Analysis of BMI GIANT GWAS data - Scott approach

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Load the relevant libraries:

```
library(readr)
library(dplyr)
library(fdrtool)
library(betareg)
library(splines)
library(Hmisc)
library(ggplot2)
library(reshape2)
library(FDRreg)
```

Load the .RData file with the BMI GIANT GWAS meta-analysis data:

```
load("BMI_GIANT_GWAS.RData")

tot <- BMI_GIANT_GWAS
```

Estimate fraction of true null hypotheses in a regression framework using the Scott approach

Create the design matrix, using natural cubic splines with 5 degrees of freedom to model `N` and 3 discrete categories for the MAFs:

```
X <- model.matrix(~ splines::ns(N,5) + Freq_MAF_Int_Hapmap, data = tot)[,-1]
dim(X)
```

```
## [1] 2500573       7
```

```
head(X)
```

```
##   splines::ns(N, 5)1 splines::ns(N, 5)2 splines::ns(N, 5)3
## 1       4.414107e-01       5.538398e-01      -0.0017421409
## 2       0.000000e+00       3.954615e-10      -0.1655612193
## 3       3.884106e-05       9.880678e-01       0.0099138318
## 4       3.209714e-04       9.891039e-01       0.0088153851
## 5       9.327150e-02       9.061998e-01       0.0002901038
## 6       6.724476e-04       9.894590e-01       0.0082264435
##   splines::ns(N, 5)4 splines::ns(N, 5)5 Freq_MAF_Int_Hapmap[0.127,0.302)
## 1       0.0034871548      -0.0017450139                                 0
## 2       0.3336072837       0.8319539352                                 0
## 3       0.0039611703      -0.0019816905                                 1
## 4       0.0035221381      -0.0017623939                                 1
## 5       0.0002264943      -0.0001133405                                 1
## 6       0.0032867973      -0.0016447160                                 0
```

```
##   Freq_MAF_Int_Hapmap[0.302,0.500]
## 1                                1
## 2                                1
## 3                                0
## 4                                0
## 5                                0
## 6                                1
```

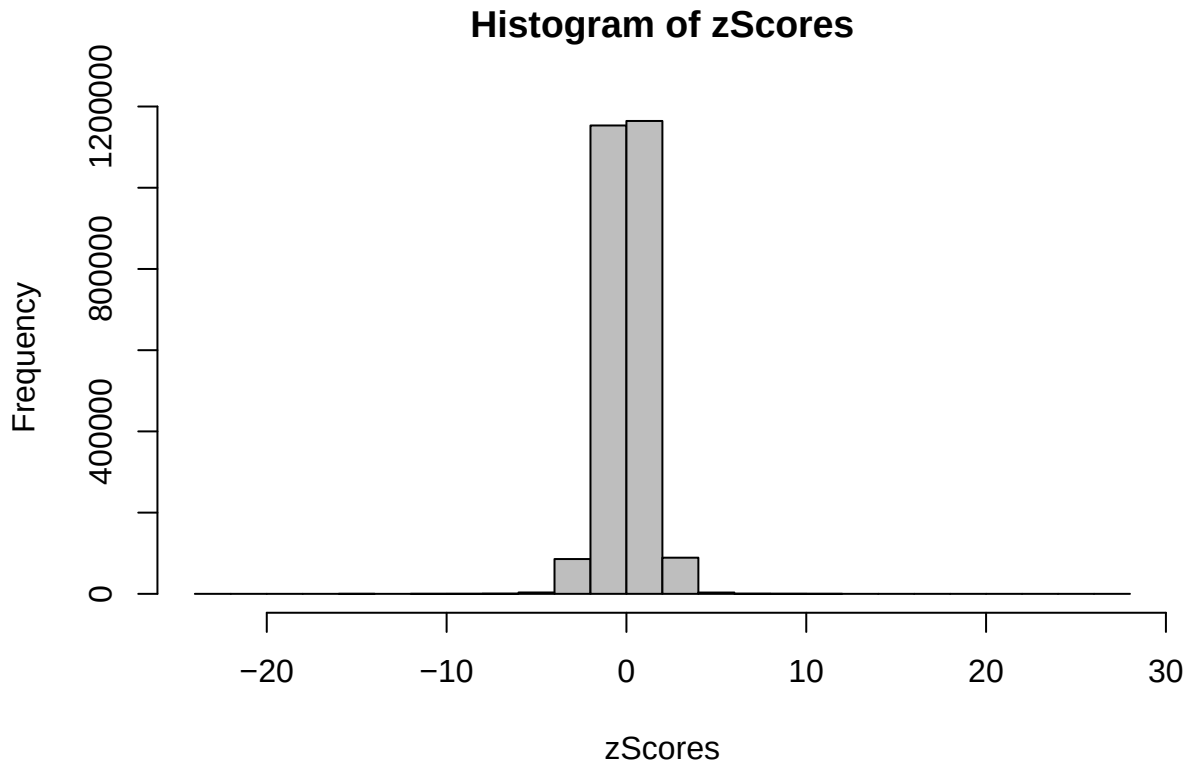
Run code to estimate the fraction of true null hypotheses within a regression framework with the design matrix specified above:

