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EPIDEMIOLOGY

Contralateral risk-reducing mastectomy in *BRCA1* and *BRCA2* mutation carriers and other high-risk women in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer (kConFab)

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Abstract The purpose of this study is to determine the prevalence and predictors of contralateral risk-reducing mastectomy (CRRM) in Australasian women at high familial risk of a second primary breast cancer (BC). Participants were women with unilateral BC and a strong family history of the disease, including *BRCA1/2* mutation carriers. Data were collected through interview, self-administered questionnaire and review of pathology and surgical reports. Associations between CRRM and potential predictors were assessed using multivariate logistic regression. Of 1,018 women (median follow-up 11.1 years), 154 (15%) underwent CRRM, 43% of these within 12 months of initial BC surgery. More likely to undergo CRRM were women who were younger at BC diagnosis (odds ratio [OR] = 0.94 per year of age, $P < 0.001$), were diagnosed more recently (OR = 1.16 per calendar year, $P < 0.001$), underwent mastectomy as initial definitive BC treatment (OR = 5.2, $P < 0.001$) and underwent risk-reducing salpingo-oophorectomy (OR = 3.4, $P < 0.001$). *BRCA1/2* mutation status, axillary nodal status and receipt of chemotherapy were not independently associated with CRRM uptake. A contralateral BC event (invasive or in situ) occurred in 177 (20.5%) of the 864 women who did not have CRRM, compared with one chest wall event (0.6%) in the 154 women post-CRRM. The contralateral event rate was 15.1 per 1,000 women-years for non-CRRM women and 0.7 per 1,000 women-years for CRRM women; $P < 0.0001$. Younger women with more recently diagnosed BC treated with mastectomy are more likely to elect CRRM. Neither *BRCA1/2* mutation status, nor the competing risk of BC recurrence and death, appears to influence decision making.

Keywords Breast cancer · Contralateral prophylactic mastectomy · BRCA1/2 · Familial breast cancer

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Introduction

Following a breast cancer (BC) diagnosis, women face both the risk of systemic and/or local recurrence of their disease and the risk of a new primary BC. For women with a strong family history of BC and for women who carry a mutation in either of the BC predisposition genes, *BRCA1* or *BRCA2,* these risks are relatively high. The contralateral BC risk is 0.6% per year overall [1], compared with 2.2%

for women with a family history [2] and up to 3% for mutation carriers [3]. Risk management strategies for contralateral BC include regular screening with mammography and magnetic resonance imaging, contralateral risk-reducing mastectomy (CRRM), risk-reducing salpingo-oophorectomy (RRSO) and chemoprevention. CRRM is the most effective strategy, reducing the risk of contralateral BC by up to 95% [3–5].

Although the effectiveness of CRRM is well established, only a relatively low proportion of women at high risk for a second primary BC elect this procedure. Internationally, uptake of CRRM for *BRCA1* and *BRCA2* mutation carriers is reported to vary between 5 and 38% [6], but the Australasian population has not been assessed. We previously published the BC risk-management choices of both unaffected female *BRCA1* and *BRCA2* mutation carriers [7] and non-carriers in carrier families [8] from a large Australasian cohort study, but to date, we have not examined the secondary prevention choices of women in this cohort. In contrast to the existing secondary prevention studies that have focused on mutation carriers [3, 4, 9], we included women with a strong family history of BC but without a documented mutation in *BRCA1* or *BRCA2*. The latter group make up the vast majority of familial BC patients seen in clinics internationally.

We aimed to determine both the prevalence of CRRM in Australasian women with familial BC and the factors associated with uptake of CRRM in this setting. The primary hypothesis, based on published literature and clinical experience, was that a minority of women would undergo CRRM. Based on our experience in Australia and knowledge of international rates for CRRM, we anticipated the Australasian CRRM prevalence would be intermediate between the prevalence reported for mutation carriers in Europe (5%) [9] and North-America (38%) [9]. We hypothesised that CRRM uptake would be associated with the following: younger age at BC diagnosis [9, 10]; higher education level; being married or living as married; being parous [8]; more recent BC diagnosis [11]; knowing one was a *BRCA1* or *BRCA2* mutation carrier [10, 12]; stronger family history [4]; features suggesting higher risk BC (axillary node involvement, receipt of chemotherapy); ipsilateral mastectomy for definitive therapeutic surgery rather than breast conservation [9]; and RRSO [4, 9, 12].

