



## Contralateral Prophylactic Mastectomy in Average Risk Women: Who Can Choose This Wisely?

Suzanne B. Coopey, MD

Allegheny Health Network, Pittsburgh, PA

The Choosing Wisely® campaign is a nationwide initiative to eliminate overtreatment and low-value care. One of the surgical de-implementation strategies identified by the American Society of Breast Surgeons as part of this campaign is not routinely performing a contralateral prophylactic mastectomy (CPM) in average risk patients with unilateral breast cancer<sup>1</sup>. There is currently insufficient evidence that CPM improves survival for average risk women, and many women who opt for CPM may be undergoing medically unnecessary surgery due to overestimation of their contralateral breast cancer (CBC) risk<sup>2</sup>.

In a recent SEER-based analysis of 812,851 women with unilateral in situ or invasive breast cancer, the annual risk of invasive CBC was only 0.37% and the 25-year actuarial risk was 9.9%<sup>3</sup>. The 25-year CBC risk was higher for black women than white women (12.7 vs. 9.7%), and higher for women with estrogen receptor negative disease than estrogen receptor positive disease (11.2 vs. 9.5%)<sup>3</sup>. Naturally, women with BRCA1, BRCA2, CHEK2 and other high-risk gene mutations and those with prior chest wall radiotherapy for childhood malignancies have much higher CBC risks and fall outside these risk estimates.

Several models have recently been developed to help predict individualized risk of CBC. In the article “Tools for Contralateral Prophylactic Mastectomy Decision Making”, recently published in the *Journal of Clinical Oncology*, authors Mitchell H. Gail and Ismail Jatoui use CBC risk predictions alongside absolute risks of regional and distant

metastases and risk of death from non-breast cancer causes to help put CPM into perspective for 10 hypothetical women<sup>4</sup>. For the non-BRCA positive patient scenarios, the CBCRisk model was utilized<sup>5</sup>.

The CBCRisk model was created in 2017, using the design steps of the Breast Cancer Risk Assessment Tool, or Gail model<sup>6</sup> [<https://bcrisktool.cancer.gov/>], as a prototype. It has been validated for 3- and 5-year CBC risks on independent cohorts of patients from Johns Hopkins University and MD Anderson Cancer Center<sup>7</sup>.

CBCRisk includes the following risk factors with the most common values highlighted in bold<sup>5</sup>:

- Age at first breast cancer diagnosis (age < 30, 30-39, **40+**)
- Anti-estrogen therapy (yes, **no**, unknown)
- Family history of breast cancer in first degree relative (yes, **no**, unknown)
- High risk pre-neoplasia (lobular carcinoma in situ and atypical hyperplasia) status (yes, **no/unknown**)
- Breast density (extremely dense, **heterogeneously dense**, scattered, unknown, almost entirely fatty)
- Estrogen receptor status (**positive**, unknown, negative)
- First breast cancer type (pure DCIS, mixed invasive-DCIS, **pure invasive**)
- Age at first birth (30-39, 40+, unknown, **<30/nulliparous**)

In a publication by Chowdhury and colleagues on the CBCRisk model, a “typical” woman, defined as a woman with the most common value for each risk factor, has low estimated 5-year and 15-year CBC risks around 1.5% and 4.5%, respectively<sup>5</sup>. Using the CBCRisk model and assuming an approximately 3.0% 10-year CBC risk in a typical woman, in “Tools for Contralateral Prophylactic Mastectomy Decision Making” Gail and Jatoui classified 10-year CBC risk as low with 0-2.49% risk, medium with

2.5–9.9% risk, and high with 10% risk or more<sup>4</sup>. Additionally, authors calculated a total risk as the sum of CBC risk, regional recurrence risk, distant recurrence risk, and mortality from non-breast cancer causes (which was largely based on patient age) and also assessed the fractional risk reduction from CPM. Based on these calculations, a high ( $\geq 10\%$ ) 10-year CBC risk justified a CPM recommendation in 3 of 3 hypothetical women, whereas a low (0–2.49%) 10-year risk directed against CPM in 1 of 1 hypothetical women. When the 10-year risk of CBC was medium (2.5–9.9%), a higher risk of mortality from non-breast cancer causes and/or a higher risk of regional or distant recurrence, decreased the fractional risk reduction from CPM, and CPM was not recommended. In medium risk women without these competing risks, CPM was a consideration. The hypothetical women with the highest CBC risks had extremely dense breast tissue, high risk pre-neoplasia, and a family history of breast cancer in a first degree relative<sup>4</sup>.

