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Selected medical interventions in women with a deleterious *BRCA* mutation: a population-based study in British Columbia

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ABSTRACT

Background We examined the uptake of risk-reducing interventions, including bilateral mastectomy, risk-reducing salpingo-oophorectomy, oral contraceptive pills, tamoxifen, and raloxifene, for the entire population of women with a deleterious *BRCA1* or *BRCA2* mutation in the Canadian province of British Columbia.

Methods This retrospective population-based study used data available in British Columbia for all women who, between 1996 and 2014, were tested and found to have a *BRCA* mutation. Rates of risk-reducing interventions stratified according to the type of *BRCA* mutation and prior history of breast or gynecologic cancer (ovary, fallopian tube, peritoneal) are presented. Cancers diagnosed in women with a *BRCA* mutation after disclosure of their mutation status are also presented.

Results The final study cohort consisted of 885 patients with a deleterious *BRCA1* (n = 474) or *BRCA2* (n = 411) mutation. Of the women with no prior breast cancer, 30.8% carrying a *BRCA1* mutation and 28.3% carrying a *BRCA2* mutation underwent bilateral mastectomy. Of women with no prior gynecologic cancer, 64.7% carrying a *BRCA1* mutation and 62.2% carrying a *BRCA2* mutation underwent risk-reducing bilateral salpingo-oophorectomy. Rates of chemoprevention with oral contraceptive pills and tamoxifen or raloxifene were low in all groups. In this cohort, 23 gynecologic and 70 breast cancers were diagnosed after disclosure of *BRCA* mutation status.

Conclusions Our results suggest reasonable uptake of risk-reducing interventions in high-risk women. To minimize the occurrence of breast and ovarian cancer in women with a *BRCA1* or *BRCA2* mutation, more attention could be paid to ensuring that affected women receive proper counselling and follow-up.

Key Words *BRCA* mutation, hereditary breast and ovarian cancer, prevention, risk reduction

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INTRODUCTION

Women with a *BRCA1* or *BRCA2* germline mutation are at increased risk for breast and ovarian cancer. Compared with the average cumulative risk of 12% and 1.4% in the general population[1], women with a germline *BRCA1* mutation have an average lifetime risk of 47%–66% for breast cancer and 35%–46% for ovarian cancer[2]. Among women with a germline *BRCA2* mutation, the average cumulative risks are 40%–57% and 13%–23% respectively[2]. In many jurisdictions, hereditary cancer programs identify women at high risk of cancer, with the goal of preventing future cases of cancer or offering enhanced screening to detect cancers earlier, when they are more treatable.

Several effective interventions to reduce the risk of future breast and ovarian cancer are available to women with *BRCA1* and *BRCA2* mutations. Those interventions include bilateral mastectomy, which has been shown to decrease the risk for breast cancer by approximately 90%[3–6], and risk-reducing bilateral salpingo-oophorectomy (RRBSO), which has been shown to decrease the risk for ovarian cancer by 80%–96%[7–12]. Chemoprevention options are also

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available (although considerably less evidence is available for their effectiveness in this population), including the use of oral contraceptive pills for prevention of ovarian cancer[13] and the use of tamoxifen[14] or raloxifene[15] for prevention of breast cancer.

Enhanced screening protocols designed for earlier detection of a possible breast cancer—for example, magnetic resonance imaging or mammography—can also be considered[16,17]. Screening for ovarian cancer is not recommended, because no mortality benefit has been demonstrated, even with strict adherence to screening protocols[18–22].

In British Columbia, women who have a mutation that increases their risk for breast or ovarian cancer or a first-degree relative with a confirmed mutation are eligible for referral to the High-Risk Clinic run by the Hereditary Cancer Program (HCP), where they will be counselled by a nurse practitioner and a medical director who arrange for appropriate screening and communicate up-to-date recommendations about risk-reducing interventions. However, not all patients with *BRCA* mutations are counselled at the High-Risk Clinic; many live too far away or opt for other forms of follow-up. A recent study of the patients counselled in the clinic reported high rates of RRBSO (>80%) in patients more than 40 years of age and a 38% rate of prophylactic mastectomy[23]. Here, we present population-based data about risk-reducing interventions in women with a *BRCA1* or *BRCA2* mutation regardless of whether those women were treated in the High-Risk Clinic or elsewhere. We hypothesized that rates of RRBSO and bilateral mastectomy in this population-based cohort of women would be lower than rates reported for the subset of women treated in the High-Risk Clinic.