Patients and methods

Study sample

Participants were women with BC who were members of multiple-case BC families enrolled in the Kathleen Cunningham Foundation Consortium for Research into Familial Breast Cancer (kConFab) [13, 14]. Families were recruited after an initial member attended a clinical consultation in one of 16 family cancer clinics in Australia and New Zealand. At enrolment, blood was drawn for possible *BRCA1* and *BRCA2* mutation analysis, and epidemiology and family history questionnaires were administered. Cancer events, screening behaviour, epidemiological and lifestyle risk factors and preventative strategies were updated on all participants every 3 years using a mailed self-administered follow-up questionnaire [15, 16]. At enrolment and during follow-up, pathology and surgical reports were obtained where possible to verify cancer events and surgeries. All participants provided written informed consent; and the study had ethics approval at all recruitment sites.

Women were eligible for the current study if they had had surgery for unilateral invasive BC, either prior to or after entering kConFab, and they had completed at least one round of three-yearly follow-up. Women from mutation-carrying families who were found not to carry the family gene mutation were excluded, as were women with a prior history of another invasive cancer (apart from non-melanoma skin cancer), bilateral synchronous BCs or metastatic disease at diagnosis.

Data collection

Demographics

Demographical information was collected by interview at entry into kConFab and subsequently three-yearly by self-administered questionnaire.

Mutation status

Mutation testing for *BRCA1* and *BRCA2* is performed only on key individuals in kConFab families. Other women are offered predictive testing through a clinical genetics service if a mutation is detected within their family but not all women elect to be tested. For the current study, *BRCA1* and *BRCA2* mutation status was determined from the kConFab database. In the self-administered follow-up questionnaire, women were asked whether they knew their mutation status, and if so, when they became aware of their result.

Breast cancer and risk-reducing surgery details

Dates of BC diagnosis and therapeutic surgery were obtained from pathology reports or self-report when no pathology report was available. Data on axillary node involvement, type of surgery (mastectomy or breast conservation) and receipt of adjuvant chemotherapy were obtained from self-report using validated questions [17]. Data on subsequent ipsilateral and contralateral breast

events (recurrences and new primary lesions), systemic recurrence of BC, risk-reducing surgery and new primary non-breast cancers, were obtained by self-report and verified where possible from pathology reports.

Statistical analysis

The proportion of women who underwent CRRM was compared across categories for each putative explanatory variable using Pearson χ^2 test. Univariate and multivariate logistic regression were used to estimate the associations between uptake of CRRM and the explanatory variables: age at diagnosis of first BC (quartiles and by year), mutation status (mutation carrier and aware of mutation status versus no identified mutation, untested or unaware of mutation status), parity (any live births versus none), highest achieved education level (tertiary versus other), marital status (married or living as married versus other), year of first BC diagnosis (quartiles and by calendar year), axillary nodal involvement for first BC (involved versus not); treatment of first BC (adjuvant chemotherapy versus not), definitive therapeutic surgery for first BC (mastectomy versus breast conserving therapy), family history of BC (at least two first- or second- degree relatives with BC versus other), family history of ovarian cancer (at least one first- or second- degree relative with ovarian cancer versus other) and occurrence of an ipsilateral breast event (any versus none). All these potential explanatory variables were included in the multivariate analysis. All were fitted as categorical variables except for age at diagnosis and year of diagnosis which were fitted as continuous variables. For the mutation status variable, the timing of the participant learning their mutation result was considered. If they learnt of their result after having a CRRM, then, they were classified as not knowing their mutation result. Women who reported they did not know when they received their mutation result in relation to CRRM were excluded from the logistic regression analysis.

