Breast Cancer Chemoprevention: Use and Views of Australian Women and Their Clinicians

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ABSTRACT

Guidelines endorse the use of chemoprevention for breast cancer risk reduction. This study examined the barriers and facilitators to chemoprevention use for Australian women at increased risk of breast cancer, and their clinicians. Surveys, based on the Theoretical Domains Framework, were mailed to 1,113 women at ≥16% lifetime risk of breast cancer who were enrolled in the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer cohort study (kConFab), and their 524 treating clinicians. Seven hundred twenty-five women (65%) and 221 (42%) clinicians responded. Only 10 (1.4%) kConFab women had ever taken chemoprevention. Three hundred seventy-eight (52%) kConFab women, two (3%) breast surgeons, and 51 (35%) family physicians were not aware of chemoprevention. For women, the strongest barriers to chemoprevention were side effects (31%) and inadequate information (23%), which operate in the Theoretical Domains Framework domains of "beliefs about consequences" and "knowledge," respectively. Strongest facilitators related to tamoxifen's long-term efficacy (35%, "knowledge," "beliefs about consequences," and "goals" domains), staying healthy for family (13%, "social role" and "goals" domains), and abnormal breast biopsy (13%, "environmental context" domain). The strongest barrier for family physicians was insufficient knowledge (45%, "knowledge" domain) and for breast surgeons was medication side effects (40%, "beliefs about consequences" domain). The strongest facilitators for both clinician groups related to clear guidelines, strong family history, and better tools to select patients ("environmental context and resources" domain). Clinician knowledge and resources, and beliefs about the side-effect consequences of chemoprevention, are key domains that could be targeted to potentially enhance uptake.

Prevention Relevance: Despite its efficacy in reducing breast cancer incidence, chemoprevention is underutilised. This survey study of Australian women and their clinicians used behavioural change theory to identify modifiable barriers to chemoprevention uptake, and to suggest interventions such as policy change, educational resources and public campaigns, that may increase awareness and use.

See related Spotlight by Vogel, p. 1

Introduction

Although breast cancer mortality has improved, incidence continues to rise, presenting a major burden for health services worldwide (1). Better implementation of evidence-based breast cancer prevention interventions, such as chemoprevention (also known as risk-reducing medication) in women at increased risk, could reduce this burden (2).

Selective estrogen receptor modulators (tamoxifen and raloxifene) and aromatase inhibitors (anastrozole and exemestane),

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taken daily for 5 years, reduce breast cancer risk by one-third to one-half in women at increased risk (3–8). For tamoxifen and anastrozole, the preventive benefit continues for at least 15 and 5 years, respectively, after completion (9, 10). Low-dose tamoxifen for only 3 years may also be an efficacious, low side-effect option for women who do not tolerate the standard 20-mg daily dose, although long-term efficacy for this shorter duration, lower dose regimen is unknown (11, 12).

Guidelines recommend consideration of risk-reducing medication for women at elevated breast cancer risk (12–15). Despite this, risk-reducing medication is underutilized. A meta-analysis, including data from 21,423 women, reported a pooled risk-reducing medication uptake estimate of 16% (16), although in individual studies, uptake ranged from 0% to 55%. Uptake was higher in trial (25%) compared with non-trial (8.7%) settings, suggesting it may be more difficult for clinicians to implement risk-reducing medication within routine practice.

Reasons for low use of risk-reducing medication are multifactorial, including patient- and physician-related factors. Concern about side effects is a well-described barrier to use (17–23). Physician recommendation, family history of breast cancer, abnormal breast biopsy, higher perceived breast cancer risk, and higher cancer-specific anxiety are associated with risk-reducing medication use (21, 24).

Tamoxifen became government subsidized for primary breast cancer prevention in Australia in 2016, but national guidelines have recommended doctors consider it for women with a lifetime risk of breast cancer at least 1.5 times population risk (i.e., ≥ 16%) since 2010 (https://www.canceraustralia.gov.au/publications-and-resources/cancer-australia-publications/advice-about-familial-aspects-breast-cancer-and-epithelial-ovarian-cancer). This study aimed to determine the past or current use of risk-reducing medication by Australian women at increased risk of breast cancer and to examine barriers and facilitators to the use of risk-reducing medication.

