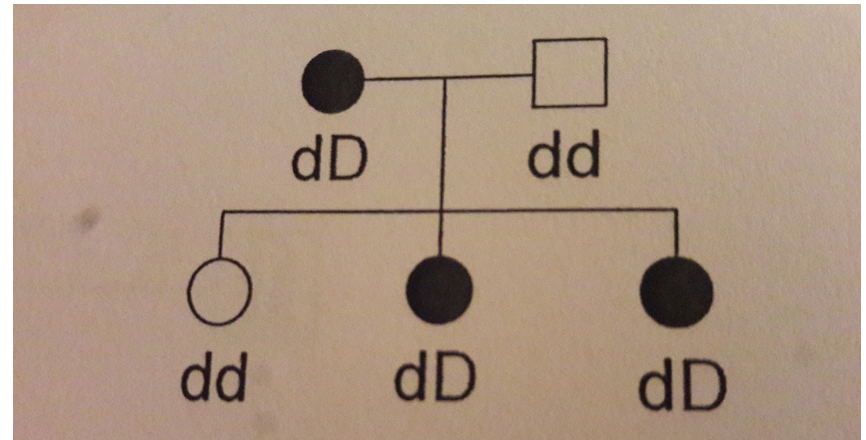


Prediction models for cancer

Probability calculations in families

Genotype - Phenotype

- Complete penetrance or reduced?
- Phenocopies?



One locus model

- Mendelian autosomal
 - Dominant
 - no phenocopies
 - complete penetrance
$$P(\text{disease} \mid dd) = 0$$
$$P(\text{disease} \mid dD) = 1$$
$$P(\text{disease} \mid DD) = 1$$
 - complex
 - phenocopies
 - incomplete penetrance
$$P(\text{disease} \mid dd) > 0$$
$$P(\text{disease} \mid dD) < 1$$
$$P(\text{disease} \mid DD) < 1$$

Diagnostic test

| | K | G | |
|----|---|---|--|
| T+ | A Test positive and disease | B Test positiv And no disease | positive predictive value = $P(K T+) = A/A+B$ |
| T- | C Test negativ und Krankheit | D Test negativ und keine Krankheit | negative prädiktive value = $P(G T-) = D/C+D$ |

Sensitivity = $P(T+|K) = A/(A+C)$

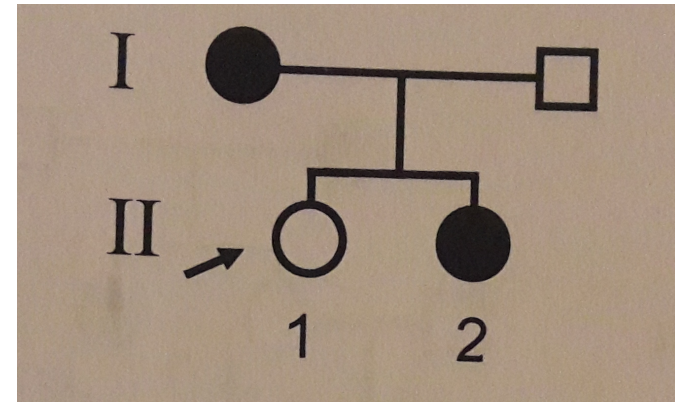
Specificity = $P(T-|G) = D/(B+D)$

Predictive values depend on prevalence

Bayes' tableau

Rare autosomal dominant disease, no phenocopies

| | Carrier | No Carrier |
|--------------|--------------|------------|
| a priori | 0.5 | 0.5 |
| condition | 1-prevalence | 1 |
| product | 0.35 | 0.5 |
| a posteriori | 0.41 | 0.59 |

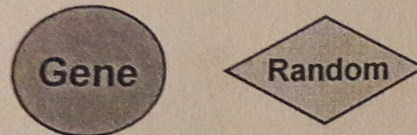


Polygenic risk score

- GWAS: first low risk variants
- Additive effect
- $PRS = \beta_1 x_1 + \beta_2 x_2 + \dots + \beta_k x_k$