```
##first get z-scores, which are needed for the Scott approach
zScores <- tot$b/tot$se

range(zScores)
```

```
## [1] -22.41379  26.96667
```

```
hist(zScores, col="grey")
```




```
##run FDRreg
fdr <- FDRreg(zScores, X,
              nulltype = 'empirical',
              control=list(lambda=1))
```

```
## Warning in doTryCatch(return(expr), name, parentenv, handler): f(z)
## misfit = -0.3. Rerun with increased df.f(z) misfit = -0.7. Rerun with
## increased df.f(z) misfit = 2.3. Rerun with increased df.f(z) misfit = 2.7.
## Rerun with increased df.f(z) misfit = -0.1. Rerun with increased df.f(z)
## misfit = 1. Rerun with increased df.f(z) misfit = 0. Rerun with increased
## df.f(z) misfit = 1. Rerun with increased df.f(z) misfit = 0. Rerun with
## increased df.f(z) misfit = 0. Rerun with increased df.f(z) misfit = 0.
## Rerun with increased df.f(z) misfit = 2. Rerun with increased df.f(z)
## misfit = 1. Rerun with increased df.f(z) misfit = 1. Rerun with increased
## df.f(z) misfit = 0. Rerun with increased df.f(z) misfit = 0. Rerun with
## increased df.f(z) misfit = 0. Rerun with increased df.f(z) misfit = 1.
## Rerun with increased df.f(z) misfit = 0. Rerun with increased df.f(z)
## misfit = 0. Rerun with increased df.f(z) misfit = 2.8. Rerun with increased
## df.f(z) misfit = 36. Rerun with increased df.f(z) misfit = 6.4. Rerun
## with increased df.f(z) misfit = 2.8. Rerun with increased df.f(z) misfit
## = 0.3. Rerun with increased df.f(z) misfit = -2.1. Rerun with increased
## df.f(z) misfit = -2. Rerun with increased df.f(z) misfit = -4.1. Rerun
## with increased df.f(z) misfit = -5.4. Rerun with increased df.f(z) misfit
## = -3.7. Rerun with increased df.f(z) misfit = -6. Rerun with increased
## df.f(z) misfit = -6.3. Rerun with increased df.f(z) misfit = -5.7. Rerun
## with increased df.f(z) misfit = -2.6. Rerun with increased df.f(z) misfit
## = -3.5. Rerun with increased df.f(z) misfit = 0.1. Rerun with increased
## df.f(z) misfit = -0.5. Rerun with increased df.f(z) misfit = 0.6. Rerun
## with increased df.f(z) misfit = 2.7. Rerun with increased df.f(z) misfit
## = 9.8. Rerun with increased df.f(z) misfit = 14.1. Rerun with increased
## df.f(z) misfit = 29.5. Rerun with increased df.f(z) misfit = 29.5. Rerun
## with increased df.f(z) misfit = 39.5. Rerun with increased df.f(z) misfit
## = 50.8. Rerun with increased df.f(z) misfit = 51.5. Rerun with increased
## df.f(z) misfit = 47.8. Rerun with increased df.f(z) misfit = 65.6. Rerun
## with increased df.f(z) misfit = 44.9. Rerun with increased df.f(z) misfit
## = 34.1. Rerun with increased df.f(z) misfit = 53.9. Rerun with increased
## df.f(z) misfit = 45.8. Rerun with increased df.f(z) misfit = 52.5. Rerun
## with increased df.f(z) misfit = 48.6. Rerun with increased df.f(z) misfit
## = 41.6. Rerun with increased df.f(z) misfit = 35.5. Rerun with increased
## df.f(z) misfit = 25.6. Rerun with increased df.f(z) misfit = 17.1. Rerun
## with increased df.f(z) misfit = -4.2. Rerun with increased df.f(z) misfit
## = -17.6. Rerun with increased df.f(z) misfit = -29.8. Rerun with increased
## df.f(z) misfit = -37.8. Rerun with increased df.f(z) misfit = -30.2. Rerun
## with increased df.f(z) misfit = -16.7. Rerun with increased df.f(z) misfit
## = 4.1. Rerun with increased df.f(z) misfit = 24.4. Rerun with increased
## df.f(z) misfit = 25.1. Rerun with increased df.f(z) misfit = 39.9. Rerun
## with increased df.f(z) misfit = 20. Rerun with increased df.f(z) misfit
## = 3.2. Rerun with increased df.f(z) misfit = -12.1. Rerun with increased
## df.f(z) misfit = -39.9. Rerun with increased df.f(z) misfit = -40. Rerun
## with increased df.f(z) misfit = -30.2. Rerun with increased df.f(z) misfit
## = -12.5. Rerun with increased df.f(z) misfit = 5.4. Rerun with increased
## df.f(z) misfit = 27.5. Rerun with increased df.f(z) misfit = 29.9. Rerun
## with increased df.f(z) misfit = 32.5. Rerun with increased df.f(z) misfit
## = 42.2. Rerun with increased df.f(z) misfit = 43.5. Rerun with increased
## df.f(z) misfit = 45.1. Rerun with increased df.f(z) misfit = 41.7. Rerun
## with increased df.f(z) misfit = 38.5. Rerun with increased df.f(z) misfit
## = 36.8. Rerun with increased df.f(z) misfit = 50.4. Rerun with increased
## df.f(z) misfit = 17.9. Rerun with increased df.f(z) misfit = 15.1. Rerun
## with increased df.f(z) misfit = 30. Rerun with increased df.f(z) misfit
```

