

BayesMendel v2.0: An R package for cancer risk prediction

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1 Introduction

The BayesMendel working group is dedicated to the development of methodologies, models, and open source software for predicting who may carry a cancer susceptibility gene. We use statistical ideas that go back to Bayes and genetic models that go back to Mendel.

This vignette will show the user how to use BRCAPRO, MMRpro, PancPRO and MelaPRO to:

- Calculate probabilities of being a germline mutation carrier.
- Calculate future risk of cancer.
- Incorporate supplementary information (marker testing results, germline testing results, tumor information) into the models.

2 Using the models

2.1 BRCAPRO

2.1.1 Family History

Before running your pedigree through `brcapro`, be sure it is structured as a numeric data frame with history of breast and ovarian cancers: n rows (where n is the number of family members, including the counselee) and 9 columns with column names:

Column Name	Content
ID	Member identifier
Gender	Gender (0=female, 1=male)
FatherID	Father's identifier number
MotherID	Mother's identifier number
AffectedBreast	Breast cancer status (0=no cancer or no information, 1=breast cancer,one breast involved; 2=bilateral breast cancer)
AffectedOvary	Ovarian cancer status (0=no cancer, 1=ovarian cancer)
AgeBreast	Age of onset of breast cancer if a breast cancer case. Current age or age of death if not a breast cancer case. 1 if unaffected and there is no age information.
AgeOvary	Age of onset of ovarian cancer if an ovarian cancer case. Current age or age of death if not an ovarian cancer case. 1 if unaffected and there is no age information.
AgeBreastContralateral	Age at onset of breast cancer, second breast. Only for members with breast cancer status=2. For the rest enter a 0.

Family members for whom no information is available should be coded with a 0 in the cancer diagnosis fields, and a 1 in the age fields. If it is known that a family member is affected, but age of diagnosis is unknown, either enter an estimate or evaluate the program at different plausible ages.

To begin using any BayesMendel models, load the package library:

```
> library(BayesMendel)
```

```
[1] "kinship is loaded"
```

The parameters used by the model, including penetrance, allele frequency, and sensitivity/specificity of testing, are set using the function `brcaparams`. Any changes to the parameters can be made by calling this function.

```
> data(BRCAPenet.metaDSL.2008, death.othercauses, CBRCAPenet.metaDSL.2009)
> data(compriskSurv)
> myparams <- brcaparams(age.by = 2)
> data(brca.fam)
> brcapro(family = brca.fam)
```

The probability of being a carrier is 0.5220824

an BRCA1 carrier 0.2864702

an BRCA2 carrier 0.2355197

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.03139229	0.03847886
2	67	0.05918727	0.08142296
3	72	0.08257729	0.12453601

4 77 0.10439096 0.16445045
 5 82 0.12357304 0.19775553

An object of class "IJBayesMendel"

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral
1	57	57	0
2	70	69	0
3	87	87	0
4	32	32	0
5	50	50	0
6	1	1	0
7	45	47	0
8	65	65	0
9	96	96	0
10	75	75	0
11	94	94	0
12	85	85	0
13	79	79	0
14	85	85	0
15	23	23	0
16	12	12	0
17	22	22	0
18	19	19	0

```

19      16      16      0
20      54      54      0
21      77      77      0

```

```

Slot "posterior":
, , BRCA

```

```

          BRCA20      BRCA21
BRCA10 0.4779176 2.355197e-01
BRCA11 0.2864702 9.243466e-05

```

```

Slot "probs":

```

```

  Pr(Being a carrier) Pr(BRCA1 mutation) Pr(BRCA2 mutation)
1          0.5220824          0.2864702          0.2355197
  Pr(Both genes mutated)
1          9.243466e-05

```

```

Slot "predictions":

```

```

  By age Contralateral Breast Ca Risk Ovarian Ca Risk
1     62                0.03139229      0.03847886
2     67                0.05918727      0.08142296
3     72                0.08257729      0.12453601
4     77                0.10439096      0.16445045
5     82                0.12357304      0.19775553

```

```

Slot "counselee.id":

```

```

[1] 1

```

```

Slot "loglik":

```

```

[1] -36.22395

```

2.1.2 Changing the penetrance or prevalence

Generally, the user can specify the prevalence of *BRCA1* and *BRCA2* directly in the `brcapro` function. Preset values for non-Ashkenazi Jewish (the default), Ashkenazi Jewish, and Italian populations are available and specified by the option “`allef.type`”.

The user can input their own values for prevalence by specifying `allef.type = “other”` and inputting the values using the `brcaparams` function.

```

> brcapro(family = brca.fam, allef.type = "AJ")

```

The probability of being a carrier is 0.7648096

an BRCA1 carrier 0.4266167

an BRCA2 carrier 0.3368202

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.04261903	0.05621519
2	67	0.07943086	0.11881667
3	72	0.10958511	0.18150634
4	77	0.13748868	0.23936908
5	82	0.16191351	0.28746941

An object of class "IJBayesMendel"

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral
1	57	57	0
2	70	69	0
3	87	87	0
4	32	32	0
5	50	50	0
6	1	1	0
7	45	47	0
8	65	65	0
9	96	96	0
10	75	75	0
11	94	94	0

12	85	85	0
13	79	79	0
14	85	85	0
15	23	23	0
16	12	12	0
17	22	22	0
18	19	19	0
19	16	16	0
20	54	54	0
21	77	77	0

Slot "posterior":

, , BRCA

	BRCA20	BRCA21
BRCA10	0.2351904	0.336820150
BRCA11	0.4266167	0.001372775

Slot "probs":

	Pr(Being a carrier)	Pr(BRCA1 mutation)	Pr(BRCA2 mutation)
1	0.7648096	0.4266167	0.3368202
	Pr(Both genes mutated)		
1	0.001372775		

Slot "predictions":

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.04261903	0.05621519
2	67	0.07943086	0.11881667
3	72	0.10958511	0.18150634
4	77	0.13748868	0.23936908
5	82	0.16191351	0.28746941

Slot "counselee.id":

[1] 1

Slot "loglik":

[1] -34.37021

```
> myparams <- brcaparams(allef = c(0.005, 0.0055))
> brcapro(family = brca.fam, allef.type = "other",
+        params = myparams)
```

The probability of being a carrier is 0.7561191
 an BRCA1 carrier 0.424327

an BRCA2 carrier 0.3306854

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.04222945	0.05572754
2	67	0.07872318	0.11776555
3	72	0.10863484	0.17986798
4	77	0.13631965	0.23717813
5	82	0.16055625	0.28481087

An object of class `AIJBayesMendel`

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral
1	57	57	0
2	70	69	0
3	87	87	0
4	32	32	0
5	50	50	0
6	1	1	0
7	45	47	0
8	65	65	0
9	96	96	0
10	75	75	0
11	94	94	0
12	85	85	0

```

13      79      79      0
14      85      85      0
15      23      23      0
16      12      12      0
17      22      22      0
18      19      19      0
19      16      16      0
20      54      54      0
21      77      77      0

```

```

Slot "posterior":
, , BRCA

```

```

          BRCA20      BRCA21
BRCA10 0.2438809 0.330685361
BRCA11 0.4243270 0.001106754

```

```

Slot "probs":