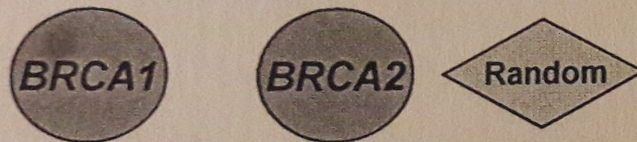
β : relative effect size

Genetic models for BC risk calculation



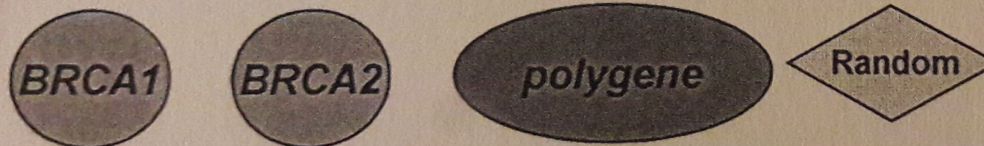
CLAUS

Claus et al. AJHG, 1991



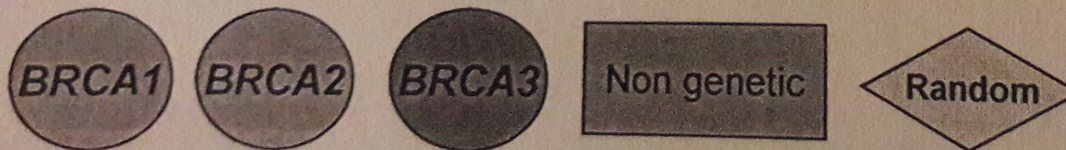
BRCAPRO

Parmigiani et al. AJHG, 1998



BOADICEA

Antoniou et al. Br J Cancer, 2002



IBIS

Tyrer et al. Stat Med, 2004

Breast Cancer Screening

Prevention

- Primary



- Secondary
 - Survival vs overdiagnosis



Risk factors

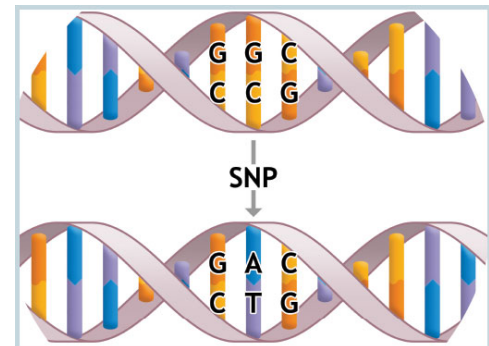
- Environmental



- Hormonal



- Genetic
 - Hereditary (BRCA1/2)
 - somatic



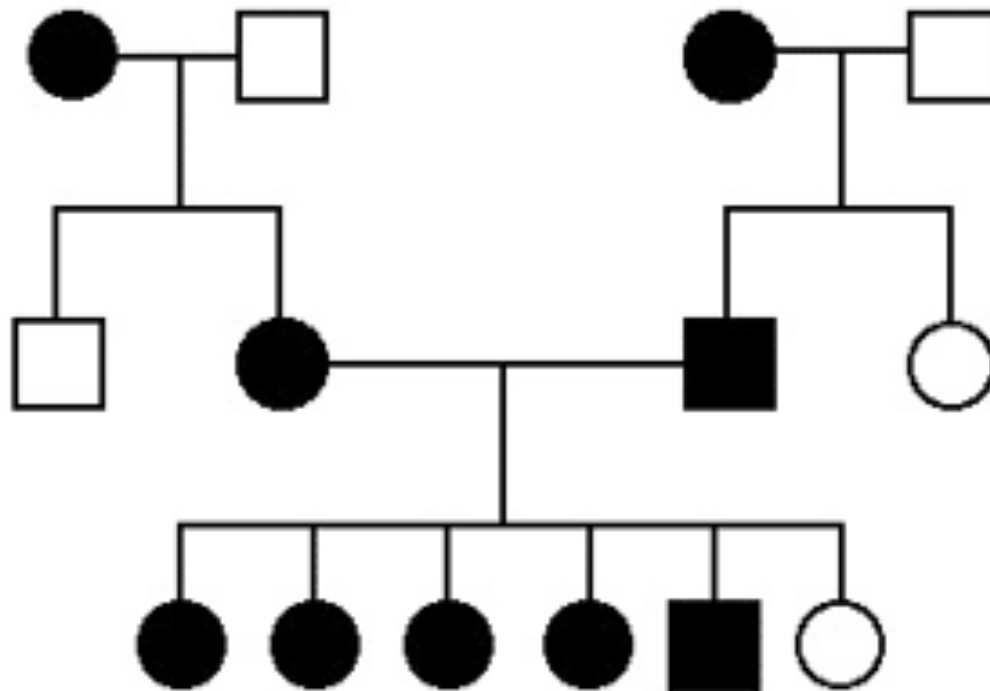
Pedigree



= Frau



= Mann



Risk models



Last modified date: 05/16/2011

IBIS Risk Assessment Tool

This tool estimates the likelihood of a woman developing breast cancer specifically within 10 years of her current age and over the course of her lifetime. The tool is utilized to inform women and help support the decision making process for genetic counseling and testing.

Note: This tool is *not* intended to assess the risk for women who have already been diagnosed with breast cancer.

System of Measurement: ☒ Metric Units ☐ Imperial Units

Personal History: Please enter the woman's age, weight and height below...

Current Age:

Weight: kg

Height: meters

What was the woman's age at the time of her first menstrual period?

Has the woman given birth to one or more children? ☒ No ☐ Yes

Has the woman gone through menopause? ☒ Don't Know ☐ No ☐ Yes
☐ In Menopause Now

Hormone Replacement Therapy (HRT) Usage? ☒ Never ☐ Stopped use 5 or more years ago
☐ Stopped use less than 5 years ago
☐ Current User

BRCA Gene: Does the woman have a mutation in either the BRCA1 or BRCA2 gene?

Get Started with the Risk Tool

About the Tool

Breast Cancer Risk Factors

Download Source Code

Page Options

Quick Links

[Breast Cancer Home Page](#)
[Breast Cancer: Prevention, Genetics, Causes](#)
[Current Clinical Trials: Breast Cancer In Situ: Treatment](#)