METHODS

In this population-based retrospective study, we analyzed all women who were tested at the HCP between 1996 and 2014 in the Canadian province of British Columbia. Subjects were eligible for the study if they were female, had tested positive for a deleterious *BRCA1* or *BRCA2* mutation (10 women also tested positive for a variant of unknown significance), had at least 1 year of follow-up data in the population-based datasets, and had been registered with the provincial health insurance program for at least 275 days in the year in which they were identified as *BRCA*-positive and in the subsequent year. Although follow-up continued until 31 December 2014, we imposed the registration criteria for only 2 calendar years to ensure that the women were residing primarily in British Columbia during the time of their of *BRCA* mutation testing and disclosure.

With approval of all data stewards, we obtained data about health services use from Population Data BC, data from the BC Cancer Registry, vital statistics death data, and data from BC PharmaNet[a]. Those data include all physician services, hospitalizations, cancer diagnoses, and prescription drug use in an outpatient setting for the entire population of British Columbia. The data were linked with data from BC Cancer's HCP—a program that provides *BRCA1* and *BRCA2* mutation testing to all patients in British Columbia. All inferences, opinions, and conclusions drawn are those of the authors and do not reflect the opinions or policies of the data stewards. Ethics approval was obtained from the University of British Columbia Behavioural Research Ethics Board.

Procedures

For all identified patients, we examined cancer histories and use of these risk-reducing interventions: mastectomy, RRBSO, and chemoprevention (oral contraceptive pills, or tamoxifen, or raloxifene). Women were stratified according to their prior history of breast cancer when examining mastectomy or chemoprevention for breast cancer, and their prior history of gynecologic cancer (defined as ovarian, fallopian tube, or peritoneal cancer) when examining RRBSO and oral contraceptive pill use. That approach allows for the presentation of data about the entire population, while acknowledging that, for women with prior breast and ovarian cancers, certain interventions—mastectomies, bilateral salpingo-oophorectomy, tamoxifen, and so on—are almost certainly being used as part of cancer treatment and not for risk reduction. We also present rates of RRBSO in women who were 40 years of age and older by the end of the follow-up period (because RRBSO is not recommended until age 40).

Cancers Diagnosed After *BRCA* Mutation Disclosure

To examine "failed" prevention opportunities, we also present the number of gynecologic and breast cancers that were diagnosed after a patient was made aware of their *BRCA* mutation status.

Statistical Analysis

The chi-square test was used to compare frequencies for categorical variables and to compare rates of intervention uptake. Mean values for all continuous variables were compared using *t*-tests. All statistical tests were performed in the Stata software application (version 13: StataCorp LP, College Station, TX, U.S.A.). When reporting certain data cells might result in inadvertent disclosure, approximate percentages are presented (rounded to the nearest multiple of 5).

RESULTS

In British Columbia, 1503 residents tested positive for a deleterious *BRCA1* or *BRCA2* mutation between 1996 and 2014. After the exclusion of male patients ($n = 211$), patients without a full year of follow-up because their *BRCA* status was disclosed too near the end of the follow-up period or because they died or moved out of province within a year of

[a] Data extracts provided by Population Data BC and the British Columbia Ministry of Health from the BC Cancer Registry (ver. 2, http://www.bccancer.bc.ca/health-professionals/professional-resources/bc-cancer-registry), the Medical Services Plan Payment Information File (ver. 2, https://www.popdata.bc.ca/data/health/msp), the BC Perinatal Data Registry (https://www.popdata.bc.ca/data/health/PSBC), and PharmaNet (https://www2.gov.bc.ca/gov/content/health/practitioner-professional-resources/pharmacare/pharmanet-bc-s-drug-information-network); and by the Canadian Institute for Health Information from the Discharge Abstract Database (ver. 2, https://www.cihi.ca/en/discharge-abstract-database-metadata); all 2015.

disclosure ($n = 353$), and patients who were not registered for health care in British Columbia for 275 days or more (75% of the calendar year, $n = 54$), the final study cohort included 885 patients with a *BRCA1* ($n = 474$) or *BRCA2* mutation ($n = 411$).

