iCARE(Individualized Coherent Absolute Risk Estimators) Package

April 10, 2025

```
> library(iCARE)
```

Example 1.A

Load the breast cancer data.

```
> data("bc_data", package="iCARE")
```

In this example, we will estimate the risk of breast cancer in ages 50-80. A SNP-only model is fit, with no specific genotypes supplied for estimation. The population disease rates are from SEER.

```
> res_snps_miss = computeAbsoluteRisk(model.snp.info = bc_72_snps,
+                       model.disease.incidence.rates = bc_inc,
+                       model.competing.incidence.rates = mort_inc,
+                       apply.age.start = 50,
+                       apply.age.interval.length = 30,
+                       return.refs.risk=TRUE)
```

```
Note: You did not provide apply.snp.profile.  Will impute SNPs for 10000 people.
If require more, please provide apply.snp.profile input.
[1] "Note: As specified, the model does not adjust SNP imputations for family history."
   user  system elapsed
 12.188   0.146  12.335
```

Compute a summary of the risks and visualize the results

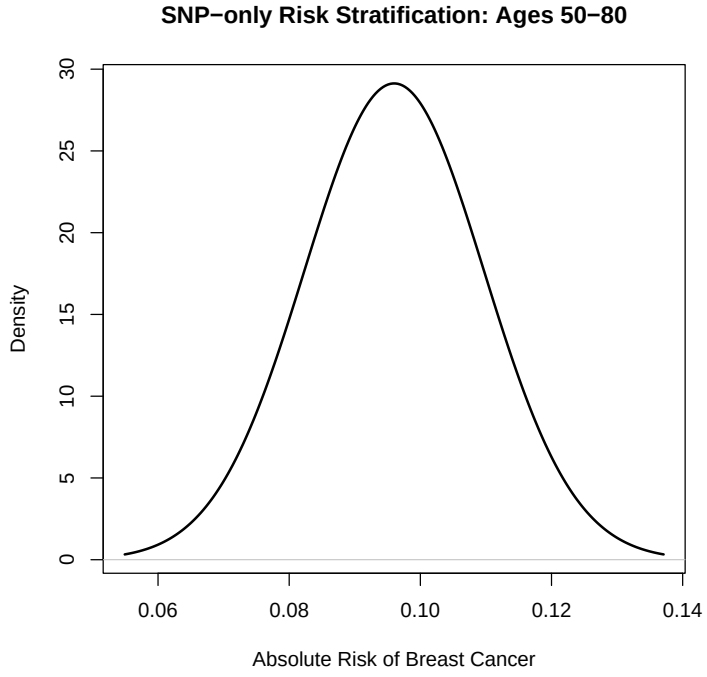
```
> summary(res_snps_miss$risk)
```

```
 Risk_Estimate
 Min.   :0.09601
 1st Qu.:0.09601
 Median :0.09601
 Mean   :0.09601
 3rd Qu.:0.09601
 Max.   :0.09601
```

```
> summary(res_snps_miss$refs.risk)
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.05347 0.08648 0.09516 0.09601 0.10428 0.16500
```

```
> plot(density(res_snps_miss$risk), lwd=2,
+   main="SNP-only Risk Stratification: Ages 50-80",
+   xlab="Absolute Risk of Breast Cancer")
```



Example 1.B

In this example, we will again estimate the risk of breast cancer in ages 50-80. This time however, three specific genotypes are supplied for estimation (with some missing data). The argument return.refs.risk = TRUE, includes the referent dataset risks be included in results.

```
> res_snps_dat = computeAbsoluteRisk(model.snp.info = bc_72_snps,
+                                    model.disease.incidence.rates = bc_inc,
+                                    model.competing.incidence.rates = mort_inc,
+                                    apply.age.start = 50,
+                                    apply.age.interval.length = 30,
+                                    apply.snp.profile = new_snp_prof,
+                                    return.refs.risk = TRUE)
```

