# Predictors of Contralateral Prophylactic Mastectomy and the Impact on Breast Reconstruction

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**Background:** Contralateral prophylactic mastectomy (CPM) is being performed with increased frequency. Predictors of CPM and their impact on breast reconstruction are examined.

**Methods:** A retrospective review of a dually trained oncologic and plastic surgeon's experience with patients undergoing total mastectomy from 2002 to 2012 was performed. Patients who underwent bilateral *therapeutic* mastectomies or who had previous contralateral mastectomy were excluded from this series.

**Results:** Four hundred forty-six patients were treated with total mastectomy and 174 (39%) underwent CPM. The incidence of CPM nearly tripled over the period studied. Compared to women treated with unilateral mastectomy, women who elected for CPM were younger (mean age, 50.4 vs 56.8 years, $P < 0.001$), leaner (mean body mass index, 26.1 vs 27.4 kg/m$^2$, $P = 0.036$), more often white (86.8% vs 73.8%, $P = 0.004$), and more often had a family history of breast cancer (52% vs 33.3%, $P < 0.001$). The CPM group was also more likely to have undergone a preoperative magnetic resonance imaging (56.3% vs 39%, $P < 0.001$) and to have stage I disease (31% vs 22.8%, $P = 0.053$). They were *less* likely to have undergone prior attempts at breast conservation (6.9% vs 15.8%, $P = 0.004$) and considerably more likely to pursue breast reconstruction (83.9% vs 63.6%, $P < 0.001$). Multivariate analysis confirmed age, white race, family history, prior attempt at breast conservation, and receipt of breast reconstruction to be independently associated with prophylactic mastectomy. Incidental contralateral cancers were discovered in 4% of women who underwent CPM (n = 7), lobular carcinoma in situ in 2.3% (n = 4), and atypical lesions in an additional 11.6% (n = 20). Women who underwent CPM favored reconstruction with breast implants (60.9% vs 17.3%), whereas the transverse rectus abdominis musculocutaneous flap predominated among their unilateral counterparts (38.6% vs 15.5%). Among women who underwent immediate breast reconstruction, the addition of a contralateral procedure expectedly increased breast complication rates (50.3% vs 35.0%, $P = 0.007$), especially the more severe complications that required hospitalization or reoperation (18.6% vs 5.0%, $P < 0.001$).

**Conclusions:** The incidence of CPM is increasing and is associated with younger age, white race, family history, and the use of breast reconstruction. Implant-based reconstructions predominate in this cohort. The added morbidity of a contralateral procedure is significant.

**Key Words:** contralateral prophylactic mastectomy, breast reconstruction, postoperative complications

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Women diagnosed with breast cancer increasingly elect to undergo a contralateral prophylactic mastectomy (CPM). Data from a large, national registry spanning most of the last decade document a more than doubling of the incidence of CPM.[1] The potential drivers of this trend are many, but in general stem from the perception of risk of a subsequent primary breast cancer on the part of patients, the medical community, and the general public. Some risk factors are better understood than others. For instance, heritable genetic mutations substantially heighten the risk of a contralateral primary breast cancer, but indeterminate findings on magnetic resonance imaging (MRI) or certain histopathologies have unknown implications. The purpose of this review was to identify factors associated with the performance of CPM, and to assess the impact of the rise of CPM on the patient's experience and breast reconstruction in general.

## METHODS

This is a single institution retrospective review of all female breast cancer patients treated with total mastectomy by a single surgeon at the Winship Cancer Institute of Emory University between 2002 and 2012. Patients who underwent bilateral *therapeutic* mastectomies or who had previous contralateral mastectomy were excluded from this series.

Institutional review board approval was obtained for this study. Data on the incidence of CPM and various potentially associated variables were collected from hospital and clinic records. Independent patient variables include age at the time of mastectomy, race/ethnicity, body mass index (BMI), smoking status, and personal or family history of breast cancer. Race and ethnicity were categorized as white, black, or other (Hispanic, Asian, other). Cancer data collected include its histology, staging according to the American Joint Committee on Cancer, preoperative imaging with MRI. Patients treated with neoadjuvant chemotherapy were categorized according to their clinical cancer stage, whereas those not treated with preoperative chemotherapy were analyzed according to their pathologic stage. It was noted if total mastectomy followed an initial attempt at breast conservation complicated by positive margins. Recurrences after remote treatment with breast conservation therapy (BCT) were not counted as BCT failures.