Table I details the characteristics of the study cohort. Approximately one third of the women with a *BRCA1* mutation (35.5%) or a *BRCA2* mutation (27.8%) knew their mutation status before age 40. No differences in the rates of breast and ovarian cancer diagnosed before *BRCA* testing were observed between women with a *BRCA1* or *BRCA2* mutation, and fewer than half the women were diagnosed with breast cancer before *BRCA* testing. Of every 10 women, approximately 1 was diagnosed with a gynecologic cancer before *BRCA* testing. No significant difference in age between the groups was observed at diagnosis of the gynecologic cancers.

TABLE I Characteristics of patients with a deleterious mutation in *BRCA1* or *BRCA2*

Characteristic	Mutation		*p* Value
	BRCA1	***BRCA2***	
Patients *(n)*	474	411	
Mean year of ...			
Birth	1959.9±14.2	1958.2±14.8	0.085
First visit to HCP	2005.3±4.7	2006.3±4.2	0.002
BRCA status disclosure	2006.4±4.6	2007.3±4.0	0.001
Mean age (years) at ...			
First visit to HCP	45.4±14.1	47.9±13.8	0.002
BRCA status disclosure	46.5±13.9	49.1±14.1	0.006
Age category at *BRCA* disclosure [*n* (%)]			
≤40 Years	156 (35.5)	108 (27.8)	
41–50 Years	133 (30.3)	105 (27.0)	
51–60 Years	79 (18.0)	100 (25.7)	
61–70 Years	45 (10.3)	37 (9.5)	
>70 Years	26 (5.9)	39 (10.0)	0.005
Index patients	213 (44.9)	185 (45.0)	0.982
Cancer before *BRCA* testing			
Breast cancer [*n* (%)]	195 (41.1)	153 (37.2)	0.235
Mean age at Dx (years)	43.8±10.8	45.9±10.9	0.075
Gynecologic cancer [*n* (%)]	41 (8.7)	43 (10.5)	0.018
Mean age at Dx (years)	49.4±11.0	55.4±11.7	0.494
Mean follow-up (years)	8.2±4.6	7.2±4.0	0.001
First-degree relatives [*n* (%)]			
0–3	176 (37.1)	143 (34.8)	
4–6	35 (7.4)	40 (9.7)	
≥7	263 (55.5)	228 (55.5)	0.413
Second-degree relatives [*n* (%)]			
0–3	100 (21.1)	74 (18.0)	
4–6	72 (15.2)	66 (16.1)	
≥7	302 (64.7)	271 (65.9)	0.510
Third-degree relatives [*n* (%)]			
0–3	112 (23.6)	81 (19.7)	
4–6	67 (14.1)	59 (14.4)	
≥7	295 (62.2)	271 (65.9)	0.362

HCP = Hereditary Cancer Program; Dx = diagnosis.

Mastectomy and Chemoprevention for Breast Cancer

Table II reports use of mastectomy and chemoprevention for breast cancer stratified by whether the women had previously been diagnosed with breast cancer. Of all patients with a *BRCA1* mutation, 40.9% underwent bilateral mastectomy (30.8% of women who had not previously had breast cancer, and 55.4% of those who had previously been diagnosed with breast cancer, $p < 0.001$). Women with a *BRCA1* mutation and no prior cancer were younger than those who had previously been diagnosed with cancer at the time of mastectomy (45.1 years vs. 49.9 years, $p = 0.006$), and they waited an average of 2.8 years between *BRCA1* mutation disclosure and mastectomy. Of women with a *BRCA2* mutation, 28.3% with no prior breast cancer and 58.2% with a prior diagnosis of breast cancer underwent bilateral mastectomy ($p < 0.001$). The average time between disclosure of the *BRCA2* mutation and mastectomy was 2.5 years in women without a prior cancer and 0.5 years in those with a prior cancer ($p < 0.001$).

With respect to chemoprevention for breast cancer, tamoxifen use was rare in women without a prior breast cancer diagnosis (1.8% for women with a *BRCA1* mutation and 6.2% for women with a *BRCA2* mutation). Very little use of raloxifene was observed in any of the groups studied (<5% in all groups).

