

iCARE(Individualized Coherent Absolute Risk Estimators) Package

October 26, 2021

```
> 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  
11.463  0.072  11.535
```

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)
```

```

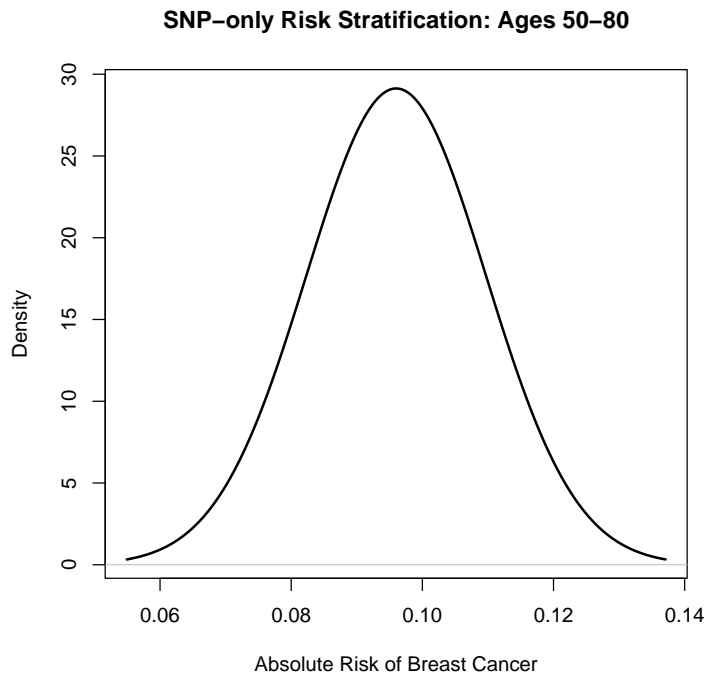
      Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
0.05319 0.08643 0.09493 0.09601 0.10450 0.15731

```

```

> 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
0.647  0.216  0.863

```

```

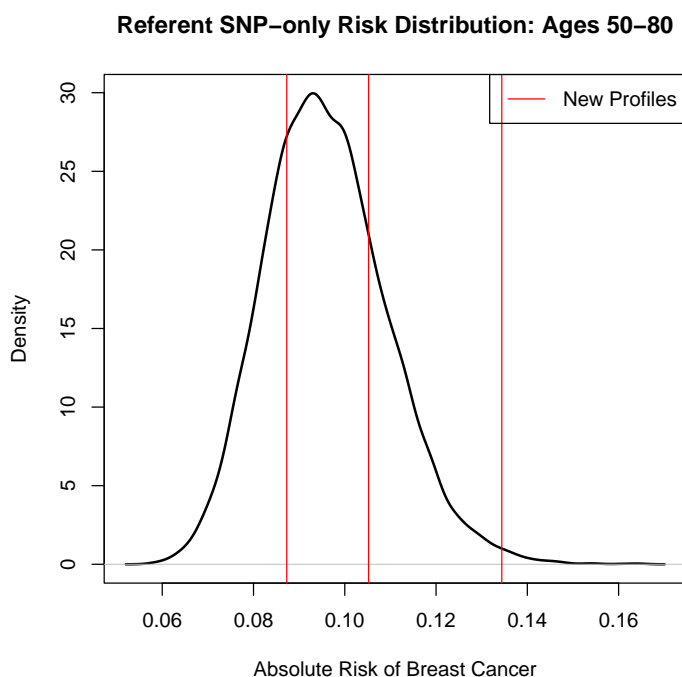
> names(res_snps_dat)

```

```
[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  
1.594 0.260 1.854
```

```
Display details of the fit
```

```
> print(res_covs_snps$details)
```

```
Int_Start Int_End Risk_Estimate rs616488 rs11552449 rs11249433 rs12405132  
1 50 80 0.1018280 NA NA NA NA  
2 50 80 0.0894485 2 0 NA NA  
3 50 80 0.1686089 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 0 1  
3 0 0 1 0 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 4.1.1 (2021-08-10)
Platform: x86_64-pc-linux-gnu (64-bit)
Running under: Ubuntu 20.04.3 LTS
```

```
Matrix products: default
```

```
BLAS: /home/biocbuild/bbs-3.14-bioc/R/lib/libRblas.so
LAPACK: /home/biocbuild/bbs-3.14-bioc/R/lib/libRlapack.so
```

```
locale:
```

```
[1] LC_CTYPE=en_US.UTF-8      LC_NUMERIC=C
[3] LC_TIME=en_GB             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_1.22.0  Hmisc_4.6-0    ggplot2_3.3.5  Formula_1.2-4
[5] survival_3.2-13 lattice_0.20-45 gtools_3.9.2   plotrix_3.8-2
```

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

```
[1] tidyselect_1.1.1  xfun_0.27      purrr_0.3.4
[4] splines_4.1.1    colorspace_2.0-2 vctrs_0.3.8
[7] generics_0.1.1   htmltools_0.5.2 base64enc_0.1-3
[10] utf8_1.2.2       rlang_0.4.12   pillar_1.6.4
[13] foreign_0.8-81   glue_1.4.2     withr_2.4.2
[16] DBI_1.1.1        RColorBrewer_1.1-2 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_1.36       fastmap_1.1.0  fansi_0.5.0
```

[28]	htmlTable_2.3.0	scales_1.1.1	backports_1.2.1
[31]	checkmate_2.0.0	gridExtra_2.3	png_0.1-7
[34]	digest_0.6.28	stringi_1.7.5	dplyr_1.0.7
[37]	grid_4.1.1	tools_4.1.1	magrittr_2.0.1
[40]	tibble_3.1.5	cluster_2.1.2	crayon_1.4.1
[43]	pkgconfig_2.0.3	ellipsis_0.3.2	Matrix_1.3-4
[46]	data.table_1.14.2	assertthat_0.2.1	rstudioapi_0.13
[49]	R6_2.5.1	rpart_4.1-15	nnet_7.3-16
[52]	compiler_4.1.1		