Limiting genetic tests for breast cancer susceptibility

June 2 2015

Screening for genes whose risk association with breast cancer has yet to be proven is not justified and potentially harmful, argue an international team of leading geneticists and oncologists in a paper published this week in the prestigious *New England Journal of Medicine*.

Among the senior authors is Dr. William Foulkes, a renowned expert in cancer genetics at the Lady Davis Institute at the Jewish General Hospital and Director of the Program in Cancer Genetics at McGill University.

"We propose that a genomic test should not be offered until its clinical

validity has been established," the authors insist. Moreover, "we believe that failing to require the clinical validation of genomic tests before they are submitted for regulatory approval is likely to lead to substantial misuse of the technology." With genetic screening having become quick and affordable, the authors have noted a trend toward offering women genetic screening tests for breast cancer that are not clinically justified and for genes without sufficient evidence of their association with high or moderate risk for breast cancer.

"In the absence of clinical validity, why would you test?" Dr. Foulkes asks. "It is really a professional duty for physicians and genetic counsellors to limit genetic testing for cancer susceptibility to those circumstances where the results are likely to provide data that you can put into action. Finding out that someone has a particular mutation for which we have not even proven that the variant discovered poses a risk to the woman simply serves no purpose."

Following the discovery that the BRCA1 and BRCA2 genes were associated with a high risk of breast cancer, there was optimism that more genes with an equally important association would be found. However, they have turned out to be rather unique and risk estimates for many other genes have proven to be too imprecise to dictate a particular clinical utility.

"Finding a mutation without knowing its association to breast cancer isthe equivalent of a false positive, where the patient ends up suffering anxiety for no reason. This is a form of harm that we, as professionals, should spare them through the exercise of proper judgement," said Dr. Foulkes. The paper argues that genetic tests should not be approved until their clinical validity has been proven – this is not without its challenges, but ignoring the need for validation could lead to harm, or at least misinformation.

The team of authors was led by Dr. Douglas Easton at the University of Cambridge, and, in addition to Dr. Foulkes, includes scientists and clinicians from the United Kingdom, Canada, United States, Netherlands, Germany, and Australia, representing a broad spectrum of experience and expertise in the field.

More information: "Gene-Panel Sequencing and the Prediction of Breast-Cancer Risk." DOI: 10.1056/NEJMsr1501341