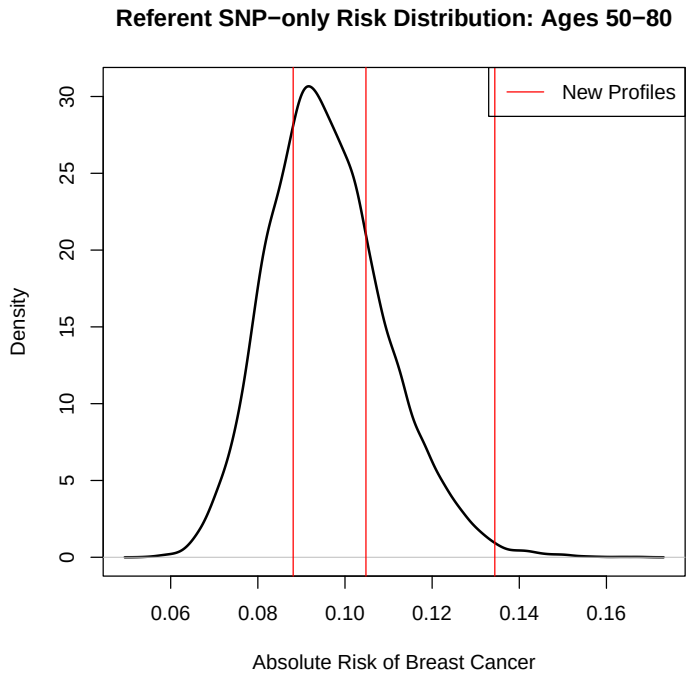
```
[1] "Note: As specified, the model does not adjust SNP imputations for family history."
   user  system elapsed
  0.344   0.032   0.375
```

```
> names(res_snps_dat)
```

```
[1] "risk"      "details"   "beta.used" "refs.risk"
```

Visualize the Results

```
> plot(density(res_snps_dat$refs.risk), lwd=2,
+    main="Referent SNP-only Risk Distribution: Ages 50-80",
+    xlab="Absolute Risk of Breast Cancer")
> abline(v=res_snps_dat$risk, col="red")
> legend("topright", legend="New Profiles", col="red", lwd=1)
```



Example 2

In this example, we will estimate the risk of breast cancer in ages 50-80 by fitting a model with 13 risk factors and 72 SNPs.

```
> res_covs_snps = computeAbsoluteRisk(model.formula=bc_model_formula,
+                                     model.cov.info=bc_model_cov_info,
+                                     model.snp.info=bc_72_snps,
+                                     model.log.RR=bc_model_log_or,
+                                     model.ref.dataset=ref_cov_dat,
+                                     model.disease.incidence.rates=bc_inc,
+                                     model.competing.incidence.rates=mort_inc,
+                                     model.bin.fh.name="famhist",
+                                     apply.age.start=50,
+                                     apply.age.interval.length=30,
+                                     apply.cov.profile=new_cov_prof,
```

```
+                                          apply.snp.profile=new_snp_prof,
+                                          return.refs.risk=TRUE)

   user  system elapsed
  1.062   0.266   1.328
```

