

iCARE(Individualized Coherent Absolute Risk Estimators) Package

April 27, 2020

```
> 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
16.225   0.432  16.667
```

Compute a summary of the risks and visualize the results

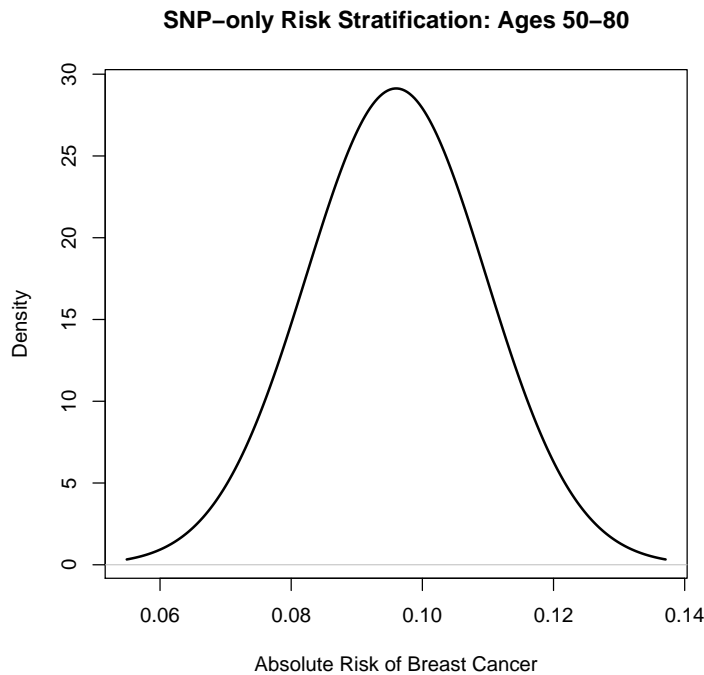
```
> summary(res_snps_miss$risk)
```

```
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.
	0.05459	0.08638	0.09489	0.09601	0.10454	0.15747

```
> 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)
```

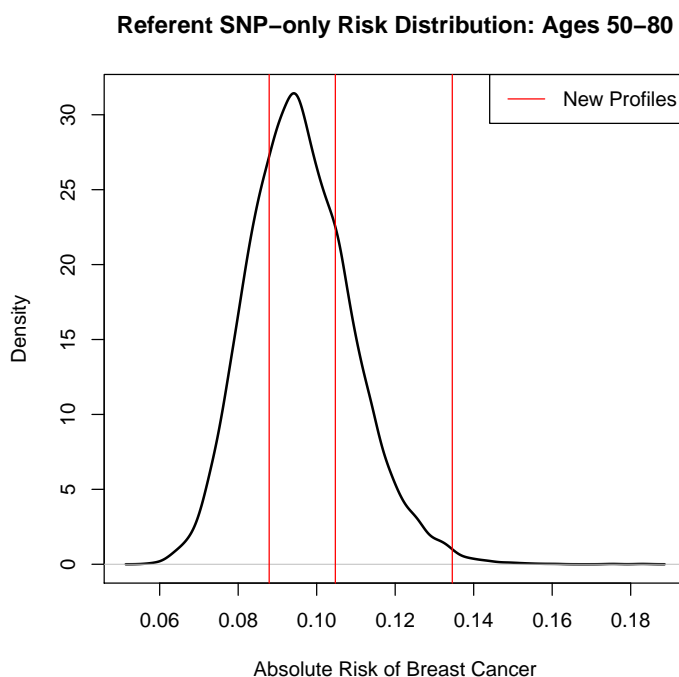
```
[1] "Note: As specified, the model does not adjust SNP imputations for family history."
      user system elapsed
0.578  0.185  0.764
```

```
> 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
2.603  0.393   3.028

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

Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132
1          50      80    0.10256525      NA      NA      NA      NA
2          50      80    0.09082911       2       0      NA      NA
3          50      80    0.16865205       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 4.0.0 (2020-04-24)
Platform: x86_64-apple-darwin17.0 (64-bit)
Running under: macOS Mojave 10.14.6
```

```
Matrix products: default
```

```
BLAS: /Library/Frameworks/R.framework/Versions/4.0/Resources/lib/libRblas.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.0/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_1.16.0    Hmisc_4.4-0    ggplot2_3.3.0  Formula_1.2-3
[5] survival_3.1-12 lattice_0.20-41 gtools_3.8.2   plotrix_3.7-8
```

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

```
[1] Rcpp_1.0.4.6      pillar_1.4.3      compiler_4.0.0
[4] RColorBrewer_1.1-2 base64enc_0.1-3    tools_4.0.0
[7] digest_0.6.25     rpart_4.1-15      checkmate_2.0.0
[10] htmlTable_1.13.3  lifecycle_0.2.0   tibble_3.0.1
[13] gtable_0.3.0      pkgconfig_2.0.3   png_0.1-7
[16] rlang_0.4.5       Matrix_1.2-18     rstudioapi_0.11
[19] xfun_0.13         gridExtra_2.3     stringr_1.4.0
[22] knitr_1.28        withr_2.2.0       dplyr_0.8.5
[25] cluster_2.1.0     htmlwidgets_1.5.1 vctrs_0.2.4
[28] grid_4.0.0        nnet_7.3-14       tidyselect_1.0.0
[31] data.table_1.12.8 glue_1.4.0        R6_2.4.1
[34] jpeg_0.1-8.1      foreign_0.8-79    latticeExtra_0.6-29
[37] purrr_0.3.4       magrittr_1.5      htmltools_0.4.0
[40] backports_1.1.6   scales_1.1.0      ellipsis_0.3.0
```

[43]	splines_4.0.0	assertthat_0.2.1	colorspace_1.4-1
[46]	stringi_1.4.6	acepack_1.4.1	munsell_0.5.0
[49]	crayon_1.3.4		