

iCARE(Individualized Coherent Absolute Risk Estimators) Package

April 26, 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
20.561   0.507   21.166
```

Compute a summary of the risks and visualize the results

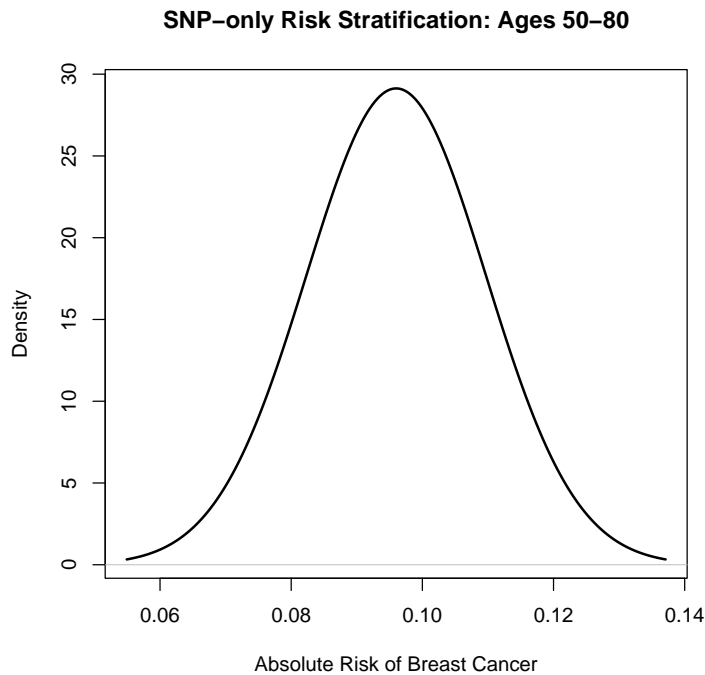
```
> summary(res_snps_miss$risk)
```

```
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. |
|--|---------|---------|---------|---------|---------|---------|
| | 0.05510 | 0.08656 | 0.09494 | 0.09601 | 0.10425 | 0.17861 |

```
> 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)
```

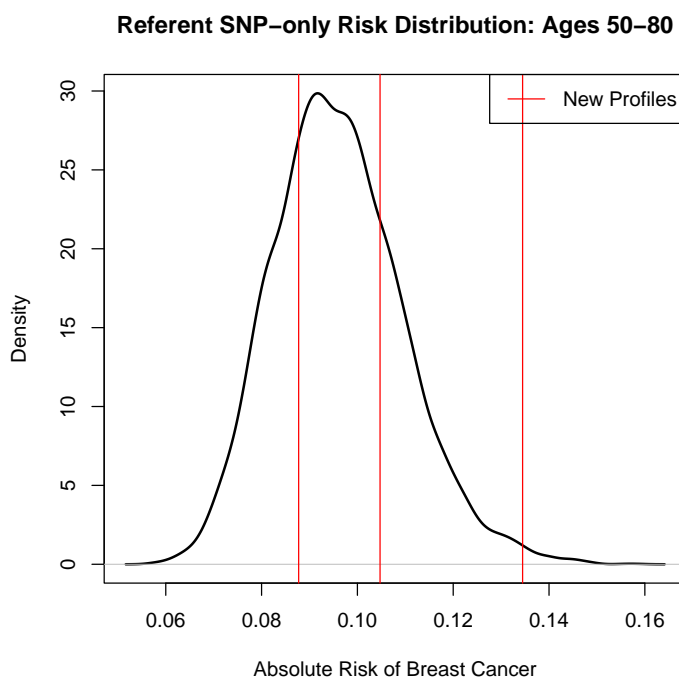
```
[1] "Note: As specified, the model does not adjust SNP imputations for family history."
      user system elapsed
0.606  0.123  0.730
```

```
> 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
2.723  0.356   3.081

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

Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132
1         50      80    0.10171652      NA      NA      NA      NA
2         50      80    0.09043045       2       0      NA      NA
3         50      80    0.16906016       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 4.2.0 RC (2022-04-19 r82224)
Platform: x86_64-apple-darwin17.0 (64-bit)
Running under: macOS Mojave 10.14.6
```

```
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_US.UTF-8/en_US.UTF-8
```

```
attached base packages:
```

```
[1] stats      graphics  grDevices  utils      datasets  methods    base
```

```
other attached packages:
```

```
[1] iCARE_1.24.0 Hmisc_4.7-0 ggplot2_3.3.5 Formula_1.2-4
[5] survival_3.3-1 lattice_0.20-45 gtools_3.9.2 plotrix_3.8-2
```

```
loaded via a namespace (and not attached):
```

```
[1] tidyselect_1.1.2 xfun_0.30 purrr_0.3.4
[4] splines_4.2.0 colorspace_2.0-3 vctrs_0.4.1
[7] generics_0.1.2 htmltools_0.5.2 base64enc_0.1-3
[10] utf8_1.2.2 rlang_1.0.2 pillar_1.7.0
[13] foreign_0.8-82 glue_1.6.2 withr_2.5.0
[16] DBI_1.1.2 RColorBrewer_1.1-3 jpeg_0.1-9
[19] lifecycle_1.0.1 stringr_1.4.0 munsell_0.5.0
[22] gtable_0.3.0 htmlwidgets_1.5.4 latticeExtra_0.6-29
[25] knitr_1.38 fastmap_1.1.0 fansi_1.0.3
[28] htmlTable_2.4.0 scales_1.2.0 backports_1.4.1
[31] checkmate_2.1.0 gridExtra_2.3 png_0.1-7
[34] digest_0.6.29 stringi_1.7.6 dplyr_1.0.8
[37] grid_4.2.0 cli_3.3.0 tools_4.2.0
[40] magrittr_2.0.3 tibble_3.1.6 cluster_2.1.3
```

| | | | |
|------|-----------------|-------------------|------------------|
| [43] | crayon_1.5.1 | pkgconfig_2.0.3 | ellipsis_0.3.2 |
| [46] | Matrix_1.4-1 | data.table_1.14.2 | assertthat_0.2.1 |
| [49] | rstudioapi_0.13 | R6_2.5.1 | rpart_4.1.16 |
| [52] | nnet_7.3-17 | compiler_4.2.0 | |