

Summaries for Patients are a service provided by *Annals* to help patients better understand the complicated and often mystifying language of modern medicine.

The full report is titled “Validity of Models for Predicting *BRCA1* and *BRCA2* Mutations.” It is in the 2 October 2007 issue of *Annals of Internal Medicine* (volume 147, pages 441–450). The authors are G. Parmigiani, S. Chen, E.S. Iversen Jr., T.M. Friebe, D.M. Finkelstein, H. Anton-Culver, A. Ziogas, B.L. Weber, A. Eisen, K.E. Malone, J.R. Daling, L. Hsu, E.A. Ostrander, L.E. Peterson, J.M. Schildkraut, C. Isaacs, C. Corio, L. Leondaridis, G. Tomlinson, C.I. Amos, L.C. Strong, D.A. Berry, J.N. Weitzel, S. Sand, D. Dutson, R. Kerber, B.N. Peshkin, and D.M. Euhus.

Validity of Models for Predicting *BRCA1* and *BRCA2* Mutations

What is the problem and what is known about it so far?

Two genes, *BRCA1* and *BRCA2*, occur infrequently in the population but are relatively common in women of Ashkenazi Jewish ancestry and in women with a strong family history of breast cancer. When a woman has defects in 1 of these genes, she is very likely to have breast (or ovarian) cancer during her lifetime. Many women are worried that they have mutations of these genes, and they seek advice about whether to be tested for it. Because the mutation test is expensive, counselors estimate the probability that a woman has the *BRCA1/BRCA2* mutations. One way to estimate the probability of the mutation is to ask questions and then use the answers to make an educated guess. The accuracy of the guess will depend on the skill and experience of the counselor. However, better ways exist. They are called *prediction models*. They use knowledge about the exact relationship between a woman’s history—including how many family members had breast cancer—and defects in the *BRCA1/BRCA2* genes. They obtain this knowledge by asking women about their medical history, testing each woman for mutations of the *BRCA1/BRCA2* genes, and doing statistical tests to identify which parts of the history are most strongly related to having the mutations. Using these models, anyone—a counselor or a patient—could calculate a woman’s probability of having *BRCA1/BRCA2* mutation. Many prediction models exist.

Why did the researchers do this particular study?

To compare 7 prediction models to determine whether any was clearly better in detecting a *BRCA1/BRCA2* gene mutation.

Who was studied?

3342 families—nearly all women—who were patients in 9 cancer counseling centers. Each person had been tested for the *BRCA1/BRCA2* gene mutation, and 17% had positive results on the genetic test.

How was the study done?

The researchers applied the 7 prediction models to every person and calculated the probability that the person had a mutation of the *BRCA1/BRCA2* gene. Because the researchers knew the results of the tests for *BRCA1/BRCA2* mutation, they could measure the accuracy of each model in people from 9 cancer practices.

What did the researchers find?

The study had 3 main findings. First, using 7 different prediction models in 1 person often gave 7 different numbers to represent that person’s probability of having a *BRCA1/BRCA2* mutation. In other words, the models often didn’t agree very well. Second, the models were similarly good at discriminating between persons with a *BRCA1/BRCA2* mutation and persons without a *BRCA1/BRCA2* gene mutation. Third, the models can make mistakes.

What were the limitations of the study?

One prediction model calculated a number that is not a probability, which makes it harder to compare it with those that do estimate a probability.

What are the implications of the study?

Although the prediction models can usually distinguish between someone with a *BRCA1/BRCA2* mutation and someone without a mutation, they can make mistakes. This means that patients should not rely entirely on the predicted probability when deciding whether to have mutation testing. Patients should discuss other factors that should be taken into consideration with their doctors.

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