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Tamoxifen and Breast Cancer Incidence Among Women with Inherited Mutations in *BRCA1* and *BRCA2*

[e-journal abstract
template on King et al](#)**Bruce K. Lin and Paula Yoon**Office of Genomics and Disease Prevention,
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The Health Outcome

As many as 192,200 new cases of invasive breast cancer will be diagnosed among women in the United States in 2001, making it the most common form of cancer in women this year. Three to five% of these breast cancer cases will be associated with mutations within the *BRCA1* or *BRCA2* genes. Despite declining mortality rates among women during 1990-1997, breast cancer remains the second-leading cause of cancer deaths among women. In addition to mutations found in the breast cancer susceptibility genes, several environmental, physical and behavioral risk factors have been identified that place some women at increased risk of developing breast cancer. Current research suggests that estrogen-receptor (ER) modulators, specifically tamoxifen, reduce breast cancer risk (1).

The Finding

King et al. (2001) reports gene-environment interaction results from a controlled clinical trial that examined the risk for breast cancer among women with *BRCA1* and *BRCA2* mutations associated with the use of tamoxifen vs. placebo (2). A detailed abstraction of this article is available online as part of the HuGE Net e-Journal club (3). Among a cohort of previously healthy women (aged 35 years and older) who developed breast cancer during the course of the clinical trial and who could be genotyped (n=288), 19 (6.6%) carried mutations within *BRCA1* and *BRCA2*. In this study, tamoxifen did not appear to decrease breast cancer incidence among healthy *BRCA1* carriers; however, the finding was not statistically significant. Based on this result for *BRCA1* carriers, the authors clarify that it is unclear whether tamoxifen use at a younger age would reduce breast cancer incidence among healthy women who have *BRCA1* mutations. In contrast, the incidence of breast cancer among patients with *BRCA2* mutations who received tamoxifen decreased by 62% (again, statistically insignificant) compared with placebo. The authors point out that the reduction is similar to the reduction in incidence of ER-positive breast cancer among all women in the clinical trial. In addition, the authors report that for this study, tumors of women with inherited *BRCA1* mutations are more frequently ER negative than tumors with *BRCA2* mutations.

Public Health Implications

Currently, screening the general population for *BRCA1* and *BRCA2* mutations for breast cancer is not recommended (1). In the context of studies that examine the treatment of breast cancer and identify *BRCA1* and *BRCA2* mutations as susceptibility genes, King et al. (2001) addressed a specific issue in their study- whether chemoprevention using tamoxifen would reduce the incidence of invasive breast cancer among previously healthy women who were either *BRCA1* or *BRCA2* carriers. The results suggest that for their study group, having *BRCA1* and *BRCA2* mutations can affect the expected effect of tamoxifen in reducing the incidence of breast cancer. In fact, results of the King et al. study show that tamoxifen's effectiveness is reduced in cancer-free women with *BRCA1* mutations. The authors note that because of the small sample size, inferences from the genetic data cannot completely answer their study hypothesis (2). King et al. state that additional research into the efficacy of tamoxifen among younger, cancer-free women with *BRCA1* mutations is needed to further clarify the issue. For the purposes of this HuGE e-journal Club, we could not comment further on gene prevalence or conduct a proper incidence-based analysis because no person-year information (or denominator data) was presented with this publication.

References

1. American Cancer Society. Cancer facts and figures 2001. Atlanta: The American Cancer Society; 2001.
2. King M-C, Wieand S, Hale K, et al. Tamoxifen and breast cancer incidence among women with inherited mutations in *BRCA1* and *BRCA2*. JAMA 2001;286:2251-6.
3. [King M-C et al. e-Journal Club abstraction template](#)

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