```

```

  Pr(Being a carrier) Pr(BRCA1 mutation) Pr(BRCA2 mutation)
1          0.7561191          0.424327          0.3306854
  Pr(Both genes mutated)
1          0.001106754

```

```

Slot "predictions":

```

```

  By age Contralateral Breast Ca Risk Ovarian Ca Risk
1    62          0.04222945          0.05572754
2    67          0.07872318          0.11776555
3    72          0.10863484          0.17986798
4    77          0.13631965          0.23717813
5    82          0.16055625          0.28481087

```

```

Slot "counselee.id":

```

```

[1] 1

```

```

Slot "loglik":

```

```

[1] -34.54357

```

The user can also specify the penetrance estimates to be used by `brcapro`. The default is the `BRCApenet.metaDSL.2008` object. To use the penetrance estimates for the Italian population:

```

> data(BRCApenet.Italian.2008)
> myparams <- brcaparams(penetrance = BRCApenet.Italian.2008)

```

```
> brcapro(family = brca.fam, allef.type = "nonAJ",
+         params = myparams)
```

```
The probability of being a carrier is 0.4183709
  an BRCA1 carrier 0.2433292
  an BRCA2 carrier 0.1749542
```

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.02677163	0.03199285
2	67	0.05080999	0.06757006
3	72	0.07134996	0.10315730
4	77	0.09059156	0.13605679
5	82	0.10755768	0.16347899

An object of class `IBayesMendel`

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral
1	57	57	0
2	70	69	0
3	87	87	0
4	32	32	0
5	50	50	0
6	1	1	0
7	45	47	0

8	65	65	0
9	96	96	0
10	75	75	0
11	94	94	0
12	85	85	0
13	79	79	0
14	85	85	0
15	23	23	0
16	12	12	0
17	22	22	0
18	19	19	0
19	16	16	0
20	54	54	0
21	77	77	0

Slot "posterior":
, , BRCA

	BRCA20	BRCA21
BRCA10	0.5816291	1.749542e-01
BRCA11	0.2433292	8.748001e-05

Slot "probs":

	Pr(Being a carrier)	Pr(BRCA1 mutation)	Pr(BRCA2 mutation)
1	0.4183709	0.2433292	0.1749542
	Pr(Both genes mutated)		
1	8.748001e-05		

Slot "predictions":

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.02677163	0.03199285
2	67	0.05080999	0.06757006
3	72	0.07134996	0.10315730
4	77	0.09059156	0.13605679
5	82	0.10755768	0.16347899

Slot "counselee.id":
[1] 1

Slot "loglik":
[1] -37.29588

2.1.3 Specifying race/ethnicity of the family

A set of race/ethnicity-specific baseline (non-carrier) penetrance values were recently added to `brcapro`. The current default assumes that the race/ethnicity of the input family is unknown, but the user can specify one of five different inputs: Asian, Black, Hispanic, NativeAmerican and White. Race/ethnicity categories and estimates were derived using the DevCan (<http://srab.cancer.gov/devcan/>) software provided by the National Cancer Institute (NCI). To specify a particular race, use the “race” input option in `brcapro`.

```
> data(BRCAbaseline.race.2008)
> brcapro(family = brca.fam, race = "Hispanic")
```

```
The probability of being a carrier is 0.6804408
  an BRCA1 carrier 0.3748946
  an BRCA2 carrier 0.3054105
```

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.03864828	0.04978498
2	67	0.07228411	0.10530551
3	72	0.10006435	0.16098799
4	77	0.12583314	0.21245735
5	82	0.14842128	0.25531509

An object of class `~IJBayesMendel~`

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0

20	20	0	21	12	0	0
21	21	1	0	0	0	0
	AgeBreast	AgeOvary	AgeBreastContralateral			
1	57	57			0	
2	70	69			0	
3	87	87			0	
4	32	32			0	
5	50	50			0	
6	1	1			0	
7	45	47			0	
8	65	65			0	
9	96	96			0	
10	75	75			0	
11	94	94			0	
12	85	85			0	
13	79	79			0	
14	85	85			0	
15	23	23			0	
16	12	12			0	
17	22	22			0	
18	19	19			0	
19	16	16			0	
20	54	54			0	
21	77	77			0	

Slot "posterior":

, , BRCA

	BRCA20	BRCA21
BRCA10	0.3195592	0.3054105038
BRCA11	0.3748946	0.0001356680

Slot "probs":

	Pr(Being a carrier)	Pr(BRCA1 mutation)	Pr(BRCA2 mutation)
1	0.6804408	0.3748946	0.3054105
	Pr(Both genes mutated)		
1	0.0001356680		

Slot "predictions":

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.03864828	0.04978498
2	67	0.07228411	0.10530551
3	72	0.10006435	0.16098799
4	77	0.12583314	0.21245735

```
5      82                0.14842128      0.25531509
```

```
Slot "counselee.id":
[1] 1
```

```
Slot "loglik":
[1] -36.84359
```

2.1.4 Germline Testing Results

If the results for *BRCA1* and *BRCA2* germline testings are available, the user can input the results in data frame `germline.testing` (0=no test, 1=positive test, 2=negative test) with column names “BRCA1”, “BRCA2” and “Test Order”.

```
> BRCA1 <- BRCA2 <- TestOrder <- rep(0, nrow(brca.fam))
> germline.testing <- data.frame(BRCA1, BRCA2, TestOrder)
> germline.testing[2, ] <- c(2, 0, 1)
> brcapro(family = brca.fam, germline.testing = germline.testing)
```

```
The probability of being a carrier is 0.4115605
  an BRCA1 carrier 0.08133249
  an BRCA2 carrier 0.3301627
```

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.02506424	0.02169108
2	67	0.04812418	0.04743364
3	72	0.06821090	0.07493449
4	77	0.08709166	0.10143088
5	82	0.10375685	0.12445081

An object of class “IJBayesMendel”

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0

12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral	BRCA1	BRCA2
1	57	57		0	0
2	70	69		0	2
3	87	87		0	0
4	32	32		0	0
5	50	50		0	0
6	1	1		0	0
7	45	47		0	0
8	65	65		0	0
9	96	96		0	0
10	75	75		0	0
11	94	94		0	0
12	85	85		0	0
13	79	79		0	0
14	85	85		0	0
15	23	23		0	0
16	12	12		0	0
17	22	22		0	0
18	19	19		0	0
19	16	16		0	0
20	54	54		0	0
21	77	77		0	0

	TestOrder
1	0
2	1
3	0
4	0
5	0
6	0
7	0
8	0
9	0
10	0
11	0
12	0

```

13      0
14      0
15      0
16      0
17      0
18      0
19      0
20      0
21      0

```

```

Slot "posterior":
, , BRCA

```

```

          BRCA20      BRCA21
BRCA10 0.58843945 0.330162688
BRCA11 0.08133249 0.000065369

```

```

Slot "probs":

```

```

  Pr(Being a carrier) Pr(BRCA1 mutation) Pr(BRCA2 mutation)
1          0.4115605          0.08133249          0.3301627
  Pr(Both genes mutated)
1          6.5369e-05

```

```

Slot "predictions":

```

```

  By age Contralateral Breast Ca Risk Ovarian Ca Risk
1     62                0.02506424          0.02169108
2     67                0.04812418          0.04743364
3     72                0.06821090          0.07493449
4     77                0.08709166          0.10143088
5     82                0.10375685          0.12445081

```

```

Slot "counselee.id":

```

```

[1] 1

```

```

Slot "loglik":

```

```

[1] -36.56195

```

2.1.5 Marker Testing Results

If the results for *BRCA1* prognostic markers are available, the user can input the results in data frame `marker.testing` with column names shown below. Note that even if not all the biomarker results listed below are available, all 4 columns must contain non-missing values, which should be set to zero for biomarkers that were not tested.