RRBSO and Chemoprevention for Ovarian Cancer

Table III outlines risk-reducing or cancer treatment interventions for ovarian cancer stratified by whether the women had previously been diagnosed with a gynecologic cancer. Most women with a *BRCA1* mutation underwent RRBSO (64.7% for those without a prior cancer and 80.5% for those with a prior cancer, $p = 0.041$). For women who were 40 years of age or older by the end of the follow-up period, rates of RRBSO uptake increased to 74.4% among women without a prior cancer and 80.0% among those with a prior cancer (RRBSO would have been part of cancer treatment for women with a gynecologic cancer). Of women with a *BRCA1* mutation, those without a prior cancer diagnosis were 49.1 years, on average, at the time of RRBSO, and they waited an average of 1.6 years after *BRCA* disclosure to undergo RRBSO; those without a prior cancer diagnosis waited an average of 3 years ($p = 0.745$). Most women with a *BRCA2* mutation underwent RRBSO (62.2% of those without a prior cancer diagnosis and 76.7% of those with a prior cancer diagnosis, $p = 0.061$). Among women who were 40 years of age or older by the end of the follow-up period, rates of RRBSO increased to 71.2% for those without a prior cancer diagnosis and 76.7% for those with a prior cancer diagnosis. The average age at RRBSO was 50.0 years for women with a *BRCA2* mutation and no prior cancer diagnosis, and they waited an average of 1.2 years after *BRCA* disclosure to undergo RRBSO.

Table III also outlines the use of oral contraceptive pills by women with a *BRCA* mutation. Of women with a

TABLE II Use of prophylactic mastectomy,[a] tamoxifen, and raloxifene by breast cancer status

Variable	Prior breast cancer					
	BRCA1 mutation			*BRCA2* mutation		
	No (*n*=279)	Yes (*n*=195)	*p* Value	No (*n*=258)	Yes (*n*=153)	*p* Value
Mastectomy						
Any bilateral mastectomy [*n* (%)]	86 (30.8)	108 (55.4)	<0.001	73 (28.3)	89 (58.2)	<0.001
Mean age at mastectomy (years)	45.1±11.7	49.9±11.7	0.006	49.2±11.4	48.5±10.4	0.694
Age category at *BRCA* disclosure [*n* (%)]						
<40 Years	35 (40.7)	19 (17.6)		12 (16.4)	20 (22.5)	
41–49 Years	26 (30.2)	42 (38.9)		29 (39.7)	33 (37.1)	
50–59 Years	15 (17.4)	25 (23.2)		19 (26.0)	25 (28.1)	
60–69 Years	7 (8.1)	14 (13.0)		9 (12.3)	9 (10.1)	
≥70 Years	(<5)[b]	(<5)[b]	0.010	(<5)[b]	(<5)[b]	0.702
Mean time from *BRCA* disclosure to mastectomy (years)	2.8±2.8	2.0±1.2	0.103	2.5±2.8	0.5±2.1	<0.001
Chemoprevention						
Any tamoxifen use [*n* (%)]	5 (1.8)	30 (15.4)	<0.001	16 (6.2)	62 (40.5)	<0.001
Any raloxifene use [*n* (%)]	7 (2.5)	(<5)[b]	0.244	(<5)[b]	(<5)[b]	

[a] Defined as mastectomy with a corresponding prophylaxis code performed after a woman was aware of her *BRCA* mutation status.
[b] Cell size suppressed because of privacy restrictions. Actual number and percentage have been replaced by an approximation.

deleterious *BRCA* mutation, approximately one third without a prior cancer diagnosis had used oral contraceptive pills (any use, defined as filling at least 1 prescription); fewer than 1 in 10 women with a prior cancer history used oral contraceptive pills ($p < 0.001$). Most of the use by women with a prior gynecologic cancer diagnosis occurred before *BRCA* disclosure, with no oral contraceptive pill use occurring in 93.3% of women with a *BRCA1* mutation and in 92.4% of women with a *BRCA2* mutation after their *BRCA* disclosure.

Cancers Diagnosed After *BRCA* Mutation Disclosure

Table IV describes cancer diagnoses in women after *BRCA* disclosure. After *BRCA* disclosure, 23 women were diagnosed with a gynecologic cancer (16 ovarian cancers). Further details about those cancers could not be reported for privacy reasons connected to small cell sizes. After *BRCA* disclosure, 70 women were diagnosed with breast cancer. Although staging data are missing for cancers diagnosed before 2010, among women with complete staging data, 60% were stage I and 30% were stage II. Of women with gynecologic cancer, 11 (47.8%) were diagnosed during their RRBSO. The number of women diagnosed with breast cancer during their bilateral mastectomy was too small to report. Of the breast cancer patients diagnosed after their genetic testing results were disclosed, 6 (8.5%) had died by the end of the follow-up period; of the gynecologic cancer patients, 7 (30.4%) had died by the end of the follow-up period.

