180	197	200	199	191	204	217	221	199	202
SNP0058	SNP0054	SNP0031	SNP0046	SNP0062	SNP0082	SNP0012	SNP0093	SNP0050	SNP0068
226	210	202	180	204	221	214	204	189	190
SNP0021	SNP0085	SNP0089	SNP0001	SNP0052	SNP0066	SNP0090	SNP0092	SNP0061	SNP0029
190	226	199	226	203	186	179	193	172	212
SNP0042	SNP0026	SNP0002	SNP0013	SNP0043	SNP0044	SNP0080	SNP0059	SNP0048	SNP0077
191	219	206	191	205	192	211	200	199	200
SNP0049	SNP0039	SNP0067	SNP0076	SNP0003	SNP0018	SNP0040	SNP0079	SNP0009	SNP0024
200	217	198	230	193	180	199	209	186	179
SNP0070	SNP0084	SNP0055	SNP0007	SNP0015	SNP0064	SNP0065	SNP0075	SNP0086	SNP0023
197	210	218	209	190	191	187	211	183	193
SNP0010	SNP0019	SNP0081	SNP0008	SNP0004	SNP0072	SNP0047	SNP0078	SNP0006	SNP0060
203	199	191	188	207	205	187	213	205	218
SNP0032	SNP0030	SNP0005	SNP0053	SNP0069	SNP0034	SNP0041	SNP0073	SNP0091	SNP0051
209	183	195	204	184	212	181	195	197	226
SNP0020	SNP0063	SNP0045	SNP0038						
217	191	228	206						

\$OUT.snp.mac\$GENE_02

SNP0167 SNP0165 SNP0172 SNP0124 SNP0115 SNP0112 SNP0174 SNP0121 SNP0103 SNP0116 SNP0141 SNP0133 SNP0134 SNP0149 SNP0099 SNP0161 SNP0095 SNP0169 SNP0164 SNP0097 SNP0143 SNP0148 SNP0114 SNP0173 SNP0160 SNP0136 SNP0108 SNP0109 SNP0105 SNP0118 SNP0150 SNP0153 SNP0126 SNP0162 SNP0119 SNP0111 SNP0129 SNP0142 SNP0145 SNP0132 SNP0177 SNP0163 SNP0107 SNP0100 SNP0154 SNP0178 SNP0146 SNP0101 SNP0144 SNP0171

							SNP0113		SNP0156
221	210	196	218	217	199	213	213	203	178
							SNP0157		SNP0138
196	197	210	208	180	202	196	191	189	200
SNP0106			SNP0168				SNP0102		SNP0159
203	208	209	211	199	191	190	194	188	197
		SNP0155	SNP0125						
166	200	239	203						
_									
_	o.mac\$GEN								
							SNP0256		
219	197	220	196	183	212	202	206	214	195
	SNP0225		SNP0270			SNP0204	SNP0264	SNP0233	SNP0279
186	207	221	198	183	211	214	196	200	189
SNP0238	SNP0250	SNP0267	SNP0226	SNP0275		SNP0280	SNP0286	SNP0207	SNP0206
205	213	231	234	185	205	199	216	213	197
SNP0222	SNP0272	SNP0245	SNP0232	SNP0241	SNP0265	SNP0230	SNP0249	SNP0269	SNP0284
202	207	206	187	220	181	195	171	207	194
SNP0262	SNP0244	SNP0283	SNP0240	SNP0218	SNP0235	SNP0237	SNP0247	SNP0242	SNP0197
192	200	188	194	212	198	190	203	185	195
SNP0210	SNP0255	SNP0278	SNP0219	SNP0276	SNP0190	SNP0277	SNP0200	SNP0179	SNP0229
193	176	211	177	203	187	199	199	195	170
SNP0183	SNP0180	SNP0194	SNP0189	SNP0212	SNP0228	SNP0202	SNP0215	SNP0261	SNP0274
186	197	212	193	200	200	220	188	179	209
SNP0223	SNP0282	SNP0239	SNP0271	SNP0227	SNP0246	SNP0285	SNP0198	SNP0217	SNP0213
214	202	193	183	193	202	217	214	188	201
SNP0184	SNP0187	SNP0193	SNP0253	SNP0251	SNP0185	SNP0201	SNP0182	SNP0258	SNP0281
170	200	183	216	196	212	186	210	202	190
SNP0234	SNP0216	SNP0211	SNP0191	SNP0192	SNP0260	SNP0221	SNP0257	SNP0181	SNP0252
184	190	208	217	207	219	199	216	193	213
SNP0243	SNP0208	SNP0259	SNP0268	SNP0203	SNP0248	SNP0231	SNP0263		
188	195	198	191	210	198	183	220		
\$OUT.snr	o.mac\$GEN	NE 04							
-			SNP0346	SNP0348	SNP0332	SNP0313	SNP0288	SNP0309	SNP0329
206	207	223	194		207	203	190	212	218
							SNP0343		
194	202	188	200	214		206	199	203	187
							SNP0380		
214	218	207	204	201	208	206	194	208	214
							SNP0357		
209	199	197	217	212	214	202	210	191	195
							SNP0383		
184	215	157	200	217		169	217	239	208
SNP0315	SNP0359	SNF0307	SNP03/1	SNP0310	SNP0366	SNF0386	SNP0379	SNF03/8	SNP03/2

100	01.0	104	010	100	177	101	100	105	005
190	216	194	219	199	177	191	192	195	205
		SNP0293							
191	211	192	211	205	201	203	211	193	197
		SNP0291							
213	190	188	200	212	208	198	198	211	187
		SNP0322							
216	191	196	222	196	209	207	211	190	201
SNP0294		SNP0361							SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
214									
_	p.mac\$GEl								
		SNP0404							
184	214	199	213	171	183	189	220	197	174
SNP0400	SNP0469	SNP0408						SNP0468	
183	197	220	197	216	202	177	216	207	211
		SNP0486						SNP0478	
182	178	198	215	182	182	210	206	199	205
SNP0442	SNP0456	SNP0447	SNP0421	SNP0444	SNP0405	SNP0414	SNP0413	SNP0475	SNP0477
222	213	212	202	205	185	212	201	225	218
SNP0450	SNP0423	SNP0452	SNP0426	SNP0403	SNP0490	SNP0402	SNP0437	SNP0445	SNP0465
207	205	177	211	213	195	193	240	194	188
SNP0430	SNP0393	SNP0481	SNP0484	SNP0439	SNP0454	SNP0389	SNP0390	SNP0459	SNP0487
183	199	174	188	208	196	208	203	187	196
SNP0470	SNP0399	SNP0428	SNP0427	SNP0472	SNP0455	SNP0397	SNP0391	SNP0453	SNP0398
188	197	203	199	195	193	216	192	197	201
SNP0417	SNP0479	SNP0446	SNP0388	SNP0407	SNP0412	SNP0431	SNP0415	SNP0441	SNP0461
202	199	198	199	207	189	201	180	206	177
SNP0418	SNP0420	SNP0438	SNP0482	SNP0396	SNP0406	SNP0483	SNP0432	SNP0451	SNP0425
190	222	197	205	169	177	202	196	201	207
SNP0436	SNP0443	SNP0464	SNP0471	SNP0433	SNP0434	SNP0485	SNP0463	SNP0489	SNP0457
181	193	208	215	201	219	196	195	211	181
SNP0440	SNP0448	SNP0411							
214	201	204							
\$OUT.snj	o.mac\$GE1	NE_06							
SNP0543	SNP0534	SNP0517	SNP0518	SNP0525	SNP0568	SNP0550	SNP0554	SNP0523	SNP0542
219	186	216	197	197	200	192	215	190	199
SNP0520	SNP0503	SNP0493	SNP0533	SNP0569	SNP0504	SNP0576	SNP0580	SNP0527	SNP0577
200	198	171	200	179	223	218	215	209	203
SNP0541	SNP0522	SNP0582	SNP0571	SNP0501	SNP0524	SNP0574	SNP0573	SNP0544	SNP0532
201	206	188	191	200	185	192	206	196	225
SNP0519	SNP0521	SNP0512	SNP0564	SNP0498	SNP0579	SNP0558	SNP0531	SNP0549	SNP0494
195	177	199	215	205	209	188	206	172	187

SNP0572	SNP0537	SNP0526	SNP0507	SNP0555	SNP0500	SNP0560	SNP0491	SNP0566	SNP0551
199	205	178	202	173	227	218	221	223	184
SNP0547	SNP0552	SNP0508				SNP0539		SNP0584	SNP0546
200	202	193	194	177	196	209	198	180	189
SNP0553	SNP0562	SNP0510	SNP0499	SNP0502	SNP0505	SNP0514	SNP0513	SNP0578	SNP0570
213	179	197	191	209	187	195	225	219	221
SNP0581	SNP0496	SNP0548	SNP0575	SNP0540	SNP0545	SNP0530	SNP0538	SNP0559	SNP0497
213	209	193	205	193	173	183	189	208	202
SNP0557	SNP0563	SNP0511	SNP0495	SNP0583	SNP0536	SNP0516	SNP0528	SNP0509	SNP0561
201	189	199	214	201	218	200	192	221	213
SNP0492	SNP0567	SNP0506	SNP0556						
202	211	183	185						
_	p.mac\$GE1								
SNP0609	SNP0649	SNP0667	SNP0685	SNP0661	SNP0597	SNP0598	SNP0623	SNP0636	SNP0603
187	185	219	201	191	212	211	207	229	205
SNP0659	SNP0657	SNP0684	SNP0616	SNP0630	SNP0629	SNP0612	SNP0677	SNP0652	SNP0672
211	211	182	192	186	193	207	200	208	222
SNP0621	SNP0670	SNP0643	SNP0619	SNP0644	SNP0686	SNP0618	SNP0655	SNP0656	SNP0653
216	215	214	187	216	224	188	197	191	203
SNP0683	SNP0663							SNP0617	SNP0634
229	203	218	201	147	202	195	211	209	208
SNP0673	SNP0660	SNP0607	SNP0678	SNP0681	SNP0606	SNP0589	SNP0591	SNP0641	SNP0613
188	193	193	216	176	209	199	198	205	194
SNP0586	SNP0687				SNP0666		SNP0671	SNP0648	SNP0608
205	202	192	206	181	190	204	180	193	201
SNP0664	SNP0626	SNP0651	SNP0602		SNP0674	SNP0642	SNP0628	SNP0662	SNP0668
193	198	198	194	205	211	201	206	194	181
	SNP0588								
213	194	213	228	190	196	186	215	213	180
	SNP0631								SNP0595
199	192	187	209	205	225	196	214	196	199
	SNP0638								SNP0646
192		217		205	202	207	210	210	190
	SNP0614								
185	211	195	179						
\$OUT sn	p.mac\$GEl	VF. 08							
_	SNP0720		SNP0733	SNP0779	SNP0732	SNP0778	SNP0703	SNP0756	SNP0705
194	195	200	196	214	209	201	200	190	194
	SNP0734								
233	205	219	191	189	201	186	198	231	184
	SNP0755								
189	179	175	199	206	193	197	189	191	212
	SNP0697								
2 0110	21.1 0001	2 0000	2 0.00	2 0.00	2 0000	~ 0 , 11	2 0.01	21.1 01 10	2111 01 20