```
## = 42.3. Rerun with increased df.f(z) misfit = 21.6. Rerun with increased
## df.f(z) misfit = 16.8. Rerun with increased df.f(z) misfit = 25. Rerun
## with increased df.f(z) misfit = 8. Rerun with increased df.f(z) misfit
## = 2. Rerun with increased df.f(z) misfit = 3.4. Rerun with increased
## df.f(z) misfit = -0.7. Rerun with increased df.f(z) misfit = -3.5. Rerun
## with increased df.f(z) misfit = -6. Rerun with increased df.f(z) misfit
## = -7.3. Rerun with increased df.f(z) misfit = -7.5. Rerun with increased
## df.f(z) misfit = -6.3. Rerun with increased df.f(z) misfit = -5. Rerun
## with increased df.f(z) misfit = -4.2. Rerun with increased df.f(z) misfit
## = -0.2. Rerun with increased df.f(z) misfit = 1.7. Rerun with increased
## df.f(z) misfit = 1.7. Rerun with increased df.f(z) misfit = 8.2. Rerun
## with increased df.f(z) misfit = 1.9. Rerun with increased df.f(z) misfit
## = 3. Rerun with increased df.f(z) misfit = 2. Rerun with increased df.f(z)
## misfit = 4. Rerun with increased df.f(z) misfit = 5. Rerun with increased
## df.f(z) misfit = 11. Rerun with increased df.f(z) misfit = 4. Rerun with
## increased df.f(z) misfit = 3. Rerun with increased df.f(z) misfit = 0.
## Rerun with increased df.f(z) misfit = 0. Rerun with increased df.f(z)
## misfit = 0. Rerun with increased df.f(z) misfit = 0. Rerun with increased
## df.f(z) misfit = 0. Rerun with increased df.f(z) misfit = 0. Rerun with
## increased df.f(z) misfit = 0. Rerun with increased df.f(z) misfit = 0.
## Rerun with increased df.f(z) misfit = 0. Rerun with increased df.f(z)
## misfit = 0. Rerun with increased df.f(z) misfit = 0. Rerun with increased
## df.f(z) misfit = 0. Rerun with increased df.f(z) misfit = 0. Rerun with
## increased df.f(z) misfit = 2. Rerun with increased df.f(z) misfit = 1.
## Rerun with increased df.f(z) misfit = 0. Rerun with increased df.f(z)
## misfit = 0.9. Rerun with increased df.f(z) misfit = -0.2. Rerun with
## increased df.f(z) misfit = 0.4. Rerun with increased df.f(z) misfit = 0.
## Rerun with increased df.f(z) misfit = -1.1. Rerun with increased df.f(z)
## misfit = 0.1. Rerun with increased df.f(z) misfit = -1.7. Rerun with
## increased df.f(z) misfit = -1.5. Rerun with increased df.f(z) misfit =
## -0.7. Rerun with increased df.f(z) misfit = -0.2. Rerun with increased
## df.f(z) misfit = 1.4. Rerun with increased df.f(z) misfit = 1.4. Rerun with
## increased df.f(z) misfit = 0.9. Rerun with increased df.f(z) misfit = -0.4.
## Rerun with increased df.f(z) misfit = -0.8. Rerun with increased df.f(z)
## misfit = 0.2. Rerun with increased df.
```

```
##get prior probabilities
pi0EstScott <- 1-fdr$priorprob
```

Save results:

```
save(x=pi0EstScott, file="BMI_GIANT_GWAS_results_Scott.RData")
```

Session Information

```
devtools::session_info()
```

```
## Session info -------------------------------------------------------------

##  setting  value
##  version  R version 3.3.1 (2016-06-21)
```

```
