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Author/s:
Macdonald, C;Chamberlain, JA;Mazza, D;Milne, RL;Phillips, KA

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Underutilisation of breast cancer prevention medication in Australia

Courtney Macdonald [a, b], James A. Chamberlain [c], Danielle Mazza [d], Roger L. Milne [c, e, f], kConFab investigators[b, g], Kelly-Anne Phillips [a, b, e, *]

[a] Department of Medical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia
[b] Sir Peter MacCallum Department of Oncology, University of Melbourne, Melbourne, Australia
[c] Cancer Epidemiology Division, Cancer Council Victoria, Melbourne, Australia
[d] Department of General Practice, Monash University, Melbourne, Australia
[e] Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, University of Melbourne, Melbourne, Australia
[f] Precision Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, Melbourne, Australia
[g] The Research Department, Peter MacCallum Cancer Centre, Melbourne, Australia

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ABSTRACT

Increased implementation of proven prevention strategies is required to combat rising breast cancer incidence. We assessed use of risk reducing medication (RRMed) by Australian women at elevated breast cancer risk. Only 2.4% had ever used RRMed. Higher breast cancer risk was statistically significantly associated with use of RRMed (OR 1.82, 95%CI: 1.08–3.07, p = 0.02 for ≥30% lifetime risk compared with 16%–29% lifetime risk), but parity, education level and family history of breast cancer were not. Breast cancer prevention medications are underutilised. Efforts are needed to incorporate breast cancer risk assessment and risk management discussions into routine health assessments for women.

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1. Introduction

Breast cancer (BC) incidence continues to rise, so implementation of prevention strategies is essential to reverse this trend [1]. Risk-reducing medications (RRMeds), such as tamoxifen and anastrozole, reduce BC risk by up to 50%, with benefit extending for at least 5–15 years after a five-year course [2,3]. In Australia, consideration of RRMed is recommended for women at moderate risk of BC (i.e.16%–29% full lifetime risk) over the age of 35 years, and for women at high BC risk (i.e. ≥30% full lifetime risk) at any age [4]. In 2016, tamoxifen became Australian government-subsidised for the primary prevention of BC for women at elevated risk. This study aimed to describe the uptake of RRMed in Australian women at elevated BC risk and to identify demographic predictors of use.

2. Materials and methods

Participants were women from multiple-case BC families in Australia enrolled in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer cohort (kConFab) between 1997 and 2008. The probands were recruited from one of fifteen cancer genetics clinics nationwide but family members could be enrolled without clinic attendance or formal risk assessment. Women were mailed a questionnaire at baseline and three yearly thereafter [5] asking about RRMed use, educational level, marital status, pregnancies, breast-feeding, cancer family history, participation in RRMed trials and bilateral mastectomy or cancer diagnoses.

Participants were eligible if, at cohort entry, they were at least 18 years old, had not had a bilateral mastectomy, invasive cancer diagnosis or ductal carcinoma in situ (DCIS) and had at least a moderate lifetime risk of BC (defined as ≥1.5 times population risk,i.e. ≥16% full lifetime risk as calculated by the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation

Abbreviations: RRMed, Risk reducing medication; BC, Breast cancer; kConFab, Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer; BOADICEA, Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm; DCIS, Ductal carcinoma in situ; LCIS, Lobular carcinoma in situ; OR, Odds ratio; CI, Confidence interval.

* Corresponding author. Department of Medical Oncology, Peter MacCallum Cancer Centre, Locked Bag 1, A'Beckett St, Victoria, 8006, Australia.
E-mail address: Kelly.Phillips@petermac.org (K.-A. Phillips).

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Algorithm: BOADICEA [6]). Participants in RRMed trials were excluded. Consistent with Australian guidelines for RRMed use, moderate-risk women who did not reach age 35 years during their follow-up period were excluded. Because RRmeds are contra-indicated during childbearing, those without a five-year pregnancy- and lactation-free period were also excluded.

Data were obtained from baseline and follow-up questionnaires. BOADICEA full lifetime risk (i.e. from age 1 to 80) was calculated (without polygenic risk scores or mammographic density, which were not available) [6]. Use of RRMed was assessed until the date of any cancer diagnosis, bilateral mastectomy, last follow up or death. Associations with RRMed use were assessed using logistic regression to estimate odds ratios (OR) and associated 95% confidence intervals (CI). The hypothesised demographic predictors of RRMed use, based on existing literature [7–10], were parity, number of first-degree relatives with BC, BOADICEA full lifetime risk, and education level.

3. Results

Of 7549 women enrolled in kConFab between 1997 and 2008, 4654 were excluded due to prior invasive cancer or DCIS (N = 2702), bilateral mastectomy (N = 37), participation in a RRMed trial (N = 79), or being at either average risk of BC or moderate risk and under age 35 (N = 1277), no follow-up (N = 509) and no five-year lactation-and pregnancy-free period (N = 50)). Characteristics of the 2895 eligible participants are shown in Table 1. The median follow-up time was 12.1 years (range 2.8–20 years). The median age at baseline was 43 years. Seventy participants (2.4%) had ever taken RRMed, most commonly tamoxifen (n = 64, 91%). The most common age to commence RRMed was 40–49 years (40%) (Table 1).