198	207	205	185	211	191	189	206	221	182	
SNP0781	SNP0710	SNP0722	SNP0742	SNP0753	SNP0689	SNP0735	SNP0730	SNP0731	SNP0768	
201	202	188	200	200	199	192	234	213	200	
SNP0762	SNP0784	SNP0706	SNP0744	SNP0757	SNP0776	SNP0760	SNP0724	SNP0751	SNP0691	
195	208	181	188	207	198	196	197	193	178	
SNP0752	SNP0750	SNP0721	SNP0704	SNP0701	SNP0713	SNP0780	SNP0743	SNP0770	SNP0718	
188	185	188	213	199	195	212	182	212	221	
SNP0782	SNP0774	SNP0737	SNP0745	SNP0769	SNP0723	SNP0693	SNP0716	SNP0758	SNP0694	
175	233	218	191	225	216	201	214	181	195	
SNP0764	SNP0767	SNP0719	SNP0739	SNP0754	SNP0783	SNP0700	SNP0759	SNP0717	SNP0728	
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SNP0841	SNP0796	SNP0880	SNP0854	SNP0821	SNP0797	SNP0882	SNP0843	SNP0828	SNP0789	
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SNP0856	SNP0884	SNP0812	SNP0799	SNP0825	SNP0850	SNP0805	SNP0877	SNP0804	SNP0864	
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SNP0842	SNP0871	SNP0790	SNP0806	SNP0863	SNP0793	SNP0846	SNP0849	SNP0873	SNP0823	
202	179	212	175	207	215	186	198	199	191	
SNP0792	SNP0831	SNP0866	SNP0858	SNP0847	SNP0860	SNP0791	SNP0824	SNP0787	SNP0819	
192	210	215	217	208	193	187	202	190	197	
SNP0839	SNP0813	SNP0803	SNP0874	SNP0876	SNP0851	SNP0794	SNP0814	SNP0827	SNP0788	
211	201	194	224	216	204	194	212	181	205	
SNP0837	SNP0832	SNP0879	SNP0817	SNP0852	SNP0815	SNP0802	SNP0857	SNP0875	SNP0818	
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SNP0809	SNP0835	SNP0800	SNP0878	SNP0801	SNP0786	SNP0870	SNP0868	SNP0844	SNP0855	
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SNP0848	SNP0798	SNP0869	SNP0822	SNP0872	SNP0867	SNP0808	SNP0861	SNP0838	SNP0883	
175	195	196	188	230	212	191	201	196	183	
SNP0826	SNP0836	SNP0785	SNP0834	SNP0820	SNP0833	SNP0865	SNP0840	SNP0862	SNP0810	
193	207	203	209	213	226	193	194	220	201	
\$OUT.snj	o.mac\$GE	NE_10								
SNP088	5 SNP090	08 SNP09	957 SNP	937 SNF	90886 SI	NP0940 S	SNP0922	SNP0980		
199.392	7 191.532	23 206.06	606 224.3	3461 190	.0407 209	5.8527 20	07.4522	187.6892		

 SNP0910
 SNP0938
 SNP0975
 SNP0965
 SNP0889
 SNP0929
 SNP0953
 SNP0921

 176.5893
 205.2578
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 SNP0916
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 181.4516
 180.4435
 200.4028
 186.6126
 196.5552

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189.0799 207.7393 192.1132 179.9798 202.2245 195.9596 184.2105 198.5816
 SNP0935 SNP0899 SNP0926 SNP0943 SNP0976
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                                                             SNP0978
184.4758 205.0761 190.3323 194.5838 218.1448 204.6606 203.2520 202.4291
 SNP0917 SNP0901 SNP0907 SNP0909 SNP0948
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178.6075 228.6002 192.3464 194.7262 204.6371 183.7563 201.6211 201.4099
 SNP0894 SNP0936 SNP0920 SNP0984
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                                                             SNP0912
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 SNP0952 SNP0924 SNP0919 SNP0925
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200.8155 229.5248 187.3112 208.4592 183.5700 212.4874 171.3710 191.1021
 SNP0972 SNP0905 SNP0979 SNP0982
                                            SNP0942 SNP0973
                                   SNP0932
                                                             SNP0892
185.2971 212.5506 200.4028 184.6620 198.9848 200.2022 195.5420 195.9799
 SNP0898 SNP0966 SNP0911 SNP0970
                                   SNP0918 SNP0967
                                                     SNP0951
200.2012 213.7097 201.0050 218.5297 198.1800 184.4758 201.0101 207.8708
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                                   SNP0887
                                            SNP0927 SNP0896 SNP0945
210.8981 177.8894 191.7255 170.7071 206.8618 223.9108 207.8708 205.8527
 SNP0888 SNP0900 SNP0893 SNP0983
208.4592 188.8889 224.9240 202.2245
```

```
attr(,"class")
[1] "SKAT_SSD_ALL"
```

> out

> File.Cov<-"./Example1.Cov"

If you have a plink covariate file, Read_Plink_FAM_Cov function can be used to read both FAM and covariate files.

```
> FAM_Cov<-Read_Plink_FAM_Cov(File.Fam, File.Cov, Is.binary=FALSE)
> # First 5 rows
> FAM_Cov[1:5,]
     FID IID PID MID Sex Phenotype
                                            X1 X2
1 FID454
                       1 0.679793 1.0297614 1
               0
                   0
2 FID977
               0
                       1 0.836566 0.1846235
3 FID462
                   0
                       1 -0.408388 -0.6141158 1
4 FID958
           1
               0
                   0
                       1 -0.522305 -2.0226759 0
5 FID668
                       1 -0.328300 -0.8213776 0
               0
> # Run with covariates
> X1 = FAM_Cov$X1
> X2 = FAM_Cov$X2
> y<-FAM_Cov$Phenotype
> obj<-SKAT_Null_Model(y ~ X1 + X2, out_type="C")</pre>
> out <- SKAT. SSD. All (SSD. INFO, obj)
```

\$results

	${\tt SetID}$	P.value	N.Marker.All	${\tt N.Marker.Test}$
1	GENE_01	0.77771227	94	94
2	GENE_02	0.06157071	84	84
3	GENE_03	0.39818504	108	108
4	GENE_04	0.46548442	101	101
5	GENE_05	0.18981516	103	103
6	GENE_06	0.94073952	94	94
7	GENE_07	0.18779019	104	104
8	GENE_08	0.74559501	96	96
9	GENE_09	0.66573796	100	100
10	GENE_10	0.40204308	100	100

\$P.value.Resampling
NULL

\$OUT.snp.mac

\$OUT.snp.mac\$GENE_01

SNP0056 SNP0083 SNP0035 SNP0027 SNP0037 SNP0011 SNP0071 SNP0033 SNP0025 SNP0088 SNP0014 SNP0036 SNP0074 SNP0017 SNP0016 SNP0022 SNP0087 SNP0094 SNP0057 SNP0028 SNP0058 SNP0054 SNP0031 SNP0046 SNP0062 SNP0082 SNP0012 SNP0093 SNP0050 SNP0068 SNP0021 SNP0085 SNP0089 SNP0001 SNP0052 SNP0066 SNP0090 SNP0092 SNP0061 SNP0029 SNP0042 SNP0026 SNP0002 SNP0013 SNP0043 SNP0044 SNP0080 SNP0059 SNP0048 SNP0077 SNP0049 SNP0039 SNP0067 SNP0076 SNP0003 SNP0018 SNP0040 SNP0079 SNP0009 SNP0024 SNP0070 SNP0084 SNP0055 SNP0007 SNP0015 SNP0064 SNP0065 SNP0075 SNP0086 SNP0023 SNP0010 SNP0019 SNP0081 SNP0008 SNP0004 SNP0072 SNP0047 SNP0078 SNP0006 SNP0060 SNP0032 SNP0030 SNP0005 SNP0053 SNP0069 SNP0034 SNP0041 SNP0073 SNP0091 SNP0051 SNP0020 SNP0063 SNP0045 SNP0038

\$OUT.snp.mac\$GENE_02

SNP0167 SNP0165 SNP0172 SNP0124 SNP0115 SNP0112 SNP0174 SNP0121 SNP0103 SNP0116 SNP0141 SNP0133 SNP0134 SNP0149 SNP0099 SNP0161 SNP0095 SNP0169 SNP0164 SNP0097 SNP0143 SNP0148 SNP0114 SNP0173 SNP0160 SNP0136 SNP0108 SNP0109 SNP0105 SNP0118

194	208	225	208	206	209	206	208	182	193
		SNP0126							
201	183	169	219	200	218	186	200	216	198
		SNP0107							
207	215	206	209	212	187	199	213	193	229
SNP0140		SNP0098						SNP0096	SNP0156
221	210	196	218	217	199	213	213	203	178
SNP0166	SNP0120	SNP0117	SNP0151	SNP0127	SNP0104	SNP0152	SNP0157	SNP0175	SNP0138
196	197	210	208	180	202	196	191	189	200
SNP0106	SNP0130	SNP0176	SNP0168	SNP0135	SNP0158	SNP0170	SNP0102	SNP0128	SNP0159
203	208	209	211	199	191	190	194	188	197
SNP0122	SNP0123	SNP0155	SNP0125						
166	200	239	203						
	o.mac\$GE1								
SNP0254	SNP0273	SNP0199					SNP0256	SNP0236	SNP0214
219	197	220	196	183	212	202	206	214	195
SNP0196	SNP0225	SNP0224						SNP0233	SNP0279
186	207	221	198	183	211	214	196	200	189
		SNP0267							
205	213	231	234	185	205	199	216	213	197
		SNP0245							
202	207	206	187	220	181	195	171	207	194
		SNP0283							
192	200	188	194	212	198	190	203	185	195
		SNP0278							
193	176	211	177	203	187	199	199	195	170
		SNP0194							
186	197	212	193	200	200	220	188	179	209
		SNP0239							
214	202	193	183	193	202	217	214	188	201
		SNP0193							
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									SNP0252
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		SNP0259							
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-		SNP0387	SNP0346	SNP0348	SNP0332	SNP0313	SNP0288	SNP0309	SNP0329
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SNP0377		SNP0320							
194	202			214	188			203	187
SNP0356	SNP0340	SNP0370	SNP0327		SNP0335	SNP0314	SNP0380	SNP0336	SNP0333
214	218	207	204	201	208	206	194	208	214

SNP0306	SNP0334	SNP0330	SNP0373	SNP0297	SNP0305	SNP0341	SNP0357	SNP0317	SNP0302
209	199	197	217	212	214	202	210	191	195
SNP0299	SNP0367	SNP0350	SNP0354	SNP0324	SNP0352	SNP0382	SNP0383	SNP0301	SNP0295
184	215	157	200	217	209	169	217	239	208
SNP0315	SNP0359	SNP0307	SNP0371	SNP0310	SNP0366	SNP0386	SNP0379	SNP0378	SNP0372
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SNP0321	SNP0385	SNP0293	SNP0376	SNP0363	SNP0308	SNP0318	SNP0323	SNP0287	SNP0381
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SNP0364	SNP0328	SNP0291	SNP0349	SNP0289	SNP0337	SNP0353	SNP0345	SNP0375	SNP0311
213	190	188	200	212	208	198	198	211	187
SNP0326	SNP0358	SNP0322	SNP0292	SNP0298	SNP0369	SNP0360	SNP0355	SNP0338	SNP0384
216	191	196	222	196	209	207	211	190	201
SNP0294	SNP0296	SNP0361	SNP0325	SNP0312	SNP0374	SNP0331	SNP0342	SNP0368	SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
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SNP0400	SNP0469	SNP0408	SNP0473	SNP0424	SNP0401	SNP0392	SNP0422	SNP0468	SNP0395
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SNP0476	SNP0488	SNP0486	SNP0435	SNP0458	SNP0467	SNP0449	SNP0480	SNP0478	SNP0394
182	178	198	215	182	182	210	206	199	205
SNP0442	SNP0456	SNP0447	SNP0421	SNP0444	SNP0405	SNP0414	SNP0413	SNP0475	SNP0477
222	213	212	202	205	185	212	201	225	218
SNP0450	SNP0423	SNP0452	SNP0426	SNP0403	SNP0490	SNP0402	SNP0437	SNP0445	SNP0465
207	205	177	211	213	195	193	240	194	188
SNP0430	SNP0393	SNP0481	SNP0484	SNP0439	SNP0454	SNP0389	SNP0390	SNP0459	SNP0487
183	199	174	188	208	196	208	203	187	196
SNP0470	SNP0399	SNP0428	SNP0427	SNP0472	SNP0455	SNP0397	SNP0391	SNP0453	SNP0398
188	197	203	199	195	193	216	192	197	201
SNP0417	SNP0479	SNP0446	SNP0388	SNP0407	SNP0412	SNP0431	SNP0415	SNP0441	SNP0461
202	199	198	199	207	189	201	180	206	177
SNP0418	SNP0420	SNP0438			SNP0406	SNP0483			SNP0425
190	222	197		169	177	202	196	201	207
SNP0436	SNP0443	SNP0464	SNP0471	SNP0433	SNP0434	SNP0485	SNP0463	SNP0489	SNP0457
181	193	208	215	201	219	196	195	211	181
SNP0440	SNP0448	SNP0411							
214	201	204							
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SNP0520	SNP0503	SNP0493	SNP0533	SNP0569	SNP0504	SNP0576	SNP0580	SNP0527	SNP0577

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SNP0541	SNP0522	SNP0582	SNP0571	SNP0501	SNP0524	SNP0574	SNP0573	SNP0544	SNP0532
201	206	188	191	200	185	192	206	196	225
SNP0519	SNP0521	SNP0512	SNP0564	SNP0498	SNP0579	SNP0558	SNP0531	SNP0549	SNP0494
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SNP0572	SNP0537	SNP0526	SNP0507	SNP0555	SNP0500	SNP0560	SNP0491	SNP0566	SNP0551
199	205	178	202	173	227	218	221	223	184
SNP0547	SNP0552	SNP0508	SNP0535	SNP0515	SNP0529	SNP0539	SNP0565	SNP0584	SNP0546
200	202	193	194	177	196	209	198	180	189
SNP0553	SNP0562	SNP0510	SNP0499	SNP0502	SNP0505	SNP0514	SNP0513	SNP0578	SNP0570
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SNP0581	SNP0496	SNP0548	SNP0575	SNP0540	SNP0545	SNP0530	SNP0538	SNP0559	SNP0497
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SNP0557	SNP0563	SNP0511	SNP0495	SNP0583	SNP0536	SNP0516	SNP0528	SNP0509	SNP0561
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SNP0492	SNP0567	SNP0506	SNP0556						
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SNP0659	SNP0657	SNP0684	SNP0616				SNP0677	SNP0652	SNP0672
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SNP0621	SNP0670	SNP0643	SNP0619	SNP0644	SNP0686	SNP0618	SNP0655	SNP0656	SNP0653
216	215	214	187	216	224	188	197	191	203
SNP0683	SNP0663	SNP0640	SNP0592	SNP0679	SNP0658	SNP0611	SNP0676	SNP0617	SNP0634
229	203	218	201	147	202	195	211	209	208
SNP0673	SNP0660	SNP0607	SNP0678	SNP0681		SNP0589	SNP0591	SNP0641	SNP0613
188	193	193	216	176	209	199	198	205	194
SNP0586	SNP0687	SNP0669	SNP0594	SNP0604	SNP0666		SNP0671	SNP0648	SNP0608
205	202	192	206	181	190	204	180	193	201
SNP0664	SNP0626	SNP0651	SNP0602	SNP0615	SNP0674	SNP0642	SNP0628	SNP0662	SNP0668
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SNP0627			SNP0625						SNP0645
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			SNP0620						SNP0595
199	192	187			225	196			199
			SNP0637						
192	167	217		205	202	207	210	210	190
		SNP0605							
185	211	195	179						
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			SNP0733						
194	195	200	196	214	209	201	200	190	194

SNP0727	SNP0734	SNP0765	SNP0772	SNP0699	SNP0775	SNP0741	SNP0763	SNP0749	SNP0715	
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SNP0725	SNP0755	SNP0707	SNP0747	SNP0702	SNP0748	SNP0714	SNP0777	SNP0771	SNP0726	
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SNP0762	SNP0784	SNP0706	SNP0744	SNP0757	SNP0776	SNP0760	SNP0724	SNP0751	SNP0691	
195	208	181	188	207	198	196	197	193	178	
SNP0752	SNP0750	SNP0721	SNP0704	SNP0701	SNP0713	SNP0780	SNP0743	SNP0770	SNP0718	
188	185	188	213	199	195	212	182	212	221	
SNP0782	SNP0774	SNP0737	SNP0745	SNP0769	SNP0723	SNP0693	SNP0716	SNP0758	SNP0694	
175	233	218	191	225	216	201	214	181	195	
SNP0764	SNP0767	SNP0719	SNP0739	SNP0754	SNP0783	SNP0700	SNP0759	SNP0717	SNP0728	
217	194	201	193	201	225	197	194	181	191	
SNP0736	SNP0690	SNP0712	SNP0692	SNP0698	SNP0709					
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SNP0841	SNP0796	SNP0880	SNP0854	SNP0821	SNP0797	SNP0882	SNP0843	SNP0828	SNP0789	
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SNP0856	SNP0884	SNP0812	SNP0799	SNP0825	SNP0850	SNP0805	SNP0877	SNP0804	SNP0864	
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SNP0842	SNP0871	SNP0790	SNP0806	SNP0863	SNP0793	SNP0846	SNP0849	SNP0873	SNP0823	
202	179	212	175	207	215	186	198	199	191	
SNP0792	SNP0831	SNP0866	SNP0858	SNP0847	SNP0860	SNP0791	SNP0824	SNP0787	SNP0819	
192	210	215	217	208	193	187	202	190	197	
SNP0839	SNP0813	SNP0803	SNP0874	SNP0876	SNP0851	SNP0794	SNP0814	SNP0827	SNP0788	
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SNP0809	SNP0835	SNP0800	SNP0878	SNP0801	SNP0786	SNP0870	SNP0868	SNP0844	SNP0855	
187	185	192	231	187	232	204	204	203	193	
SNP0848	SNP0798	SNP0869	SNP0822	SNP0872	SNP0867	SNP0808	SNP0861	SNP0838	SNP0883	
175	195	196	188	230	212	191	201	196	183	
SNP0826	SNP0836	SNP0785	SNP0834	SNP0820	SNP0833	SNP0865	SNP0840	SNP0862	SNP0810	
193	207	203	209	213	226	193	194	220	201	
\$OUT.snj	p.mac\$GEl	NE_10								

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                                                      SNP0958
189.0799 207.7393 192.1132 179.9798 202.2245 195.9596 184.2105 198.5816
 SNP0935 SNP0899
                 SNP0926 SNP0943
                                   SNP0976
                                             SNP0955
                                                     SNP0946
                                                               SNP0978
184.4758 205.0761 190.3323 194.5838 218.1448 204.6606 203.2520 202.4291
 SNP0917 SNP0901 SNP0907 SNP0909
                                    SNP0948
                                             SNP0939
                                                      SNP0906
                                                               SNP0977
178.6075 228.6002 192.3464 194.7262 204.6371 183.7563 201.6211 201.4099
 SNP0894 SNP0936
                  SNP0920 SNP0984
                                    SNP0981
                                             SNP0931
                                                      SNP0928
                                                               SNP0912
210.1010 203.6290 212.1212 227.4549 198.5816 185.4103 196.3746 226.3959
 SNP0952 SNP0924 SNP0919 SNP0925
                                    SNP0930
                                             SNP0941
                                                      SNP0974
                                                               SNP0903
200.8155 229.5248 187.3112 208.4592 183.5700 212.4874 171.3710 191.1021
 SNP0972 SNP0905 SNP0979 SNP0982
                                    SNP0932
                                             SNP0942
                                                     SNP0973
                                                               SNP0892
185.2971 212.5506 200.4028 184.6620 198.9848 200.2022 195.5420 195.9799
 SNP0898 SNP0966 SNP0911 SNP0970
                                    SNP0918
                                             SNP0967
                                                      SNP0951
                                                               SNP0964
200.2012 213.7097 201.0050 218.5297 198.1800 184.4758 201.0101 207.8708
 SNP0947 SNP0944 SNP0891 SNP0961
                                    SNP0887
                                             SNP0927
                                                      SNP0896
210.8981 177.8894 191.7255 170.7071 206.8618 223.9108 207.8708 205.8527
 SNP0888 SNP0900 SNP0893 SNP0983
208.4592 188.8889 224.9240 202.2245
```

```
attr(,"class")
[1] "SKAT_SSD_ALL"
```

