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 appli

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

```
[1] 0.1338658

>
```

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="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 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 ρs. 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 boostrap.
> 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-O
> 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.

```
> data(SKAT.example.ChrX)
> attach(SKAT.example.ChrX)
> Z = SKAT.example.ChrX$Z
> ############################################################
> #        Compute the P-value of SKAT
>
> # binary trait
> obj.x<-SKAT_Null_Model_ChrX(y ~ x1 +x2 + Gender, SexVar="Gender", out_type="D", data=SKAT.ex
> # run SKAT-O
> SKAT_ChrX(Z, obj.x, method="SKATO")$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-O
> 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
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SNP0557 SNP0563 SNP0511 SNP0495 SNP0583 SNP0536 SNP0516 SNP0528 SNP0509 SNP0561
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SNP0492 SNP0567 SNP0506 SNP0556
    202     211     183     185

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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
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SNP0683 SNP0663 SNP0640 SNP0592 SNP0679 SNP0658 SNP0611 SNP0676 SNP0617 SNP0634
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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
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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
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SNP0680 SNP0638 SNP0665 SNP0637 SNP0622 SNP0647 SNP0654 SNP0601 SNP0585 SNP0646
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SNP0650 SNP0614 SNP0605 SNP0590
    185     211     195     179

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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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SNP0773 SNP0697 SNP0696 SNP0766 SNP0708 SNP0695 SNP0711 SNP0761 SNP0746 SNP0729
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SNP0762 SNP0784 SNP0706 SNP0744 SNP0757 SNP0776 SNP0760 SNP0724 SNP0751 SNP0691
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SNP0752 SNP0750 SNP0721 SNP0704 SNP0701 SNP0713 SNP0780 SNP0743 SNP0770 SNP0718
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SNP0782 SNP0774 SNP0737 SNP0745 SNP0769 SNP0723 SNP0693 SNP0716 SNP0758 SNP0694
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SNP0764 SNP0767 SNP0719 SNP0739 SNP0754 SNP0783 SNP0700 SNP0759 SNP0717 SNP0728
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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
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SNP0792 SNP0831 SNP0866 SNP0858 SNP0847 SNP0860 SNP0791 SNP0824 SNP0787 SNP0819
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SNP0839 SNP0813 SNP0803 SNP0874 SNP0876 SNP0851 SNP0794 SNP0814 SNP0827 SNP0788
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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
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SNP0826 SNP0836 SNP0785 SNP0834 SNP0820 SNP0833 SNP0865 SNP0840 SNP0862 SNP0810
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$OUT.snp.mac$GENE_10
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 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
```

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 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
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SNP0014 SNP0036 SNP0074 SNP0017 SNP0016 SNP0022 SNP0087 SNP0094 SNP0057 SNP0028
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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
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SNP0049 SNP0039 SNP0067 SNP0076 SNP0003 SNP0018 SNP0040 SNP0079 SNP0009 SNP0024
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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
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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
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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
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    194      208      225      208      206      209      206      208      182      193
SNP0150 SNP0153 SNP0126 SNP0162 SNP0119 SNP0111 SNP0129 SNP0142 SNP0145 SNP0132
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SNP0177 SNP0163 SNP0107 SNP0100 SNP0154 SNP0178 SNP0146 SNP0101 SNP0144 SNP0171
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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
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SNP0122 SNP0123 SNP0155 SNP0125
    166      200      239      203