Outcomes considered include the pathology of the CPM breast where applicable; utilization of breast reconstruction, including the timing and method of reconstruction; and the incidence of complications. Among patients who underwent CPM, it was noted if complications occurred in the therapeutically treated breast, prophylactic breast, or both. Complications were classified as major if they required repeat hospitalization or reoperation.

### Statistical Analysis

Bivariate analyses were performed to compare patients who underwent CPM and those who did not. Continuous variables (eg, age and BMI) were compared using a 2-tailed *t* test. Differences across categorical variables (eg, race) were assessed using a $\chi^2$ test, or Fisher exact test in the case of small sample sizes. Multivariate logistic regression was used to measure the relationship between various predictive variables and the use of CPM while adjusting for potentially confounding variables. An initial model contained all variables that were significant at $P < 0.1$ on bivariate analysis, and sequential backward elimination was used to determine a best-fit

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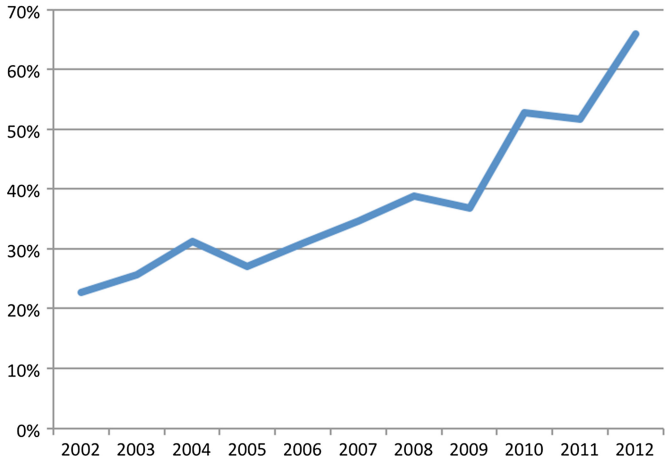


**FIGURE 1.** Contralateral prophylactic mastectomy as percentage of therapeutic mastectomies.

logistic regression model. A $P$ value less than 0.05 was considered statistically significant in all cases.

## RESULTS

Four hundred forty-six patients were treated with total mastectomy between 2002 and 2012, and 174 (39%) underwent CPM.

**TABLE 1.** Patient Characteristics by Performance of CPM

| | CPM, n = 174 | No CPM, n = 272 | *P* |
|---|---|---|---|
| Age (mean), y | 50.4 | 56.8 | <0.001 |
| BMI (mean), kg/m$^2$ | 26.1 | 27.4 | 0.036 |
| Race* | | | 0.004 |
| White | 151 (86.8%) | 200 (73.8%) | |
| Black | 18 (10.3%) | 60 (22.1%) | |
| Other | 5 (2.9%) | 11 (4.1%) | |
| Family history of breast cancer | 90 (52%) | 90 (33.3%) | <0.001 |
| Personal history of breast cancer | 18 (10.3%) | 37 (13.6%) | 0.307 |
| Preoperative breast MRI | 98 (56.3%) | 106 (39%) | <0.001 |
| BCT attempted | 12 (6.9%) | 43 (15.8%) | 0.004 |
| Histology | | | |
| DCIS | 39 (22.4%) | 66 (24.3%) | 0.653 |
| Ductal | 107 (61.5%) | 171 (62.9%) | 0.770 |
| Lobular | 24 (13.8%) | 32 (11.8%) | 0.528 |
| Other | 4 (2.3%) | 3 (1.1%) | 0.439 |
| Stage | | | |
| 0 | 36 (20.7%) | 64 (23.5%) | 0.483 |
| I | 54 (31%) | 62 (22.8%) | 0.053 |
| II | 45 (25.9%) | 75 (27.6%) | 0.691 |
| III | 30 (17.2%) | 56 (20.6%) | 0.382 |
| IV | 2 (1.1%) | 4 (1.5%) | 1.00 |
| Recurrent | 7 (4%) | 11 (4%) | 0.991 |
| Smoking | 10 (5.8%) | 17 (6.3%) | 0.844 |
| Reconstruction | | | |
| Immediate | 145 (83.3%) | 160 (58.8%) | |
| Delayed | 1 (0.6%) | 13 (4.8%) | |
| None | 28 (16.1%) | 99 (36.4%) | <0.001 |

*Race unknown for 1 patient.
DCIS indicates ductal carcinoma in situ.

The incidence of CPM rose dramatically over the period studied, increasing from less than a quarter of therapeutic mastectomies in 2002 to 66% in 2012 (Fig. 1).