To use custom weight, you need to make a weight file and read it using "Read_SNP_WeightFile" function. The weight file should have two columns, SNP ID and weight values. The output object of "Read_SNP_WeightFile" can be used as a parameter in SKAT.SSD functions

```
> # Custom weight
```

- > # File: Example1_Weight.txt
- > obj.SNPWeight<-Read_SNP_WeightFile("./Example1_Weight.txt")
- > out<-SKAT.SSD.All(SSD.INFO, obj, obj.SNPWeight=obj.SNPWeight)
- > out

\$results

	${\tt SetID}$	P.value	N.Marker.All	${\tt N.Marker.Test}$
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2	GENE_02	0.03286684	84	84
3	GENE_03	0.25752493	108	108
4	GENE_04	0.18486050	101	101
5	GENE 05	0.43670123	103	103

6	GENE_06	0.98039703	94	94
7	GENE_07	0.12460640	104	104
8	GENE_08	0.78814493	96	96
9	GENE_09	0.80206141	100	100
10	GENE 10	0.34070404	100	100

\$P.value.Resampling NULL

\$OUT.snp.mac

\$OUT.snp.mac\$GENE_01

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SNP0014	SNP0036	SNP0074	SNP0017	SNP0016	SNP0022	SNP0087	SNP0094	SNP0057	SNP0028
180	197	200	199	191	204	217	221	199	202
SNP0058	SNP0054	SNP0031	SNP0046	SNP0062	SNP0082	SNP0012	SNP0093	SNP0050	SNP0068
226	210	202	180	204	221	214	204	189	190
SNP0021	SNP0085	SNP0089	SNP0001	SNP0052	SNP0066	SNP0090	SNP0092	SNP0061	SNP0029
190	226	199	226	203	186	179	193	172	212
SNP0042	SNP0026	SNP0002	SNP0013	SNP0043	SNP0044	SNP0080	SNP0059	SNP0048	SNP0077
191	219	206	191	205	192	211	200	199	200
SNP0049	SNP0039	SNP0067	SNP0076	SNP0003	SNP0018	SNP0040	SNP0079	SNP0009	SNP0024
200	217	198	230	193	180	199	209	186	179
SNP0070	SNP0084	SNP0055	SNP0007	SNP0015	SNP0064	SNP0065	SNP0075	SNP0086	SNP0023
197	210	218	209	190	191	187	211	183	193
SNP0010	SNP0019	SNP0081	SNP0008	SNP0004	SNP0072	SNP0047	SNP0078	SNP0006	SNP0060
203	199	191	188	207	205	187	213	205	218
SNP0032	SNP0030	SNP0005	SNP0053	SNP0069	SNP0034	SNP0041	SNP0073	SNP0091	SNP0051
209	183	195	204	184	212	181	195	197	226
SNP0020	SNP0063	SNP0045	SNP0038						
217	191	228	206						

\$OUT.snp.mac\$GENE_02

SNP0167 SNP0165 SNP0172 SNP0124 SNP0115 SNP0112 SNP0174 SNP0121 SNP0103 SNP0116 SNP0141 SNP0133 SNP0134 SNP0149 SNP0099 SNP0161 SNP0095 SNP0169 SNP0164 SNP0097 SNP0143 SNP0148 SNP0114 SNP0173 SNP0160 SNP0136 SNP0108 SNP0109 SNP0105 SNP0118 SNP0150 SNP0153 SNP0126 SNP0162 SNP0119 SNP0111 SNP0129 SNP0142 SNP0145 SNP0132 SNP0177 SNP0163 SNP0107 SNP0100 SNP0154 SNP0178 SNP0146 SNP0101 SNP0144 SNP0171 SNP0140 SNP0139 SNP0098 SNP0110 SNP0147 SNP0131 SNP0137 SNP0113 SNP0096 SNP0156