##  system   x86_64, mingw32
##  ui       RTerm
##  language (EN)
##  collate  English_United States.1252
##  tz       America/New_York
##  date     2016-10-26

## Packages -----------------------------------------------------------------

##  package      * version date       source
##  acepack        1.3-3.3 2014-11-24 CRAN (R 3.3.0)
##  assertthat     0.1     2013-12-06 CRAN (R 3.3.1)
##  BayesLogit   * 0.5.1   2014-07-21 CRAN (R 3.3.0)
##  betareg      * 3.0-5   2014-09-25 CRAN (R 3.3.1)
##  BiocStyle    * 2.0.2   2016-05-16 Bioconductor
##  chron          2.3-47  2015-06-24 CRAN (R 3.3.1)
##  cluster        2.0.4   2016-04-18 CRAN (R 3.3.1)
##  codetools      0.2-14  2015-07-15 CRAN (R 3.3.1)
##  colorspace     1.2-6   2015-03-11 CRAN (R 3.3.1)
##  data.table     1.9.6   2015-09-19 CRAN (R 3.3.1)
##  DBI            0.4-1   2016-05-08 CRAN (R 3.3.1)
##  devtools       1.12.0  2016-06-24 CRAN (R 3.3.1)
##  digest         0.6.9   2016-01-08 CRAN (R 3.3.1)
##  dplyr        * 0.5.0   2016-06-24 CRAN (R 3.3.1)
##  evaluate       0.9     2016-04-29 CRAN (R 3.3.1)
##  fda          * 2.4.4   2014-12-16 CRAN (R 3.3.1)
##  FDRreg       * 0.2-1   2016-08-30 Github (jgscott/FDRreg@8025d1a)
##  fdrtool      * 1.2.15  2015-07-08 CRAN (R 3.3.0)
##  flexmix        2.3-13  2015-01-17 CRAN (R 3.3.1)
##  foreign        0.8-66  2015-08-19 CRAN (R 3.3.1)
##  formatR        1.4     2016-05-09 CRAN (R 3.3.1)
##  Formula      * 1.2-1   2015-04-07 CRAN (R 3.3.0)
##  ggdendro       0.1-20  2016-04-27 CRAN (R 3.3.1)
##  ggplot2      * 2.1.0   2016-03-01 CRAN (R 3.3.1)
##  gridExtra      2.2.1   2016-02-29 CRAN (R 3.3.1)
##  gtable         0.2.0   2016-02-26 CRAN (R 3.3.1)
##  Hmisc        * 3.17-4  2016-05-02 CRAN (R 3.3.1)
##  htmltools      0.3.5   2016-03-21 CRAN (R 3.3.1)
##  knitr          1.13    2016-05-09 CRAN (R 3.3.1)
##  lattice      * 0.20-33 2015-07-14 CRAN (R 3.3.1)
##  latticeExtra   0.6-28  2016-02-09 CRAN (R 3.3.1)
##  lazyeval       0.2.0   2016-06-12 CRAN (R 3.3.1)
##  lmtest         0.9-34  2015-06-06 CRAN (R 3.3.1)
##  magrittr       1.5     2014-11-22 CRAN (R 3.3.1)
##  MASS           7.3-45  2016-04-21 CRAN (R 3.3.1)
##  Matrix       * 1.2-6   2016-05-02 CRAN (R 3.3.1)
##  memoise        1.0.0   2016-01-29 CRAN (R 3.3.1)
##  modeltools     0.2-21  2013-09-02 CRAN (R 3.3.0)
##  mosaic         0.14.4  2016-07-29 CRAN (R 3.3.1)
##  mosaicData     0.14.0  2016-06-17 CRAN (R 3.3.1)
##  munsell        0.4.3   2016-02-13 CRAN (R 3.3.1)
##  mvtnorm      * 1.0-5   2016-02-02 CRAN (R 3.3.0)
##  nnet           7.3-12  2016-02-02 CRAN (R 3.3.1)
##  plyr           1.8.4   2016-06-08 CRAN (R 3.3.1)
```

```
##  R6             2.1.2   2016-01-26 CRAN (R 3.3.1)
##  RColorBrewer   1.1-2   2014-12-07 CRAN (R 3.3.0)
##  Rcpp           0.12.6  2016-07-19 CRAN (R 3.3.1)
##  readr        * 0.2.2   2015-10-22 CRAN (R 3.3.1)
##  reshape2     * 1.4.1   2014-12-06 CRAN (R 3.3.1)
##  rmarkdown      1.0     2016-07-08 CRAN (R 3.3.1)
##  rpart          4.1-10  2015-06-29 CRAN (R 3.3.1)
##  sandwich       2.3-4   2015-09-24 CRAN (R 3.3.1)
##  scales         0.4.0   2016-02-26 CRAN (R 3.3.1)
##  stringi        1.1.1   2016-05-27 CRAN (R 3.3.0)
##  stringr        1.0.0   2015-04-30 CRAN (R 3.3.1)
##  survival     * 2.39-4  2016-05-11 CRAN (R 3.3.1)
##  tibble         1.1     2016-07-04 CRAN (R 3.3.1)
##  tidyr          0.5.1   2016-06-14 CRAN (R 3.3.1)
##  withr          1.0.2   2016-06-20 CRAN (R 3.3.1)
##  yaml           2.1.13  2014-06-12 CRAN (R 3.3.1)
##  zoo            1.7-13  2016-05-03 CRAN (R 3.3.1)
```