### Factors Predictive of CPM

Compared to women treated with unilateral mastectomy, women who elected for CPM were younger (mean age, 50.4 vs 56.8 years; $P < 0.001$), leaner (mean BMI, 26.1 vs 27.4 kg/m$^2$; $P = 0.036$), and more often white (86.8% vs 73.8%, $P = 0.004$, Table 1). They more often reported a family history of breast cancer (52% vs 33.3%, $P < 0.001$), especially among first-degree relatives (27.6% vs 14.3%, $P = 0.001$). The CPM group was also more likely to have undergone a preoperative MRI (56.3% vs 39%, $P < 0.001$) and to have stage I disease (31% vs 22.8%, $P = 0.053$). They were *less* likely to have undergone prior attempts at breast conservation (6.9% vs 15.8%, $P = 0.004$). The pursuit of breast reconstruction was also more frequent among women who chose to undergo contralateral mastectomy (83.9% vs 63.6%, $P < 0.001$). Prevalence of a smoking habit, personal history of breast cancer, and tumor histology were no different between patients who underwent CPM and those who did not.

Multivariate analysis confirmed age, race, family history, prior attempt at breast conservation, and breast reconstruction with implants or transverse rectus abdominis musculocutaneous (TRAM) flap to be independently associated with prophylactic mastectomy (Table 2). With each additional year of age, patients were 5% less likely to pursue CPM. Compared to their white counterparts, black women were less than half as likely to undergo CPM. On the other hand, having a first-degree relative with a history of breast cancer increased by 2.5-fold the odds of prophylactic mastectomy. Women with a failed initial attempt at breast conservation were much less likely to pursue additional prophylactic surgery. The choice of postmastectomy breast reconstruction was also an independent predictor of CPM, with women who underwent implant-based breast reconstruction being more than 4 times as likely to undergo CPM, and women who received TRAM flap reconstruction being one-half as likely.

### Impact of CPM

Most of the patients who underwent CPM had benign pathology of the prophylactically removed breast (82.2%). However, 7 (4%) patients were found to have occult cancer in the CPM specimen

**TABLE 2.** Multivariate Analysis of Factors Associated With CPM

| | CPM vs No CPM | | |
|---|---|---|---|
| Factor | Odds Ratio | 95% Confidence Interval | *P* |
| Age (each incremental year) | 0.95 | 0.93–0.98 | <0.001 |
| Race | | | |
| White | 1.00 | Referent | |
| Black | 0.44 | 0.23–0.83 | 0.011 |
| Other | 0.34 | 0.09–1.37 | 0.130 |
| Family history of breast cancer | | | |
| No family history | 1.00 | Referent | |
| First-degree relative | 2.49 | 1.37–4.53 | 0.003 |
| Second-degree relative | 2.06 | 1.17–3.63 | 0.013 |
| BCT attempted | 0.30 | 0.14–0.66 | 0.003 |
| Breast reconstruction | | | |
| None | 1.00 | Referent | |
| Expander/implant | 4.44 | 2.40–8.21 | <0.001 |
| Latissimus dorsi flap | 1.57 | 0.65–3.79 | 0.321 |
| TRAM flap | 0.50 | 0.26–0.99 | 0.046 |