Materials and Methods

Setting

Participants were women (and their clinicians) from multiple-case breast cancer families recruited to the Kathleen Cuningham Foundation Consortium for Research into Familial Breast Cancer cohort (kConFab) between 1997 and 2008 (https://www.kconfab.org/). Multiple-case breast cancer families were defined as families where a *BRCA1* or *BRCA2* mutation, or a mutation in another breast cancer susceptibility gene, had been identified, or families where no predisposing mutation had been identified but two or more family members on the same side of the family were affected by breast cancer. The proband was recruited after a clinic consultation in any of 15 Australian genetics clinics. Other family members were not required to attend a genetics clinic to enroll. kConFab women were mailed follow-up questionnaires every 3 years (25) asking questions regarding doctors involved in their care, use of risk-reducing medication, educational level, parity, pregnancy, breastfeeding, marital status, family history, participation in clinical trials of risk-reducing medication, and details of any bilateral mastectomy or cancer diagnoses. In addition to follow-up questionnaires, all kConFab women eligible for the study reported here were sent a survey on risk-reducing medication in late 2018 (see surveys of kConFab women section below). This study was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent and the kConFab cohort study has Human Research Ethics Committee approval at all participating sites, and this survey study has Human Research Ethics Committee approval at the Peter MacCallum Cancer Centre.

Surveys of kConFab women and clinicians

Understanding the behavioral determinants of use of risk-reducing medication for both clinicians and patients is the first step in implementing practice change to increase use of risk-reducing medication. We used the Theoretical Domains Framework (26) to guide the development of survey questions. The Theoretical Domains Framework was developed to identify the cognitive, affective, social, and environmental influences on health professional and patient behavior related to implementation of evidence-based recommendations. It consists of 84 theoretical constructs grouped into 14 domains and maps directly to the COM-B (capability, opportunity, motivation, behavior) behavioral change model (27), to suggest intervention functions and relevant policy categories to guide pathways to behavioral change.

kConFab women

A 68-item survey (Supplementary data 1) was developed based on a literature review and semi-structured interviews with 62 kConFab women from different geographical locations, socioeconomic status, and ethnicities to identify barriers and facilitators to using risk-reducing medication. Survey questions, based on the Theoretical Domains Framework (**Tables 1** and **2**), were developed by the research team, including experts in health sociology, qualitative research, breast surgery, and primary care. The survey was piloted for usability with nine kConFab women in face-to-face cognitive interviews and refined. kConFab women were eligible if, at the time of survey, they were aged between 25 and 70 years, resided in Australia, and had a BOADICEA (28) lifetime breast cancer risk of ≥16% but had not had bilateral mastectomy, previous breast cancer ever, or other invasive cancer in the previous 6 years. Women who had participated in the IBIS prevention trials (3, 6) or the survey pilot study were also excluded. The survey was mailed or emailed, and non-responders were followed up three times.

Clinicians

In Australia, family physicians and breast surgeons primarily undertake breast cancer prevention. Medical oncologists do not have a primary role in discussion of risk-reducing medication. A literature review and focus group interviews were undertaken with family physicians and breast surgeons to inform survey development (29, 30). The 49-item clinician survey (Supplementary Data 2) was developed using the Theoretical Domains

Table 1. Barriers: relationship between survey statement, Theoretical Domains Framework domain, and COM-B source of behavior and intervention function.

TDF domain	Domain description	Statement (barrier)		COM-B source of behavior	Intervention function
		kConFab women	Clinicians		
Social/professional role and identity	A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting	Not applicable	It is not my role to discuss RRM		
Goals	Mental representations of outcomes or end states that an individual wants to achieve	I have another medical condition that outweighs my BC concerns	There are other things I wish to achieve in most consultations that interfere with my ability to discuss RRMs		Education
Beliefs about capabilities	Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use	I have trouble remembering to take a daily tablet	Patients don't ask me about RRMs I am not confident in providing advice/ information to pts about RRMs I have inadequate training and confidence in BC risk assessment I have difficultly explaining to pts the pros and cons of RRMs	Reflective motivation	Persuasion Incentivization Coercion
Optimism	The confidence that things will happen for the best or that desired goals will be attained	I'm too old to bother trying to prevent BC If cancer is going to happen it will happen, I do not believe you can change your own risk I don't believe RRMs would reduce my risk of BC at all I don't believe RRMs would reduce my risk of BC enough to make it worthwhile	Not applicable		
Beliefs about consequences	Acceptance of the truth, reality, or validity about outcomes of a behavior in a given situation	I am concerned about drug interactions I am worried my family/friends would assume I have been diagnosed with BC or may ask questions about our family history I wouldn't know whether RRMs were actually working My risk of BC is not high enough to justify taking RRMs Possible side effects I've seen family/friends experience side effects when taking medicines like this, so I am likely to experience the same If cancer is going to happen it will happen, I do not believe you can change your own risk I don't believe RRMs would reduce my risk of BC at all I don't believe RRMs would reduce my risk of BC enough to make it worthwhile	There is no evidence that they reduce mortality Medication side effects I don't believe they decrease the risk of BC I'm concerned I might increase the patient's worry about BC		