Column Name	Content
ER	ER testing result. (0=no test, 1=positive test, 2=negative test)
CK14	CK14 testing result. (0=no test, 1=positive test, 2=negative test)
CK5.6	CK5/6 testing result. (0=no test, 1=positive test, 2=negative test)
PR	PR testing result. (0=no test, 1=positive test, 2=negative test)

When the testing result for ER is negative, and the results for CK14 and CK5/6 are both also available, these 3 markers are treated as a group, and the calculations of carrier probabilities will incorporate the joint conditional probabilities of them given genetic status. If the result for either CK14 or CK5/6 is not available, the calculations of carrier probabilities will only involve the marginal conditional probability of ER given genetic status. Note that when ER is positive, only the marginal conditional probability for ER+ is used even if the testing results for CK14 or CK5/6 is available (which is very rare). For any family member, if the testing result for ER is available, the testing result for PR will be ignored even though it's also available. That is, PR will not be included in carrier prediction when ER is available.

```
> marker.testing <- data.frame(matrix(rep(0, nrow(brca.fam) *
+   4), ncol = 4))
> colnames(marker.testing) <- c("ER", "CK14", "CK5.6",
+   "PR")
> brca.fam[1, "AffectedBreast"] <- 1
> marker.testing[1, "ER"] <- 2
> brcapro(family = brca.fam, germline.testing = germline.testing,
+   marker.testing = marker.testing)
```

The probability of being a carrier is 0.4782926

an BRCA1 carrier 0.1854231

an BRCA2 carrier 0.2927205

The risks of developing cancers are

	By age	Contralateral Breast Ca Risk	Ovarian Ca Risk
1	62	0.02871438	0.03060766
2	67	0.05454488	0.06558120
3	72	0.07659463	0.10157075
4	77	0.09722369	0.13543448
5	82	0.11539026	0.16416779

An object of class "BayesMendel"

Slot "family":

ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	1
2	2	0	9	8	0
3	3	1	11	10	0
4	4	0	0	1	0
5	5	1	3	2	0

6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral	BRCA1	BRCA2
1	57	57		0	0
2	70	69		0	2
3	87	87		0	0
4	32	32		0	0
5	50	50		0	0
6	1	1		0	0
7	45	47		0	0
8	65	65		0	0
9	96	96		0	0
10	75	75		0	0
11	94	94		0	0
12	85	85		0	0
13	79	79		0	0
14	85	85		0	0
15	23	23		0	0
16	12	12		0	0
17	22	22		0	0
18	19	19		0	0
19	16	16		0	0
20	54	54		0	0
21	77	77		0	0

	TestOrder	ER	CK14	CK5.6	PR
1	0	2	0	0	0
2	1	0	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0
5	0	0	0	0	0
6	0	0	0	0	0

```

7      0 0 0 0 0
8      0 0 0 0 0
9      0 0 0 0 0
10     0 0 0 0 0
11     0 0 0 0 0
12     0 0 0 0 0
13     0 0 0 0 0
14     0 0 0 0 0
15     0 0 0 0 0
16     0 0 0 0 0
17     0 0 0 0 0
18     0 0 0 0 0
19     0 0 0 0 0
20     0 0 0 0 0
21     0 0 0 0 0

```

Slot "posterior":

, , BRCA

```

          BRCA20      BRCA21
BRCA10 0.5217074 0.2927205344
BRCA11 0.1854231 0.0001490293

```

Slot "probs":

```

Pr(Being a carrier) Pr(BRCA1 mutation) Pr(BRCA2 mutation)
1      0.4782926      0.1854231      0.2927205
Pr(Both genes mutated)
1      0.0001490293

```

Slot "predictions":

```

By age Contralateral Breast Ca Risk Ovarian Ca Risk
1      62      0.02871438      0.03060766
2      67      0.05454488      0.06558120
3      72      0.07659463      0.10157075
4      77      0.09722369      0.13543448
5      82      0.11539026      0.16416779

```

Slot "counselee.id":

[1] 1

Slot "loglik":

[1] -37.49141

2.1.6 Oophorectomy

If women in the pedigree have had an oophorectomy, this information can be included in the calculation by creating a data frame `oophorectomy`. Set up a data frame with two columns, one indicating if oophorectomy was done and the other with the age at oophorectomy. If no oophorectomy was done, an individual's current age should be used.

Column Name	Content
Oophorectomy	Oophorectomy yes/no. (0=no oophorectomy, 1=oophorectomy)
AgeOophorectomy	Age at Oophorectomy.

```
> Oophorectomy <- c(1, rep(0, (nrow(brca.fam) - 1)))
> AgeOophorectomy <- c(30, rep(1, (nrow(brca.fam) -
+   1)))
> oophorectomy <- data.frame(Oophorectomy, AgeOophorectomy)
> brcapro(family = brca.fam, germline.testing = germline.testing,
+   marker.testing = marker.testing, oophorectomy = oophorectomy)
```

The probability of being a carrier is 0.5590058
 an BRCA1 carrier 0.2453306
 an BRCA2 carrier 0.3135274

The risks of developing cancers are

	By age	Breast Ca Risk	Ovarian Ca Risk
1	35	0.005061704	1.456496e-05
2	40	0.013358649	3.750186e-05
3	45	0.024844277	7.944420e-05
4	50	0.037229520	1.497457e-04
5	55	0.048354543	2.484134e-04
6	60	0.058395153	3.717900e-04
7	65	0.067456569	5.226497e-04
8	70	0.075193441	6.884074e-04
9	75	0.082136091	8.644992e-04
10	80	0.088380692	1.041285e-03
11	85	0.093266946	1.199922e-03

An object of class "IJBayesMendel"

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedBreast	AffectedOvary
1	1	0	3	2	0	0
2	2	0	9	8	0	1
3	3	1	11	10	0	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	1

9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	1	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeBreast	AgeOvary	AgeBreastContralateral	BRCA1	BRCA2
1	30	30		0	0
2	70	69		0	2
3	87	87		0	0
4	32	32		0	0
5	50	50		0	0
6	1	1		0	0
7	45	47		0	0
8	65	65		0	0
9	96	96		0	0
10	75	75		0	0
11	94	94		0	0
12	85	85		0	0
13	79	79		0	0
14	85	85		0	0
15	23	23		0	0
16	12	12		0	0
17	22	22		0	0
18	19	19		0	0
19	16	16		0	0
20	54	54		0	0
21	77	77		0	0