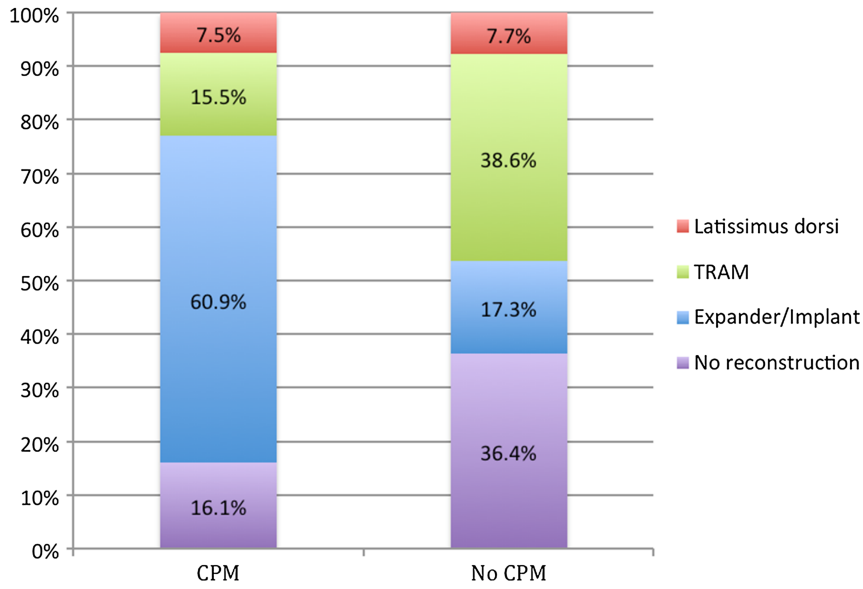


**FIGURE 2.** Reconstructive methods in patients undergoing therapeutic mastectomy with and without CPM.

(ductal carcinoma in situ in 4 and stage I cancer in 3) and 24 (13.9%) were found to have high-risk pathology (lobular carcinoma in situ, 4; atypical ductal hyperplasia, 11; and atypical lobular hyperplasia, 9).

Women who underwent CPM were far more likely to undergo breast reconstruction, which almost uniformly took place at the time of mastectomy (immediate, 83.3%; delayed, 0.6%). Reconstruction was most often performed with breast implants, whereas the TRAM flap predominated among unilateral mastectomies ($P < 0.001$, Fig. 2).

Among women who underwent immediate breast reconstruction, the addition of a contralateral procedure expectedly increased overall breast complication rates (50.3% vs 35.0%, $P = 0.007$), especially the more severe complications that required hospitalization or reoperation (18.6% vs 5.0%, $P < 0.001$). Among patients who underwent CPM, the therapeutically treated breast more often bore the complication, although nearly a quarter of patients experienced a complication in the prophylactically removed breast (Fig. 3).

Stratifying by *type* of reconstruction, bilateral implant-based reconstructions were more often complicated than their unilateral counterparts (51.0% vs 34.0%, $P = 0.059$), with major complications occurring more than 5 times as often with the addition of a contralateral procedure (23.6% vs 4.5%, $P = 0.006$, Table 3). An excess of complications was also observed for bilateral autologous reconstructions, but those differences were nonsignificant.

The performance of a contralateral mastectomy and reconstruction significantly increased the incidence of certain types of complications. In the expander population, the incidence of skin and nipple necrosis nearly doubled (26.4% vs 13.6%, $P = 0.089$), and the incidence of infection more than tripled (16.0% vs 4.5%, $P = 0.054$, Table 4). Among women reconstructed with a TRAM flap, the rate of infection was 10-fold higher for bilateral reconstructions (11.5% vs 1.1%, $P = 0.031$).

The main drivers of complications in this cohort were the performance of contralateral mastectomy and breast reconstruction. Various potential risk factors were considered, including age, BMI, smoking status, receipt of radiation therapy, chemotherapy, or an axillary procedure, performance of CPM, and type of breast reconstruction. On multivariate analysis, all types of breast reconstruction conferred a greater than 20-fold increase in the odds of experiencing a complication relative to no reconstruction (Table 5). Contralateral prophylactic mastectomy was another independent risk factor that more than doubled the odds of experiencing a complication (odds ratio, 2.11; 95% confidence interval, 1.28–3.49; $P = 0.004$).

## DISCUSSION

Consistent with national trends, the incidence of CPM in our experience markedly increased during the last decade. Although the rapid rate of increase is in line with large national registries, our utilization of CPM is considerably higher (26% vs 11.0% in 2003).[2,3] This likely reflects our setting—a tertiary care referral center—and a degree of selection bias, as our patients are cared for by a dually trained oncologic and reconstructive surgeon.

Younger age has been widely demonstrated to increase the likelihood of electing for CPM.[2–8] Among women with early stage disease, younger women face a longer life expectancy and thus

