Published in final edited form as:

JAMA Oncol. 2019 January 01; 5(1): 111. doi:10.1001/jamaoncol.2018.5058.

Competing Risks for a Diagnosis of Invasive Breast Cancer- Reply

Adam R. Brentnall, PhD,

Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, United Kingdom

Diana S. M. Buist, PhD,

Kaiser Permanente Washington Health Research Institute, Seattle

Jack Cuzick, PhD

Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, London, United Kingdom

In Reply

Syn expresses concern that our analysis of the long-term accuracy of breast cancer risk assessment in a cohort of women who underwent breast cancer screening could be inadequate because some women could have undergone risk-reducing surgery or preventive therapy.¹ Although we do not have data to directly assess this issue, we believe that our findings are robust; this is an average-risk cohort, and very few women are likely to have received these interventions.^{2–5} This view is supported by 4 observations.

First, Pocobelli et al³ assessed a cohort of 18 390 women, including a subcohort from our analysis, who were 35 years or older and reported a personal or family history consistent with an inherited susceptibility to breast and/or ovarian cancer between 2004 and 2009. Those authors reported a low incidence rate for prophylactic oophorectomy of approximately 1 per 1000 person-years.

Second, on the basis of assumptions used by Manchanda et al⁴ to calculate the probability of having a family history strong enough to fulfill genetic testing criteria, to be *BRCA1/2* positive once tested, and to make a subsequent decision to undergo risk-reducing surgery, we estimate that only 61 of the 132 139 women in our cohort would have undergone a risk-reducing mastectomy.

Third, use of preventive therapy is still uncommon.⁵ In the United States in 2010, the use of tamoxifen preventive therapy was estimated to be approximately 30 per 100 000 women aged 35 to 79 years. The estimated use of raloxifene was higher (approximately 210 per 100 000 women aged 50–79 years) than that of tamoxifen, but raloxifene has only been licensed

Corresponding Author: Adam R. Brentnall, PhD, Centre for Cancer Prevention, Wolfson Institute of Preventive Medicine, Queen Mary University of London, Charterhouse Square, London EC1M 6BQ, United Kingdom (a.brentnall@qmul.ac.uk).

Conflict of Interest Disclosures: Drs Cuzick and Brentnall report receiving royalty payments through Cancer Research UK for commercial use of the Tyrer-Cuzick algorithm. No other disclosures are reported.

for prevention in the United States since 2007, and our cohort was observed from 1996 to 2014.

Finally, even in an extreme scenario in which 100 women underwent risk-reducing mastectomy shortly after entry to the cohort and had a 100% reduction in risk, and 750 women received preventive therapy at entry and had a 30% reduction in risk,⁴ we might expect 39 more cancer diagnoses at most if these interventions were not carried out (assuming an average 6-year follow-up, a risk of 2.0% per year for the *BRCA1/2* carriers who did not undergo mastectomy, and an incidence of 0.6% per year for the potential preventive therapy group if preventive therapy was not given⁶). If these women were all in the high-risk group, then the number of breast cancer diagnoses would increase from 273 to 312, compared with 349 cancers expected based on our model¹; there would be a slight improvement in model calibration, but it would not change our conclusions.

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