Mathematical Name	SNP0166	SNP0120	SNP0117	SNP0151	SNP0127	SNP0104	SNP0152	SNP0157	SNP0175	SNP0138
Name	196	197	210	208	180	202	196	191	189	200
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191 197	\$OUT.snp	o.mac\$GEN	NE_03							
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Name	219	197	220	196	183	212	202	206	214	195
SNP0238 SNP0250 SNP0267 SNP0226 SNP0275 SNP0280 SNP0280 SNP0280 SNP0206 SNP0206 SNP0206 SNP0207 SNP0208 SNP0228 SNP0229 SNP0228 SNP0229 SNP0228 SNP0229 SNP0228 SNP0229 SNP0228 SNP0229 SNP0228 SNP0238 SNP0	SNP0196	SNP0225	SNP0224	SNP0270	SNP0188	SNP0209	SNP0204	SNP0264	SNP0233	SNP0279
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202 207 206 187 220 181 195 171 207 194 SNP0262 SNP0244 SNP0238 SNP0240 SNP0218 SNP0235 SNP0237 SNP0247 SNP0242 SNP0197 192 200 188 194 212 198 190 203 185 195 SNP0210 SNP0255 SNP0278 SNP0219 SNP0169 SNP0190 SNP0277 SNP0278 SNP0290 SNP0271 SNP0283 SNP0200 SNP0199 195 170 SNP0138 SNP0190 SNP0189 SNP0212 SNP0228 SNP0202 SNP0215 SNP0261 SNP0215 SNP0261 SNP0271 SNP0228 SNP0202 SNP0215 SNP0215 SNP0216 SNP0217 SNP0218 SNP0221 SNP0228 SNP0218 SNP0218 <td>205</td> <td>213</td> <td>231</td> <td>234</td> <td>185</td> <td>205</td> <td>199</td> <td>216</td> <td>213</td> <td>197</td>	205	213	231	234	185	205	199	216	213	197
SNP0262 SNP0244 SNP0283 SNP0240 SNP0218 SNP0235 SNP0247 SNP0242 SNP019 192 200 188 194 212 198 190 203 185 195 SNP0210 SNP0255 SNP0278 SNP0219 SNP0190 SNP0177 SNP0200 SNP0179 SNP0229 193 176 211 177 203 187 199 199 195 170 SNP0183 SNP0180 SNP0194 SNP0189 SNP0212 SNP0222 SNP02025 SNP0215 SNP0274 180 200 200 220 188 179 209 SNP0223 SNP0217 SNP0218 SNP0228 SNP0218 SNP02	SNP0222	SNP0272	SNP0245	SNP0232	SNP0241	SNP0265	SNP0230	SNP0249	SNP0269	SNP0284
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186 197 212 193 200 200 220 188 179 209 SNP0223 SNP0282 SNP0239 SNP0271 SNP0227 SNP0246 SNP0285 SNP0198 SNP0217 SNP0213 214 202 193 183 193 202 217 214 188 201 SNP0184 SNP0187 SNP0185 SNP0201 SNP0182 SNP0201 SNP0258 SNP0281 170 200 183 216 196 212 186 210 202 190 SNP0234 SNP0216 SNP0111 SNP0191 SNP0192 SNP0260 SNP0221 SNP0257 SNP0181 SNP0252 184 190 208 217 207 219 199 216 193 213 SNP0243 SNP0208 SNP0268 SNP0203 SNP0231 SNP0263 SNP0263 SNP0231 SNP0263 SNP0263 SNP0231 SNP0263 SNP0263 SNP0233	193	176	211	177	203	187	199	199	195	170
SNP0223 SNP0282 SNP0299 SNP0271 SNP0227 SNP0246 SNP0285 SNP0198 SNP0217 SNP0213 214 202 193 183 193 202 217 214 188 201 SNP0184 SNP0187 SNP0183 SNP0251 SNP0185 SNP0201 SNP0182 SNP0281 SNP0282 SNP0281 SNP0282 SNP0282 SNP0282 SNP0282 SNP0283 SNP0262 SNP0263	SNP0183	SNP0180	SNP0194	SNP0189	SNP0212	SNP0228	SNP0202	SNP0215	SNP0261	SNP0274
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SNP0184 SNP0187 SNP0193 SNP0253 SNP0251 SNP0185 SNP0201 SNP0182 SNP0284 SNP0281 170 200 183 216 196 212 186 210 202 190 SNP0234 SNP0216 SNP0211 SNP0191 SNP0192 SNP0260 SNP0221 SNP0257 SNP0181 SNP0252 184 190 208 217 207 219 199 216 193 213 SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0231 SNP0263 SNP0263 193 213 SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0231 SNP0263 3 213 \$0017 \$198 191 210 198 183 220 3 193 213 \$0017 \$198 199 191 210 198 183 220 190 212 218 \$0017 \$199 190 20	SNP0223	SNP0282	SNP0239	SNP0271	SNP0227	SNP0246	SNP0285	SNP0198	SNP0217	SNP0213
170 200 183 216 196 212 186 210 202 190 SNP0234 SNP0216 SNP0211 SNP0191 SNP0192 SNP0260 SNP0221 SNP0257 SNP0181 SNP0252 184 190 208 217 207 219 199 216 193 213 SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0248 SNP0231 SNP0263 206 193 213 \$0UT.snp.mac\$GENE_04 SNP0348 SNP0348 SNP0332 SNP0313 SNP0288 SNP0309 SNP0329 \$NP0303 SNP0362 SNP0387 SNP0346 SNP0348 SNP0332 SNP0313 SNP0288 SNP0309 SNP0329 \$NP0303 SNP0362 SNP0387 SNP0346 SNP0348 SNP03342 SNP0313 SNP0348 SNP03039 SNP0329 SNP0349 SNP0343 SNP0339 SNP0349 SNP0349 SNP0349 SNP0349 SNP0349 SNP0349 SNP0349 SNP0349 <td>214</td> <td>202</td> <td>193</td> <td>183</td> <td>193</td> <td>202</td> <td>217</td> <td>214</td> <td>188</td> <td>201</td>	214	202	193	183	193	202	217	214	188	201
SNP0234 SNP0216 SNP0211 SNP0191 SNP0192 SNP0260 SNP0221 SNP0257 SNP0181 SNP0262 184 190 208 217 207 219 199 216 193 213 SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0248 SNP0231 SNP0263 SNP0264 SNP0363 SNP0363 SNP0365 SNP0387 SNP0346 SNP0348 SNP0332 SNP0313 SNP0288 SNP0309 SNP0329 SNP0363 SNP0288 SNP0309 SNP0329 SNP0331 SNP0288 SNP0309 SNP0329 SNP0331 SNP0288 SNP0309 SNP0329 SNP0341 SNP0388 SNP0309 SNP0329 SNP0344 SNP0319 SNP0334 SNP0339 SNP0334 SNP0334 SNP0334 SNP0334 SNP0334 SNP0334	SNP0184	SNP0187	SNP0193	SNP0253	SNP0251	SNP0185	SNP0201	SNP0182	SNP0258	SNP0281
184 190 208 217 207 219 199 216 193 213 SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0248 SNP0231 SNP0263 Lead of the content	170	200	183	216	196	212	186	210	202	190
SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0248 SNP0231 SNP0263 SNP0264 SNP0264 SNP0340 SNP0348 SNP0332 SNP0313 SNP0288 SNP0309 SNP0329 SNP0343 SNP0309 SNP0329 SNP0313 SNP0288 SNP0309 SNP0329 SNP0343 SNP0309 SNP0329 SNP0343 SNP0309 SNP0329 SNP0344 SNP0319 SNP0343 SNP0339 SNP0304 SNP0330 SNP0330 SNP0330 SNP0330 SNP0330 SNP0330 SNP0333 SNP0334 SNP0336 SNP0333 SNP0341 SNP0360 SNP0346 SNP0330 SNP0303 SNP0303 <t< td=""><td>SNP0234</td><td>SNP0216</td><td>SNP0211</td><td>SNP0191</td><td>SNP0192</td><td>SNP0260</td><td>SNP0221</td><td>SNP0257</td><td>SNP0181</td><td>SNP0252</td></t<>	SNP0234	SNP0216	SNP0211	SNP0191	SNP0192	SNP0260	SNP0221	SNP0257	SNP0181	SNP0252
\$OUT.snp.mac\$GENE_04 \$NPO303 \$NPO362 \$NPO387 \$NPO346 \$NPO348 \$NPO332 \$NPO313 \$NPO288 \$NPO309 \$NPO329 \$206 207 223 194 191 207 203 190 212 218 \$NPO377 \$NPO300 \$NPO320 \$NPO347 \$NPO290 \$NPO344 \$NPO319 \$NPO343 \$NPO343 \$NPO339 \$NPO344 \$NPO356 \$NPO345 \$NPO370	184	190	208	217	207	219	199	216	193	213
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194 202 188 200 214 188 206 199 203 187 SNP0356 SNP0340 SNP0370 SNP0327 SNP0351 SNP0335 SNP0314 SNP0380 SNP0336 SNP0333 214 218 207 204 201 208 206 194 208 214 SNP0306 SNP0334 SNP0330 SNP0373 SNP0297 SNP0305 SNP0341 SNP0357 SNP0317 SNP0302 SNP0299 199 197 217 212 214 202 210 191 195 SNP0299 SNP0367 SNP0350 SNP0354 SNP0324 SNP0352 SNP0382 SNP0383 SNP0301 SNP0295 184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 <td>206</td> <td>207</td> <td>223</td> <td>194</td> <td>191</td> <td>207</td> <td>203</td> <td>190</td> <td>212</td> <td>218</td>	206	207	223	194	191	207	203	190	212	218
SNP0356 SNP0340 SNP0370 SNP0327 SNP0351 SNP0335 SNP0314 SNP0380 SNP0336 SNP0333 214 218 207 204 201 208 206 194 208 214 SNP0306 SNP0334 SNP0330 SNP0373 SNP0297 SNP0305 SNP0341 SNP0357 SNP0317 SNP0302 209 199 197 217 212 214 202 210 191 195 SNP0299 SNP0367 SNP0350 SNP0354 SNP0324 SNP0352 SNP0382 SNP0383 SNP0301 SNP0295 184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	SNP0377	SNP0300	SNP0320	SNP0347	SNP0290	SNP0344	SNP0319	SNP0343	SNP0339	SNP0304
214 218 207 204 201 208 206 194 208 214 SNP0306 SNP0334 SNP0330 SNP0373 SNP0297 SNP0305 SNP0341 SNP0357 SNP0317 SNP0302 209 199 197 217 212 214 202 210 191 195 SNP0299 SNP0367 SNP0350 SNP0354 SNP0324 SNP0352 SNP0382 SNP0383 SNP0301 SNP0295 184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	194	202	188	200	214	188	206	199	203	187
SNP0306 SNP0334 SNP0330 SNP0373 SNP0297 SNP0305 SNP0341 SNP0357 SNP0317 SNP0302 209 199 197 217 212 214 202 210 191 195 SNP0399 SNP0367 SNP0350 SNP0354 SNP0324 SNP0352 SNP0382 SNP0383 SNP0301 SNP0295 184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	SNP0356	SNP0340	SNP0370	SNP0327	SNP0351	SNP0335	SNP0314	SNP0380	SNP0336	SNP0333
209 199 197 217 212 214 202 210 191 195 SNP0299 SNP0367 SNP0350 SNP0354 SNP0324 SNP0352 SNP0382 SNP0383 SNP0301 SNP0295 184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	214	218	207	204	201	208	206	194	208	214
SNP0299 SNP0367 SNP0350 SNP0354 SNP0324 SNP0352 SNP0382 SNP0383 SNP0301 SNP0295 184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	SNP0306	SNP0334	SNP0330	SNP0373	SNP0297	SNP0305	SNP0341	SNP0357	SNP0317	SNP0302
184 215 157 200 217 209 169 217 239 208 SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	209	199	197	217	212	214	202	210	191	195
SNP0315 SNP0359 SNP0307 SNP0371 SNP0310 SNP0366 SNP0386 SNP0379 SNP0378 SNP0372 190 216 194 219 199 177 191 192 195 205	SNP0299	SNP0367	SNP0350	SNP0354	SNP0324	SNP0352	SNP0382	SNP0383	SNP0301	SNP0295
190 216 194 219 199 177 191 192 195 205	184	215	157	200	217	209	169	217	239	208
	SNP0315	SNP0359	SNP0307	SNP0371	SNP0310	SNP0366	SNP0386	SNP0379	SNP0378	SNP0372
SNP0321 SNP0385 SNP0293 SNP0376 SNP0363 SNP0308 SNP0318 SNP0323 SNP0287 SNP0381	190	216	194	219	199	177	191	192	195	205
	SNP0321	SNP0385	SNP0293	SNP0376	SNP0363	SNP0308	SNP0318	SNP0323	SNP0287	SNP0381