DISCUSSION AND CONCLUSIONS

Testing for *BRCA1* and *BRCA2* mutations is a cancer prevention initiative. The two most effective interventions for significantly reducing the risk of breast and ovarian cancer in women with a *BRCA1* or *BRCA2* germline mutation are risk-reducing bilateral mastectomy (approximately 90% risk reduction)[3–6] and RRBSO (80%–96% risk reduction)[7–12]. Our data indicate that, of women not previously diagnosed with a breast cancer, approximately 30% with a deleterious *BRCA* mutation underwent bilateral mastectomy after disclosure of their *BRCA* status.

The decision-making process for bilateral mastectomy is complex, given the effectiveness of mammography and magnetic resonance imaging for breast cancer screening in this high-risk population[24]. Our data likely reflect the choice by many women for enhanced screening in preference to mastectomy. The number of women with a prior breast cancer diagnosis undergoing mastectomy is higher, reflecting mastectomies performed for treatment purposes.

There are no effective screening methods for ovarian cancer, and 5-year overall survival remains low[25,26]. As a result, close to two thirds of B.C. women with a deleterious *BRCA1* or *BRCA2* mutation and no prior gynecologic cancer underwent RRBSO for prevention. That proportion exceeded 70% when looking solely at women who were 40 years of age or older at the end of study follow-up.

We found that very few high-risk women were using medications for prevention. Fewer than 10% of women with no prior gynecologic cancer used oral contraceptives after disclosure of their *BRCA* status. That observation is likely at least partly explained by the age of the women in our cohort (most were more than 45 years of age at the time of *BRCA* disclosure), the fact that use of oral contraceptive pills for ovarian cancer prevention in high-risk women is less well supported by the evidence, and the fact that most women proceed to RRBSO after disclosure. No randomized controlled trials have been reported, but observational studies have shown associations between the use of oral contraceptives and a reduced risk of ovarian cancer for

TABLE III Bilateral salpingo-oophorectomy (BSO) and oral contraceptive pill use by gynecologic cancer status

Variable	Prior gynecologic cancer					
	***BRCA1* mutation**			***BRCA2* mutation**		
	No (*n*=433)	**Yes (*n*=41)**	***p* Value**	**No (*n*=368)**	**Yes (*n*=43)**	***p* Value**
Risk-reducing BSO						
Use of risk-reducing BSO [*n* (%)]						
Any	280 (64.7)	33 (80.5)	0.041	229 (62.2)	33 (76.7)	0.061
In women ≥40 years of age	267 (74.4)	32 (80.0)	0.436	220 (71.2)	33 (76.7)	0.448
Mean age at time of procedure (years)	49.1±10.0	50.6±9.7	0.410	50.0±9.3	58.6±1.7	<0.001
Age group at time of procedure [*n* (%)]						
<40 Years	50 (17.9)	(<5)[a]		30 (13.1)	(<5)[a]	
41–49 Years	122 (43.6)	11 (33.3)		94 (41.1)	5 (15.2)	
50–59 Years	64 (22.9)	11 (33.3)		79 (34.5)	12 (36.4)	
60–69 Years	35 (12.5)	7 (21.2)		20 (8.7)	10 (30.3)	
≥70 Years	9 (3.2)	(<5)[a]	0.251	6 (2.6)	(<5)[a]	<0.001
Mean time from *BRCA* disclosure to procedure (years)	1.6±2.4	3.0±2.0	0.7452	1.2±2.0	2.9±2.0	0.135
Chemoprevention						
Use by duration-of-use group [*n* (%)]						
Overall						
None	298 (68.8)	37 (90.2)		254 (69.0)	40 (93.0)	
0–1 Years	24 (5.5)	(<5)[a]		19 (5.2)	(<5)[a]	
2–5 Years	49 (11.3)	(<5)[a]		46 (12.5)	(<5)[a]	
5–10 Years	45 (10.4)	(<5)[a]		37 (10.1)	(<5)[a]	
≥10 Years	17 (3.9)	(<5)[a]		12 (3.3)	(<5)[a]	0.015
After *BRCA* disclosure						
None	404 (93.3)	41 (100)		340 (92.4)	43 (100)	
0–1 Years	14 (13.2)	0		12 (3.3)	0	
2–5 Years	8 (1.9)	0		9 (2.5)	0	
5–10 Years	5 (1.4)	0		5 (1.4)	0	
≥10 Years	(<5)[a]	0	0.570	(<5)[a]	0	0.476

[a] Cell size suppressed because of privacy restrictions. Actual number and percentage have been replaced by an approximation.