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Table 1. Barriers: relationship between survey statement, Theoretical Domains Framework domain, and COM-B source of behavior and intervention function. (Cont'd)

TDF domain	Domain description	Statement (barrier)		COM-B source of behavior	Intervention function
		kConFab women	Clinicians		
Intentions	A conscious decision to perform a behavior or a resolve to act in a certain way	I prefer healthy lifestyle choices alone to medications I don't believe in taking medicines for prevention, only for illness RRMs are unnatural	I don't routinely assess BC risk with my pts		
Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	Not applicable	There are no incentives/rewards for discussing RRMs with pts		Persuasion
Emotion	A complex reaction pattern, involving experiential, behavioral, and physiologic elements, by which the individual attempts to deal with a personally significant matter or event	It would be a reminder of family members or friends cancer experiences	I feel uncomfortable prescribing a "cancer drug" to healthy women	Automatic motivation	Incentivization Coercion Environmental restructuring
		Taking a daily tablet for 5 years would be a daily reminder of my cancer risk	I'm concerned I might increase the pt's worry about BC		Modeling Enablement
Memory, attention, and decision processes	The ability to retain information, focus selectively on aspects of the environment, and choose between two or more alternatives	I would prefer to have both breasts removed rather than take the medication I would prefer BC screening (e.g., mammograms) alone, rather than screening and taking RRMs	I forget to discuss RRMs with pts		Education
		I have trouble remembering to take a daily tablet		Psychological capability	Training Enablement
Knowledge	An awareness of the existence of something	I don't know what my BC risk is I don't know how much they cost I think of these as medicines to treat BC, not prevent it I don't have enough information about RRMs to make an informed decision	I have insufficient knowledge of RRMs		
Behavioral regulation	Anything aimed at managing or changing objectively observed or measured actions	My doctor doesn't talk to me enough about RRMs	There are no procedures (e.g., a checklist that facilitates discussion) that encourage me to discuss RRMs		
Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior	I am already taking too many medications	It is difficult to measure whether the medication is working	Physical opportunity	Restriction
		The inconvenience of taking a daily tablet	I find it hard to access tools/resources to help me estimate patients BC risk		Environmental restructuring
		Taking them would mean I couldn't take the OCP	I find it hard to access good information/ resources for my pts, e.g., pt information sheets		Enablement
		Taking them would mean I would have to delay becoming pregnant	Lack of time during consultations		

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Table 1. Barriers: relationship between survey statement, Theoretical Domains Framework domain, and COM-B source of behavior and intervention function. (Cont'd)

TDF domain	Domain description	Statement (barrier)		COM-B source of behavior	Intervention function
		kConFab women	Clinicians		
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors	If family/friends did not think taking RRM was a good idea	I don't think pts want to discuss taking medications for prevention of BC	Social opportunity	Restriction Environmental restructuring Enablement
Skills	An ability or proficiency acquired through practice	Not applicable	I have difficulty identifying pts suitable for RRM I have inadequate training and confidence in BC risk assessment I have difficulty explaining to pts the pros and cons of RRMs	Physical capability	Training Enablement

Abbreviations: BC, breast cancer; COM-B system, capability, opportunity and motivation behavior system; TDF, Theoretical Domains Framework; OCP, oral contraceptive pill; RRM, risk reducing medication.

Framework (**Tables 1** and **2**). Eligible clinicians were family physicians or breast surgeons involved in the care of kConFab women and practicing in Australia with a valid address. Non-responders to the mailed questionnaire were followed up.

