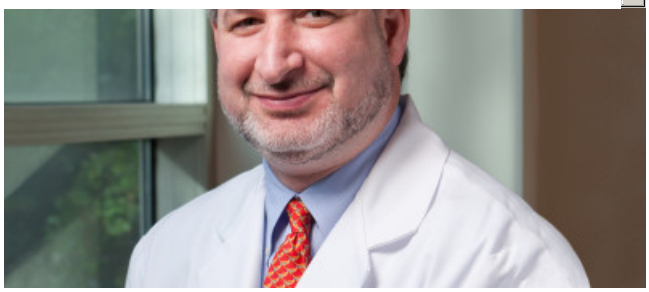
led by researchers at Memorial Sloan Kettering Cancer Center (MSKCC) is the first prospective examination of the impact of this procedure in which *BRCA2* mutation carriers were analyzed separately from *BRCA1* mutation carriers. All previous studies evaluating this approach have only examined *BRCA1* and *BRCA2* mutation carriers together or have limited their analysis to *BRCA1* mutation carriers alone.



Noah D. Kauff

The findings of the new study, to be published in the March 2008 issue of the *Journal of Clinical Oncology* may have important implications for women comparing the risks and benefits of specific cancer-risk-reduction options. [PubMed Abstract]

> "These findings will allow doctors to better tailor risk-reduction approaches for women at inherited risk for breast

and ovarian cancer."

Noah Kauff, MD, study's lead author and a gynecologist and geneticist at MSKCC

According to the research, the surgery - called risk-reducing salpingo-oophorectomy (RRSO) - may confer different benefits for women at inherited risk for breast and ovarian cancer depending upon whether *BRCA1* or *BRCA2* is abnormal. The efficacy of this procedure for the prevention of breast and gynecologic cancer had never been evaluated in groups of women stratified according to mutation type, despite 17 percent to 39 percent of all *BRCA* mutation carriers having a mutation in the *BRCA2* gene.

"These findings will allow doctors to better tailor risk-reduction approaches for women at inherited risk for breast and ovarian cancer," said the study's lead author, Noah Kauff, MD, a gynecologist and geneticist at MSKCC. "Given these results, further studies evaluating the efficacy of risk-reduction strategies in *BRCA* mutation carriers will likely need to stratify by the specific gene mutated," he added.

Researchers compared the incidence of breast and gynecologic cancers between a group of 509 women 30 years of age or older who carried a *BRCA1* or *BRCA2* mutation and had undergone RRSO, and a group of 283 women with these mutations who did not have the surgery. The women were followed prospectively for three years via questionnaire and medical record review.

Investigators found that RRSO was associated with a 72 percent breast cancer risk reduction in women with *BRCA2* mutations - nearly twice the reduction in breast cancer risk compared to women with *BRCA1* mutations. The surgery also reduced the risk of gynecologic cancer by 85 percent in women with a *BRCA1* mutation. While protection against gynecologic cancer was suggested in women with a *BRCA2* mutation, researchers were not able to estimate the level of reduced risk due to the low incidence of gynecologic cancers among women with these mutations.

Further analyses demonstrated that RRSO appeared to reduce the risk of estrogen receptor (ER)-positive breast cancer by 78 percent in women with a mutation in either *BRCA1* or *BRCA2*, but had no effect on the development of ER-negative breast cancers. Because *BRCA1* carriers are more likely to be diagnosed with ER-negative breast cancers, the authors note that carriers of these mutations need to consider additional breast-cancer-risk-reduction strategies, such as intensive screening with breast MRI or prophylactic mastectomy.

"While our results suggest that removal of the ovaries in women with *BRCA1* or *BRCA2* mutations is highly protective against ER-positive breast cancers, further research is urgently needed to develop effective

non-surgical prevention strategies for the ER-negative cancers that are frequently associated with these mutations," said Dr. Kauff.

Researchers from the following institutions also contributed to this study: University of Pennsylvania, Philadelphia, PA; Dana-Farber Cancer Institute, Boston, MA; Lombardi Comprehensive Cancer Center, Washington, DC; Manchester Regional Genetics Service, Manchester, United Kingdom; Creighton University School of Medicine, Omaha, NE; The Institute of Cancer Research, Sutton, United Kingdom; University of California at Irvine, Irvine, CA; Fox Chase Cancer Center, Philadelphia, PA; Yale University, New Haven, CT; and Baylor-Charles A. Sammons Cancer Center, Dallas, TX.

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