	TestOrder	ER	CK14	CK5.6	PR	Oophorectomy	AgeOophorectomy
1	0	2	0	0	0	1	30
2	1	0	0	0	0	0	1
3	0	0	0	0	0	0	1
4	0	0	0	0	0	0	1
5	0	0	0	0	0	0	1
6	0	0	0	0	0	0	1
7	0	0	0	0	0	0	1
8	0	0	0	0	0	0	1
9	0	0	0	0	0	0	1

10	0	0	0	0	0	1
11	0	0	0	0	0	1
12	0	0	0	0	0	1
13	0	0	0	0	0	1
14	0	0	0	0	0	1
15	0	0	0	0	0	1
16	0	0	0	0	0	1
17	0	0	0	0	0	1
18	0	0	0	0	0	1
19	0	0	0	0	0	1
20	0	0	0	0	0	1
21	0	0	0	0	0	1

Slot "posterior":

, , BRCA

	BRCA20	BRCA21
BRCA10	0.4409942	0.3135274113
BRCA11	0.2453306	0.0001477409

Slot "probs":

	Pr(Being a carrier)	Pr(BRCA1 mutation)	Pr(BRCA2 mutation)
1	0.5590058	0.2453306	0.3135274
	Pr(Both genes mutated)		
1	0.0001477409		

Slot "predictions":

	By age	Breast Ca Risk	Ovarian Ca Risk
1	35	0.005061704	1.456496e-05
2	40	0.013358649	3.750186e-05
3	45	0.024844277	7.944420e-05
4	50	0.037229520	1.497457e-04
5	55	0.048354543	2.484134e-04
6	60	0.058395153	3.717900e-04
7	65	0.067456569	5.226497e-04
8	70	0.075193441	6.884074e-04
9	75	0.082136091	8.644992e-04
10	80	0.088380692	1.041285e-03
11	85	0.093266946	1.199922e-03

Slot "counselee.id":

[1] 1

Slot "loglik":

[1] -38.07909

2.2 MMRpro

2.2.1 Family History

Before running your pedigree through **MMRpro**, be sure it is structured as a numeric data frame with history of colon and endometrial cancers: *n* rows (where *n* is the number of family members, including the counselee) and 8 columns with required column names described below.

The family history includes the information on the counselee and his/her relatives. For each member, we need information on whether he or she has been diagnosed with colorectal cancer and either the age at diagnosis or, if cancer free, the current age or the age at death. We do the same for endometrial cancer, if the member is female.

The family cancer history must be entered in data frame form, with one row for each family member and columns containing the following information:

Column	Content
ID	Member identifier
Gender	Gender (0=female, 1=male)
FatherID	Father's identifier number
MotherID	Mother's identifier number
AffectedColon	Colorectal cancer status (0=no cancer or no information,1=colon/rectum cancer)
AffectedEndometrium	Endometrial cancer status (0=no cancer, 1=ovarian cancer)
AgeColon	Age of onset of colorectal cancer if a colorectal cancer case. Current age or age of death if not a colorectal cancer case. 1 if unaffected and there is no age information.
AgeEndometrium	Age of onset of endometrial cancer if an endometrial cancer case. Current age or age of death if not an endometrial cancer case. 1 if unaffected and there is no age information.

Family members for whom no information is available should be coded with a 0 in the cancer diagnosis fields, and a 1 in the age fields. If it is known that a family member is affected, but age of diagnosis is unknown, either enter an estimate or evaluate the program at different plausible ages.

The parameters used by the model, including penetrance, allele frequency, and sensitivity/specificity of testing, are set using the function **MMRparams**. Any changes to the parameters can be made by calling this function.

```
> data(MMRpenet.2008, death.othercauses)
> data(MMR.fam)
```

```
> myparams <- MMRparams(age.to = 95)
> MMRpro(family = MMR.fam, params = myparams)
```

```
The probability of being a carrier is 0.1544784
  an MLH1 carrier 0.06100283
  an MSH2 carrier 0.06912988
  an MSH6 carrier 0.02438393
```

The risks of developing cancers are

	By age	Colorectal Ca Risk	Endometrial Ca Risk
1	60	NA	0.02553414
2	65	NA	0.04417356
3	70	NA	0.05301416
4	75	NA	0.05816094
5	80	NA	0.06187595
6	85	NA	0.06434005
7	90	NA	0.06565629
8	95	NA	0.06612507

An object of class "IJBayesMendel"

Slot "family":

ID	Gender	FatherID	MotherID	AffectedColon	AffectedEndometrium	
1	1	0	3	2	1	0
2	2	0	9	8	0	0
3	3	1	11	10	1	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	0	0
8	8	0	0	0	0	0
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	0	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeColon	AgeEndometrium
1	55	55
2	70	70
3	57	57

4	32	32
5	50	50
6	1	1
7	47	47
8	65	65
9	66	66
10	30	30
11	74	74
12	85	85
13	79	79
14	79	79
15	23	23
16	12	12
17	22	22
18	19	19
19	16	16
20	54	54
21	77	77

Slot "posterior":

, , MSH60

	MSH20	MSH21	MSH22
MLH10	0.84552162	6.910083e-02	0
MLH11	0.06097501	1.860968e-05	0
MLH12	0.00000000	0.000000e+00	0

, , MSH61

	MSH20	MSH21	MSH22
MLH10	2.436428e-02	1.044151e-05	0
MLH11	9.213615e-06	1.719177e-09	0
MLH12	0.000000e+00	0.000000e+00	0

, , MSH62

	MSH20	MSH21	MSH22
MLH10	1.704936e-127	0	0
MLH11	0.000000e+00	0	0
MLH12	0.000000e+00	0	0

Slot "probs":

	Pr(Being a carrier)	Pr(MLH1 mutation)	Pr(MSH2 mutation)
1	0.1544784	0.06100283	0.06912988

```
Pr(MSH6)
1 0.02438393
```

```
Slot "predictions":
```

```
By age Colorectal Ca Risk Endometrial Ca Risk
1 60 NA 0.02553414
2 65 NA 0.04417356
3 70 NA 0.05301416
4 75 NA 0.05816094
5 80 NA 0.06187595
6 85 NA 0.06434005
7 90 NA 0.06565629
8 95 NA 0.06612507
```

```
Slot "counselee.id":
```

```
[1] 1
```

```
Slot "loglik":
```

```
[1] -15.34516
```

2.2.2 Germline Testing

Information about germline testing results is included in the `germline.testing` object. If the results of germline testing are available, the user can input them into a data frame with `n` rows and 4 columns with column names “MLH1”, “MSH2”, “MSH6”, and Test Order which stores the mutation testing results for *MLH1*, *MSH2*, and *MSH6* (0=no test, 1=positive test, 2=negative test) and order in which family members were tested. If the testing order is unknown, we suggest evaluating the model multiple times, allowing each tested family member to be indicated as the first person tested.

```
> MLH1 <- MSH2 <- MSH6 <- TestOrder <- rep(0, nrow(MMR.fam))
> germline.testing = data.frame(MLH1, MSH2, MSH6, TestOrder)
> germline.testing[3, ] <- c(2, 2, 0, 1)
> MMRpro(family = MMR.fam, germline.testing = germline.testing)
```

```
The probability of being a carrier is 0.07071813
```

```
an MLH1 carrier 0.02053903
```

```
an MSH2 carrier 0.02327619
```

```
an MSH6 carrier 0.02691327
```

```
The risks of developing cancers are
```

```
By age Colorectal Ca Risk Endometrial Ca Risk
1 60 NA 0.01152636
2 65 NA 0.02168490
```