191	211	192	211	205	201	203	211	193	197
		SNP0291							
213	190	188	200	212	208	198	198	211	187
		SNP0322							
216	191	196	222	196	209	207	211	190	201
		SNP0361							
190	193	186	192	166	190	223	194	222	184
SNP0316	133	100	132	100	130	220	134	222	104
214									
214									
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-	•	SNP0404	SNP0466	SNP0462	SNP0429	SNP0410	SNP0419	SNP0409	SNP0416
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SNP0400	SNP0469	SNP0408	SNP0473	SNP0424	SNP0401	SNP0392	SNP0422	SNP0468	SNP0395
183	197	220	197	216	202	177	216	207	211
SNP0476	SNP0488	SNP0486	SNP0435	SNP0458	SNP0467	SNP0449	SNP0480	SNP0478	SNP0394
182	178	198	215	182	182	210	206	199	205
SNP0442	SNP0456	SNP0447	SNP0421	SNP0444	SNP0405	SNP0414	SNP0413	SNP0475	SNP0477
222	213	212	202	205	185	212	201	225	218
SNP0450	SNP0423	SNP0452	SNP0426	SNP0403	SNP0490	SNP0402	SNP0437	SNP0445	SNP0465
207	205	177	211	213	195	193	240	194	188
SNP0430	SNP0393	SNP0481	SNP0484	SNP0439	SNP0454	SNP0389	SNP0390	SNP0459	SNP0487
183	199	174	188	208	196	208	203	187	196
SNP0470	SNP0399	SNP0428	SNP0427	SNP0472	SNP0455	SNP0397	SNP0391	SNP0453	SNP0398
188	197	203	199	195	193	216	192	197	201
SNP0417	SNP0479	SNP0446	SNP0388	SNP0407	SNP0412	SNP0431	SNP0415	SNP0441	SNP0461
202	199	198	199	207	189	201	180	206	177
SNP0418	SNP0420	SNP0438	SNP0482	SNP0396	SNP0406	SNP0483	SNP0432	SNP0451	SNP0425
190	222	197	205	169	177	202	196	201	207
SNP0436	SNP0443	SNP0464	SNP0471	SNP0433	SNP0434	SNP0485	SNP0463	SNP0489	SNP0457
181	193	208	215	201	219	196	195	211	181
SNP0440	SNP0448	SNP0411							
214	201	204							
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SNP0543	SNP0534	SNP0517	SNP0518	SNP0525	SNP0568	SNP0550	SNP0554	SNP0523	SNP0542
219	186	216	197	197	200	192	215	190	199
SNP0520	SNP0503	SNP0493	SNP0533	SNP0569	SNP0504	SNP0576	SNP0580	SNP0527	SNP0577
200	198	171	200	179	223	218	215	209	203
SNP0541	SNP0522	SNP0582	SNP0571	SNP0501	SNP0524	SNP0574	SNP0573	SNP0544	SNP0532
201	206	188	191	200	185	192	206	196	225
SNP0519	SNP0521	SNP0512	SNP0564	SNP0498	SNP0579	SNP0558	SNP0531	SNP0549	SNP0494
195	177	199	215	205	209	188	206	172	187
SNP0572	SNP0537	SNP0526	SNP0507	SNP0555	SNP0500	SNP0560	SNP0491	SNP0566	SNP0551
199	205	178	202	173	227	218	221	223	184

GNDOE 47	QNIDAEEA.	QNIDAEAA	QNIDAE SE	ONDOE 1 E	QNIDOE OO	and a co	QNIDOE CE	CMDOEO4	CMDOE 4.C
	SNP0552								
200	202	193	194	177	196	209	198	180	189
	SNP0562								
213	179	197	191	209	187	195	225	219	221
	SNP0496								
213	209	193	205	193	173	183	189	208	202
SNP0557	SNP0563								SNP0561
201	189	199	214	201	218	200	192	221	213
SNP0492	SNP0567	SNP0506	SNP0556						
202	211	183	185						
\$OUT.sn	p.mac\$GE1	NE_07							
SNP0609	SNP0649	SNP0667	SNP0685	SNP0661	SNP0597	SNP0598	SNP0623	SNP0636	SNP0603
187	185	219	201	191	212	211	207	229	205
SNP0659	SNP0657	SNP0684	SNP0616	SNP0630	SNP0629	SNP0612	SNP0677	SNP0652	SNP0672
211	211	182	192	186	193	207	200	208	222
SNP0621	SNP0670	SNP0643	SNP0619	SNP0644	SNP0686	SNP0618	SNP0655	SNP0656	SNP0653
216	215	214	187	216	224	188	197	191	203
SNP0683	SNP0663	SNP0640	SNP0592	SNP0679	SNP0658	SNP0611	SNP0676	SNP0617	SNP0634
229	203	218	201	147	202	195	211	209	208
SNP0673	SNP0660	SNP0607	SNP0678	SNP0681	SNP0606	SNP0589	SNP0591	SNP0641	SNP0613
188	193	193	216	176	209	199	198	205	194
SNP0586	SNP0687	SNP0669	SNP0594	SNP0604	SNP0666	SNP0688	SNP0671	SNP0648	SNP0608
205	202	192	206	181	190	204	180	193	201
SNP0664	SNP0626	SNP0651	SNP0602	SNP0615	SNP0674	SNP0642	SNP0628	SNP0662	SNP0668
193	198	198	194	205	211	201	206	194	181
SNP0627	SNP0588	SNP0624	SNP0625	SNP0639	SNP0599	SNP0635	SNP0593	SNP0596	SNP0645
213	194	213	228	190	196	186	215	213	180
SNP0675	SNP0631	SNP0682	SNP0620	SNP0633	SNP0587	SNP0610	SNP0600	SNP0632	SNP0595
199	192	187	209	205	225	196	214	196	199
SNP0680	SNP0638	SNP0665	SNP0637	SNP0622	SNP0647	SNP0654	SNP0601	SNP0585	SNP0646
192	167	217	204	205	202	207	210	210	190
SNP0650	SNP0614	SNP0605	SNP0590						
185	211	195	179						
\$OUT.sn	p.mac\$GE1	NE_08							
SNP0740	SNP0720	SNP0738	SNP0733	SNP0779	SNP0732	SNP0778	SNP0703	SNP0756	SNP0705
194	195	200	196	214	209	201	200	190	194
SNP0727	SNP0734	SNP0765	SNP0772	SNP0699	SNP0775	SNP0741	SNP0763	SNP0749	SNP0715
233	205	219	191	189	201	186	198	231	184
SNP0725	SNP0755	SNP0707	SNP0747	SNP0702	SNP0748	SNP0714	SNP0777	SNP0771	SNP0726
189	179	175	199	206	193	197	189	191	212
SNP0773	SNP0697	SNP0696	SNP0766	SNP0708	SNP0695	SNP0711	SNP0761	SNP0746	SNP0729
198	207	205	185	211	191	189	206	221	182
SNP0781	SNP0710	SNP0722					SNP0730	SNP0731	SNP0768

201	202	188	200	200	199	192	234	213	200
SNP0762	SNP0784	SNP0706	SNP0744	SNP0757	SNP0776	SNP0760	SNP0724	SNP0751	SNP0691
195	208	181	188	207	198	196	197	193	178
SNP0752	SNP0750	SNP0721	SNP0704	SNP0701	SNP0713	SNP0780	SNP0743	SNP0770	SNP0718
188	185	188	213	199	195	212	182	212	221
SNP0782	SNP0774	SNP0737	SNP0745	SNP0769	SNP0723	SNP0693	SNP0716	SNP0758	SNP0694
175	233	218	191	225	216	201	214	181	195
SNP0764	SNP0767	SNP0719	SNP0739	SNP0754	SNP0783	SNP0700	SNP0759	SNP0717	SNP0728
217	194	201	193	201	225	197	194	181	191
SNP0736	SNP0690	SNP0712	SNP0692	SNP0698	SNP0709				
217	223	200	217	191	221				
\$OUT.snp	o.mac\$GEN	VE_09							
SNP0795	SNP0859	SNP0845	SNP0816	SNP0829	SNP0881	SNP0830	SNP0811	SNP0807	SNP0853
190	183	182	197	205	202	212	193	195	194
SNP0841	SNP0796	SNP0880	SNP0854	SNP0821	SNP0797	SNP0882	SNP0843	SNP0828	SNP0789
193	219	198	203	182	228	185	217	193	207
SNP0856	SNP0884	SNP0812	SNP0799	SNP0825	SNP0850	SNP0805	SNP0877	SNP0804	SNP0864
188	217	196	207	203	189	215	211	201	194
SNP0842	SNP0871	SNP0790	SNP0806	SNP0863	SNP0793	SNP0846	SNP0849	SNP0873	SNP0823
202	179	212	175	207	215	186	198	199	191
SNP0792	SNP0831	SNP0866	SNP0858	SNP0847	SNP0860	SNP0791	SNP0824	SNP0787	SNP0819
192	210	215	217	208	193	187	202	190	197
SNP0839	SNP0813	SNP0803	SNP0874	SNP0876	SNP0851	SNP0794	SNP0814	SNP0827	SNP0788
211	201	194	224	216	204	194	212	181	205
SNP0837	SNP0832	SNP0879	SNP0817	SNP0852	SNP0815	SNP0802	SNP0857	SNP0875	SNP0818
198	186	213	225	214	203	211	194	171	207
SNP0809	SNP0835	SNP0800	SNP0878	SNP0801	SNP0786	SNP0870	SNP0868	SNP0844	SNP0855
187	185	192	231	187	232	204	204	203	193
SNP0848	SNP0798	SNP0869	SNP0822	SNP0872	SNP0867	SNP0808	SNP0861	SNP0838	SNP0883
175	195	196	188	230	212	191	201	196	183
SNP0826	SNP0836	SNP0785	SNP0834	SNP0820	SNP0833	SNP0865	SNP0840	SNP0862	SNP0810
193	207	203	209	213	226	193	194	220	201
\$OUT.snp	o.mac\$GE1	VE_10							
SNP0885	5 SNP090	08 SNP09	957 SNP(0937 SNI	90886 SI	NP0940	SNP0922	SNP0980	
199.3927	7 191.532	23 206.06	606 224.3	3461 190	.0407 20	5.8527 2	07.4522	187.6892	
SNP0910	SNP093	38 SNP09	975 SNP	0965 SNI	0889 SI	NP0929	SNP0953	SNP0921	
176.5893	3 205.257	78 181.08	365 205.6	6738 184	.7390 210	0.7396 1	95.5645	189.1348	
SNP0916	SNP090	04 SNPOS	915 SNP(0913 SNF	0949 SI	NP0890	SNP0933	SNP0969	

219.7581 214.3579 200.0000 217.3038 188.3182 194.7262 214.3579 223.2323 SNP0934 SNP0960 SNP0956 SNP0963 SNP0895 SNP0950 SNP0962 SNP0923 176.1134 208.9249 196.1577 181.4516 180.4435 200.4028 186.6126 196.5552 SNP0914 SNP0959 SNP0897 SNP0971 SNP0968 SNP0954 SNP0958 SNP0902 189.0799 207.7393 192.1132 179.9798 202.2245 195.9596 184.2105 198.5816

```
SNP0935 SNP0899 SNP0926 SNP0943 SNP0976 SNP0955 SNP0946 SNP0978
184.4758 205.0761 190.3323 194.5838 218.1448 204.6606 203.2520 202.4291
 SNP0917 SNP0901 SNP0907 SNP0909 SNP0948
                                            SNP0939 SNP0906 SNP0977
178.6075 228.6002 192.3464 194.7262 204.6371 183.7563 201.6211 201.4099
 SNP0894 SNP0936 SNP0920 SNP0984 SNP0981
                                            SNP0931
                                                    SNP0928
                                                            SNP0912
210.1010 203.6290 212.1212 227.4549 198.5816 185.4103 196.3746 226.3959
 SNP0952 SNP0924 SNP0919 SNP0925
                                   SNP0930
                                            SNP0941
                                                    SNP0974
                                                             SNP0903
200.8155 229.5248 187.3112 208.4592 183.5700 212.4874 171.3710 191.1021
 SNP0972 SNP0905 SNP0979 SNP0982 SNP0932 SNP0942 SNP0973
                                                            SNP0892
185.2971 212.5506 200.4028 184.6620 198.9848 200.2022 195.5420 195.9799
 SNP0898 SNP0966 SNP0911 SNP0970 SNP0918
                                            SNP0967
                                                    SNP0951
                                                             SNP0964
200.2012 213.7097 201.0050 218.5297 198.1800 184.4758 201.0101 207.8708
 SNP0947 SNP0944 SNP0891 SNP0961
                                  SNP0887 SNP0927
                                                    SNP0896
210.8981 177.8894 191.7255 170.7071 206.8618 223.9108 207.8708 205.8527
 SNP0888 SNP0900 SNP0893 SNP0983
208.4592 188.8889 224.9240 202.2245
```

```
attr(,"class")
[1] "SKAT_SSD_ALL"
```

