

iCARE(Individualized Coherent Absolute Risk Estimators) Package

October 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  
14.024 0.028 14.068
```

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)
```

```

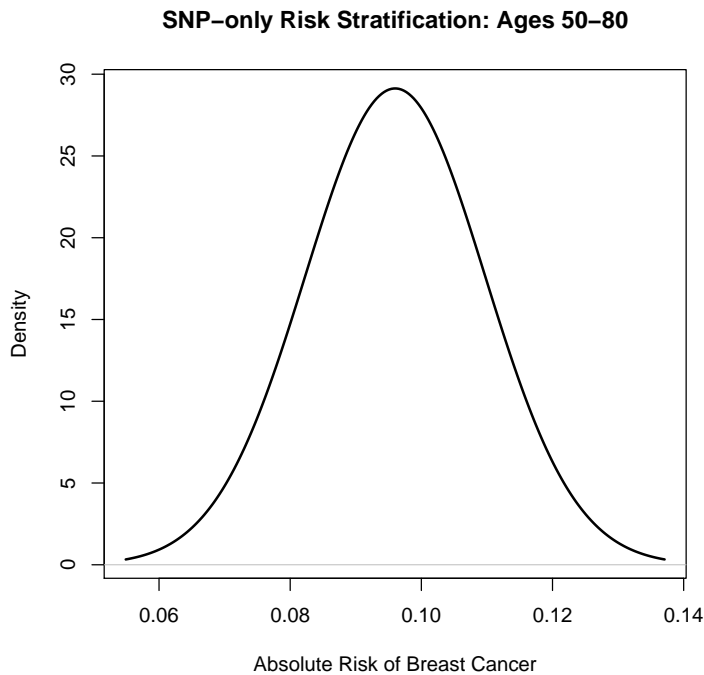
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.05492 0.08662 0.09499 0.09601 0.10431 0.15405

```

```

> 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
0.556  0.004  0.560

```

```

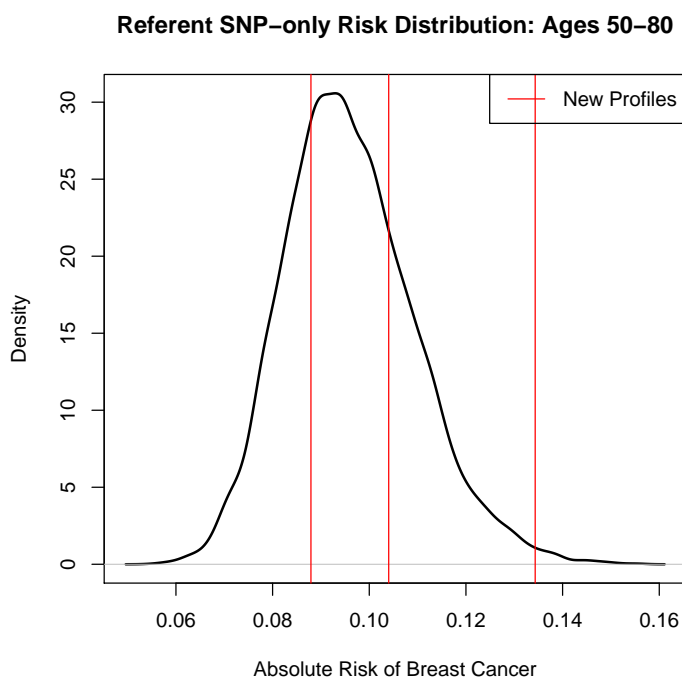
> names(res_snps_dat)

```

```
[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
1.304 0.212 1.516

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

Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132
1          50         80 0.10251274      NA          NA          NA          NA
2          50         80 0.09052638         2           0          NA          NA
3          50         80 0.16910419         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 4.0.3 (2020-10-10)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Ubuntu 18.04.5 LTS
```

```
Matrix products: default
```

```
BLAS: /home/biocbuild/bbs-3.12-bioc/R/lib/libRblas.so
```

```
LAPACK: /home/biocbuild/bbs-3.12-bioc/R/lib/libRlapack.so
```

```
locale:
```

```
[1] LC_CTYPE=en_US.UTF-8      LC_NUMERIC=C
[3] LC_TIME=en_US.UTF-8      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
```

```
attached base packages:
```

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

```
other attached packages:
```

```
[1] iCARE_1.18.0  Hmisc_4.4-1  ggplot2_3.3.2  Formula_1.2-4
[5] survival_3.2-7  lattice_0.20-41  gtools_3.8.2  plotrix_3.7-8
```

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

```
[1] pillar_1.4.6      compiler_4.0.3  RColorBrewer_1.1-2
[4] base64enc_0.1-3   tools_4.0.3     digest_0.6.27
[7] rpart_4.1-15     checkmate_2.0.0  lifecycle_0.2.0
[10] tibble_3.0.4     gtable_0.3.0    htmlTable_2.1.0
[13] pkgconfig_2.0.3  png_0.1-7       rlang_0.4.8
[16] Matrix_1.2-18    rstudioapi_0.11  xfun_0.18
[19] gridExtra_2.3    stringr_1.4.0   knitr_1.30
[22] withr_2.3.0     dplyr_1.0.2     cluster_2.1.0
[25] htmlwidgets_1.5.2  generics_0.0.2  vctrs_0.3.4
```

[28]	grid_4.0.3	nnet_7.3-14	tidyselect_1.1.0
[31]	data.table_1.13.2	glue_1.4.2	R6_2.4.1
[34]	jpeg_0.1-8.1	foreign_0.8-80	latticeExtra_0.6-29
[37]	purrr_0.3.4	magrittr_1.5	htmltools_0.5.0
[40]	backports_1.1.10	scales_1.1.1	ellipsis_0.3.1
[43]	splines_4.0.3	colorspace_1.4-1	stringi_1.5.3
[46]	munsell_0.5.0	crayon_1.3.4	