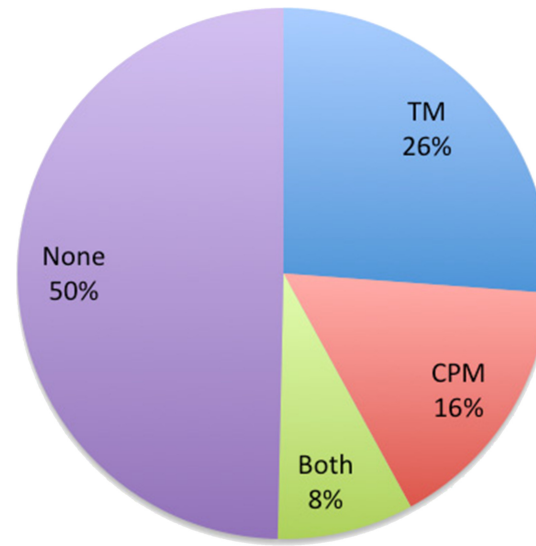


**FIGURE 3.** Distribution of complications among patients treated with CPM and immediate breast reconstruction.

**TABLE 3.** Severity of Complications by CPM Versus None

| Reconstruction Type*/Complication | CPM | No CPM | *P* |
|---|---|---|---|
| Expander/implant | 106 | 44 | |
| Major | 25 (23.6%) | 2 (4.5%) | 0.006 |
| Minor | 29 (27.4%) | 13 (29.5%) | 0.786 |
| None | 52 (49.1%) | 29 (65.9%) | 0.059 |
| Latissimus | 13 | 21 | |
| Major | 0 | 1 (4.8%) | 1.00 |
| Minor | 7 (53.8%) | 6 (28.6%) | 0.168 |
| None | 6 (46.2%) | 14 (66.7%) | 0.238 |
| TRAM | 26 | 95 | |
| Major | 2 (7.7%) | 5 (5.3%) | 0.642 |
| Minor | 10 (38.5%) | 29 (30.5%) | 0.443 |
| None | 14 (53.8%) | 61 (64.2%) | 0.335 |
| All immediate reconstructions | 145 | 160 | |
| Major | 27 (18.6%) | 8 (5.0%) | <0.001 |
| Minor | 46 (31.7%) | 48 (30.0%) | 0.745 |
| None | 72 (49.7%) | 104 (65.0%) | 0.007 |
| No reconstruction | 28 | 99 | |
| Major | 1 (3.6%) | 0 | 0.220 |
| Minor | 1 (3.6%) | 1 (1.0%) | 0.394 |
| None | 26 (92.9%) | 98 (99.0%) | 0.122 |
| Total | 173 | 259 | |
| Major | 28 (16.2%) | 8 (3.1%) | <0.001 |
| Minor | 47 (27.2%) | 49 (18.9%) | 0.043 |
| None | 98 (56.6%) | 202 (78.0%) | <0.001 |

*Delayed reconstructions excluded.

**TABLE 4.** Type of Complications Among Immediately Reconstructed Patients by CPM Versus None

| | CPM* (n = 145), % | No CPM (n = 160), % | *P* |
|---|---|---|---|
| Expander/implant (n = 150) | | | |
| Skin/nipple necrosis | 26.4 | 13.6 | 0.089 |
| Infection | 16.0 | 4.5 | 0.054 |
| Fat necrosis | 0.0 | 0.0 | — |
| Hematoma | 3.8 | 9.1 | 0.234 |
| Flap necrosis | — | — | — |
| Implant or expander failure | 2.8 | 4.5 | 0.631 |
| Implant exposure | 4.7 | 0.0 | 0.322 |
| Seroma | 0.9 | 2.3 | 0.502 |
| Latissimus dorsi flap (n = 34) | | | |
| Skin/nipple necrosis | 38.5 | 19.0 | 0.254 |
| Infection | 15.4 | 14.3 | 1.000 |
| Fat necrosis | 0.0 | 0.0 | — |
| Hematoma | 0.0 | 0.0 | — |
| Flap necrosis | 0.0 | 0.0 | — |
| Implant or expander failure | 0.0 | 0.0 | — |
| Implant exposure | 0.0 | 0.0 | — |
| Seroma | 7.7 | 0.0 | 0.382 |
| TRAM flap (n = 121) | | | |
| Skin/nipple necrosis | 23.1 | 15.8 | 0.390 |
| Infection | 11.5 | 1.1 | 0.031 |
| Fat necrosis | 7.7 | 12.6 | 0.732 |
| Hematoma | 3.8 | 1.1 | 0.385 |
| Flap necrosis | 7.7 | 5.3 | 0.642 |
| Implant or expander failure | — | — | — |
| Implant exposure | — | — | — |
| Seroma | 3.8 | 0.0 | 0.215 |

*Nine patients developed >1 complication.

longer window in which to develop a second primary breast cancer. On the other hand, younger women with very early presenting cancers may be more likely to harbor a predisposing genetic mutation, which clearly confers an increased risk of a subsequent cancer to the opposite breast and may motivate the pursuit of CPM. It is also known that younger women are more likely to pursue postmastectomy breast reconstruction in general.[9–17] Some have postulated that better symmetry and a superior aesthetic outcome can be achieved with bilateral breast reconstruction, which may make some women more accepting of a contralateral procedure.