$OUT.snp.mac$GENE_03
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SNP0196 SNP0225 SNP0224 SNP0270 SNP0188 SNP0209 SNP0204 SNP0264 SNP0233 SNP0279
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SNP0238 SNP0250 SNP0267 SNP0226 SNP0275 SNP0205 SNP0280 SNP0286 SNP0207 SNP0206
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SNP0222 SNP0272 SNP0245 SNP0232 SNP0241 SNP0265 SNP0230 SNP0249 SNP0269 SNP0284
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SNP0262 SNP0244 SNP0283 SNP0240 SNP0218 SNP0235 SNP0237 SNP0247 SNP0242 SNP0197
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SNP0223 SNP0282 SNP0239 SNP0271 SNP0227 SNP0246 SNP0285 SNP0198 SNP0217 SNP0213
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SNP0184 SNP0187 SNP0193 SNP0253 SNP0251 SNP0185 SNP0201 SNP0182 SNP0258 SNP0281
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SNP0234 SNP0216 SNP0211 SNP0191 SNP0192 SNP0260 SNP0221 SNP0257 SNP0181 SNP0252
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SNP0243 SNP0208 SNP0259 SNP0268 SNP0203 SNP0248 SNP0231 SNP0263
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$OUT.snp.mac$GENE_04
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SNP0356 SNP0340 SNP0370 SNP0327 SNP0351 SNP0335 SNP0314 SNP0380 SNP0336 SNP0333
    214      218      207      204      201      208      206      194      208      214
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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
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SNP0326 SNP0358 SNP0322 SNP0292 SNP0298 SNP0369 SNP0360 SNP0355 SNP0338 SNP0384
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SNP0294 SNP0296 SNP0361 SNP0325 SNP0312 SNP0374 SNP0331 SNP0342 SNP0368 SNP0365
    190     193     186     192     166     190     223     194     222     184
SNP0316
    214

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SNP0476 SNP0488 SNP0486 SNP0435 SNP0458 SNP0467 SNP0449 SNP0480 SNP0478 SNP0394
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SNP0442 SNP0456 SNP0447 SNP0421 SNP0444 SNP0405 SNP0414 SNP0413 SNP0475 SNP0477
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SNP0430 SNP0393 SNP0481 SNP0484 SNP0439 SNP0454 SNP0389 SNP0390 SNP0459 SNP0487
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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
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SNP0418 SNP0420 SNP0438 SNP0482 SNP0396 SNP0406 SNP0483 SNP0432 SNP0451 SNP0425
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SNP0436 SNP0443 SNP0464 SNP0471 SNP0433 SNP0434 SNP0485 SNP0463 SNP0489 SNP0457
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SNP0520 SNP0503 SNP0493 SNP0533 SNP0569 SNP0504 SNP0576 SNP0580 SNP0527 SNP0577
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SNP0519 SNP0521 SNP0512 SNP0564 SNP0498 SNP0579 SNP0558 SNP0531 SNP0549 SNP0494
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SNP0557 SNP0563 SNP0511 SNP0495 SNP0583 SNP0536 SNP0516 SNP0528 SNP0509 SNP0561
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SNP0492 SNP0567 SNP0506 SNP0556
    202     211     183     185

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SNP0683 SNP0663 SNP0640 SNP0592 SNP0679 SNP0658 SNP0611 SNP0676 SNP0617 SNP0634
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SNP0627 SNP0588 SNP0624 SNP0625 SNP0639 SNP0599 SNP0635 SNP0593 SNP0596 SNP0645
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SNP0680 SNP0638 SNP0665 SNP0637 SNP0622 SNP0647 SNP0654 SNP0601 SNP0585 SNP0646
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SNP0650 SNP0614 SNP0605 SNP0590
    185     211     195     179

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SNP0773 SNP0697 SNP0696 SNP0766 SNP0708 SNP0695 SNP0711 SNP0761 SNP0746 SNP0729
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SNP0781 SNP0710 SNP0722 SNP0742 SNP0753 SNP0689 SNP0735 SNP0730 SNP0731 SNP0768
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SNP0762 SNP0784 SNP0706 SNP0744 SNP0757 SNP0776 SNP0760 SNP0724 SNP0751 SNP0691
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SNP0752 SNP0750 SNP0721 SNP0704 SNP0701 SNP0713 SNP0780 SNP0743 SNP0770 SNP0718
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SNP0792 SNP0831 SNP0866 SNP0858 SNP0847 SNP0860 SNP0791 SNP0824 SNP0787 SNP0819
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    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

$OUT.snp.mac$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"
```

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
[1] 0

$ID
NULL
```

```
> # 1 gene is significnat with controling 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
```

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    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: /private/var/folders/1n/hmqxyn1x5vz9669g58n65_f40000gn/T/RtmpoeEF0f
```

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-O
> 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 (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 βs, and p_2 is the proportion of negative (or positive) βs among the non-zero βs.

```
> 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

>
```