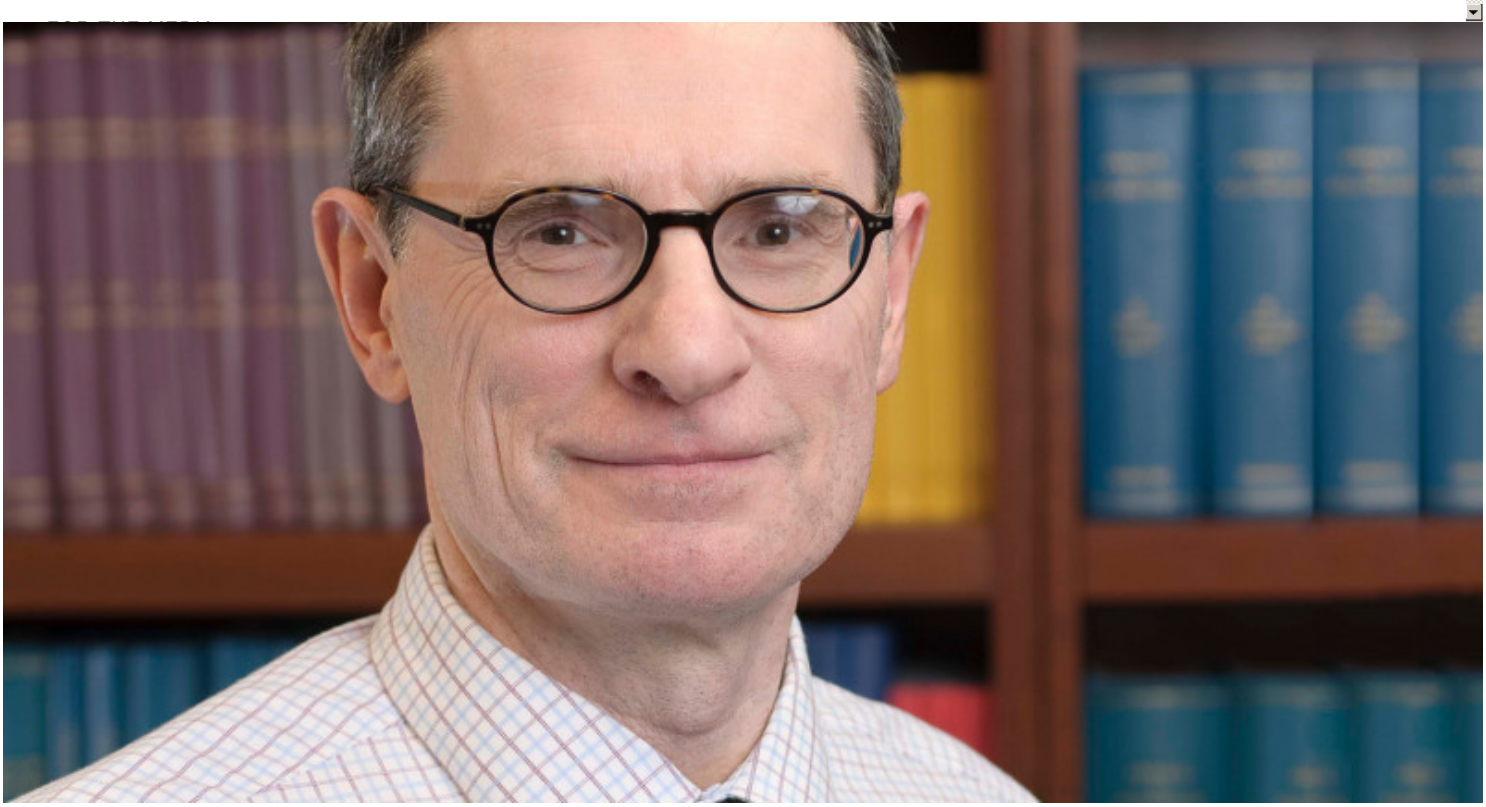

Breast cancer risk varies widely among women who are carriers of the *BRCA1* and *BRCA2* mutations, according to a new study published in the January 9, 2008, issue of the *Journal of the American Medical Association* (*JAMA*). "Our results underscore the conclusion that there is no single risk associated with *BRCA1* or *BRCA2* carrier status," said lead author Colin Begg, PhD, Chair of the Department of Epidemiology and Biostatistics at Memorial Sloan Kettering Cancer Center, "and the risks in carriers and their relatives must be influenced by other risk factors." [PubMed Abstract]

Previous studies have reported on the overall increased breast cancer risk among carriers of the *BRCA1* and *BRCA2* mutations, with little attention paid to the degree with which risk may vary among carriers. "We found evidence that some carriers have a much higher risk and some have a much lower risk," said Dr. Begg. "The presumptive explanation is that there are other, unknown genes that influence breast cancer risk in *BRCA1* and *BRCA2* carriers."

The research team analyzed epidemiological data from more than 2,000 women who participated in the study, called the WECARE Study. One of the largest studies of its type, the WECARE Study was an international, multi-institutional, population-based study that involved 1,394 women with breast cancer and an additional 704 women with contralateral breast cancer (separate occurrences of cancer in both breasts). The women were diagnosed with breast cancer between 1985 and 2000, prior to age 55 and without evidence of spread beyond the regional lymph nodes.

> Our results underscore the conclusion that there is no single risk associated with BRCA1 or BRCA2 carrier status, and the risks in carriers and their relatives must be influenced by other risk factors.
>
> Colin Begg, PhD, Chair of the Department of Epidemiology and Biostatistics

The study focused on the incidence of breast cancer in the first-degree relatives of the 181 women who tested positive for a mutation in *BRCA1* or *BRCA2*. The results showed that relatives of the women diagnosed at younger ages (35 years or younger) had significantly higher incidence of breast cancer than relatives of women diagnosed between the ages of 45 and 54. “Our statistical analysis also demonstrated that risk varied significantly from family to family,” said Dr. Begg.

“Although our study did not address this directly, our findings imply the additional genes affecting risk in these carrier families might also affect the risk of breast cancer in both the carriers and the non-carriers in the families, suggesting that risks are generally higher in families with multiple cases of breast cancer,” said Jonine Bernstein, PhD, the lead investigator for the WECARE Study. “Conversely, the likelihood of breast cancer developing in a healthy woman without a family history of breast cancer after testing positive for a *BRCA1* or *BRCA2* mutation is likely to be much lower than current estimates of lifetime risk in carriers.”

The findings from the study have implications for the future of genetic screening for breast cancer and for understanding who is at greatest risk. According to Dr. Begg, they also underscore that “research to identify new genes that influence breast cancer is worthwhile and should ultimately be fruitful.”

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