[Current Clinical Trials: Breast Cancer Prevention](#)

The Breast Cancer Risk Assessment Tool is an interactive tool designed by scientists at the National Cancer Institute (NCI) and the [National Surgical Adjuvant Breast and Bowel Project \(NSABP\)](#) to estimate a woman's risk of developing [invasive breast cancer](#). See [About the Tool](#) for more information.

The Breast Cancer Risk Assessment Tool may be updated periodically as new data or research becomes available.

Risk Tool

(Click a question number for a brief explanation, or [read all explanations.](#))

1. Does the woman have a medical history of any breast cancer or of ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS) or has she received previous radiation therapy to the chest for treatment of Hodgkin lymphoma?
2. Does the woman have a mutation in either the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?
3. What is the woman's age?
This tool only calculates risk for women 35 years of age or older.

Consultand Consultand

Enter details of the consultand...

Clinical history **Breast cancer pathology**

First name/ID

Personal details

Sex and status ☐ Male ☒ Female ☐ Alive ☐ Dead ☐ Ashkenazi origin

Age or Age at death ☒ Exact ☐ Approx ☐ Unknown

Year of birth ☒ Exact ☐ Approx ☐ Unknown

Breast cancer ☐ Age at diagnosis ☒ Exact ☐ Approx ☐ Unknown

Contralateral BC ☐ Age at diagnosis ☒ Exact ☐ Approx ☐ Unknown

Ovarian cancer ☐ Age at diagnosis ☒ Exact ☐ Approx ☐ Unknown

Prostate cancer ☐ Age at diagnosis ☒ Exact ☐ Approx ☐ Unknown

Pancreatic cancer ☐ Age at diagnosis ☒ Exact ☐ Approx ☐ Unknown

Genetic testing

Genetic test type ☒ Untested ☐ Mutation search ☐ Direct gene test

Mutation ☒ None ☐ BRCA1 ☐ BRCA2

Consultand Consultand

Enter details of the consultand...

Clinical history **Breast cancer pathology**

☐ Estrogen Receptor (ER) ☒ Unknown ☐ Positive ☐ Negative

☐ Progesterone Receptor (PR) ☒ Unknown ☐ Positive ☐ Negative