

# Breast Cancer Risk Associated With Reproductive Factors in Younger Women

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Younger women have a lower risk of breast cancer. But when the disease does strike in these women, it tends to be more aggressive. Breast cancer is increasingly being recognized as a heterogeneous group of distinct diseases, with different survival rates, genetic characteristics, and recommended treatment regimens. For example, triple-negative and HER2-overexpressing breast cancers are more aggressive and have poorer prognoses than estrogen receptor positive (ER+) subtypes. Improving our understanding of what causes of each of these subtypes is key for preventing future cases of breast cancer. Some of the most well-established risk factors for breast cancer as a whole include reproductive characteristics (early menarche, late age at first birth, not breastfeeding after childbirth). Few studies, however, have investigated how these reproductive factors affect risk of the different types of breast cancer in younger women, whose breast cancer is more likely to be one of the more aggressive types.

Dr. Christopher Li and colleagues in Public Health Sciences addressed this question in a group of 1,021 women ages 20-44 diagnosed with ER+, triple-negative, or HER2-overexpressing breast cancer. They interviewed these women, along with a comparison group of 941 similarly aged controls, about their reproductive histories, to assess whether such factors influence the risk of some types of breast cancer differently than others. They checked for confounding by demographic and reproductive factors, and included any potential confounders in their analyses.

Dr. Li and colleagues found that certain factors did not affect the risk of all breast cancer subtypes equally. In particular, some factors were associated with a lower risk of triple-negative breast cancer in younger women, but were not associated with ER+ or HER2-overexpressing breast cancers. These included, surprisingly, having a first child at an older age, which was associated with a 60% lower risk of triple-negative breast cancer [odds ratio (OR) 0.4, 95% CI 0.2-0.8 for >34 years versus 20-24 years old). Additionally, a 50% reduction in risk was seen in women with a longer interval between menarche and their first child (OR 0.5, 95% CI 0.3-0.9 for >20 versus <10 years), and in those mothers who breastfed (OR 0.5, 95% CI 0.3-0.9 for >12 months of breastfeeding compared to none, among women who had children). There was less evidence for an association between these factors and ER+ or HER2-overexpressing breast cancers. Other factors, including age at menarche,

parity (any childbirth), and the number of full-term pregnancies, did not appear to be differentially associated with the various types of breast cancer.

This work added to evidence from previous studies for a protective effect of breastfeeding on risk of triple-negative breast cancer in younger women. Both childbirth and breastfeeding induce structural changes and further development of breast tissue, which may make women less susceptible to breast cancer. Of note, this was the first study to observe a lower risk of triple-negative breast cancer in association with an older age at first childbirth, in contrast with six earlier studies. However, those studies included relatively small numbers of older first-time mothers, and therefore had less statistical power to address this question. These findings are surprising, as older age at first birth is associated with an increased risk of breast cancer overall; thus, further research into this question is needed.

This work contributes to our understanding of what causes the different types of breast cancer, and could ultimately impact prevention of this set of diseases, particularly the more aggressive triple-negative breast cancers.

Li CI, Beaver EF, Tang MT, Porter PL, Daling JR, Malone KE. [Reproductive factors and risk of estrogen receptor positive, triple-negative, and HER2-neu overexpressing breast cancer among women 20-44 years of age](#). *Breast Cancer Res Treat.* 2013 Jan;137(2):579-87. doi: 10.1007/s10549-012-2365-1. Epub 2012 Dec 9.



*Photo by Dean Forbes*

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