European Journal of Cancer 124 (2020) 204–206

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Editorial

New evidence confirms that reproductive risk factors can be used to stratify breast cancer risks: Implications for a new population screening paradigm

An article in the current issue of the journal based on data from the Swedish national registry databases on over 4 million women, from birth cohorts spanning 1932–1980, shows that age at first pregnancy and number of pregnancies alone provides sufficient information to change a threshold driven starting age for national 2-yearly screening mammography [1]. They show a 12-year difference in the age at which the 10-year risk of breast cancer reached 2.2% (age 50 in the overall population), between women with multiple births from a young age to those with only one or two births at age 30 years or older. The authors excluded women with a personal or family history of breast cancer as these women often start screening earlier based on national guidelines such as National Institute for Healthcare and Clinical Excellence (NICE) in the UK [2], National Comprehensive Cancer Network (NCCN) in the USA [3] and INSERM in France [4]. As such, the study deals with the 76–86% of the population with no close (first or second degree) family history of breast cancer in their forties [5] who in all probability have no idea that they may be at increased risk from their absent or late first pregnancy or indeed protected by early multiple births. The datasets from Sweden are almost unique and certainly the largest available to assess this. They have been able to exclude family history in 85% of the 5 million women assessed to at least second degree relatives. The data sources are indeed remarkable as they can also be linked to cancer incidence and live births meaning that the investigators could identify the age at first live birth for all women. The results are well presented and show a meaningful change in starting age based on the two parameters. Among women with first birth at maternal age <25 years, those who had parity ≥4 reached the average risk of a 50-year-old (2.2% 10-year) at age 59 years. In contrast, women with age at first birth ≥30 years and parity 1–2 reached a similar 2.2% risk at age 47 years. The present study clearly justifies the inclusion of age at first pregnancy in existing risk prediction models such as Tyrer-Cuzick (IBIS) and Gail for women without a family history of breast cancer [6]. The new BOADICEA model also contains both reproductive parameters [7].

Whilst in Sweden, it might be possible to connect databases to automatically initiate screening at different ages these data would not be available in other countries. As such this would require data collection from women themselves. The predicting the risk of cancer at screening (PROCAS) study in the UK has shown that is feasible to collect and collate risk information necessary to populate existing models, and that incorporation of other important risk factors such as mammographic density improves the accuracy of breast cancer risk prediction [5,6]. There is a great deal of interest in the concept of risk-adapted screening and indeed evidence that this would likely be cost-effective [8,9]. As such, a number of large-scale studies assessing the feasibility of collecting information electronically from women and incorporating this with mammographic density and common genetic variants, including the women informed to screen depending on measures of risk (WISDOM) study in the USA and 'My Personal estimate of Breast cancer risk at Screening (MyPeBS)' in Europe, are underway [10,11]. Of course, this would increase the costs, particularly in obtaining and analysing DNA samples, but the risks obtained are more accurate and substantially improve population risk stratification [12].

DOI of original article: https://doi.org/10.1016/j.ejca.2019.10.011.

https://doi.org/10.1016/j.ejca.2019.10.012
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Whilst in Sweden it may be possible, at little extra cost, to implement a risk-stratified programme in women with no family history of breast cancer; this would miss the high precision of adding mammographic density and polygenic risk scores (PRSs). In addition, misclassification of women in to incorrect risk groups could occur, for example, in those who had a term stillbirth at a young age or an abnormal breast biopsy. Ultimately, however, women will require a mammogram to assess their breast density and therefore an initial assessment with a PRS and standard risk factors at a younger age of around 35–40 years would potentially identify those at high enough risk to at least have a first baseline mammogram and consider lifestyle and therapeutic breast cancer prevention strategies. Although population screening in the forties has been rejected in most countries and is even now being doubted in the USA [13], there is clearly a group of women in their forties who could benefit from early screening based on accurately defined breast cancer risks. How the additional parity-based factors (over age at first full-term pregnancy alone) described in the accompanying article fit into the more complete risk prediction algorithms will need to be formally tested.

Conflict of interest statement

Authors declare no conflict of interest.

Acknowledgements

DGE, SH and AH are supported through the NIHR Manchester Biomedical Research Centre (IS-BRC1215-20007).

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18 October 2019