3	70	NA	0.02882039
4	75	NA	0.03408755
5	80	NA	0.03799758
6	85	NA	0.04058723

An object of class "IJBayesMendel"

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedColon	AffectedEndometrium
1	1	0	3	2	1	0
2	2	0	9	8	0	0
3	3	1	11	10	1	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	0	0
8	8	0	0	0	0	0
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	0	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeColon	AgeEndometrium	MLH1	MSH2	MSH6	TestOrder
1	55	55	0	0	0	0
2	70	70	0	0	0	0
3	57	57	2	2	0	1
4	32	32	0	0	0	0
5	50	50	0	0	0	0
6	1	1	0	0	0	0
7	47	47	0	0	0	0
8	65	65	0	0	0	0
9	66	66	0	0	0	0
10	30	30	0	0	0	0
11	74	74	0	0	0	0
12	85	85	0	0	0	0
13	79	79	0	0	0	0
14	79	79	0	0	0	0
15	23	23	0	0	0	0
16	12	12	0	0	0	0

17	22	22	0	0	0	0
18	19	19	0	0	0	0
19	16	16	0	0	0	0
20	54	54	0	0	0	0
21	77	77	0	0	0	0

Slot "posterior":

, , MSH60

	MSH20	MSH21	MSH22
MLH10	0.92928187	2.326938e-02	0
MLH11	0.02053269	2.774639e-06	0
MLH12	0.00000000	0.000000e+00	0

, , MSH61

	MSH20	MSH21	MSH22
MLH10	2.690568e-02	4.030641e-06	0
MLH11	3.556590e-06	2.794389e-10	0
MLH12	0.000000e+00	0.000000e+00	0

, , MSH62

	MSH20	MSH21	MSH22
MLH10	1.882909e-127	0	0
MLH11	0.000000e+00	0	0
MLH12	0.000000e+00	0	0

Slot "probs":

	Pr(Being a carrier)	Pr(MLH1 mutation)	Pr(MSH2 mutation)
1	0.07071813	0.02053903	0.02327619
	Pr(MSH6)		
1	0.02691327		

Slot "predictions":

	By age	Colorectal Ca Risk	Endometrial Ca Risk
1	60	NA	0.01152636
2	65	NA	0.02168490
3	70	NA	0.02882039
4	75	NA	0.03408755
5	80	NA	0.03799758
6	85	NA	0.04058723

Slot "counselee.id":

```
[1] 1
```

```
Slot "loglik":
```

```
[1] -15.44486
```

2.2.3 Marker Testing

Information about the colorectal tumor is included in the `marker.testing` object. This object is a data frame with `n` rows and 2 columns with information about MSI testing and location of the colorectal tumor. For more information on determining MSI, please refer to Boland (1998). If immunohistochemistry (IHC) was performed, enter 1 if any protein expression was shown to be abnormal or 2 if all were normal.

Column Name	Content
MSI	Microsatellite instability result enter 1 if high instability is present 2 if low instability or stability is present, or 0 if no MSI test has been performed.
location	Location of the colorectal tumor: enter 1 if found in the proximal colon 2 if found in the distal colon, or 0 if the location of the tumor is unknown.

```
> MMR.fam[7, "AffectedColon"] <- 1
> MSI <- location <- rep(0, nrow(MMR.fam))
> marker.testing <- data.frame(MSI, location)
> marker.testing[7, "MSI"] <- 1
> MMRpro(family = MMR.fam, marker.testing = marker.testing)
```

The probability of being a carrier is 0.946165

an MLH1 carrier 0.3662159

an MSH2 carrier 0.4147153

an MSH6 carrier 0.1678773

The risks of developing cancers are

By age	Colorectal Ca Risk	Endometrial Ca Risk
1 60	NA	0.1418469
2 65	NA	0.2389525
3 70	NA	0.2766201
4 75	NA	0.2931617
5 80	NA	0.3036418
6 85	NA	0.3102919

An object of class `"IJBayesMendel"`

```
Slot "family":
```

ID	Gender	FatherID	MotherID	AffectedColon	AffectedEndometrium	
1	1	0	3	2	1	0
2	2	0	9	8	0	0
3	3	1	11	10	1	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	0
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	0	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0
17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

	AgeColon	AgeEndometrium	MSI	location
1	55	55	0	0
2	70	70	0	0
3	57	57	0	0
4	32	32	0	0
5	50	50	0	0
6	1	1	0	0
7	47	47	1	0
8	65	65	0	0
9	66	66	0	0
10	30	30	0	0
11	74	74	0	0
12	85	85	0	0
13	79	79	0	0
14	79	79	0	0
15	23	23	0	0
16	12	12	0	0
17	22	22	0	0
18	19	19	0	0
19	16	16	0	0
20	54	54	0	0
21	77	77	0	0

Slot "posterior":

, , MSH60

	MSH20	MSH21	MSH22
MLH10	0.05383502	0.412730703	0
MLH11	0.36431890	0.001238119	0
MLH12	0.00000000	0.000000000	0

, , MSH61

	MSH20	MSH21	MSH22
MLH10	0.1664728726	7.454496e-04	0
MLH11	0.0006579279	1.006465e-06	0
MLH12	0.0000000000	0.000000e+00	0

, , MSH62

	MSH20	MSH21	MSH22
MLH10	1.608333e-126	0	0
MLH11	0.000000e+00	0	0
MLH12	0.000000e+00	0	0

Slot "probs":

	Pr(Being a carrier)	Pr(MLH1 mutation)	Pr(MSH2 mutation)
1	0.946165	0.3662159	0.4147153

Pr(MSH6)

1	0.1678773
---	-----------

Slot "predictions":

	By age	Colorectal Ca Risk	Endometrial Ca Risk
1	60	NA	0.1418469
2	65	NA	0.2389525
3	70	NA	0.2766201
4	75	NA	0.2931617
5	80	NA	0.3036418
6	85	NA	0.3102919

Slot "counselee.id":

[1] 1

Slot "loglik":

[1] -26.91065

2.2.4 Extra-colonic cancers

Information on extra-colonic cancer diagnosis is included in the `extra.colonic` object. Other cancer diagnoses that are considered to be HNPCC-associated cancers per the revised Bethesda Guidelines (see Umar et.al) can be included for all family members. The user can input this information into a data frame with `n` rows and 1 column with column name "ECC", which stores extra-colonic cancer status: enter 1 if affected, enter 0 if unaffected.

```
> ECC <- rep(0, nrow(MMR.fam))
> ECC[5] <- 1
> extra.colonic <- data.frame(ECC)
> MMRpro(family = MMR.fam, extra.colonic = extra.colonic)
```

```
The probability of being a carrier is 0.9514625
  an MLH1 carrier 0.3622179
  an MSH2 carrier 0.4104018
  an MSH6 carrier 0.1795903
```