We found no evidence of an association between uptake of RRMed and parity or education. BC risk was associated with use; those with a full lifetime risk ≥30% were 82% (OR = 1.82, 95% CI = 1.08–3.07) more likely to take RRMed than those with a 16%–29% risk (Table 2). There was weak evidence that uptake was more likely by women with more affected first-degree relatives (P = 0.06). An exploratory analysis did not suggest that BC risk was associated with adherence to RRMed (Supplement 1).

Table 1
Demographic characteristics.

Characteristic	Number of kConFab women (%)
Age started RRMed (years)	
20-29	1 (1.5)
30-39	10 (14)
40-49	28 (40)
50-59	18 (26)
60-69	8 (11)
70-79	1 (1.5)
Don't know	4 (5.7)
Age at cohort entry	
<20	28 (1)
20-29	364 (12.6)
30-39	793 (27.4)
40-49	698 (24.1)
50-59	607 (21)
60-69	265 (9.1)
70-79	117 (4)
≥80	23 (0.8)
Parity	
Nulliparous	387 (13.4)
1	270 (9.3)
2+	2238 (77.3)
Education	
Pre-tertiary	1990 (68.7)
Tertiary	905 (31.3)
Marital status	
Married/living as married	2048 (70.7)
Other	847 (29.3)
BRCA mutation status	
BRCA1	195 (6.7)
BRCA2	162 (5.6)
No known BRCA1/2 mutation	2538 (87.7)
Affected 1st degree relative (Invasive/DCIS)	
None	288 (9.9)
1	1666 (57.6)
2	650 (22.5)
3	224 (7.7)
≥4	67 (2.3)
Full lifetime breast cancer risk[a]	
16%–29%	2075 (71.7)
≥30%	820 (28.3)
Risk reducing medication	
Yes	70 (2.4)
Tamoxifen	64 (91.4)
Raloxifene	4 (5.7)
Anastrozole	2 (2.9)
No	2825 (97.6)

[a] Lifetime breast cancer risk from age 1 to age 80 as calculated by BOADICEA.

4. Discussion

This study of a large number of women from a familial breast cancer cohort found that use of BC RRMed in Australia is low, compared with that in the international literature, with one meta-analysis reporting a pooled estimated uptake of 16.3% (range 0%–55%) [10]. Use may be even lower for women at increased BC risk in the general Australian population, given our participants likely had greater exposure to information about RRMed due to their enrolment in a familial cohort study. We excluded women who had participated in a placebo-controlled RRMed trial, however if these women were included, still only 5% of women would have used RRMed. Higher lifetime BC risk was associated with use, highlighting the importance of risk stratification and personal knowledge of BC risk. Previous research has shown that higher perceived BC risk in women with elevated objective risk is associated with consideration of RRMed [11].

In a recent survey of a subgroup of the current study sample and their clinicians, for the majority (82%) of women, knowledge of their increased BC risk would facilitate use of RRMed [12]. Although the women in the current study knew they had a family history of BC and that they were therefore at increased risk, a quantitative risk assessment was not provided as part of the kConFab study. Thus the level of knowledge of the women in this study is representative of the "real world" quantitative knowledge about their risk that women obtain from other sources. The study also identified that most family physicians lacked awareness of the existence of RRMeds, and/or lack confidence in providing advice about RRMeds. Thus, taken together, our studies suggest that not knowing one's personal BC risk, and other potentially modifiable clinician and patient factors, act as barriers to the uptake of RRMed in Australia, and that the mostly unmodifiable demographic factors examined in this study are of much less importance. These barriers are not unique to Australia. Tamoxifen was recently listed in the National Health Service Rapid Uptake Products programme [13], which aims to increase uptake of effective health interventions in the UK.

5. Conclusion

Use of breast cancer RRMed by eligible women in Australia is very low. Increasing the use of RRMed requires a precision prevention approach incorporating individualised BC risk assessment and risk management discussions in routine woman's health care.

Table 2
Potential predictors of risk reducing medication use.

Characteristic	Odds ratio	95% confidence interval	P-value
Parity			.17
0	1.0 (reference)	–	
1	0.96	0.34–2.73	
2	1.22	0.55–2.71	
3+	0.90	0.43–1.90	
No. of 1st degree relatives with BC			.06
0	1.0 (reference)	–	
1	2.23	0.68–7.34	
2	3.05	0.88–10.6	
3+	3.11	0.84–11.5	
Education			.48
Pre-tertiary	1.0 (reference)	–	
Tertiary	0.82	0.48–1.42	
BC risk[a]			.02
16–29%	1.0 (reference)	–	
≥30%	1.82	1.08–3.07	

[a] Full Lifetime risk. BC = breast cancer; odds ratios and confidence intervals were calculated from separate logistic regression models with a single categorical predictor. P values for parity and number of first-degree relatives with BC were calculated using a Z-test on the linear term modelling the relevant count variable; P values for education and BC risk were calculated using a Z-test on the coefficient of the relevant indicator variable.

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Ethical approval

The kConFab study is approved by the Peter MacCallum Cancer Centre Human.

Research Ethics Committee. All participants provided written informed consent.

Declaration of competing interest

All authors report no potential conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.breast.2021.08.013.

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