

# 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	1	2	4	577	432	4	4	2	3	2	1	34
VAR14	VAR15	VAR16	VAR17	VAR18	VAR19	VAR20	VAR21	VAR22	VAR23	VAR24	VAR25	VAR26
657	2	82	1	25	328	465	2	4	85	430	3	6
VAR27	VAR28	VAR29	VAR30	VAR31	VAR32	VAR33	VAR34	VAR35	VAR36	VAR37	VAR38	VAR39
29	82	1	1	1	15	19	1	657	1	35	4	29
VAR40	VAR41	VAR42	VAR43	VAR44	VAR45	VAR46	VAR47	VAR48	VAR49	VAR50	VAR51	VAR52
2	913	1	423	2	2	1	1	29	2	1	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	3	1
VAR66	VAR67											
2	1											

```
>
```

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 applied.

```
> SKAT(Z[IDX,], obj.s, kernel = "linear.weighted")$p.value
```

```
[1] 0.1322476
```

```
>
```

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  $W = \text{diag}\{w_1, \dots, w_m\}$  is a weight matrix. In the previous examples, we used the default  $\text{beta}(1,25)$  weight,  $w_i = \text{dbeta}(p_i, 1, 25)$ , where  $\text{dbeta}$  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, `weights.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="l")
> plot(MAF[1:100],W[1:100],xlab="MAF",ylab="Weights",type="l")
> 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  $\rho$  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  $\rho$  values from 0 to 1 as a grid of  $\rho$ 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.

```
> # parametric bootstrap.
> obj<-SKAT_Null_Model(y.b ~ X, out_type="D", n.Resampling=5000,
+ type.Resampling="bootstrap")
> # SKAT p-value
> re<- SKAT(Z, obj, kernel = "linear.weighted")
> re$p.value # SKAT p-value
```

```
[1] 0.1401991
```

```

> 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="SKAT0")$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.

```

> data(SKAT.example.ChrX)
> attach(SKAT.example.ChrX)
> Z = SKAT.example.ChrX$Z
> #####
> #          Compute the P-value of SKAT
>
> # binary trait
> obj.x<-SKAT_Null_Model_ChrX(y ~ x1 +x2 + Gender, SexVar="Gender", out_type="D", data=SKAT.ex
> # run SKAT-0
> SKAT_ChrX(Z, obj.x, method="SKATO")$p.value

[1] 0.9156629

>
>
>

```

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.

```

> #####
> #          Compute the P-value of SKAT
>
> # binary trait
> obj.x<-SKAT_Null_Model_ChrX(y ~ x1 +x2 + Gender, SexVar="Gender", out_type="D", data=SKAT.ex
Sample size (non-missing y and X) = 1000, which is < 2000. The small sample adjustment is appl
> # run SKAT-0
> SKAT_ChrY(Z, obj.x, method="SKATO")$p.value

[1] 0.8682478

> detach(SKAT.example.ChrX)

```

### 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.

```

> # To run this code, first download and unzip example files
>
> #####
> #          Generate SSD file
>

```

```

> # Create the MW File
> File.Bed<-"./Example1.bed"
> File.Bim<-"./Example1.bim"
> File.Fam<-"./Example1.fam"
> 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")

```

```

> 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
3	GENE_03	0.38416582	108	108

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
184	197	216	208	198	184	210	173	189	201
SNP0141	SNP0133	SNP0134	SNP0149	SNP0099	SNP0161	SNP0095	SNP0169	SNP0164	SNP0097
221	173	220	203	217	202	200	213	223	201
SNP0143	SNP0148	SNP0114	SNP0173	SNP0160	SNP0136	SNP0108	SNP0109	SNP0105	SNP0118
194	208	225	208	206	209	206	208	182	193
SNP0150	SNP0153	SNP0126	SNP0162	SNP0119	SNP0111	SNP0129	SNP0142	SNP0145	SNP0132
201	183	169	219	200	218	186	200	216	198
SNP0177	SNP0163	SNP0107	SNP0100	SNP0154	SNP0178	SNP0146	SNP0101	SNP0144	SNP0171
207	215	206	209	212	187	199	213	193	229

