Cost-effectiveness of a Genetic Test for Breast Cancer Risk – Letter

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We read with great interest the paper by Folse et al (1). Their conclusion that “risk modeling may provide information that allows stratification of patients by disease risk, with alternate strategies of … screening and/or preventative treatment” has major potential implications. However, care needs to be taken with respect to the specific methods used, potential for acceptance of stratification by all actors (including subjects), and generalizability beyond the United States (as mentioned in the Discussion).

Folse et al. assume an interest of alternative screening methods when lifetime risk exceeds 20%, regardless of the reasons for such risk. The only current demonstration of the value of adding MRI to mammography is applicable to genetic high-risk populations, who develop very early, aggressive cancers in dense breasts. This value is related to cancer detection, and as of yet shows no influence on survival. Such benefits may be very different if the expected cancers occur later and are less aggressive. Indeed MRI currently shows little added value after the age of 60-70, even in BRCA carriers (2), and the value of MRI was previously documented in addition to current strategies, including mammography. The assumption made in this paper that MRI may lead to the elimination of mammography remains a hypothesis and is the object of currently ongoing trials (3). Furthermore, breast density, which is currently considered a major risk factor, is included in all recently-developed or updated models (including Gail), and may be linked to the potential benefit of MRI screening3. Adding density as a basic marker may refine the prediction and modify need for MRI.

Finally, Folse et al. evaluate the added value of the first 7 breast cancer polymorphisms described by GWAS, whereas more than 70 have been published, all with roughly equivalent predictive value (4). It is likely that the inclusion of 70 (or more) polymorphisms will largely increase the discrimination capability of current models. The per-SNP costs proposed are excessive, and a conservative estimate for cost-per-genotype in our laboratory is more than 10-times lower. Considerably more SNPs could be evaluated with higher discrimination and much lower costs using currently available techniques (PCR-based assays in custom microarrays, for example).

Exploring further the potential of stratifying women based on risk estimated from epidemiologic and genetic models, as well as how this stratification is viewed by the women themselves, is of importance to predictive medicine, and is the objective of our ongoing study, Primrose.


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Cancer Prev Res Published OnlineFirst February 5, 2014.

Updated version

Access the most recent version of this article at:
doi:10.1158/1940-6207.CAPR-13-0429

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