iCARE(Individualized Coherent Absolute Risk Estimators) Package

November 8, 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
 14.713   0.220  19.108
```

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.
0.05525 0.08655 0.09509 0.09601 0.10447 0.15815

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

SNP−only Risk Stratification: Ages 50−80
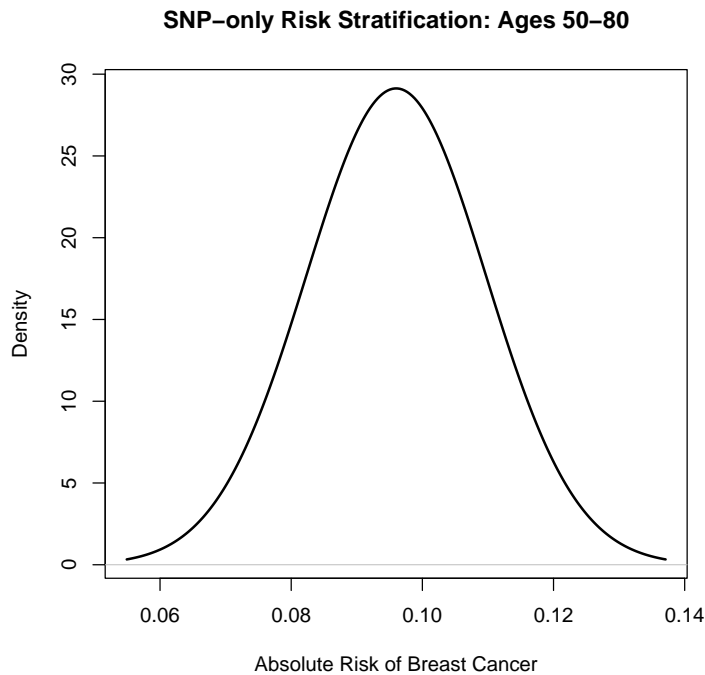
Example 1.B

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
  0.559    0.066    0.803

> names(res_snps_dat)
```
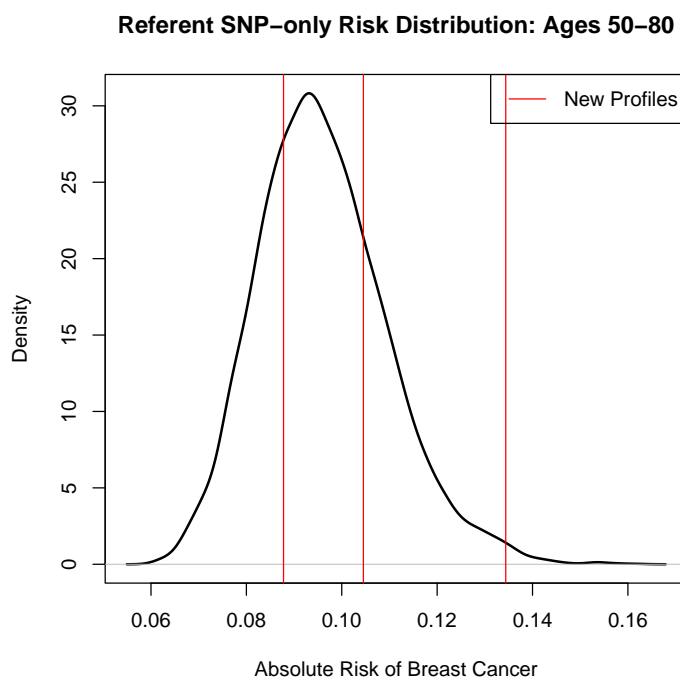
```
[1] "risk"      "details"   "beta.used" "refs.risk"
```

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)
```

Referent SNP−only Risk Distribution: Ages 50−80

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
  2.187   0.163   3.007
```

Display details of the fit

```
> print(res_covs_snps$details)

  Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132
1        50      80    0.10167868       NA         NA         NA         NA
2        50      80    0.09077494        2          0         NA         NA
3        50      80    0.16880605        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
```

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```
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 4.2.1 (2022-06-23)
Platform: aarch64-apple-darwin20 (64-bit)
Running under: macOS Ventura 13.0

Matrix products: default
BLAS:   /Library/Frameworks/R.framework/Versions/4.2-arm64/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.2-arm64/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_1.26.0   Hmisc_4.7-0     ggplot2_3.3.6   Formula_1.2-4
[5] survival_3.3-1  lattice_0.20-45 gtools_3.9.3    plotrix_3.8-2

loaded via a namespace (and not attached):
 [1] tidyselect_1.1.2   xfun_0.31          purrr_0.3.4
 [4] splines_4.2.1      colorspace_2.0-3   vctrs_0.4.1
 [7] generics_0.1.3     htmltools_0.5.2    base64enc_0.1-3
[10] utf8_1.2.2         rlang_1.0.4        pillar_1.7.0
[13] foreign_0.8-82     glue_1.6.2         withr_2.5.0
[16] DBI_1.1.3          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_0.6-30
[25] knitr_1.39         fastmap_1.1.0      fansi_1.0.3
[28] htmlTable_2.4.1    Rcpp_1.0.9         scales_1.2.0
[31] backports_1.4.1    checkmate_2.1.0    deldir_1.0-6
[34] interp_1.1-3       gridExtra_2.3      png_0.1-7
[37] digest_0.6.29      stringi_1.7.8      dplyr_1.0.9
[40] grid_4.2.1         cli_3.3.0          tools_4.2.1
```

```
[43] magrittr_2.0.3     tibble_3.1.7       cluster_2.1.3
[46] crayon_1.5.1       pkgconfig_2.0.3    ellipsis_0.3.2
[49] Matrix_1.4-1       data.table_1.14.2  assertthat_0.2.1
[52] rstudioapi_0.13    R6_2.5.1           rpart_4.1.16
[55] nnet_7.3-17        compiler_4.2.1
```