The output object of SKAT.SSD.All has an output dataframe object "results". You can save it using write.table function.

```
> output.df = out$results
> write.table(output.df, file="./save.txt", col.names=TRUE, row.names=FALSE)
>
```

If more than one gene/SNP sets are to be tested, multiple test should be adjusted to control for family-wise error rate. It can be done by the bonferroni correction. If gene/SNP sets are correlated, however, this approach can be conservative. Alternatively, you can directly control family wise error rate (FWER) using the resampling method.

```
> obj<-SKAT_Null_Model(y ~ 1, out_type="C", n.Resampling=1000, type.Resampling="bootstrap")
> out<-SKAT.SSD.All(SSD.INFO, obj)

> # No gene is significant with controling FWER = 0.05
> Resampling_FWER(out,FWER=0.05)

$result
NULL
$n
```

\$ID NULL

[1] 0

```
> # 1 gene is significant with controling FWER = 0.5
> Resampling_FWER(out,FWER=0.5)
$result
             P.value N.Marker.All N.Marker.Test
    SetID
2 GENE_02 0.06245208
                                84
$n
[1] 1
$ID
[1] 2
   "SKAT.SSD.OneSet" or "SKAT.SSD.OneSet_SetIndex" functions can be used to test for a sin-
gle gene/SNP set. Alternatively, you can obtain a genotype matrix using "Get_Genotypes_SSD"
function and then run SKAT.
> obj<-SKAT_Null_Model(y ~ 1, out_type="C")</pre>
> # test the second gene
> id<-2
> SetID<-SSD.INFO$SetInfo$SetID[id]
> SKAT.SSD.OneSet(SSD.INFO,SetID, obj)$p.value
[1] 0.06245208
> SKAT.SSD.OneSet_SetIndex(SSD.INFO,id, obj)$p.value
[1] 0.06245208
> # test the second gene with the logistic weight.
> Z<-Get_Genotypes_SSD(SSD.INFO, id)
> weights = Get_Logistic_Weights(Z, par1=0.07, par2=150)
> SKAT(Z, obj, weights=weights)$p.value
[1] 0.7227001
>
   SKAT_CommonRare function also can be used with SSD files.
> # test all genes in SSD file
> obj<-SKAT_Null_Model(y ~ X1 + X2, out_type="C")</pre>
> out <- SKAT_CommonRare.SSD.All(SSD.INFO, obj)
> out
```

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	${\tt SetID}$	P.value	Q	N.Marker.All	N.Marker.Test	N.Marker.Rare
1	GENE_01	0.69065787	7793.492	94	94	0
2	GENE_02	0.01627559	10487.653	84	84	0
3	GENE_03	0.57047824	9340.646	108	108	0
4	GENE_04	0.31381746	9743.714	101	101	0
5	GENE_05	0.21088057	10224.331	103	103	0
6	GENE_06	0.91250955	6734.116	94	94	0
7	GENE_07	0.26552996	10193.704	104	104	0
8	GENE_08	0.64072991	8087.342	96	96	0
9	GENE_09	0.65984552	8376.438	100	100	0
10	GENE_10	0.28938130	9502.883	100	100	0

N.Marker.Common

1	94
2	84
3	108
4	101
5	103
6	94
7	104
8	96
9	100
10	100

\$P.value.Resampling
NULL

\$OUT.snp.mac

\$0UT.snp.mac\$GENE_01

SNP0056 SNP0083 SNP0035 SNP0027 SNP0037 SNP0011 SNP0071 SNP0033 SNP0025 SNP0088 SNP0014 SNP0036 SNP0074 SNP0017 SNP0016 SNP0022 SNP0087 SNP0094 SNP0057 SNP0028 SNP0058 SNP0054 SNP0031 SNP0046 SNP0062 SNP0082 SNP0012 SNP0093 SNP0050 SNP0068 SNP0021 SNP0085 SNP0089 SNP0001 SNP0052 SNP0066 SNP0090 SNP0092 SNP0061 SNP0029 SNP0042 SNP0026 SNP0002 SNP0013 SNP0043 SNP0044 SNP0080 SNP0059 SNP0048 SNP0077 SNP0049 SNP0039 SNP0067 SNP0076 SNP0003 SNP0018 SNP0040 SNP0079 SNP0009 SNP0024 SNP0070 SNP0084 SNP0055 SNP0007 SNP0015 SNP0064 SNP0065 SNP0075 SNP0086 SNP0023 SNP0010 SNP0019 SNP0081 SNP0008 SNP0004 SNP0072 SNP0047 SNP0078 SNP0006 SNP0060

SNP0032 209	SNP0030 183	SNP0005 195	SNP0053 204	SNP0069 184	SNP0034 212	SNP0041 181	SNP0073 195	SNP0091 197	SNP0051 226
SNP0020	SNP0063	SNP0045	SNP0038						
217	191	228	206						
211	101	220	200						
\$OUT sn	p.mac\$GE1	JE 02							
_	SNP0165		SNP0124	SNP0115	SNP0112	SNP0174	SNP0121	SNP0103	SNP0116
184	197	216	208	198	184	210	173	189	201
	SNP0133								
221	173	220	203	217	202	200	213	223	201
	SNP0148								
194	208	225	208	206	209	206	208	182	193
	SNP0153								
201	183	169	219	200	218	186	200	216	198
	SNP0163								
207	215	206	209	212	187	199	213	193	229
	SNP0139								
221	210	196	218	217	199	213	213	203	178
	SNP0120								
196	197	210	208	180	202	196	191	189	200
	SNP0130								
203	208	209	211	199	191	190	194	188	197
SNP0122	SNP0123	CMD0155	SNP0125						
DIVIOIZZ	DIVI 0120	DIVI OTOO	DIVI OIZO						
166	200	239	203						
166	200	239							
166 \$OUT.snj	200 p.mac\$GEI	239 NE_03	203	SNP0195	SNP0186	SNP0220	SNP0256	SNP0236	SNP0214
166 \$OUT.snj SNP0254	200 p.mac\$GEI SNP0273	239 NE_03 SNP0199	203 SNP0266						
166 \$OUT.snj SNP0254 219	200 p.mac\$GEI SNP0273 197	239 NE_03 SNP0199 220	203 SNP0266 196	183	212	202	206	214	195
\$0UT.snj SNP0254 219 SNP0196	200 p.mac\$GEN SNP0273 197 SNP0225	239 NE_03 SNP0199 220 SNP0224	203 SNP0266 196 SNP0270	183 SNP0188	212 SNP0209	202 SNP0204	206 SNP0264	214 SNP0233	195 SNP0279
\$0UT.snj SNP0254 219 SNP0196 186	200 p.mac\$GEI SNP0273 197 SNP0225 207	239 NE_03 SNP0199 220 SNP0224 221	203 SNP0266 196 SNP0270 198	183 SNP0188 183	212 SNP0209 211	202 SNP0204 214	206 SNP0264 196	214 SNP0233 200	195 SNP0279 189
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250	239 NE_03 SNP0199 220 SNP0224 221 SNP0267	203 SNP0266 196 SNP0270 198 SNP0226	183 SNP0188 183 SNP0275	212 SNP0209 211 SNP0205	202 SNP0204 214 SNP0280	206 SNP0264 196 SNP0286	214 SNP0233 200 SNP0207	195 SNP0279 189 SNP0206
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205	200 p.mac\$GEN SNP0273 197 SNP0225 207 SNP0250 213	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231	203 SNP0266 196 SNP0270 198 SNP0226 234	183 SNP0188 183 SNP0275 185	212 SNP0209 211 SNP0205 205	202 SNP0204 214 SNP0280 199	206 SNP0264 196 SNP0286 216	214 SNP0233 200 SNP0207 213	195 SNP0279 189 SNP0206 197
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232	183 SNP0188 183 SNP0275 185 SNP0241	212 SNP0209 211 SNP0205 205 SNP0265	202 SNP0204 214 SNP0280 199 SNP0230	206 SNP0264 196 SNP0286 216 SNP0249	214 SNP0233 200 SNP0207 213 SNP0269	195 SNP0279 189 SNP0206 197 SNP0284
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187	183 SNP0188 183 SNP0275 185 SNP0241 220	212 SNP0209 211 SNP0205 205 SNP0265 181	202 SNP0204 214 SNP0280 199 SNP0230 195	206 SNP0264 196 SNP0286 216 SNP0249 171	214 SNP0233 200 SNP0207 213 SNP0269 207	195 SNP0279 189 SNP0206 197 SNP0284 194
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\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202 SNP0262 192	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207 SNP0244 200	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206 SNP0283 188	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187 SNP0240 194	183 SNP0188 183 SNP0275 185 SNP0241 220 SNP0218 212	212 SNP0209 211 SNP0205 205 SNP0265 181 SNP0235 198	202 SNP0204 214 SNP0280 199 SNP0230 195 SNP0237 190	206 SNP0264 196 SNP0286 216 SNP0249 171 SNP0247 203	214 SNP0233 200 SNP0207 213 SNP0269 207 SNP0242 185	195 SNP0279 189 SNP0206 197 SNP0284 194 SNP0197 195
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202 SNP0262 192 SNP0210	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207 SNP0244 200 SNP0255	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206 SNP0283 188 SNP0278	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187 SNP0240 194 SNP0219	183 SNP0188 183 SNP0275 185 SNP0241 220 SNP0218 212 SNP0276	212 SNP0209 211 SNP0205 205 SNP0265 181 SNP0235 198 SNP0190	202 SNP0204 214 SNP0280 199 SNP0230 195 SNP0237 190 SNP0277	206 SNP0264 196 SNP0286 216 SNP0249 171 SNP0247 203 SNP0200	214 SNP0233 200 SNP0207 213 SNP0269 207 SNP0242 185 SNP0179	195 SNP0279 189 SNP0206 197 SNP0284 194 SNP0197 195 SNP0229
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\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202 SNP0262 192 SNP0210 193 SNP0183 186 SNP0223	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207 SNP0244 200 SNP0255 176 SNP0180 197 SNP0282	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206 SNP0283 188 SNP0278 211 SNP0194 212 SNP0239	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187 SNP0240 194 SNP0219 177 SNP0189 193 SNP0271	183 SNP0188 183 SNP0275 185 SNP0241 220 SNP0218 212 SNP0276 203 SNP0212 200 SNP0227	212 SNP0209 211 SNP0205 205 SNP0265 181 SNP0235 198 SNP0190 187 SNP0228 200 SNP0246	202 SNP0204 214 SNP0280 199 SNP0230 195 SNP0237 190 SNP0277 199 SNP0202 220 SNP0285	206 SNP0264 196 SNP0286 216 SNP0249 171 SNP0247 203 SNP0200 199 SNP0215 188 SNP0198	214 SNP0233 200 SNP0207 213 SNP0269 207 SNP0242 185 SNP0179 195 SNP0261 179 SNP0217	195 SNP0279 189 SNP0206 197 SNP0284 194 SNP0197 195 SNP0229 170 SNP0274 209 SNP0213
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202 SNP0262 192 SNP0210 193 SNP0183 186 SNP0223 214	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207 SNP0244 200 SNP0255 176 SNP0180 197 SNP0282 202	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206 SNP0283 188 SNP0278 211 SNP0194 212 SNP0239 193	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187 SNP0240 194 SNP0219 177 SNP0189 193 SNP0271 183	183 SNP0188 183 SNP0275 185 SNP0241 220 SNP0218 212 SNP0276 203 SNP0212 200 SNP0227 193	212 SNP0209 211 SNP0205 205 SNP0265 181 SNP0235 198 SNP0190 187 SNP0228 200 SNP0246 202	202 SNP0204 214 SNP0280 199 SNP0230 195 SNP0237 190 SNP0277 199 SNP0202 220 SNP0285 217	206 SNP0264 196 SNP0286 216 SNP0249 171 SNP0247 203 SNP0200 199 SNP0215 188 SNP0198 214	214 SNP0233 200 SNP0207 213 SNP0269 207 SNP0242 185 SNP0179 195 SNP0261 179 SNP0217 188	195 SNP0279 189 SNP0206 197 SNP0284 194 SNP0197 195 SNP0229 170 SNP0274 209 SNP0213 201
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202 SNP0262 192 SNP0210 193 SNP0183 186 SNP0223 214	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207 SNP0244 200 SNP0255 176 SNP0180 197 SNP0282	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206 SNP0283 188 SNP0278 211 SNP0194 212 SNP0239 193	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187 SNP0240 194 SNP0219 177 SNP0189 193 SNP0271 183	183 SNP0188 183 SNP0275 185 SNP0241 220 SNP0218 212 SNP0276 203 SNP0212 200 SNP0227 193	212 SNP0209 211 SNP0205 205 SNP0265 181 SNP0235 198 SNP0190 187 SNP0228 200 SNP0246 202 SNP0185	202 SNP0204 214 SNP0280 199 SNP0230 195 SNP0237 190 SNP0277 199 SNP0202 220 SNP0285 217	206 SNP0264 196 SNP0286 216 SNP0249 171 SNP0247 203 SNP0200 199 SNP0215 188 SNP0198 214	214 SNP0233 200 SNP0207 213 SNP0269 207 SNP0242 185 SNP0179 195 SNP0261 179 SNP0217 188	195 SNP0279 189 SNP0206 197 SNP0284 194 SNP0197 195 SNP0229 170 SNP0274 209 SNP0213 201
\$0UT.snj SNP0254 219 SNP0196 186 SNP0238 205 SNP0222 202 SNP0262 192 SNP0210 193 SNP0183 186 SNP0223 214	200 p.mac\$GEI SNP0273 197 SNP0225 207 SNP0250 213 SNP0272 207 SNP0244 200 SNP0255 176 SNP0180 197 SNP0282 202	239 NE_03 SNP0199 220 SNP0224 221 SNP0267 231 SNP0245 206 SNP0283 188 SNP0278 211 SNP0194 212 SNP0239 193	203 SNP0266 196 SNP0270 198 SNP0226 234 SNP0232 187 SNP0240 194 SNP0219 177 SNP0189 193 SNP0271 183 SNP0253	183 SNP0188 183 SNP0275 185 SNP0241 220 SNP0218 212 SNP0276 203 SNP0212 200 SNP0227 193 SNP0251	212 SNP0209 211 SNP0205 205 SNP0265 181 SNP0235 198 SNP0190 187 SNP0228 200 SNP0246 202	202 SNP0204 214 SNP0280 199 SNP0230 195 SNP0237 190 SNP0277 199 SNP0202 220 SNP0285 217	206 SNP0264 196 SNP0286 216 SNP0249 171 SNP0247 203 SNP0200 199 SNP0215 188 SNP0198 214	214 SNP0233 200 SNP0207 213 SNP0269 207 SNP0242 185 SNP0179 195 SNP0261 179 SNP0217 188	195 SNP0279 189 SNP0206 197 SNP0284 194 SNP0197 195 SNP0229 170 SNP0274 209 SNP0213 201