The risks of developing cancers are

	By age	Colorectal Ca Risk	Endometrial Ca Risk
1	60	NA	0.1412477
2	65	NA	0.2385546
3	70	NA	0.2771776
4	75	NA	0.2945922
5	80	NA	0.3056667
6	85	NA	0.3126874

An object of class "IBayesMendel"

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedColon	AffectedEndometrium
1	1	0	3	2	1	0
2	2	0	9	8	0	0
3	3	1	11	10	1	0
4	4	0	0	1	0	0
5	5	1	3	2	0	0
6	6	0	0	0	0	0
7	7	0	3	2	1	0
8	8	0	0	0	0	0
9	9	1	0	0	0	0
10	10	0	0	0	0	0
11	11	1	0	0	0	0
12	12	0	9	8	0	0
13	13	0	9	8	0	0
14	14	0	11	10	0	0
15	15	1	5	6	0	0
16	16	1	0	7	0	0

17	17	0	0	7	0	0
18	18	0	0	7	0	0
19	19	0	0	7	0	0
20	20	0	21	12	0	0
21	21	1	0	0	0	0

AgeColon AgeEndometrium

1	55	55
2	70	70
3	57	57
4	32	32
5	50	50
6	1	1
7	47	47
8	65	65
9	66	66
10	30	30
11	74	74
12	85	85
13	79	79
14	79	79
15	23	23
16	12	12
17	22	22
18	19	19
19	16	16
20	54	54
21	77	77

Slot "posterior":
, , MSH60

	MSH20	MSH21	MSH22
MLH10	0.04853754	0.4098431181	0
MLH11	0.36168433	0.0003447228	0
MLH12	0.00000000	0.0000000000	0

, , MSH61

	MSH20	MSH21	MSH22
MLH10	0.1791875390	2.139156e-04	0
MLH11	0.0001887668	6.188713e-08	0
MLH12	0.0000000000	0.000000e+00	0

, , MSH62

	MSH20	MSH21	MSH22
MLH10	2.365088e-126	0	0
MLH11	0.000000e+00	0	0
MLH12	0.000000e+00	0	0

Slot "probs":

	Pr(Being a carrier)	Pr(MLH1 mutation)	Pr(MSH2 mutation)
1	0.9514625	0.3622179	0.4104018

Pr(MSH6)

1	0.1795903
---	-----------

Slot "predictions":

	By age	Colorectal Ca Risk	Endometrial Ca Risk
1	60	NA	0.1412477
2	65	NA	0.2385546
3	70	NA	0.2771776
4	75	NA	0.2945922
5	80	NA	0.3056667
6	85	NA	0.3126874

Slot "counselee.id":

[1] 1

Slot "loglik":

[1] -18.67546

2.3 PancPRO

2.3.1 Family History

Before running your pedigree through **pancpro**, be sure it is structured as a numeric data frame with history of pancreas cancer: n rows (where n is the number of family members, including the counselee) and 6 columns with required column names described below.

The family history includes the information on the counselee and his/her relatives. For each member, we need information on whether he or she has been diagnosed with colorectal cancer and either the age at diagnosis or, if cancer free, the current age or the age at death. We do the same for endometrial cancer, if the member is female.

The family cancer history must be entered in data frame form, with one row for each family member and columns containing the following information:

Column	Content
ID	Member identifier
Gender	Gender (0=female, 1=male)
FatherID	Father's identifier number
MotherID	Mother's identifier number
AffectedPancreas	Pancreatic cancer status (0=no cancer or no information,1=pancreatic cancer)
AgePancreas	Age of onset of pancreatic cancer if a pancreas cancer case. Current age or age of death if not a pancreas cancer case. 1 if unaffected and there is no age information.

Family members for whom no information is available should be coded with a 0 in the cancer diagnosis fields, and a 1 in the age fields. If it is known that a family member is affected, but age of diagnosis is unknown, either enter an estimate or evaluate the program at different plausible ages.

The parameters used by the model, including penetrance, allele frequency, and sensitivity/specificity of testing, are set using the function `pancparams`. Any changes to the parameters can be made by calling this function.

```
> data(pancpenet.2008, death.othercauses)
> myparams <- pancparams(age.by = 1, age.to = 65)
> data(panc.fam)
> pancpro(family = panc.fam, params = myparams)
```

The probability of being a carrier is 0.1694682

The risks of developing cancers are

By age	Pancreatic Ca Risk	
1	58	0.001253662
2	59	0.002612585
3	60	0.004078487
4	61	0.005651623
5	62	0.007330114
6	63	0.009110159
7	64	0.010985948
8	65	0.012949658

An object of class "IJBayesMendel"

Slot "family":

ID	Relation	Gender	FatherID	MotherID	AffectedPancreas	
1	1	1	0	3	2	0
2	2	4	0	9	8	0
3	3	4	1	11	10	0
4	4	3	0	0	1	0
5	5	2	1	3	2	0
6	6	15	0	0	0	0
7	7	2	0	3	2	1
8	8	7	0	0	0	0

9	9	7	1	0	0	0
10	10	5	0	0	0	0
11	11	5	1	0	0	0
12	12	8	0	9	8	0
13	13	8	0	9	8	0
14	14	6	0	11	10	1
15	15	13	1	5	6	0
16	16	13	1	0	7	0
17	17	13	0	0	7	0
18	18	13	0	0	7	0
19	19	13	0	0	7	0

AgePancreas

1	57
2	70
3	87
4	32
5	50
6	1
7	45
8	65
9	96
10	75
11	94
12	85
13	79
14	85
15	23
16	12
17	22
18	19
19	16

Slot "posterior":

PANCO	PANC1	PANC2
0.830531809	0.169207734	0.000260457

Slot "probs":

Pr(Being a carrier)	0.1694682
---------------------	-----------

Slot "predictions":

By age	Pancreatic Ca Risk
1 58	0.001253662
2 59	0.002612585
3 60	0.004078487

```

4      61      0.005651623
5      62      0.007330114
6      63      0.009110159
7      64      0.010985948
8      65      0.012949658

```

```
Slot "counselee.id":
```

```
[1] 1
```

```
Slot "loglik":
```

```
[1] -17.08565
```

2.3.2 Germline and Marker Testing

Because the PANC gene is a hypothetical gene, there are no germline or marker testing results to add to the calculation.

2.4 MelaPRO

2.4.1 Family History

Before running your pedigree through `melapro`, be sure it is structured as a numeric data frame with history of melanomas: n rows (where n is the number of family members, including the counselee) and 6 columns with required column names described below.

The family history includes the information on the counselee and his/her relatives. For each member, we need information on whether he or she has been diagnosed with colorectal cancer and either the age at diagnosis or, if cancer free, the current age or the age at death. We do the same for endometrial cancer, if the member is female.

The family cancer history must be entered in data frame form, with one row for each family member and columns containing the following information:

Column	Content
ID	Member identifier
Gender	Gender (0=female, 1=male)
FatherID	Father's identifier number
MotherID	Mother's identifier number
AffectedSkin	Number of diagnosed melanomas (0=no cancer or no information, 1=single melanoma, 2=multiple melanomas)
AgeSkin	Age of onset of melanomas if a cancer case. Current age or age of death if not a cancer case. 1 if unaffected and there is no age information.