The survey responses for both clinicians and kConFab women were analyzed using descriptive statistics (numbers and percentages) in R-version 3.6.1 (R Core Team (2015; ref. 31).

Results

Survey of kConFab women

Demographics

Of the 5,231 women unaffected with breast cancer when enrolled in kConFab between 1997 and 2008, 1,097 declined follow-up, 332 died during follow-up, and 2,689 were excluded based on their characteristics at the time of survey (previous breast cancer (1,045), not aged between 25 to 70 years (499), not residing in Australia or invalid address (294), participation in pilot study (9), invasive cancer in last 6 years (61), bilateral mastectomy (191), <16% lifetime breast cancer risk (537), or participation in IBIS trials (53)). Of 1,113 eligible women, 725 (65%) responded to the survey. **Table 3** describes responder characteristics. A minority (7%) were *BRCA1* or *BRCA2* mutation carriers. Only 16% had a high lifetime breast cancer risk (≥ 30%) but 30% of respondents had high perceived breast cancer risk.

Risk-reducing medication awareness, use, and side-effect concerns

Approximately half (48%) of respondents were aware of medications to reduce breast cancer risk. Few (1.4%) had ever taken risk-reducing medication (**Table 3**).

kConFab women were asked to rank side effects of risk-reducing medication from most to least important to them. The side effects most frequently ranked as most important were endometrial cancer (45%) and blood clots (36%; **Fig. 1**). Of the 322 women who ranked endometrial cancer as most important, 201 (62%) were under age 50 years. Only 21 (3%) women ranked vasomotor symptoms as most important.

Barriers to and facilitators of use of risk-reducing medication

kConFab women ($n = 715$) who had not taken risk-reducing medication were asked to identify the strongest of 29 possible barriers to taking it (Supplementary Data 3) and to rate the strength of each barrier (**Fig. 2**). The barriers most frequently identified as the strongest were side effects (31%) and side-effect experiences of family or friends when taking similar medications (4%; both map to the "beliefs about consequences" in the Theoretical Domains Framework), as well as inadequate information to make a decision (23%, Theoretical Domains Framework "knowledge" domain) and preferring healthy lifestyle choices to medication (6%, Theoretical Domains Framework "intentions" domain).

The information ranked most important by women before deciding whether to take risk-reducing medication

Table 2. Facilitators: relationship between survey statement, TDF domain, and COM-B source of behavior, and intervention function.

TDF domain	Domain description	Statement (facilitator)		COM-B source of behavior	Intervention function
		kConFab women	Clinicians		
Social/professional role and identity	A coherent set of behaviors and displayed personal qualities of an individual in a social or work setting	If I thought RRMs would improve the chance I will stay healthy for my family	If it were endorsed as part of my professional role by the relevant college or other peak body		
Goals	Mental representations of outcomes or end states that an individual wants to achieve	Taking RRMs can reduce BC risk for up to 20 years If I thought RRMs would improve the chance I will stay healthy for my family	The beneficial effects of RRMs, e.g., better blood lipid profile and improvements in bone density with tamoxifen		Education Persuasion
Beliefs about capabilities	Acceptance of the truth, reality or validity about an ability, talent or facility that a person can put to constructive use	Not applicable	Not applicable	Reflective motivation	Incentivization Coercion
Optimism	The confidence that things will happen for the best or that desired goals will be attained	Not applicable	I expect positive outcomes for women who take RRMs		
Beliefs about consequences	Acceptance of the truth, reality, or validity about outcomes of a behavior in a given situation	Taking RRMs can reduce BC risk for up to 20 years	I expect positive outcomes for women who take RRMS		
Intentions	A conscious decision to perform a behavior or a resolve to act in a certain way	Not applicable	Not applicable		
Reinforcement	Increasing the probability of a response by arranging a dependent relationship, or contingency, between the response and a given stimulus	If family/friends were supportive of me taking RRMs	Not applicable		Persuasion
Emotion	A complex reaction pattern, involving experiential, behavioral, and physiologic elements, by which the individual attempts to deal with a personally significant matter or event	Because they would reduce my stress and worry about BC	Sometimes it is easier to discuss RRMs than bilateral mastectomy	Automatic motivation	Incentivization Coercion Environmental restructuring Modeling Enablement
Memory, attention, and decision processes	The ability to retain information, focus selectively on aspects of the environment, and choose between two or more alternatives	Taking a daily tablet to reduce my BC risk would make me feel more in control of my health	If my medical software prompted me to discuss RRMs		
Knowledge	An awareness of the existence of something	Taking RRMs can reduce BC risk for up to 20 years Knowing RRMs can be taken prior to risk-reducing surgery Knowing I have high breast cancer risk Once I stop taking RRMs any side-effects will diminish	Knowing some RRMs are PBS funded	Psychological capability	Education Training Enablement