All analysis was carried out using STATA version 8.0 (STATA Corp, College Station, TX).

Results

Population characteristics

As of March 2008, 1,469 women enrolled in kConFab had had surgery for unilateral invasive BC. Of these, 230 were not eligible for the present study because they had not completed a follow-up questionnaire. Of the remaining 1,239 women, a further 221 were ineligible; 81 were found to not carry the family *BRCA1* or *BRCA2* mutation, 62 had another invasive cancer prior to their BC diagnosis, 63 had synchronous bilateral BC, 2 had metastatic disease at diagnosis, 11 had a diagnosis of DCIS treated with mastectomy prior to their first invasive BC and 2 women had incomplete data. See Fig. 1—Study Schema.

Characteristics of the remaining 1,018 participants are described in Table 1. BC was verified with pathology reports for 920 participants (90%). For 54 participants (5%), the first BC occurred after enrolment in the cohort study. A *BRCA1* or *BRCA2* mutation was detected in 288 women (29%), and 217 carriers were aware of their mutation result at last follow-up. The median time from first BC diagnosis to last follow-up was 11.1 years (8 years for women who underwent CRRM and 11.7 years for women who did not).

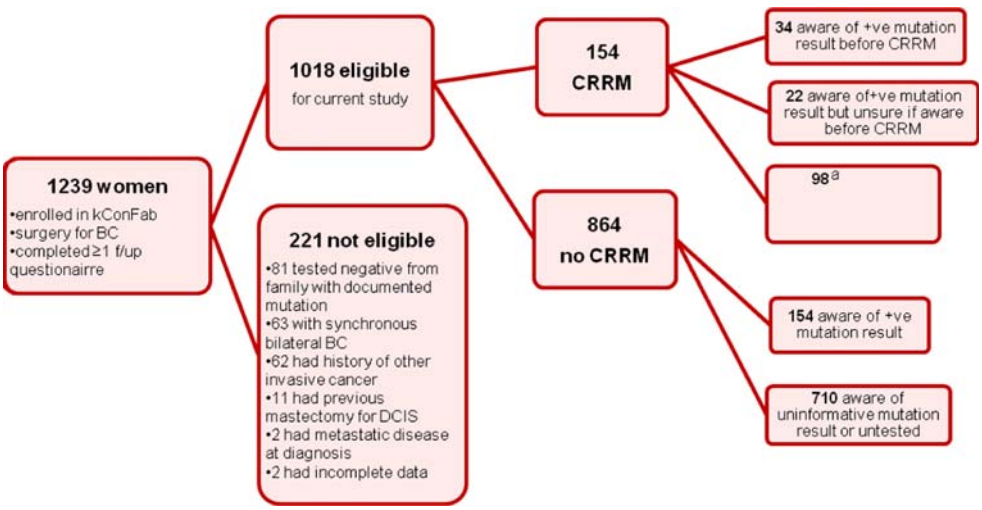

Fig. 1 Schema for patients BC = breast cancer; CRRM = contralateral risk-reducing mastectomy; DCIS = ductal carcinoma in situ; f/up = follow-up; +ve = positive.[a] Includes seven women who learnt positive mutation result after CRRM