Women of racial minorities are less likely to choose CPM, a trend that likely reflects cultural preferences and socioeconomic differences.[2,3,5,7,18] As has been shown elsewhere, a family history of breast cancer was a strong predictor of prophylactic mastectomy in our series.[4,7,8,19] Family history is among the indications for prophylactic mastectomy put forth by the Society of Surgical Oncology, although they specify multiple affected first-degree relatives, criteria that are not likely met by all of our patients who report a positive family history.[20]

The use of MRI in the diagnostic workup of a breast cancer increases the use of CPM by 2- to 3-fold.[7,19,21] Sorbero et al[21] propose 2 mechanisms for this association. In the first, women imaged by MRI are more likely to choose mastectomy over breast conserving surgery, which introduces the option of CPM, which a subset of women will take. In the second mechanism, indeterminate findings in the contralateral breast, some of which will necessitate further breast biopsies, generate uncertainty and distress for the patient and perhaps even their surgeon, which then spurs a decision for CPM.

Women who initially sought breast conserving treatment but ultimately required mastectomy due to persistently positive margins less often underwent CPM, a phenomenon that reflects their original goal of breast preservation. Interestingly, the opposite association was identified by King et al[7] in their review of Memorial Sloan Kettering's experience with CPM. Among those patients, repeat excisions after BCT may have heightened their anxiety surrounding their cancer.

Four percent of our CPM cohort was discovered to have a contralateral breast cancer. Although those lesions may have been identified on surveillance imaging and effectively treated, most evidence points to an overall improvement in disease-free survival after CPM, at least among women at high risk, such as those with a strong family history or hormone receptor negative cancer.[21–24]

Nationwide data on breast reconstruction have demonstrated an overall increase in immediate breast reconstruction, as well as a

**TABLE 5.** Multivariate Analysis of Factors Predicting Development of a Postoperative Complication

| Factor | Odds Ratio | 95% Confidence Interval | *P* |
|---|---|---|---|
| CPM | 2.11 | 1.28–3.49 | 0.004 |
| Breast reconstruction | | | |
| None | 1.00 | Referent | |
| Expander/implant | 24.89 | 7.46–83.05 | <0.001 |
| Latissimus dorsi flap | 26.72 | 6.99–102.12 | <0.001 |
| TRAM flap | 24.09 | 7.23–80.33 | <0.001 |

significant increase in the use of breast implants.[25] The increasing proportion of women who undergo CPM is undoubtedly a substantial contributor to these trends. The benefits of prophylactic mastectomy must be weighed against the added morbidity of a second procedure, which in most of the cases involves not only mastectomy but also reconstruction. Because the procedure is elective and the breast healthy, patients and even clinicians may underestimate the potential risks. Crosby et al[26] examined immediate postmastectomy bilateral reconstruction for an index cancer combined with a CPM in 497 patients. One hundred fifty-four patients developed a complication in the reconstruction. Forty-two (27.3%) patients developed a complication on the prophylactic side. In implant reconstruction, they found a 22.5% complication rate in the index breast and a 19.2% risk of a complication in the prophylactic breast. The risk of having a complication in both breasts was 11.1%.

In our experience, patients who underwent CPM and immediate breast reconstruction experienced 40% more complications overall and almost 4 times as many severe complications requiring readmission or reoperation. Some of this added morbidity can be explained by the different distribution of reconstructive methods, with implants predominating in the CPM cohort. However, comparison of unilateral and bilateral implant reconstructions still shows a 50% greater burden of complications when CPM is performed. The considerable added morbidity of prophylactic mastectomy has been demonstrated in other series.[26–28] Miller et al[27] reviewed a single institution experience of 600 patients treated by total mastectomy (unilateral, 391; CPM, 209). When adjusting for confounding variables (age, BMI, smoking, diabetes, reconstruction, and radiation), patients undergoing CPM were 1.5 times more likely to have an operative complication ($P = 0.029$) and 2.7 times more likely to have a major complication ($P = 0.004$) compared with patients undergoing unilateral mastectomy.

## CONCLUSIONS

The incidence of CPM has risen dramatically over recent years. Women who choose CPM are more often young, white, and have a family history of breast cancer. Failure of breast conservation and pursuit of postmastectomy breast reconstruction are other contributing factors. Reconstructive trends in this cohort, namely the prevalence of immediate implant-based reconstruction, are mirrored by national trends among *all* patients who undergo mastectomy. As the incidence of CPM continues to increase, the outcomes of this procedure must be critically assessed. The added morbidity seems to be substantial.

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