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Table 2. Facilitators: relationship between survey statement, TDF domain, and COM-B source of behavior, and intervention function. (Cont'd)

TDF domain	Domain description	Statement (facilitator)		COM-B source of behavior	Intervention function
		kConFab women	Clinicians		
Behavioral regulation	Anything aimed at managing or changing objectively observed or measured actions	Taking a daily tablet to reduce my BC would reassure me			
Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behavior	Having an abnormal biopsy that increased my risk of developing BC Knowing that some of these medicines help prevent or treat osteoporosis Knowing some of these medicines reduce cholesterol levels Having a family history of BC	If the patient is diagnosed with atypical hyperplasia that increases their risk of BC If the patient is diagnosed with LCIS that increases their risk of BC If a patient has a strong family history of BC If I had better tools to help me identify patients who were suitable Clear guidelines/recommendations e.g., RACGP and Cancer Australia guidelines Support from specialists Support from peers	Physical opportunity	Restriction Environmental restructuring Enablement
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviors	If my family/friends recommended taking RRMs If my doctor recommend taking RRMs	If I knew my colleagues discuss it with their pts	Social opportunity	Restriction Environmental restructuring Enablement
Skills	An ability or proficiency acquired through practice	Not applicable	Not applicable	Physical capability	Training Enablement

Abbreviations: BC, breast cancer; COM-B system, capability, opportunity, and motivation behavior system; LCIS, lobular carcinoma *in situ*; pts, patients; RACGP, Royal Australian College of General Practitioners; RRM, risk-reducing medication; TDF, Theoretical Domains Framework.

Table 3. Characteristics of survey respondents.

Characteristic	kConFab women *n* (%)	Family physicians *n* (%)	Breast surgeons *n* (%)
Age[a]			
18–29	1 (0)	0	0
30–39	83 (12)	5 (3)	1 (1)
40–49	186 (26)	21 (14)	21 (28)
50–59	235 (32)	66 (45)	30 (41)
60+	220 (30)	55 (38)	21 (28)
Not disclosed	0	0	1 (1)
Gender			
Female	725 (100)	99 (67)	30 (41)
Male	0	48 (33)	43 (58)
Not disclosed	0	0	1 (1)
BRCA mutation status[a]			
BRCA1	21 (3)	n/a	n/a
BRCA2	27 (4)	n/a	n/a
No known mutation	677 (93)	n/a	n/a
Number of first- and second-degree relatives with breast cancer			
0	128 (17)	n/a	n/a
1	280 (39)	n/a	n/a
2	216 (30)	n/a	n/a
≥ 3	101 (14)	n/a	n/a
BOADICEA lifetime risk[a]			
16 – 29%	608 (84)	n/a	n/a
≥ 30%	117 (16)	n/a	n/a
Perceived breast cancer risk[b]			
Low	10 (1)	n/a	n/a
Average	173 (24)	n/a	n/a
Moderately increased	302 (42)	n/a	n/a
High	219 (30)	n/a	n/a
Don't know	21 (3)	n/a	n/a
Marital status[a]			
Married/living as married	547 (75)	n/a	n/a
Other	178 (25)	n/a	n/a
Parity[a]			
0	127 (18)	n/a	n/a
1	190 (26)	n/a	n/a
2+	408 (56)	n/a	n/a
Educational status[a]			
Tertiary	328 (45)	n/a	n/a
Less than tertiary	397 (55)	n/a	n/a
Annual screening[c]			
Yes	418 (58)	n/a	n/a
No	198 (27)	n/a	n/a
Unknown	11 (2)	n/a	n/a
Not applicable	98 (13)	n/a	n/a
Awareness of risk-reducing medication			
Yes	347 (48)	96 (65)	72 (97)
No	378 (52)	51 (35)	2 (3)
Source of information[d]			
Family/friends	223 (64)	n/a	n/a
Cancer genetics clinic	70 (20)	n/a	n/a
Family physician	52 (15)	n/a	n/a
Breast surgeon	46 (13)	n/a	n/a
Other	46 (13)	n/a	n/a
TV	43 (12)	n/a	n/a
Internet	37 (11)	n/a	n/a
Magazines	26 (7)	n/a	n/a
Radio	13 (4)	n/a	n/a
Gynecologist	10 (3)	n/a	n/a
Risk-reducing medication use			
Yes	10 (1)	n/a	n/a
No	715 (99)	n/a	n/a