Table 1 Participant characteristics

Characteristic	Number (%)[a]
Age (years) at 1st BC diagnosis	
Mean	46.7
Median (range)	47 (22–85)
<40	265 (26)
40–47	278 (27)
48–54	225 (22)
>54	250 (25)
Time from 1st BC diagnosis to last f/up	
Median	11.1 years
Range	1 week to 63 years
Year of BC diagnosis	
Mean	1993
Median (range)	1997 (1944–2007)
Before 1990	282 (28)
1991–1995	266 (26)
1996–1999	257 (25)
Since 2000	213 (21)
Surgery type for treatment of 1st BC[b]	
Breast conserving surgery	401 (39)
Mastectomy	607 (60)
Unknown	10 (1)
Axillary nodal involvement	
Yes	370 (36)
No	628 (62)
Unknown	20 (2)
Received adjuvant chemotherapy	
Yes	391 (38)
No	578 (57)
Unknown	49 (5)
Risk-reducing salpingo-oophorectomy	
Yes	326 (32)
No	692 (68)
Mutation status	
BRCA1 mutation carrier	161 (16)
BRCA2 mutation carrier	127 (12)
No documented mutation (includes untested)	730 (72)
Educational level	
Tertiary/vocational	406 (40)
Less than tertiary	608 (60)
unknown	4 (<1)
Marital status	
Married or living as married	741 (73)
Never married, divorced or widowed	269 (26)
Unknown	8 (1)
Parity (number of live births)	
0	40 (4)
≥1	912 (90)
Unknown	66 (6)
Family history of BC (no. FDR and SDR)	
<2	285 (28)
≥2	733 (72)
Family history of OC (no. FDR and SDR)	
0	789 (78)
≥1	229 (22)
Ethnicity	
Caucasian	966 (95)
Asian	8 (1)
Other	22 (2)
Unknown	22 (2)

BC Breast cancer, *no.* number, *FDR* first degree relatives, *f/up* follow-up, *OC* ovarian cancer, *SDR* second degree relatives

[a] Unless otherwise indicated

[b] Does not include subsequent ipsilateral surgery, e.g. ipsilateral risk-reducing mastectomy at time of contralateral risk-reducing mastectomy

Risk-reducing surgery

CRRM was undertaken by 154 women (15%), and 326 women (32%) had a RRSO. Thirty-seven women who elected CRRM (24%) had had ipsilateral breast conservation as definitive treatment for their initial BC. All of these women later underwent ipsilateral mastectomy. Twenty-one (57%) had ipsilateral risk-reducing completion mastectomy at the time of CRRM, and 16 had ipsilateral mastectomy as treatment for a recurrent cancer event either concurrent with CRRM or prior to CRRM.

Table 2 describes the characteristics of participants by CRRM status and the results of the unadjusted and adjusted analyses estimating the associations between those characteristics and CRRM uptake. The independent predictors of CRRM from the adjusted analysis were as follows: younger age at BC diagnosis (odds of CRRM decreased 6% per year of age at diagnosis [95% CI 4%–9%], $P < 0.001$); more recent diagnosis (odds of CRRM increased 16% per calendar year [95% CI 11%–21%], $P < 0.001$); having a RRSO (odds ratio 3.35 [95% CI 2.08–5.40], $P < 0.001$); and having a mastectomy as treatment for first BC (odds ratio 5.25 [95% CI 3.08–8.95], $P < 0.001$).

Twenty-two mutation carriers who elected CRRM but did not know whether they received their mutation result before or after their surgery were excluded from the analysis. Seven carriers learned their mutation result after their CRRM and were categorised with the women who did not know their mutation status at the time of CRRM. Of the 188 women who knew they carried a *BRCA1* or *BRCA2* mutation, 34 (18%) elected CRRM. Of the 808 women

Table 2 Characteristics of women by CRRM status and associations with CRRM uptake in unadjusted and adjusted analyses