Family members for whom no information is available should be coded with a 0 in the cancer

diagnosis fields, and a 1 in the age fields. If it is known that a family member is affected, but age of diagnosis is unknown, either enter an estimate or evaluate the program at different plausible ages.

The parameters used by the model, including penetrance, allele frequency, and sensitivity/specificity of testing, are set using the function `melaparams`. Any changes to the parameters can be made by calling this function.

```
> data(melapenet.HBI.2009, death.othercauses)
> data(mela.fam)
> myparams <- melaparams(spm.lr.noncarrier = 0.8)
> melapro(family = mela.fam, params = myparams)
```

The probability of being a carrier is 0.9644958

The risk of developing cancer is

	By age	Melanoma Risk
1	35	NA
2	40	NA
3	45	NA
4	50	NA
5	55	NA
6	60	NA
7	65	NA
8	70	NA
9	75	NA
10	80	NA
11	85	NA

An object of class `"IBayesMendel"`

Slot "family":

	ID	Gender	FatherID	MotherID	Affected	Skin	AgeSkin
1	1	0	2	3	2	30	
2	2	1	20	21	1	40	
3	3	0	11	12	0	36	
4	4	0	2	3	1	29	
5	5	0	2	3	0	50	
6	6	1	0	1	0	24	
7	7	0	0	1	0	23	
8	8	1	0	1	0	20	
9	9	0	0	5	0	26	
10	10	0	0	5	0	22	
11	11	1	0	0	0	63	
12	12	0	0	0	0	92	
13	13	1	11	12	0	64	
14	14	1	11	12	0	74	
15	15	0	14	0	1	25	

16	16	0	14	0	0	1
17	17	1	14	0	0	1
18	18	1	14	0	0	1
19	19	1	14	0	0	1
20	20	1	0	0	0	99
21	21	0	0	0	0	100
22	22	0	20	21	0	1
23	23	0	20	21	1	35
24	24	0	20	21	1	35
25	25	1	20	21	0	16
26	26	0	0	24	0	1
27	27	1	0	24	0	1
28	28	1	0	23	0	1

Slot "posterior":

	P160	P161	P162
	3.550425e-02	9.644558e-01	3.994792e-05

Slot "probs":

Pr(Being a carrier)	0.9644958
---------------------	-----------

Slot "predictions":

	By age	Melanoma Risk
1	35	NA
2	40	NA
3	45	NA
4	50	NA
5	55	NA
6	60	NA
7	65	NA
8	70	NA
9	75	NA
10	80	NA
11	85	NA

Slot "counselee.id":

[1] 1

Slot "loglik":

[1] -47.9441

2.4.2 Germline and Marker Testing

Information about germline testing results is included in the `germline.testing` object. If the results of germline testing are available, the user can input them into a data frame with `n` rows and 2 columns with column names “P16”, and “Test Order” which stores the mutation testing results for *P16* (0=no test, 1=positive test, 2=negative test) and order in which family members were tested. If the testing order is unknown, we suggest evaluating the model multiple times, allowing each tested family member to be indicated as the first person tested.

```
> P16 <- TestOrder <- rep(0, nrow(mela.fam))
> germline.testing = data.frame(P16, TestOrder)
> germline.testing[4, ] <- c(1, 1)
> germline.testing[1, ] <- c(2, 2)
> melapro(family = mela.fam, germline.testing = germline.testing)
```

The probability of being a carrier is 0.02308667

The risk of developing cancer is

	By age	Melanoma Risk
1	35	NA
2	40	NA
3	45	NA
4	50	NA
5	55	NA
6	60	NA
7	65	NA
8	70	NA
9	75	NA
10	80	NA
11	85	NA

An object of class `BayesMendel`

Slot "family":

	ID	Gender	FatherID	MotherID	AffectedSkin	AgeSkin	P16
1	1	0	2	3	2	30	2
2	2	1	20	21	1	40	0
3	3	0	11	12	0	36	0
4	4	0	2	3	1	29	1
5	5	0	2	3	0	50	0
6	6	1	0	1	0	24	0
7	7	0	0	1	0	23	0
8	8	1	0	1	0	20	0
9	9	0	0	5	0	26	0
10	10	0	0	5	0	22	0
11	11	1	0	0	0	63	0
12	12	0	0	0	0	92	0

13	13	1	11	12	0	64	0
14	14	1	11	12	0	74	0
15	15	0	14	0	1	25	0
16	16	0	14	0	0	1	0
17	17	1	14	0	0	1	0
18	18	1	14	0	0	1	0
19	19	1	14	0	0	1	0
20	20	1	0	0	0	99	0
21	21	0	0	0	0	100	0
22	22	0	20	21	0	1	0
23	23	0	20	21	1	35	0
24	24	0	20	21	1	35	0
25	25	1	20	21	0	16	0
26	26	0	0	24	0	1	0
27	27	1	0	24	0	1	0
28	28	1	0	23	0	1	0

TestOrder

1	2
2	0
3	0
4	1
5	0
6	0
7	0
8	0
9	0
10	0
11	0
12	0
13	0
14	0
15	0
16	0
17	0
18	0
19	0
20	0
21	0
22	0
23	0
24	0
25	0
26	0
27	0
28	0

```
Slot "posterior":
      P160          P161          P162
9.769133e-01 2.308559e-02 1.081983e-06
```

```
Slot "probs":
  Pr(Being a carrier)
      0.02308667
```

```
Slot "predictions":
  By age Melanoma Risk
1      35          NA
2      40          NA
3      45          NA
4      50          NA
5      55          NA
6      60          NA
7      65          NA
8      70          NA
9      75          NA
10     80          NA
11     85          NA
```

```
Slot "counselee.id":
[1] 1
```

```
Slot "loglik":
[1] -52.5884
```

