

# iCARE(Individualized Coherent Absolute Risk Estimators) Package

November 1, 2022

```
> 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
9.508   0.275   9.790
```

Compute a summary of the risks and visualize the results

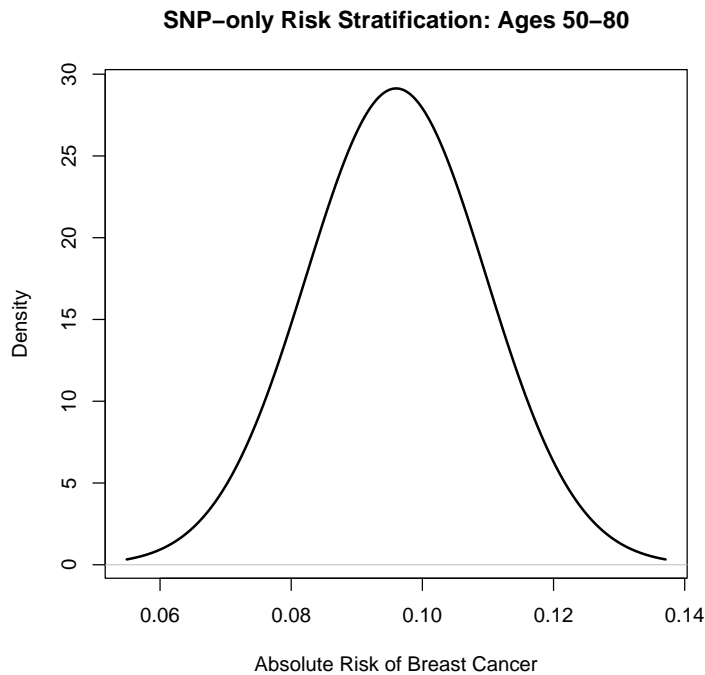
```
> summary(res_snps_miss$risk)
```

```
Risk_Estimate
Min.      :0.096
1st Qu.  :0.096
Median   :0.096
Mean     :0.096
3rd Qu.  :0.096
Max.     :0.096
```

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

| Min.    | 1st Qu. | Median  | Mean    | 3rd Qu. | Max.    |
|---------|---------|---------|---------|---------|---------|
| 0.05605 | 0.08656 | 0.09503 | 0.09600 | 0.10432 | 0.16371 |

```
> 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)
```

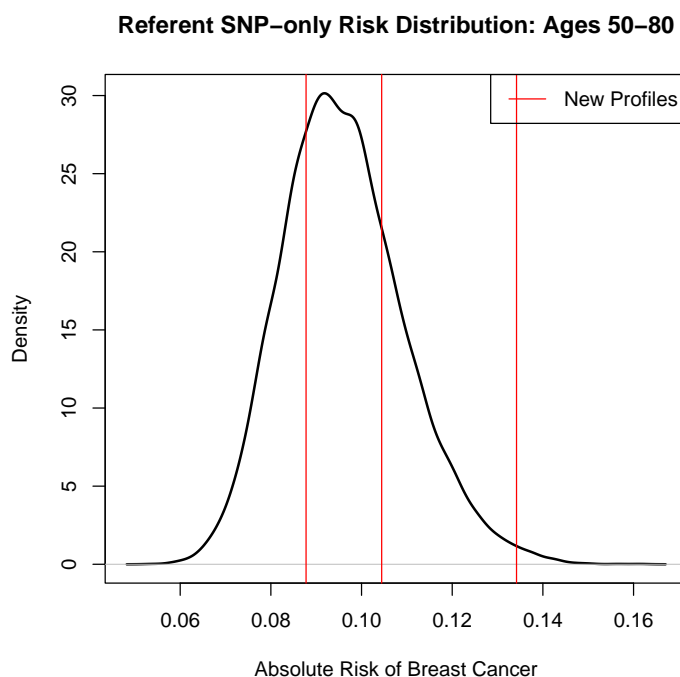
```
[1] "Note: As specified, the model does not adjust SNP imputations for family history."
      user system elapsed
0.353   0.231   0.588
```

```
> 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
1.622  0.345   1.970

Display details of the fit
> print(res_covs_snps$details)

Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132
1         50      80    0.10205812      NA      NA      NA      NA
2         50      80    0.08989262       2       0      NA      NA
3         50      80    0.16884863       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 | alcoholweek_dec | ever_smoke |            |               |    |   |
| 1 | 0             | 0           |                 | 1          | 1          |               |    |   |
| 2 | 0             | 0           |                 | 6          | 0          |               |    |   |
| 3 | 0             | 0           |                 | 1          | 1          |               |    |   |

## Session Information

```
> sessionInfo()
```

R version 4.2.1 Patched (2022-07-09 r82577)

Platform: x86\_64-apple-darwin17.0 (64-bit)

Running under: macOS Big Sur ... 10.16

Matrix products: default

BLAS: /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRblas.0.dylib

LAPACK: /Library/Frameworks/R.framework/Versions/4.2/Resources/lib/libRlapack.dylib

locale:

[1] C/en\_US.UTF-8/en\_US.UTF-8/C/en\_GB/en\_US.UTF-8

attached base packages:

[1] stats graphics grDevices utils datasets methods base

other attached packages:

[1] iCARE\_1.26.0 Hmisc\_4.7-1 ggplot2\_3.3.6 Formula\_1.2-4

[5] survival\_3.4-0 lattice\_0.20-45 gtools\_3.9.3 plotrix\_3.8-2

loaded via a namespace (and not attached):

|                         |                     |                 |
|-------------------------|---------------------|-----------------|
| [1] tidyselect_1.2.0    | xfun_0.34           | splines_4.2.1   |
| [4] colorspace_2.0-3    | vctr_0.5.0          | generics_0.1.3  |
| [7] htmltools_0.5.3     | base64enc_0.1-3     | utf8_1.2.2      |
| [10] rlang_1.0.6        | pillar_1.8.1        | foreign_0.8-83  |
| [13] glue_1.6.2         | withr_2.5.0         | DBI_1.1.3       |
| [16] RColorBrewer_1.1-3 | jpeg_0.1-9          | lifecycle_1.0.3 |
| [19] stringr_1.4.1      | munsell_0.5.0       | gtable_0.3.1    |
| [22] htmlwidgets_1.5.4  | latticeExtra_0.6-30 | knitr_1.40      |
| [25] fastmap_1.1.0      | fansi_1.0.3         | htmlTable_2.4.1 |
| [28] Rcpp_1.0.9         | scales_1.2.1        | backports_1.4.1 |
| [31] checkmate_2.1.0    | deldir_1.0-6        | interp_1.1-3    |
| [34] gridExtra_2.3      | png_0.1-7           | digest_0.6.30   |
| [37] stringi_1.7.8      | dplyr_1.0.10        | grid_4.2.1      |
| [40] cli_3.4.1          | tools_4.2.1         | magrittr_2.0.3  |

|      |                 |                   |                  |
|------|-----------------|-------------------|------------------|
| [43] | tibble_3.1.8    | cluster_2.1.4     | pkgconfig_2.0.3  |
| [46] | Matrix_1.5-1    | data.table_1.14.4 | assertthat_0.2.1 |
| [49] | rstudioapi_0.14 | R6_2.5.1          | rpart_4.1.19     |
| [52] | nnet_7.3-18     | compiler_4.2.1    |                  |