SNP0140	SNP0139	SNP0098	SNP0110	SNP0147	SNP0131	SNP0137	SNP0113	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						

\$OUT.snp.mac\$GENE\_03

SNP0254	SNP0273	SNP0199	SNP0266	SNP0195	SNP0186	SNP0220	SNP0256	SNP0236	SNP0214
219	197	220	196	183	212	202	206	214	195
SNP0196	SNP0225	SNP0224	SNP0270	SNP0188	SNP0209	SNP0204	SNP0264	SNP0233	SNP0279
186	207	221	198	183	211	214	196	200	189
SNP0238	SNP0250	SNP0267	SNP0226	SNP0275	SNP0205	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.snp.mac\$GENE\_04

SNP0303	SNP0362	SNP0387	SNP0346	SNP0348	SNP0332	SNP0313	SNP0288	SNP0309	SNP0329
206	207	223	194	191	207	203	190	212	218
SNP0377	SNP0300	SNP0320	SNP0347	SNP0290	SNP0344	SNP0319	SNP0343	SNP0339	SNP0304
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
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	SNP0363	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	SNP0325	SNP0312	SNP0374	SNP0331	SNP0342	SNP0368	SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
214									

\$OUT.snp.mac\$GENE\_05

SNP0460	SNP0474	SNP0404	SNP0466	SNP0462	SNP0429	SNP0410	SNP0419	SNP0409	SNP0416
184	214	199	213	171	183	189	220	197	174
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							

\$OUT.snp.mac\$GENE\_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	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
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						

\$OUT.snp.mac\$GENE\_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.snp.mac\$GENE\_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	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
217	194	201	193	201	225	197	194	181	191
SNP0736	SNP0690	SNP0712	SNP0692	SNP0698	SNP0709				
217	223	200	217	191	221				

\$OUT.snp.mac\$GENE\_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.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	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 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"

```

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

```

> File.Cov<-"./Example1.Cov"
> 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  0  1  0.679793  1.0297614  1
2 FID977  1  0  0  1  0.836566  0.1846235  1
3 FID462  1  0  0  1 -0.408388 -0.6141158  1
4 FID958  1  0  0  1 -0.522305 -2.0226759  0
5 FID668  1  0  0  1 -0.328300 -0.8213776  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")

> out<-SKAT.SSD.All(SSD.INFO, obj)

> out

```

\$results

	SetID	P.value	N.Marker.All	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
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
184	197	216	208	198	184	210	173	189	201
SNP0141	SNP0133	SNP0134	SNP0149	SNP0099	SNP0161	SNP0095	SNP0169	SNP0164	SNP0097
221	173	220	203	217	202	200	213	223	201
SNP0143	SNP0148	SNP0114	SNP0173	SNP0160	SNP0136	SNP0108	SNP0109	SNP0105	SNP0118

194	208	225	208	206	209	206	208	182	193
SNP0150	SNP0153	SNP0126	SNP0162	SNP0119	SNP0111	SNP0129	SNP0142	SNP0145	SNP0132
201	183	169	219	200	218	186	200	216	198
SNP0177	SNP0163	SNP0107	SNP0100	SNP0154	SNP0178	SNP0146	SNP0101	SNP0144	SNP0171
207	215	206	209	212	187	199	213	193	229
SNP0140	SNP0139	SNP0098	SNP0110	SNP0147	SNP0131	SNP0137	SNP0113	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						

\$OUT.snp.mac\$GENE\_03

SNP0254	SNP0273	SNP0199	SNP0266	SNP0195	SNP0186	SNP0220	SNP0256	SNP0236	SNP0214
219	197	220	196	183	212	202	206	214	195
SNP0196	SNP0225	SNP0224	SNP0270	SNP0188	SNP0209	SNP0204	SNP0264	SNP0233	SNP0279
186	207	221	198	183	211	214	196	200	189
SNP0238	SNP0250	SNP0267	SNP0226	SNP0275	SNP0205	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.snp.mac\$GENE\_04

SNP0303	SNP0362	SNP0387	SNP0346	SNP0348	SNP0332	SNP0313	SNP0288	SNP0309	SNP0329
206	207	223	194	191	207	203	190	212	218
SNP0377	SNP0300	SNP0320	SNP0347	SNP0290	SNP0344	SNP0319	SNP0343	SNP0339	SNP0304
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
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	SNP0363	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	SNP0325	SNP0312	SNP0374	SNP0331	SNP0342	SNP0368	SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
214									

\$OUT.snp.mac\$GENE\_05

SNP0460	SNP0474	SNP0404	SNP0466	SNP0462	SNP0429	SNP0410	SNP0419	SNP0409	SNP0416
184	214	199	213	171	183	189	220	197	174
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							

\$OUT.snp.mac\$GENE\_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	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
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						

\$OUT.snp.mac\$GENE\_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						

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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	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
217	194	201	193	201	225	197	194	181	191
SNP0736	SNP0690	SNP0712	SNP0692	SNP0698	SNP0709				
217	223	200	217	191	221				

\$OUT.snp.mac\$GENE\_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.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  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  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"

