Performance of BCRAT in high-risk patients with breast cancer

In their Article in *The Lancet Oncology*, Mary Beth Terry and colleagues[1] did an excellent study of risk models by use of the Breast Cancer Prospective Family Study Cohort (Prof-SC), of whom 12 927 (82·17%) of 15 732 participants had at least one affected first-degree relative and 1075 (6·83%) participants carried a *BRCA1/2* mutation. I calculated an incidence of 508 cases of breast cancer per 100 000 people annually, under my assumption that breast cancers, deaths, and censoring occurred at year 5, on average. This incidence is 3·04 times higher than the 167 cases of breast cancer per 100 000 people annually that I calculated by weighting incidence data[2] for the US National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results Program regarding white women (from 2011 to 2015) by the Prof-SC age distribution. Thus, Prof-SC is a high-risk cohort.

The NCI Breast Cancer Risk Assessment Tool (BCRAT) was designed for use in the general US population and its instructions warn that it cannot be accurately used for women carrying *BRCA1* or *BRCA2* mutations. In fact, BCRAT recommends the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) model for such women.

To evaluate BCRAT, one should restrict attention to those without *BRCA1* or *BRCA2* mutations, in whom BCRAT performed surprisingly well.[1] The expected-to-observed ratio was 0·97 (95% CI 0·89–1·06), indicating excellent overall calibration. Moreover, the concordance statistic for BRCAT (0·64) differed little from the values attained by the BOADICEA (0·65) and International Breast Cancer Intervention Study (0·66) models, which require more extensive information. In those without *BRCA1* or *BRCA2* mutations who were younger than 50 years, BCRAT had the same concordance statistic result; however, the expected-to-observed ratio was 0·78 (95% CI 0·68–0·89). This underprediction could represent systematic bias, but it might be partly due to chance, because even a model that is well calibrated can be poorly calibrated by chance in some data subsets. In the Nurses' Health Study,[3] expected-to-observed ratios for BCRAT varied little by age.

Terry and colleagues conclude that "all risk models would be improved by inclusion of pedigree information". However, BCRAT only used the number (0, 1, or ≥2) of affected first-degree relatives. Models with pedigree data had substantially higher concordance statistics (near 0·7) than BCRAT in the entire Prof-SC, but not in those without *BRCA1* or *BRCA2* mutations, suggesting that mutation information, rather than pedigree data, improved concordance. I calculated the concordance for a risk model with no risk factors except mutations and with the mutation carrier prevalence 6·83% found in Prof-SC. With a relative risk of 17·17 (ie, the Prof-SC age-weighted and BRCA type-weighted average of relative risks from a previous study),[4] the concordance statistic would be 0·773. This simplified calculation shows that mutations alone provide notable discrimination in Prof-SC; at a mutation prevalence of 0·32%,[4] the concordance statistic would be 0·526.

Complex models with pedigree, mutation, mammographic density, and polygenic risk score data can increase discriminatory accuracy[1,5] and improve the usefulness of risk models in some, but not all applications.[6] However, data in the study by Terry and colleagues indicate that the simple BCRAT could be useful, not only in general populations, but in those individuals without *BRCA1* or *BRCA2* mutations at high risk.

I declare no competing interests.

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For the **Breast Cancer Risk Assessment Tool** see https://bcrisktool.cancer.gov/