

Breast Cancer Risk Models

What are breast cancer risk models?

Breast cancer risk models are used to calculate a woman's risk for developing breast cancer over the course of her lifetime, based on a wide variety of personal and familial risk factors. Some risk models calculate a patient's risk of having a *BRCA1/2* mutation. These risk models can be used to determine breast surveillance, and eligibility for chemoprevention.

Models to Assess Breast Cancer Risks in Unaffected Women

The Gail Model

Risk Factors

- Proband age, medical, and reproductive history
- Family history

Relative Risk Assessment

- Combination of risk factors
- Logistic regression provides summary RR
- Calculates lifetime and 5-year breast cancer risk
- Women with a lifetime risk >20% should consider breast MRI
- Women with a 5-year Gail risk score of >1.67% are eligible for chemoprevention

Main Limitations

- Family history limited to two 1st degree relatives
- Validated only for certain ethnic/racial groups
- Age of cancer onset not factored into calculation
- Not validated in women under age 35
- Used only for women with no history of breast cancer or high-risk lesions and no known gene mutations associated with cancer
- A good population-based model, but not very good at predicting risk at the individual level

The Claus Model (Table Based)

Risk Factors

- Proband age
- Family history of female breast cancer (invasive and DCIS)
- Age of onset in affected relatives

Relative Risk Assessment

- Data compiled from a research study and organized into sets of tables for more general use
- Various mathematical equations were tested to see which fit the data set best
- Women with a lifetime risk >20% should consider breast MRI

Main Limitations

- Family history is not extensive
- Maximum of two 1st or 2nd degree relatives
- Male breast cancer not included in model
- Does not take any personal medical history/reproductive history into account
- Used only for unaffected probands when there is no concern for a genetic mutation

Model to Assess the Risk of a *BRCA1* or *BRCA2* Gene Mutation

Myriad Prevalence Tables

Risk Factors

- Personal and family history of cancer as reported on Myriad Laboratories test requisition forms

Relative Risk Assessment

- Determined by a compilation of data from Myriad Laboratories' sequencing of acquired *BRCA1/BRCA2* samples

Main Limitations

- This is not a model – it is a compilation of data put into a categorical table
- This is a biased sample and may not be representative of the general population
- These tables rely on information provided on the test requisition form

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Models to Assess the Risk of Developing Breast Cancer AND of a *BRCA1* or *BRCA2* Mutation

BRCAPro

Risk Factors

- Breast or ovarian cancer in proband and all affected 1st or 2nd degree relatives
- Age(s) of onset for all cancers, age(s) of unaffected relatives, age(s) of oophorectomy
- Proband age at menarche and first live birth, height, weight, biopsy history, and mutation carrier status if known

Risk Assessment

- Bayesian analysis
- Mutation frequency and penetrance estimates derived from Breast Cancer Linkage Consortium data

Main Limitations

- Dependent on current mutation frequency and penetrance data
- Assumes all familial cancers are due to *BRCA1/2*
- Inaccuracies in placing value on certain cancers

- Calculates likelihood of *BRCA* mutation using Bayesian analysis
- Calculates breast cancer risk based on:
 - Likelihood of *BRCA* mutation
 - Likelihood of hypothetical autosomal dominant gene mutation
- Personal risk factors

Main Limitations

- Not based on an actual population of women
- Proband cannot have breast cancer (but can have ovarian cancer)
- Dependent on current mutation frequency and penetrance data
- Hypothetical gene mutation
- Cannot account prophylactic surgery; bilateral breast cancer in 2nd and 3rd degree relatives; other cancers

Tyrer-Cuzick Model

Risk Factors

- Proband age, reproductive factors, hormonal risk factors, height, weight, HRT use, breast density
- Ashkenazi Jewish ancestry
- Family history of cancer
- Mothers and sisters (affected and unaffected)
 - Presence of breast cancer (and if bilateral), ovarian cancer, and age of diagnosis
- Daughters, maternal and paternal aunts and grandmothers (affected and unaffected)
 - Presence of breast or ovarian cancer and age at diagnosis
- Can also add affected half-siblings, cousins, and nieces
- Accounts for affected male relatives

Risk Assessment

- Proportional hazards model

Resources

For information about genetic testing and genetic counseling, visit the [UT Southwestern Cancer Genetics for Health Professionals site](#).

For additional resources on coordinating genetics counseling and testing for patients, or providing genetics services, visit the [Genetic Screening and Navigation Toolkit](#).

To find a genetic counselor near you, visit the National Society of Genetic Counselors [Find a Genetic Counselor Tool](#).

References

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