```

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
      SetID      P.value N.Marker.All N.Marker.Test
1  GENE_01 0.58647860           94           94
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

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
184	197	216	208	198	184	210	173	189	201
SNP0141	SNP0133	SNP0134	SNP0149	SNP0099	SNP0161	SNP0095	SNP0169	SNP0164	SNP0097
221	173	220	203	217	202	200	213	223	201
SNP0143	SNP0148	SNP0114	SNP0173	SNP0160	SNP0136	SNP0108	SNP0109	SNP0105	SNP0118
194	208	225	208	206	209	206	208	182	193
SNP0150	SNP0153	SNP0126	SNP0162	SNP0119	SNP0111	SNP0129	SNP0142	SNP0145	SNP0132
201	183	169	219	200	218	186	200	216	198
SNP0177	SNP0163	SNP0107	SNP0100	SNP0154	SNP0178	SNP0146	SNP0101	SNP0144	SNP0171
207	215	206	209	212	187	199	213	193	229
SNP0140	SNP0139	SNP0098	SNP0110	SNP0147	SNP0131	SNP0137	SNP0113	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						

\$OUT.snp.mac\$GENE\_03

SNP0254	SNP0273	SNP0199	SNP0266	SNP0195	SNP0186	SNP0220	SNP0256	SNP0236	SNP0214
219	197	220	196	183	212	202	206	214	195
SNP0196	SNP0225	SNP0224	SNP0270	SNP0188	SNP0209	SNP0204	SNP0264	SNP0233	SNP0279
186	207	221	198	183	211	214	196	200	189
SNP0238	SNP0250	SNP0267	SNP0226	SNP0275	SNP0205	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.snp.mac\$GENE\_04

SNP0303	SNP0362	SNP0387	SNP0346	SNP0348	SNP0332	SNP0313	SNP0288	SNP0309	SNP0329
206	207	223	194	191	207	203	190	212	218
SNP0377	SNP0300	SNP0320	SNP0347	SNP0290	SNP0344	SNP0319	SNP0343	SNP0339	SNP0304
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
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	SNP0363	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	SNP0325	SNP0312	SNP0374	SNP0331	SNP0342	SNP0368	SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
214									

\$OUT.snp.mac\$GENE\_05

SNP0460	SNP0474	SNP0404	SNP0466	SNP0462	SNP0429	SNP0410	SNP0419	SNP0409	SNP0416
184	214	199	213	171	183	189	220	197	174
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							

\$OUT.snp.mac\$GENE\_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	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
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						

\$OUT.snp.mac\$GENE\_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						

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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	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
217	194	201	193	201	225	197	194	181	191
SNP0736	SNP0690	SNP0712	SNP0692	SNP0698	SNP0709				
217	223	200	217	191	221				

\$OUT.snp.mac\$GENE\_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.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	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 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"

```

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 controlling FWER = 0.05
> Resampling_FWER(out,FWER=0.05)

```

```

$result
NULL

```

```

$n
[1] 0

```

```

$ID
NULL

```

```
> # 1 gene is significant with controlling FWER = 0.5
> Resampling_FWER(out,FWER=0.5)
```

```
$result
```

```
      SetID      P.value N.Marker.All N.Marker.Test
2 GENE_02 0.06245208           84           84
```

```
$n
```

```
[1] 1
```

```
$ID
```

```
[1] 2
```