Display details of the fit

```
> print(res_covs_snps$details)

  Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132
1        50      80     0.1024411       NA         NA         NA         NA
2        50      80     0.0901060        2          0         NA         NA
3        50      80     0.1687748        2          0          1          1
  rs12048493 rs6678914 rs4245739 rs72755295 rs12710696 rs4849887 rs2016394
1         NA         0         0          0          0         0         0
2         NA        NA        NA         NA          1         1         0
3          1         1         1          0          2         0         0
  rs1550623 rs16857609 rs6762644 rs4973768 rs12493607 rs6796502 rs9790517
1         0          0         0         1          1         0         1
2         0          2         1         1          1         1         2
3         0          0         0         2          1         0         1
  rs6828523 rs10069690 rs13162653 rs2012709 rs10941679 rs10472076 rs1353747
1         0          1          2         0          0          2         0
2         0          0          1         0          0          1         1
3         0          0          1         0          0          0         1
  rs7707921 rs1432679 rs11242675 rs204247 rs9257408 rs4593472 rs720475
1         0         1          2        0         0         1        1
2         0         0          1        2         1         1        0
3         1         2          1        2         1         1        0
  rs9693444 rs13365225 rs6472903 rs2943559 rs13267382 rs11780156 rs1011970
1         1          1         1         0          0          0         0
2         0          0         1         0          2          1         1
3         1          1         0         0          1          0         0
  rs10759243 rs2380205 rs7072776 rs11814448 rs7904519 rs11199914 rs554219
1          0         2         2          0         0          1        1
2          1         0         0          0         0          0        0
3          1         1         1          0         2          0        1
  rs75915166 rs11820646 rs12422552 rs17356907 rs1292011 rs11571833 rs2236007
1          0          1          1          0         1          0         1
2          0          0          0          0         0          0         0
3          0          1          1          0         2          0         0
  rs2588809 rs999737 rs941764 rs11627032 rs17817449 rs11075995 rs13329835
1         0        0        1          0          1          1          1
2         1        0        0          1          1          1          0
3         0        0        1          0          0          1          1
  rs146699004 rs745570 rs527616 rs1436904 rs6507583 rs4808801 rs3760982
1           0        0        0         0         0         1         0
2           1        2        0         0         0         1         1
3           1        2        1         1         0         1         1
  rs2284378 rs2823093 rs17879961 rs132390 rs6001930 famhist menarche_dec parity
```

```
1         1         1          0        0         0       0            8      0
2         1         0          0        0         0       0           10      0
3         0         0          0        0         0       0            1      0
  birth_dec agemeno_dec height_dec bmi_dec rd_menohrt rd2_everhrt_e
1         2           2          6      10          1             0
2         2           1          6       4          1             0
3         1           7          1      10          1             0
  rd2_everhrt_c rd2_currhrt alcoholdweek_dec ever_smoke
1             0           0                1          1
2             0           0                6          0
3             0           0                1          1
```

Session Information

```
> sessionInfo()

R version 4.5.0 beta (2025-04-02 r88102)
Platform: x86_64-pc-linux-gnu
Running under: Ubuntu 24.04.2 LTS

Matrix products: default
BLAS:   /home/biocbuild/bbs-3.22-bioc/R/lib/libRblas.so
LAPACK: /usr/lib/x86_64-linux-gnu/lapack/liblapack.so.3.12.0  LAPACK version 3.12.0

locale:
 [1] LC_CTYPE=en_US.UTF-8       LC_NUMERIC=C
 [3] LC_TIME=en_GB              LC_COLLATE=C
 [5] LC_MONETARY=en_US.UTF-8    LC_MESSAGES=en_US.UTF-8
 [7] LC_PAPER=en_US.UTF-8       LC_NAME=C
 [9] LC_ADDRESS=C               LC_TELEPHONE=C
[11] LC_MEASUREMENT=en_US.UTF-8 LC_IDENTIFICATION=C

time zone: America/New_York
tzcode source: system (glibc)

attached base packages:
[1] stats     graphics  grDevices utils     datasets  methods   base

other attached packages:
[1] iCARE_1.35.0  Hmisc_5.2-3   gtools_3.9.5  plotrix_3.8-4

loaded via a namespace (and not attached):
 [1] gtable_0.3.6      dplyr_1.1.4       compiler_4.5.0    rpart_4.1.24
 [5] tidyselect_1.2.1  htmlTable_2.4.3   stringr_1.5.1     gridExtra_2.3
 [9] cluster_2.1.8.1   scales_1.3.0      fastmap_1.2.0     ggplot2_3.5.2
[13] R6_2.6.1          generics_0.1.3    Formula_1.2-5     knitr_1.50
[17] htmlwidgets_1.6.4 backports_1.5.0   checkmate_2.3.2   tibble_3.2.1
[21] munsell_0.5.1     nnet_7.3-20       pillar_1.10.2     rlang_1.1.5
[25] stringi_1.8.7     xfun_0.52         cli_3.6.4         magrittr_2.0.3
```

```
[29] digest_0.6.37     grid_4.5.0        rstudioapi_0.17.1 base64enc_0.1-3
[33] lifecycle_1.0.4   vctrs_0.6.5       data.table_1.17.0 evaluate_1.0.3
[37] glue_1.8.0        colorspace_2.1-1  rmarkdown_2.29    foreign_0.8-90
[41] tools_4.5.0       pkgconfig_2.0.3   htmltools_0.5.8.1
```