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Table 3. Characteristics of survey respondents. (Cont'd)

[a]At the time of survey.
[b]Response options were: "Low—lower than most other women," "Average—about the same as most other women," "Moderately increased—about 2 or 3 times that of most other women," "High—more than 3 times that of most other women."
[c]Annual screening with mammogram, magnetic resonance imaging, or both reported in the 9 years prior to being sent the risk-reducing medication survey. Not applicable for 98 women as they were at moderate risk of breast cancer and under the age of 40 at the time of the survey ($n = 98$).
[d]Multiple responses allowed.
n/a: not asked.

pertained to side effects (33%) and extent of breast cancer risk reduction (31%).

Respondents also identified the strongest of 16 facilitators for taking risk-reducing medication (Supplementary Data 3) and rated the strength of each facilitator (**Fig. 2**). The strongest facilitator was that taking risk-reducing medication can reduce breast cancer risk for up to 20 years (35%, Theoretical Domains Framework "knowledge", "beliefs about consequences", and "goals" domains). Additional strong facilitators were knowledge of being at high risk of breast cancer (11%, Theoretical Domains Framework "knowledge" domain), if risk-reducing medications would improve the chance of staying healthy for family (13%, Theoretical Domains Framework "social role/identity" and "goals" domains), and having an abnormal biopsy that increases breast cancer risk (13%, Theoretical Domains Framework "environmental context and resources" domain). Doctor's recommendation was the strongest facilitator for 10% of women, but family or friend recommendation only for 1%. Cholesterol reduction (with tamoxifen) and reduced osteoporosis (with tamoxifen or raloxifene in postmenopausal women) were infrequently identified as the strongest facilitators (1% and 4%, respectively) but most women did identify them as facilitators (55% and 79%, respectively).

Clinician survey

Demographics

Of 554 breast surgeons and family physicians identified by women as involved in their care, 30 were excluded (13 not currently practicing and 17 invalid address). Of 524 eligible clinicians (394 family physicians and 130 breast surgeons) mailed the survey, 221 (42%) responded (57% of breast surgeons and 37% of family physicians). Clinician characteristics are shown in **Table 3**.

Risk-reducing medication awareness, confidence, and roles

Most (76%) clinicians had heard of risk-reducing medication (97% of breast surgeons and 65% of family physicians). Few (3%) family physicians were "very confident" in providing