“SKAT.SSD.OneSet” or “SKAT.SSD.OneSet\_SetIndex” functions can be used to test for a single 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")
> # 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")
> out<-SKAT_CommonRare.SSD.All(SSD.INFO, obj)
```

```
>
```

```
> out
```

\$results

	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

\$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
184	197	216	208	198	184	210	173	189	201
SNP0141	SNP0133	SNP0134	SNP0149	SNP0099	SNP0161	SNP0095	SNP0169	SNP0164	SNP0097
221	173	220	203	217	202	200	213	223	201
SNP0143	SNP0148	SNP0114	SNP0173	SNP0160	SNP0136	SNP0108	SNP0109	SNP0105	SNP0118
194	208	225	208	206	209	206	208	182	193
SNP0150	SNP0153	SNP0126	SNP0162	SNP0119	SNP0111	SNP0129	SNP0142	SNP0145	SNP0132
201	183	169	219	200	218	186	200	216	198
SNP0177	SNP0163	SNP0107	SNP0100	SNP0154	SNP0178	SNP0146	SNP0101	SNP0144	SNP0171
207	215	206	209	212	187	199	213	193	229
SNP0140	SNP0139	SNP0098	SNP0110	SNP0147	SNP0131	SNP0137	SNP0113	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						

\$OUT.snp.mac\$GENE\_03

SNP0254	SNP0273	SNP0199	SNP0266	SNP0195	SNP0186	SNP0220	SNP0256	SNP0236	SNP0214
219	197	220	196	183	212	202	206	214	195
SNP0196	SNP0225	SNP0224	SNP0270	SNP0188	SNP0209	SNP0204	SNP0264	SNP0233	SNP0279
186	207	221	198	183	211	214	196	200	189
SNP0238	SNP0250	SNP0267	SNP0226	SNP0275	SNP0205	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.snp.mac\$GENE\_04

SNP0303	SNP0362	SNP0387	SNP0346	SNP0348	SNP0332	SNP0313	SNP0288	SNP0309	SNP0329
206	207	223	194	191	207	203	190	212	218
SNP0377	SNP0300	SNP0320	SNP0347	SNP0290	SNP0344	SNP0319	SNP0343	SNP0339	SNP0304
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
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	SNP0363	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	SNP0325	SNP0312	SNP0374	SNP0331	SNP0342	SNP0368	SNP0365
190	193	186	192	166	190	223	194	222	184
SNP0316									
214									

\$OUT.snp.mac\$GENE\_05

SNP0460	SNP0474	SNP0404	SNP0466	SNP0462	SNP0429	SNP0410	SNP0419	SNP0409	SNP0416
184	214	199	213	171	183	189	220	197	174
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							

\$OUT.snp.mac\$GENE\_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	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
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						

\$OUT.snp.mac\$GENE\_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.snp.mac\$GENE\_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	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
217	194	201	193	201	225	197	194	181	191
SNP0736	SNP0690	SNP0712	SNP0692	SNP0698	SNP0709				
217	223	200	217	191	221				

\$OUT.snp.mac\$GENE\_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.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	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	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"
```

After finishing to use SSD files, please close them.

```
> Close_SSD()
```

Close the opened SSD file: /tmp/RtmpAbF76/Rbuild2fc483a52fb/SKAT/vignettes/Example1.SSD

### 3.1 Plink Binary format files: SKATBinary

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,]
```

	SetID	P.value	N.Marker.All	N.Marker.Test	MAC	m	Method.bin	MAP
1	1	0.92753378	11	11	18	17	ER	2.512149e-07
2	2	0.24947578	2	2	3	3	ER	3.544808e-02
3	3	0.60706345	7	7	19	19	ER	3.312382e-08
4	4	0.08566388	11	11	19	18	ER	6.640864e-08
5	5	0.63625247	4	4	18	18	ER	2.721199e-07

```
>
```

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 ( $\rho$ ). 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  $\beta$ s, and  $p_2$  is the proportion of negative (or positive)  $\beta$ s among the non-zero  $\beta$ 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
      0.01      0.001      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

```

```

>

```