Characteristic	CRRM $n = 154$ n (%)	No CRRM $n = 864$ n (%)	Odds ratio (unadjusted) (95% CI), P value	Odds ratio (adjusted)
Mean age at BC diagnosis (years)	43.9	48.3	0.96 per year (0.94–0.98), $P < 0.001$	0.94 per year (0.91–0.96), $P < 0.001$
Age range at diagnosis (years)				
<40	53 (20)	212(80)	1.0 (baseline)	
40–47 years	45 (17)	233 (83)	0.78 (0.50–1.20)	
48–54	33 (15)	192 (85)	0.69 (0.43–1.11)	
>54	23 (9)	227 (91)	0.41 (0.24–0.68)	
Mean year of BC diagnosis	1997	1992	1.09 per year (1.06–1.12), $P < 0.001$	1.16 per year (1.11–1.21), $P < 0.001$
Year of diagnosis				
Prior to 1990	16 (6)	266 (94)	1.0 (baseline)	
1991–1995	44 (17)	222 (83)	3.30 (1.81–6.00)	
1996–1999	43 (17)	214 (83)	3.34 (1.83–6.10)	
Since 2000	51 (24)	162 (76)	5.23 (2.89–9.49)	
BRCA result known by patient				
Yes	34[a] (18)	154 (82)	1.60 (1.04–2.45), $P = 0.03$	0.78 (0.43–1.40), $P = 0.40$
No	98 (12)	710 (88)	1.0 (baseline)	1.0 (baseline)
Axillary nodal involvement				
Yes	54 (15)	316 (85)	0.94 (0.65–1.34), $P = 0.72$	0.66 (0.40–1.11), $P = 0.12$
No	97 (15)	531 (85)	1.0 (baseline)	1.0 (baseline)
Adjuvant chemotherapy				
Yes	70 (18)	321 (82)	1.44 (1.01–2.05), $P = 0.043$	0.76 (0.45–1.29), $P = 0.31$
No	76 (13)	502 (87)	1.0 (baseline)	1.0 (baseline)
RRSO				
Yes	86 (26)	240 (74)	3.29 (2.31–4.67), $P < 0.001$	3.35 (2.08–5.40), $P < 0.001$
No	68 (10)	624 (90)	1.0 (baseline)	1.0 (baseline)
Surgery type for treatment of 1st BC				
Breast conserving	37 (9)	364 (91)	1.0 (baseline)	1.0 (baseline)
Mastectomy	115 (19)	492 (82)	2.22 (1.50–3.28), $P < 0.001$	5.25 (3.08–8.94), $P < 0.001$
Education				
Tertiary	68 (17)	338 (83)	1.27 (0.90–1.80), $P = 0.18$	0.70 (0.44–1.12), $P = 0.15$
Less than tertiary	83 (14)	525 (86)	1.0 (baseline)	1.0 (baseline)
Ipsilateral event				
Yes	16 (19)	68 (81)	1.37 (0.77–2.43), $P = 0.29$	1.59 (0.74–3.40), $P = 0.23$
No	137 (15)	796 (85)	1.0 (baseline)	1.0 (baseline)
Family history of BC (FDR and SDR)				
Less than 2	50 (17)	235 (82)	1.0 (baseline)	1.0 (baseline
2 or more	104 (14)	629 (86)	0.78 (0.53–1.15), $P = 0.18$	1.46 (0.87–2.42), $P = 0.15$

Table 2 continued

Characteristic	CRRM $n = 154$ n (%)	No CRRM $n = 864$ n (%)	Odds ratio (unadjusted) (95% CI), P value	Odds ratio (adjusted)
Family history of OC (FDR and SDR)				
0	107 (14)	682 (86)	1.0 (baseline)	1.0 (baseline)
1 or more	47 (21)	182 (79)	1.65 (1.13–2.41), $P = 0.10$	0.93 (0.54–1.59), $P = 0.78$
Marital status				
Married/living as married	120 (17)	621 (84)	1.38 (0.91–2.09), $P = 0.13$	1.46 (0.79–2.69), $P = 0.23$
Other	33 (12)	236 (88)	1.0 (baseline)	1.0 (baseline)
Parity				
Any children	134 (15)	778 (85)	0.80 (0.70–0.93), $P = 0.003$	0.87 (0.72–1.06), $P = 0.16$
No children	8 (20)	32 (80)	1.0 (baseline)	1.0 (baseline)

BC Breast cancer, *Yrs* years, *FDR* first degree relative, *SDR* second degree relative, *OC* ovarian cancer, *RRSO* risk-reducing salpingo-oophorectomy

[a] Only includes women who knew their positive mutation result prior to CRRM

who did not know their mutation result or knew they had no documented mutation, 98 (12%) elected CRRM. The crude odds ratio (unadjusted for other variables) was 1.60 (95% CI 1.04–2.45), $P = 0.03$. However, after adjusting for other factors, *BRCA1* and *BRCA2* mutation status was not a statistically significant predictor of CRRM ($P = 0.4$).