BRCA1 and *BRCA2* carriers, with odds ratios suggesting a 40%–50% reduction in risk[13]. Two meta-analyses have not supported an increased risk of breast cancer for high-risk women using oral contraceptive pills[13,27]. Our results suggest that tamoxifen and raloxifene are not being regularly used as primary chemoprevention. Data about the use of tamoxifen for prevention of breast cancer in *BRCA1* and *BRCA2* carriers are limited, but there is some indication of effectiveness in *BRCA2* carriers[14]. Trials of raloxifene use have not included many *BRCA* carriers, which makes drawing conclusions about its effectiveness difficult[28]. Thus, the low rates of use in our cohort are not surprising and not indicative of a failure to provide an effective chemoprevention option.

With respect to how our results compare with publications examining women who were seen at the HCP's High-Risk Clinic at BC Cancer, 24% of woman more than 40 years of age received prophylactic mastectomies[23]. We report that approximately 30% of our *BRCA1* and *BRCA2* mutation carriers without a prior breast cancer diagnosis underwent bilateral mastectomy. The difference is likely explained by the fact that women who want to proceed directly to mastectomy after disclosure of their test result would not necessarily be seen at the High-Risk Clinic. The number of women undergoing RRBSO for prevention in our study (approximately 70% of those without a history of gynecologic cancer who were 40 years of age or older at the end of the follow-up period) is lower than that reported from the High-Risk Clinic, where 80% of women more than 40 years of age had undergone RRBSO, suggesting that those counselled in the clinic are more likely to undergo that important preventive intervention. Our work differs from previous publications in that we included the entire population of women with a *BRCA* mutation in British Columbia regardless of where they were treated. We also present data about chemoprevention.

TABLE IV Characteristics of 70 breast cancer diagnoses in the follow-up period

Variable	Value
Mutation status [*n* (%)]	
BRCA1	30 (42.9)
BRCA2	31 (44.3)
Unknown variant	9 (13.0)
Stage [*n* (%)]	
All women	
I	18 (25.7)
II	9 (12.9)
≥III	(<5)[a]
Missing	(<5)[a]
Carrier women	48 (68.6)
I	15 (31.3)
II	5 (10.4)
≥III	(<5)[a]
Missing	(>50)
Index women	22 (31.4)
I	(~15)
II	(~20)
≥III	0
Missing	>65

[a] Cell size suppressed because of privacy restrictions.

Our work was strengthened by its population-based nature and our ability to access long-term follow-up data with procedure codes revealing all surgeries that the women had undergone (with exact dates) and all medicines that were dispensed (with dates). Thus, we were not forced to rely on patient recall. Limitations of our work include a lack of data about screening for breast cancer. We were unable to ascertain whether bilateral mastectomy in women with a prior breast cancer diagnosis was undertaken partly as a preventive measure if the woman had cancer only in one breast. Unfortunately, the data do not provide that level of detail. We also lacked data about which of the women included in our study were seen at the High-Risk Clinic, but that proportion of our study population would be expected to be approximately 75%, meaning that most women in the present study would have received some counselling about their best prevention and screening approaches. We also lacked a negative control group to determine whether rates of risk-reducing interventions were comparatively higher for women who screened positive than for women who screened negative. Such a comparison is especially important, given recent reports by Kurian *et al.*[29] indicating that average-risk patients are frequently undergoing bilateral mastectomy despite lack of evidence for a survival advantage[30–32]. Finally, we lacked information about whether women consider these risk-reducing interventions acceptable—an important consideration in whether an intervention will be used. Although we cannot report those data, previous studies into the psychological effects of bilateral mastectomy and RRBSO have reported significantly less worry after the surgery and a high quality of physical and mental well-being[33–36].

We also report 70 breast and 23 gynecologic cancers diagnosed after *BRCA* disclosure. Although some of those cancers were diagnosed at the time of risk-reducing surgery, most occurred in women who had not yet undergone any risk-reducing interventions. Future work should seek to illuminate why these high-risk women are not undergoing risk-reducing interventions to improve rates of cancer prevention and to lower the number of breast and gynecologic cancers for known high-risk women.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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