While “Tools for Contralateral Prophylactic Mastectomy Decision Making” offers useful guidance when considering CPM for various patient scenarios, there are some limitations. First, the decision to have a CPM is often made before final pathology is available, which may directly impact regional and distant recurrence risks, making these risks essentially unknown during the pre-operative surgical discussion for many patients. Also, the thresholds used for low, medium, and high CBC risk defined by Gail and Jatoi were arbitrary and could vary for individual patients based on their own values and capacity to accept risk. This is also true of the weighted risk, where patients could assign different weights to CBC risk and regional recurrence, distant recurrence, and non-breast cancer death based on their own preferences. Furthermore, patients often consider many things besides level of CBC risk when choosing CPM, such as breast symmetry, avoiding future breast screening and potential biopsies, and peace of mind. Risks of surgical complications based on patient factors would need to be separately discussed when counseling patients on the pros and cons of CPM as the tool does not take these into account.

The development of the CBCRisk model, as well as others like CBCRisk-Black (designed for prediction of CBC risk in black women) and Predict-CBC (includes

BRCA mutation status), are important steps forward in estimating individualized CBC risk<sup>8,9</sup>. Validation of these models in larger cohorts with known values for all risk factors, plus incorporation of regional and distant recurrence risks based on cancer subtype, stage, and treatments received, and including risk of non-breast cancer mortality (like Gail and Jatoi have shown), can help create a CPM decision tool that is personalized. Applying these models has the potential to identify a subset of otherwise average risk women who have a high risk of contralateral breast cancer and for whom contralateral prophylactic mastectomy is a wise choice.

## REFERENCES

1. Landercasper J, Bailey L, Berry TS, et al. Measures of appropriateness and value for surgeons and their patients: the American society of breast surgeons Choosing Wisely® Initiative. *Ann Surg Oncol*. 2016;23:3112–8.
2. Carbine NE, Lostumbo L, Wallace J, Ko H. Risk-reducing mastectomy for the prevention of primary breast cancer. *Cochrane Database Syst Rev*. 2018. <https://doi.org/10.1002/14651858.CD002748.pub4>.
3. Giannakeas V, Lim DW, Narod SA. The risk of contralateral breast cancer: a SEER-based analysis. *Br J Cancer*. 2021;125:601–10.
4. Gail MH, Jatoi I. Tools for contralateral prophylactic mastectomy decision making. *J Clin Oncol*. 2022. <https://doi.org/10.1200/JCO.21.02782>.
5. Chowdhury M, Euhus D, Omega T, Biswas S, Choudhary PK. A model for individualized risk prediction of contralateral breast cancer. *Breast Cancer Res Treat*. 2017;161(1):153–60.
6. Gail MH, Brinton LA, Byar DP, et al. Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl Cancer Inst*. 1989;81:1879–86.
7. Chowdhury M, Euhus D, Arun B, Umbricht C, Biswas S, Choudhary PK. Validation of a personalized risk prediction model for contralateral breast cancer. *Breast Cancer Res Treat*. 2018;170(2):415–23.
8. Sajal IH, Chowdhury M, Wang T, Euhus D, Choudhary PK. CBCRisk-black: a personalized contralateral breast cancer risk prediction model for black women. *Breast Cancer Res Treat*. 2022;194:179–86.
9. Giardiello D, Steyerberg EW, Hauptmann M, et al. Prediction and clinical utility of a contralateral breast cancer risk model. *Breast Cancer Res*. 2019;21:144.

**Publisher’s Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.