Sixty-six women (43%) underwent CRRM within 12 months of BC diagnosis. The only independent predictor of early (<1 year from BC diagnosis) versus late (>1 year from BC diagnosis) CRRM was having mastectomy as definitive surgery for first BC (adjusted OR 4.5; 95% CI 1.6–12.7, $P = 0.005$).

Four incidental BCs (two invasive and two in situ) were detected at the time of surgery in the 57 women who had CRRM after recruitment to the study.

Seventy-five women who had CRRM underwent breast reconstruction (49%) and most reconstruction (73%) occurred within 1 year of CRRM. The average age of first BC diagnosis in women electing reconstruction was 6 years younger than for women not having reconstruction (40.8 versus 46.8 years, mean age difference 5.9 years, SE 1.4 years, $P < 0.0001$). The reconstruction rate was 56% in women diagnosed with BC before age 50 years and 28% in women diagnosed with BC at age 50 years or older ($P = 0.08$).

New cancers and recurrences

There were 177 contralateral BC events (invasive or in situ) during 11,759 women-years of observation for the 864 women who did not elect CRRM and one chest wall event during 1,440 women-years of observation for the 154 women who elected CRRM (15.1 versus 0.7 per 1,000 women-years; $P < 0.0001$). Of the 177 women who developed contralateral BC, 82 (46%) were mutation carriers (54 *BRCA1* and 28 *BRCA2*), 71 had uninformative results, and 24 were untested. The single chest wall recurrence following CRRM occurred in a *BRCA2* mutation carrier.

At last follow-up, 144 of the CRRM women (93.5%) and 800 of the non-CRRM women (92.6%) were still alive. Systemic BC recurrence was reported in 95 women during the study follow-up period, at a median time of 5 years following initial BC diagnosis. The systemic recurrence rate was 6.2 per 1,000 women-years for CRRM women and 10.4 per 1,000 women-years for non-CRRM women; $P = 0.04$. A new non-breast primary cancer was reported by 89 women (9%).

Discussion

This study of contralateral BC in Australasian BC patients with a strong family history found that only a minority undergo CRRM. The finding that younger age at BC diagnosis, mastectomy as definitive therapeutic surgery for BC, and RRSO are independent predictors of electing CRRM is consistent with a recent study of predictors of CRRM that was limited to mutation carriers [9]. In addition, the current study showed that more recent calendar year of BC diagnosis was associated with higher likelihood of undergoing CRRM. Importantly, in this study, which

included mutation carriers as well as women at high risk for contralateral BC on the basis of family history alone, neither *BRCA1* nor *BRCA2* mutation status was an independent predictor of undergoing CRRM. Features of the first BC, including axillary nodal status, and receipt of chemotherapy were also not associated with CRRM uptake.

The Australasian CRRM prevalence of 15% (18% in known *BRCA1* and *BRCA2* mutation carriers and 12% in women with no documented mutation) is higher than the prevalence reported for mutation carriers in Europe (5%) [9] and in the United Kingdom (10%) [18], but lower than that for mutation carriers in North America (38%) [9]. Although caution must be exercised in directly comparing these estimates, given the differing follow-up times and study participant characteristics, similar international variation has also been reported for risk-reducing bilateral mastectomy and RRSO for unaffected women [6, 7]. This variation likely reflects cultural differences in attitudes towards these procedures by both doctors and patients, as well as other differences such as health system and insurance coverage. Qualitative studies in this area would be of interest.

The CRRM rate was higher for women with more recently diagnosed BC, reflecting the increasing trend for CRRM in mutation carriers [4] as well as in the general population [11]. As awareness of familial BC increases and more women are considered at high risk for contralateral BC, surgeons may increasingly offer CRRM at the time of definitive therapeutic surgery for BC.

