

Genomic sequencing more efficient in predicting breast cancer risk than previously thought

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Using genomic sequencing data on all currently known genetic alterations in breast cancer, it is possible to identify a woman's genetic risk for the disease, and this approach can bring greater gains in disease prevention than previously estimated, according to a study published in *Cancer Epidemiology, Biomarkers & Prevention*, a journal of the American Association for Cancer Research.

Results of this study suggest that it is feasible to use genomic sequencing to identify women who would benefit most from [breast cancer](#) screening practices, such as mammography. Further, knowing one's risk for breast cancer at birth may help women take measures to modify their nongenetic risk factors, such as diet and lifestyle, and lower their risk, according to the study.

"We need low-cost screening tools that can discriminate between women who will and won't develop fatal breast cancer that are more effective than those currently available," said Alice S. Whittemore, PhD, professor of epidemiology and biostatistics in the Department of Health Research and Policy at Stanford Cancer Institute in California.

"Previous studies using theoretical models have predicted that sequencing the genomes of women, ranking them by risk, and then targeting those at highest risk will provide little gain in cost-effective disease prevention," added Whittemore. "However, our estimates suggest

that preventive strategies based on genome sequencing will bring greater gains in [disease prevention](#) than previously projected. Moreover, these gains will increase with increased understanding of the genetic etiology of breast cancer," she said.

Whittemore and colleagues used data from published literature on the frequency of 86 known breast cancer variants associated with breast cancer risk. They then developed a computational model to estimate a woman's lifetime probability of developing breast cancer by calculating the [risk score](#). The risk score is the sum of the breast cancer-related genetic variants a woman carries, multiplied by the effect of the variants, Whittemore explained.

The researchers estimated that the variance of the risk score based on the 86 known breast cancer susceptibility variants for the population as a whole is 0.35, which is higher than the variance of 0.07 estimated by an earlier study. "Variance is a relative measure of the heterogeneity of breast cancer risks in the population," explained Whittemore. "The more genetic variants we discover, the more heterogeneous our genetic risks will be, and the more effective it will be to target those at highest risk."

Weiva Sieh, MD, PhD, assistant professor and epidemiologist at Stanford and first author on this study, said, "As we keep identifying additional breast cancer variants that can further explain the difference between my risk versus yours, the variance of the [genetic risk](#) score in the population will increase, and the potential utility of [genomic sequencing](#) will grow.

"Our ability to predict the probability of disease based on genetics is the starting point," Sieh added. "If a girl knew, from birth, what her inborn risk was, she could then make more informed choices to alter her future risk by altering her modifiable factors, such as diet and lifestyle."

More information: "The Role of Genome Sequencing in Personalized Breast Cancer Prevention" Weiva Sieh, Joseph H. Rothstein, Valerie McGuire, and Alice S. Whittemore *Cancer Epidemiol Biomarkers*, Prev Published OnlineFirst October 23, 2014; [DOI: 10.1158/1055-9965.EPI-14-0559](https://doi.org/10.1158/1055-9965.EPI-14-0559)

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