3 Other Features

3.1 Plotting a pedigree

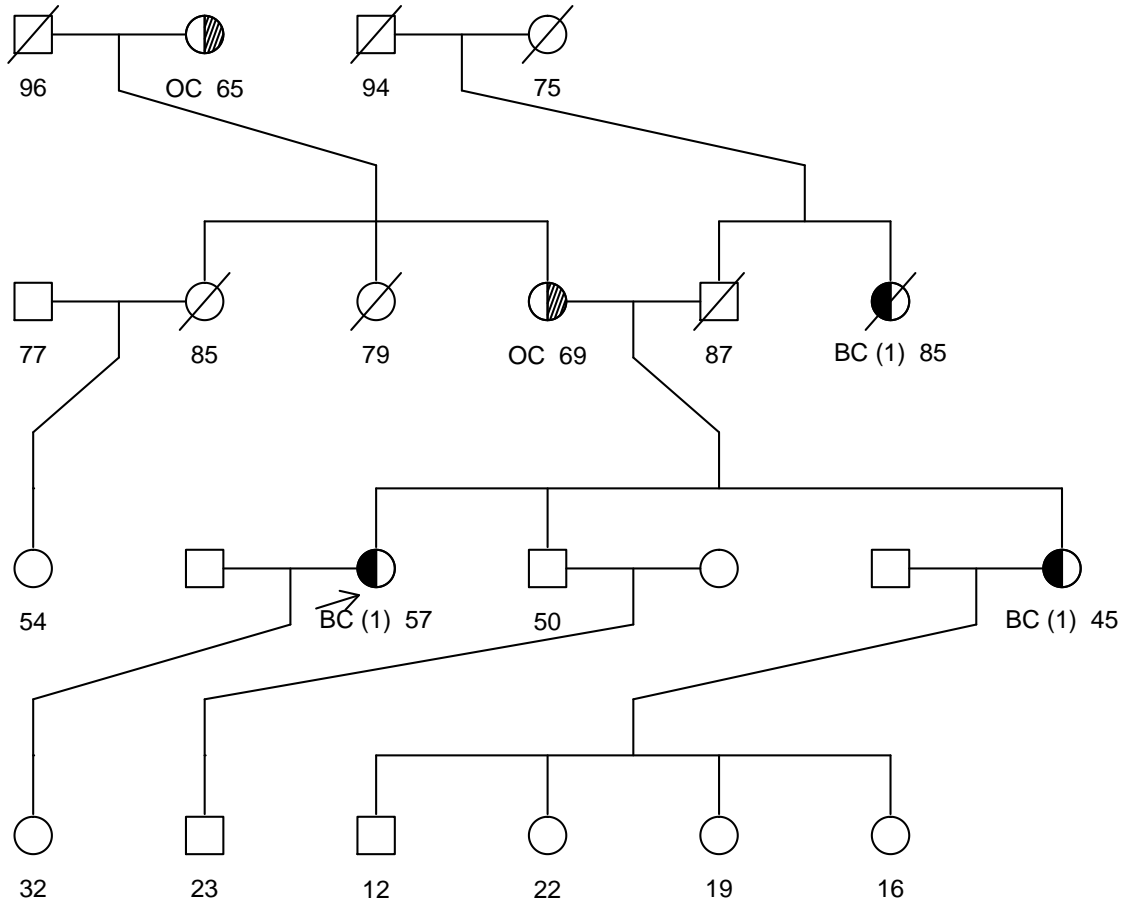
The family history data frame can be displayed graphically in a traditional pedigree plot. There are two options for plotting your pedigree. If you want to plot your pedigree without running it through any of the models, the family history data frame `family` must be set to be part of the `BayesMendel` class and then plotted by simply using the generic function `plot`. If the vital status of family members is known, it can be included by adding a column labeled “status” can be added to the family data frame. Enter 0 if the individual is alive, or 1 if not alive.

```
> status <- c(0, 0, 1, 0, 0, 0, 0, 0, 1, 1, 1, 1, 1,
+            1, 0, 0, 0, 0, 0, 0, 0)
> brca.fam <- data.frame(brca.fam, status)
```

```

> myfamily <- new("BayesMendel", family = brca.fam,
+   counselee.id = 1)
> plot(myfamily)

```



The pedigree can also be run through any of the models and plotted with the carrier probabilities displayed on the graph.

```

> mmrpro.out <- MMRpro(family = MMR.fam, counselee.id = 1)

```

The probability of being a carrier is 0.8617582
 an MLH1 carrier 0.3330994

an MSH2 carrier 0.377442

an MSH6 carrier 0.1516471

The risks of developing cancers are

	By age	Colorectal Ca Risk	Endometrial Ca Risk
1	60	NA	0.1292149
2	65	NA	0.2177639
3	70	NA	0.2522371
4	75	NA	0.2674864
5	80	NA	0.2771938
6	85	NA	0.2833653

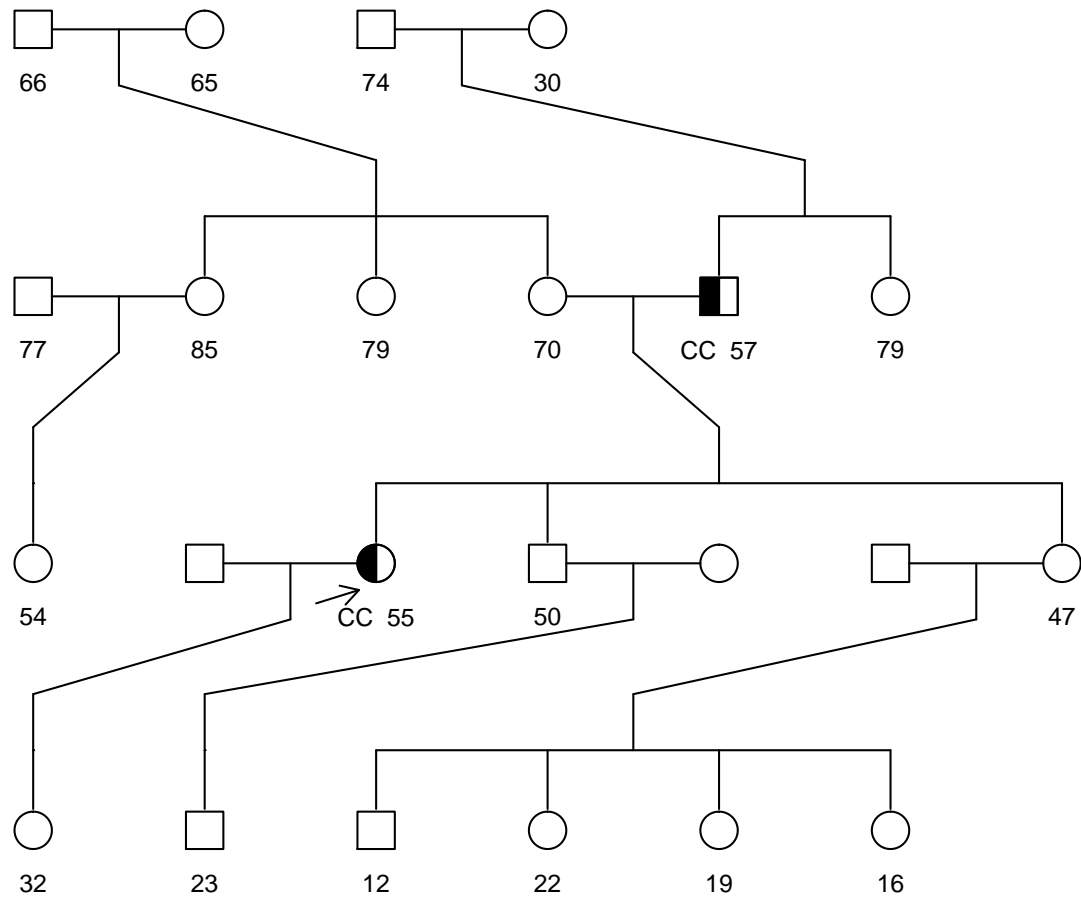
> plot(mmrpro.out)

Noncarrier probability = 0.846

MLH1 carrier probability = 0.061

MSH2 carrier probability = 0.069

MSH6 carrier probability = 0.024



4 Further Information

More information about our methods and software can be found at our website <http://astor.som.jhmi.edu/BayesMendel>. We can also be reached by email at BayesMendel@jhu.edu.