Of the women undergoing CRRM, 49% had breast reconstruction. This is much lower than the 89% we reported for mutation carriers unaffected by cancer who undergo bilateral risk-reducing mastectomy [7, 19], and perhaps, highlights the differing priorities of these two groups of women. Prior cancer treatments that consume time, energy and finances may influence the decision for reconstruction.

The *BRCA1* or *BRCA2* mutation carriers who knew their genetic test result were not more likely to elect CRRM than the women with no known mutation. This differs from a study from the Lombardi Comprehensive Cancer Center of women affected with BC where the CRRM rate in the year following mutation testing was higher for mutation carriers (18%) compared with women who had uninformative results (3%) [10]. Another study of 194 women with newly diagnosed BC from the same single institution found that those who carried a mutation were more likely to elect bilateral mastectomy (48%) compared with women who were untested or received uninformative results (28%) [12]. The fact that mutation status appears to be associated with uptake of CRRM at that US centre but not in our multi-institutional Australasian setting may reflect differences in counselling content.

Other factors such as cancer-specific distress, the desire for reassurance, having relatives with bilateral BC or relatives that have died of BC and physician recommendation, may be important in driving the decision process for CRRM, but we were unable to examine these factors in the current study.

CRRM reduces the risk of contralateral BC by up to 95% [3–5]. Because the risk of distant metastases and subsequent death from BC often exceeds the risk of contralateral BC, a CRRM survival benefit has been difficult to establish. A Cochrane review of eight studies including 1,708 women, across all levels of familial risk, who underwent CRRM, concluded that CRRM decreased the incidence of contralateral BC, but was not associated with any survival improvement [20]. However, a more recent retrospective cohort study of women with BC across all levels of familial risk reported that CRRM decreased BC mortality (HR = 0.57; 95% CI = 0.45–0.72) and overall mortality (HR = 0.60; 95% CI 0.50–0.72) [21]. Our study, with a median follow-up of 11.1 years, found a reduced rate of contralateral BC for the women who underwent CRRM (0.7 v 15.1 per 1,000 women-years; $P < 0.0001$) but no apparent difference in overall survival (93.5% for CRRM v 92.6% for non-CRRM). The potential survival benefit of CRRM for women at high familial risk of BC requires further evaluation.

This study has several limitations. Much of the information on cancer features and treatment, and potential predictors of CRRM, was retrospective and self-reported. However, data were verified where possible with pathology and operation reports. In addition, there may be a survivorship bias due to 95% of the BC cases being prevalent rather than incident. We had no information on the means of detection of the primary cancer. Women with BC that was occult on diagnostic imaging may be more likely to elect CRRM rather than rely on breast surveillance and it would be interesting to study this. To improve understanding of the uptake and predictors of CRRM and to estimate the survival benefit, longitudinal studies following women with strong family histories of BC from the time of BC diagnosis are underway using this and other cohorts. Women who agree to participate in kConFab might represent a highly motivated group more likely to elect risk-reducing surgery than the general population, so these data may overestimate the true CRRM prevalence.

Despite the limitations, this is the first study to examine uptake of CRRM in Australasian women with familial BC. It is also the largest study and the only multi-institutional study to include women with no identified genetic mutation. Understanding predictors in these women is important, as most women with a strong family history of BC do not have a documented gene mutation.

Genetic testing is becoming more accessible, faster and less expensive. As the awareness of the clinical significance of family history increases, and a larger number of genetic abnormalities contributing to BC risk are identified, cancer clinicians will increasingly need to counsel women on how best to manage the risk of related cancers. The decision process for CRRM must take into consideration the risk of a subsequent BC and the competing risk of dying from the initial BC. In this study, the risk of dying (as assessed by axillary nodal status and receipt of chemotherapy) did not seem to influence the decisions made by our participants. The first two years following BC diagnosis tend to be the highest risk period for systemic recurrence yet most of the women electing CRRM did so within this period. Women may not always fully comprehend their risk of systemic disease recurrence and death, and clinicians have an important role in assisting them to understand these risks and to make appropriate and timely management decisions.

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