184	190	208	217	207	219	199	216	193	213
			SNP0268					193	213
188	195	198	191	210	198	183	220		
\$OUT.sn:	o.mac\$GE1	NE 04							
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SNP0377	SNP0300	SNP0320	SNP0347				SNP0343	SNP0339	SNP0304
194	202	188	200	214	188	206	199	203	187
SNP0356	SNP0340						SNP0380		SNP0333
214	218	207	204	201	208	206	194	208	214
SNP0306	SNP0334	SNP0330	SNP0373	SNP0297		SNP0341	SNP0357	SNP0317	SNP0302
209	199	197	217	212	214	202	210	191	195
SNP0299	SNP0367	SNP0350	SNP0354	SNP0324	SNP0352	SNP0382	SNP0383	SNP0301	SNP0295
184	215	157	200	217	209	169	217	239	208
SNP0315	SNP0359	SNP0307	SNP0371	SNP0310	SNP0366	SNP0386	SNP0379	SNP0378	SNP0372
190	216	194	219	199	177	191	192	195	205
SNP0321	SNP0385	SNP0293	SNP0376		SNP0308	SNP0318	SNP0323	SNP0287	SNP0381
191	211	192	211	205	201	203	211	193	197
SNP0364	SNP0328	SNP0291	SNP0349	SNP0289	SNP0337	SNP0353	SNP0345	SNP0375	SNP0311
213	190	188	200	212	208	198	198	211	187
SNP0326	SNP0358	SNP0322	SNP0292	SNP0298	SNP0369	SNP0360	SNP0355	SNP0338	SNP0384
216	191	196	222	196	209	207	211	190	201
SNP0294	SNP0296	SNP0361					SNP0342	SNP0368	SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
214									
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SNP0400	SNP0469	SNP0408	SNP0473	SNP0424	SNP0401	SNP0392	SNP0422	SNP0468	SNP0395
183	197	220	197	216	202	177	216	207	211
SNP0476	SNP0488	SNP0486	SNP0435	SNP0458	SNP0467	SNP0449	SNP0480	SNP0478	SNP0394
182	178	198	215	182	182	210	206	199	205
SNP0442	SNP0456	SNP0447	SNP0421	SNP0444	SNP0405	SNP0414	SNP0413	SNP0475	SNP0477
222	213	212	202	205	185	212	201	225	218
SNP0450	SNP0423	SNP0452	SNP0426	SNP0403	SNP0490	SNP0402	SNP0437	SNP0445	SNP0465
207	205	177	211	213	195	193	240	194	188
SNP0430	SNP0393	SNP0481	SNP0484	SNP0439	SNP0454	SNP0389	SNP0390	SNP0459	SNP0487
183	199	174	188	208	196	208	203	187	196
SNP0470	SNP0399	SNP0428	SNP0427	SNP0472	SNP0455	SNP0397	SNP0391	SNP0453	SNP0398
188	197	203	199	195	193	216	192	197	201
SNP0417	SNP0479	SNP0446	SNP0388	SNP0407	SNP0412	SNP0431	SNP0415	SNP0441	SNP0461
202	199	198	199	207	189	201	180	206	177

SNP0418 190	SNP0420 222	SNP0438 197	SNP0482 205	SNP0396 169	SNP0406 177	SNP0483 202	SNP0432 196	SNP0451 201	SNP0425 207
							SNP0463		
181	193	208	215	201	219	196	195		181
			215	201	219	190	195	211	101
	SNP0448								
214	201	204							
\$NIT snr	o.mac\$GE1	JF. 06							
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							SNP0580		
200	198	171	200	179	223	218	215	209	203
							SNP0573		
201	206	188	191	200	185	192	206	196	225
SNP0519	SNP0521						SNP0531	SNP0549	SNP0494
195	177	199	215	205	209	188	206	172	187
SNP0572	SNP0537						SNP0491		SNP0551
199	205	178	202	173	227	218	221	223	184
							SNP0565		
200	202	193	194	177	196	209	198	180	189
							SNP0513		
213	179	197	191	209	187	195	225	219	221
							SNP0538		
213	209	193	205	193	173	183	189	208	202
							SNP0528		
201	189	199	214	201	218	200	192	221	213
	SNP0567								
202	211	183	185						
\$OUT.snp	o.mac\$GE1	VE_07							
SNP0609	SNP0649	SNP0667	SNP0685	SNP0661	SNP0597	SNP0598	SNP0623	SNP0636	SNP0603
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SNP0659	SNP0657	SNP0684	SNP0616	SNP0630	SNP0629	SNP0612	SNP0677	SNP0652	SNP0672
211	211	182	192	186	193	207	200	208	222
SNP0621	SNP0670	SNP0643	SNP0619	SNP0644	SNP0686	SNP0618	SNP0655	SNP0656	SNP0653
216	215	214	187	216	224	188	197	191	203
SNP0683	SNP0663	SNP0640	SNP0592	SNP0679	SNP0658	SNP0611	SNP0676	SNP0617	SNP0634
229	203	218	201	147	202	195	211	209	208
SNP0673	SNP0660	SNP0607	SNP0678	SNP0681	SNP0606	SNP0589	SNP0591	SNP0641	SNP0613
188	193	193	216	176	209	199	198	205	194
SNP0586	SNP0687	SNP0669	SNP0594	SNP0604	SNP0666	SNP0688	SNP0671	SNP0648	SNP0608
205	202	192	206	181	190	204	180	193	201
SNP0664	SNP0626	SNP0651	SNP0602	SNP0615	SNP0674	SNP0642	SNP0628	SNP0662	SNP0668
193	198	198	194	205	211	201	206	194	181
SNP0627	SNP0588	SNP0624	SNP0625	SNP0639	SNP0599	SNP0635	SNP0593	SNP0596	SNP0645

	213	194	213	228	190	196	186	215	213	180	
	SNP0675	SNP0631			SNP0633					SNP0595	
	199	192	187	209	205	225	196	214	196	199	
	SNP0680	SNP0638			SNP0622						
	192	167	217	204	205	202	207	210	210	190	
	SNP0650		SNP0605								
	185	211	195	179							
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	-			SNP0733	SNP0779	SNP0732	SNP0778	SNP0703	SNP0756	SNP0705	
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	SNP0727	SNP0734	SNP0765	SNP0772	SNP0699	SNP0775	SNP0741	SNP0763	SNP0749	SNP0715	
	233	205	219	191	189	201	186	198	231	184	
	SNP0725	SNP0755	SNP0707		SNP0702			SNP0777	SNP0771	SNP0726	
	189	179	175	199	206	193	197	189	191	212	
	SNP0773	SNP0697	SNP0696		SNP0708		SNP0711	SNP0761	SNP0746	SNP0729	
	198	207	205	185	211	191	189	206	221	182	
	SNP0781		SNP0722		SNP0753					SNP0768	
	201	202	188	200	200	199	192	234	213	200	
	SNP0762				SNP0757		SNP0760				
	195	208	181	188	207	198	196	197	193	178	
	SNP0752				SNP0701					SNP0718	
	188	185	188	213	199	195	212	182	212	221	
	SNP0782				SNP0769					SNP0694	
	175	233	218	191	225	216	201	214	181	195	
					SNP0754						
	217	194	201	193	201	225	197	194	181	191	
					SNP0698			-0-			
	217	223	200	217	191	221					
					-0-						
	\$OUT.snp.mac\$GENE_09										
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	193	219	198	203		228	185	217	193	207	
	SNP0856				SNP0825				SNP0804		
	188	217	196	207		189	215	211	201	194	
					SNP0863						
	202	179	212	175	207	215	186	198	199	191	
					SNP0847						
	192	210	215	217		193	187	202	190	197	
					SNP0876						
	211	201	194	224		204	194		181	205	
					SNP0852						
	198	186	213	225	214	203	211	194	171	207	
	100	100	210	220	1	200		101		201	

```
SNP0809 SNP0835 SNP0800 SNP0878 SNP0801 SNP0786 SNP0870 SNP0868 SNP0844 SNP0855
    187
            185
                     192
                             231
                                      187
                                              232
                                                       204
                                                                204
                                                                        203
                                                                                 193
SNP0848 SNP0798 SNP0869 SNP0822 SNP0872 SNP0867 SNP0808 SNP0861 SNP0838 SNP0883
    175
            195
                     196
                             188
                                      230
                                              212
                                                       191
                                                                201
                                                                        196
                                                                                 183
SNP0826 SNP0836 SNP0785 SNP0834 SNP0820 SNP0833 SNP0865 SNP0840 SNP0862 SNP0810
    193
            207
                     203
                             209
                                      213
                                              226
                                                       193
                                                                194
                                                                        220
                                                                                201
```

