

University of Pennsylvania BRCA1/BRCA2 prediction model

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Abstract

Background. Strategies such as prophylactic oophorectomy and mastectomy are effective in preventing ovarian and breast cancer in women with BRCA1 and BRCA2 mutations. These successful interventions highlight the need for appropriate identification of individuals at sufficient risk of carrying a mutation to justify genetic testing. Several models, each with inherent limitations, have been developed to predict the probability that an individual carries a mutation in BRCA1 or BRCA2. Here, we have refined our previously published prediction model (Couch, 1997, #1) to predict the presence of BRCA1 and BRCA2 mutations in families attending high-risk breast cancer clinics.

Methods. Nine hundred sixty-six families with at least two individuals affected with breast or ovarian cancer and tested for mutations in BRCA1 and BRCA2 were identified from four high-risk breast cancer screening clinics. A complete pedigree, cancer history, and genetic testing information were obtained. Chi-squared and univariate regression analyses were used to examine associations between familial characteristics and the presence of a BRCA1 or BRCA2 mutation. Multivariable logistic models were generated. Predicted probabilities were generated from the best-fitting logistic models.

Result. For mutations in either BRCA1 or BRCA2, predictive factors on the best-fitting model were the number of breast cancers under the age of 50, presence of male breast cancer, presence of breast and ovarian cancer in an individual, ovarian cancer in the family, and Ashkenazi [Jewish] descent.

Conclusion. Based on the number and diversity of contributing referral centers, this model should be generalizable to most families seeking genetic counseling for breast and ovarian cancer.