\$OUT.snp.mac\$GENE_10 SNP0885 SNP0908 SNP0957 SNP0937 SNP0886 SNP0940 SNP0922 SNP0980 199.3927 191.5323 206.0606 224.3461 190.0407 205.8527 207.4522 187.6892 SNP0910 SNP0938 SNP0975 SNP0965 SNP0889 SNP0929 SNP0953 SNP0921 176.5893 205.2578 181.0865 205.6738 184.7390 210.7396 195.5645 189.1348 SNP0916 SNP0904 SNP0915 SNP0913 SNP0949 SNP0890 SNP0933 219.7581 214.3579 200.0000 217.3038 188.3182 194.7262 214.3579 223.2323 SNP0934 SNP0960 SNP0956 SNP0963 SNP0895 SNP0950 SNP0962 SNP0923 176.1134 208.9249 196.1577 181.4516 180.4435 200.4028 186.6126 196.5552 SNP0914 SNP0959 SNP0897 SNP0971 SNP0968 SNP0954 SNP0958 SNP0902 189.0799 207.7393 192.1132 179.9798 202.2245 195.9596 184.2105 198.5816 SNP0935 SNP0899 SNP0926 SNP0943 SNP0976 SNP0955 SNP0946 SNP0978 184.4758 205.0761 190.3323 194.5838 218.1448 204.6606 203.2520 202.4291 SNP0917 SNP0901 SNP0907 SNP0909 SNP0948 SNP0939 SNP0906 178.6075 228.6002 192.3464 194.7262 204.6371 183.7563 201.6211 201.4099 SNP0894 SNP0936 SNP0920 SNP0984 SNP0981 SNP0931 SNP0928 SNP0912 210.1010 203.6290 212.1212 227.4549 198.5816 185.4103 196.3746 226.3959 SNP0952 SNP0924 SNP0919 SNP0925 SNP0930 SNP0941 SNP0974 SNP0903 200.8155 229.5248 187.3112 208.4592 183.5700 212.4874 171.3710 191.1021 SNP0972 SNP0905 SNP0979 SNP0982 SNP0932 SNP0942 SNP0973 SNP0892 185.2971 212.5506 200.4028 184.6620 198.9848 200.2022 195.5420 195.9799 SNP0898 SNP0966 SNP0911 SNP0970 SNP0918 SNP0967 SNP0951 200.2012 213.7097 201.0050 218.5297 198.1800 184.4758 201.0101 207.8708 SNP0947 SNP0944 SNP0891 SNP0961 SNP0887 SNP0927 SNP0896 210.8981 177.8894 191.7255 170.7071 206.8618 223.9108 207.8708 205.8527 SNP0888 SNP0900 SNP0893 SNP0983

```
attr(,"class")
[1] "SKAT_SSD_ALL"
```

After finishing to use SSD files, please close them.

208.4592 188.8889 224.9240 202.2245

> Close_SSD()

Close the opened SSD file: /private/var/folders/g1/xq8b2nf54zbg8x6srcmmzvpw0000gn/T/RtmpSvl2

3.1 Plink Binary format files: SKATBinary

5 0.63625247

SKATBinary functions can also be used with plink formatted files. This section shows an example code. Example plink files can be found on the SKAT/MetaSKAT google group page.

```
> # File names
> File.Bed<-"./SKATBinary.example.bed"
> File.Bim<-"./SKATBinary.example.bim"
> File.Fam<-"./SKATBinary.example.fam"
> File.Cov<-"./SKATBinary.example.cov"
> File.SetID<-"./SKATBinary.example.SetID"
> File.SSD<-"./SKATBinary.example.SSD"
> File.Info<-"./SKATBinary.example.SSD.info"
> # Generate SSD file, and read fam and cov files
> # If you already have a SSD file, you do not need to call this function.
> Generate_SSD_SetID(File.Bed, File.Bim, File.Fam, File.SetID, File.SSD, File.Info)
Check duplicated SNPs in each SNP set
No duplicate
2000 Samples, 30 Sets, 340 Total SNPs
[1] "SSD and Info files are created!"
> FAM<-Read_Plink_FAM_Cov(File.Fam, File.Cov, Is.binary=TRUE, cov_header=FALSE)
> # open SSD files
> SSD.INFO<-Open_SSD(File.SSD, File.Info)
2000 Samples, 30 Sets, 340 Total SNPs
Open the SSD file
> # No adjustment is needed
> obj<-SKAT_Null_Model(Phenotype ~ COV1 + COV2, out_type="D", data=FAM, Adjustment=FALSE)
> # SKAT
> out.skat<-SKATBinary.SSD.All(SSD.INFO, obj, method="SKAT")
> # SKAT-0
> out.skato<-SKATBinary.SSD.All(SSD.INFO, obj, method="SKATO")
> # First 5 variant sets, SKAT
> out.skat$results[1:5,]
           P.value N.Marker.All N.Marker.Test MAC m Method.bin
  SetID
                                                                          MAP
1
      1 0.92753378
                             11
                                           11 18 17
                                                             ER 2.512149e-07
                              2
2
      2 0.24947578
                                            2
                                                3 3
                                                             ER 3.544808e-02
                              7
                                            7 19 19
3
      3 0.60706345
                                                             ER 3.312382e-08
      4 0.08566388
                             11
                                           11 19 18
                                                             ER 6.640864e-08
```

4 18 18

ER 2.721199e-07

4

The effective number of tests and QQ plots can be obtained using the minimum achievable p-values (MAP).

```
> # Effective number of test is smaller than 30 (number of variant sets)
> # Use SKAT results
> Get_EffectiveNumberTest(out.skat$results$MAP, alpha=0.05)

[1] 28
> # QQ plot
> QQPlot_Adj(out.skat$results$P.value, out.skat$results$MAP)
>
```

4 Power/Sample Size calculation.

4.1 Dataset

>

SKAT package provides a haplotype dataset (SKAT.haplotypes) which contains a haplotype matrix of 10,000 haplotypes over 200kb region (Haplotype), and a dataframe with information on each SNP. These haplotypes were simulated using a calibrated coalescent model (cosi) with mimicking linkage disequilibrium structure of European ancestry. If no haplotype data are available, this dataset can be used to compute power/sample size.

```
> data(SKAT.haplotypes)
> names(SKAT.haplotypes)
[1] "Haplotype" "SNPInfo"
> attach(SKAT.haplotypes)
```

4.2 Power/Sample Size calculation

The following example uses the haplotypes in SKAT.haplotypes with the following parameters.

- 1. Subregion length = 3k bp
- 2. Causal percent = 20%
- 3. Negative percent = 20%
- 4. For continuous traits, $\beta = c|log_{10}(MAF)|$ (BetaType = "Log") with $\beta = 2$ at MAF = 10^{-4}
- 5. For binary traits, $log(OR) = c|log_{10}(MAF)|$ (OR.Type = "Log") with OR = 2 at MAF = 10^{-4} , and 50% of samples are cases and 50% of samples are controls

```
> set.seed(500)
```

- > out.c<-Power_Continuous(Haplotype,SNPInfo\$CHROM_POS, SubRegion.Length=5000,
- + Causal.Percent= 20, N.Sim=10, MaxBeta=2, Negative.Percent=20)

```
[1] "10/10"
> out.b<-Power_Logistic(Haplotype,SNPInfo$CHROM_POS, SubRegion.Length=5000,
+ Causal.Percent= 20, N.Sim=10 ,MaxOR=7, Negative.Percent=20)
[1] "10/10"
> out.c
$Power
          0.01
                   0.001
                             1e-06
500 0.6175978 0.4876905 0.2812231
1000 0.8196568 0.6959138 0.4967577
1500 0.9260644 0.8176848 0.6047217
2000 0.9795038 0.9033846 0.6978467
2500 0.9964443 0.9611981 0.7625096
3000 0.9996061 0.9888946 0.8168844
3500 0.9999708 0.9977467 0.8687841
4000 0.9999985 0.9996697 0.9163105
4500 0.9999999 0.9999641 0.9541347
5000 1.0000000 0.9999970 0.9789134
$R.sq
[1] 0.07804945
attr(,"class")
[1] "SKAT_Power"
> out.b
$Power
          0.01
                   0.001
                              1e-06
500 0.3195274 0.1838831 0.03372994
1000 0.5729441 0.3887094 0.15492725
1500 0.7488294 0.5687846 0.25885689
2000 0.8557195 0.7085993 0.37007813
2500 0.9189064 0.8044937 0.48059575
3000 0.9569876 0.8689837 0.58421719
3500 0.9790826 0.9146539 0.67116819
4000 0.9907789 0.9475064 0.73753304
4500 0.9963200 0.9700309 0.78656221
5000 0.9986658 0.9842302 0.82447737
attr(,"class")
[1] "SKAT_Power"
```

> Get_RequiredSampleSize(out.c, Power=0.8)

```
$`alpha = 1.00e-02`
[1] 951.3587

$`alpha = 1.00e-03`
[1] 1427.385

$`alpha = 1.00e-06`
[1] 2844.741

> Get_RequiredSampleSize(out.b, Power=0.8)

$`alpha = 1.00e-02`
[1] 1739.361

$`alpha = 1.00e-03`
[1] 2476.569

$`alpha = 1.00e-06`
[1] 4677.209

>
```

In this example, N.Sim=10 was used to get the result quickly. When you run the power calculation, please increase it to more than 100. When BetaType = "Log" or OR.Type = "Log", the effect size of continuous trait and the log odds ratio of binary traits are $c|log_{10}(MAF)|$, where c is determined by Max_Beta or Max_OR. For example, c = 2/4 = 0.5 when the Max_Beta = 2. In this case, a causal variant with MAF=0.01 has $\beta = 1$. For binary traits, c = log(7)/4 = 0.486 with MAX_OR=7. And thus, a causal variant with MAF=0.01 has log OR = 0.972.

Power_Continuous_R or Power_Logistic_R functions can be used to compute power with with non-zero r.corr (ρ). Since these functions use slightly different method to compute power, power estimates from Power_Continuous_R and Power_Logistic_R can be slightly different from estimates from Power_Continuous and Power_Logistic even when r.corr=0. If you want to computer the power of SKAT-O by estimating the optimal r.corr, please use r.corr=2. The estimated optimal r.corr is

$$r.corr = p_1^2 (2p_2 - 1)^2,$$

where p_1 is the proportion of nonzero β s, and p_2 is the proportion of negative (or positive) β s among the non-zero β s.

```
> set.seed(500)
> out.c<-Power_Continuous_R(Haplotype,SNPInfo$CHROM_POS, SubRegion.Length=5000,
+ Causal.Percent= 20, N.Sim=10, MaxBeta=2,Negative.Percent=20, r.corr=2)
[1] "10/10"
> out.c
```

```
$Power
                   0.001
          0.01
                             1e-06
500 0.6143437 0.4867279 0.2821814
1000 0.8155499 0.6904465 0.4962072
1500 0.9246785 0.8124547 0.5991376
2000 0.9798723 0.9006001 0.6923563
2500 0.9967484 0.9611003 0.7558941
3000 0.9996732 0.9894869 0.8095854
3500 0.9999783 0.9980407 0.8629075
4000 0.9999990 0.9997413 0.9136032
4500 1.0000000 0.9999749 0.9542956
5000 1.0000000 0.9999981 0.9801759
$R.sq
[1] 0.07804945
$r.corr
[1] 0.0144
attr(,"class")
[1] "SKAT_Power"
> Get_RequiredSampleSize(out.c, Power=0.8)
\alpha = 1.00e-02
[1] 961.3582
\alpha = 1.00e-03
[1] 1448.959
\alpha = 1.00e-06
[1] 2910.736
```