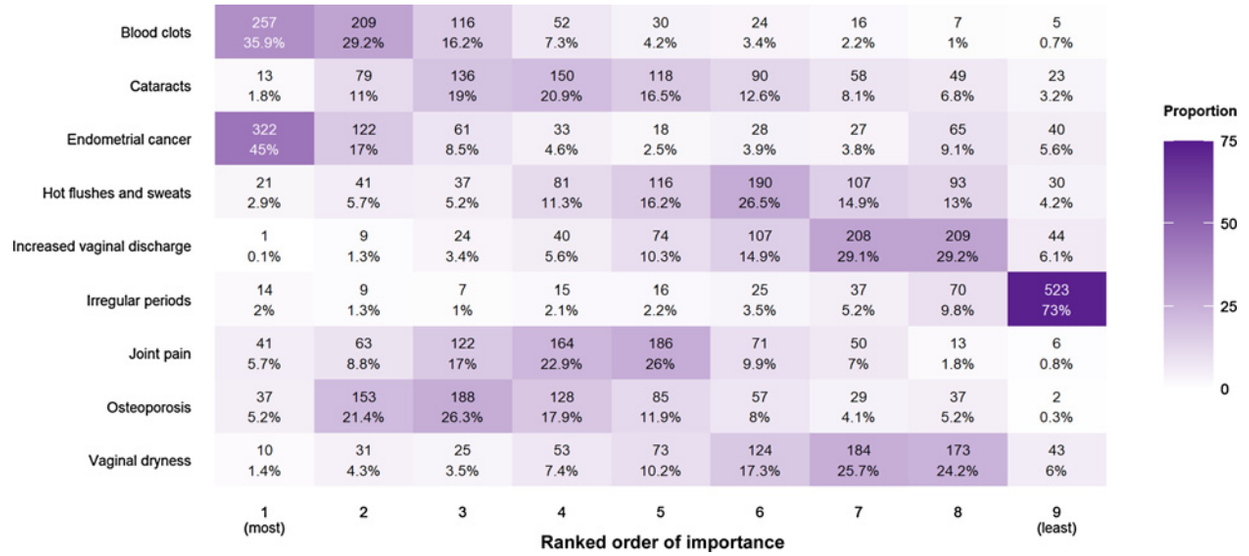

Figure 1.

Heat map of the importance of potential risk-reducing medication side effects as ranked by kConFab women ($n = 716$). Women were asked to rank each potential side effect from most (1) to least (9) important to them when considering taking risk-reducing medication. Numbers and proportions of women who endorsed each level of ranking for each side effect are indicated. Proportions are also indicated by shading, with darker shading representing higher proportions of women endorsing that ranking compared with lighter shading. Data are missing for 9 women who did not answer this question.

information about risk-reducing medication, compared with 56% of breast surgeons. Many family physicians (32%) were "not at all confident" compared with 1% of breast surgeons. Approximately one third (29%) of family physicians had never discussed or prescribed cancer risk-reducing medication, although most (75%) responded it was their role to initiate such discussions and 98% that it was their role to write ongoing prescriptions. Only three (4%) surgeons had never discussed or prescribed risk-reducing medications. Most surgeons perceived their role as initiating discussion and writing first prescriptions (89% and 81%, respectively). Almost half of breast surgeons (47%) but only 10% of family physicians had heard of the iPrevent tool, an Australian tool for women and clinicians to assess and manage breast cancer risk (https://www.canceraustralia.gov.au/affected-cancer/check-your-cancer-risk-online; refs. 32, 33).

Clinician barriers to and facilitators of discussing or prescribing risk-reducing medication

Clinicians who had heard of risk-reducing medication (168) were asked to identify the strongest of 22 barriers to discussing or prescribing risk-reducing medication (Supplementary Data 4) and to rate the strength of individual barriers (**Fig. 3**). The strongest barriers for family physicians were insufficient knowledge (45%, Theoretical Domains Framework "knowledge" domain), lack of confidence in providing advice about risk-reducing medications, and inadequate training and confidence in breast cancer risk assessment (9% and 6%, respectively, Theoretical Domains Framework "beliefs about capabilities" and "skills" domains), medication side effects (7%, Theoretical Domains Framework "beliefs about consequences" domain), difficulty identifying suitable patients (7%, Theoretical Domains Framework "skills" domain), and wanting to achieve other things during a consultation (6%, Theoretical Domains Framework "goals" domain). For breast surgeons, the strongest barriers were medication side effects (40%, Theoretical Domains Framework "beliefs about consequences" domain) and lack of time during a consultation (14%), lack of surrogate markers of medication efficacy (7%), difficulty accessing good patient information (7%), and difficulty finding resources to estimate a patients risk (5%), all operating within the "environmental context and resources" domain of the Theoretical Domains Framework.

Of 14 facilitators, the strongest for family physicians was clear guidelines and recommendations (50%), better tools to identify suitable patients (12%), strong family history of breast cancer (10%), and specialist support (9%), all of which operate within the "environmental context and resources" domain of the Theoretical Domains Framework. For surgeons the strongest facilitators were strong family history (28%), clear guidelines and recommendations (22%), and patients with lobular carcinoma *in situ* (20%), all of which operate in the "environmental context and resources" domain of the Theoretical Domains Framework, as well as expecting positive outcomes for women who take risk-reducing medications (11%, "optimism" and "beliefs about consequences" domains).

Discussion

This Australia-wide study of women at increased risk of breast cancer, and their clinicians, demonstrates very low use of risk-reducing medication (1.4%) by international

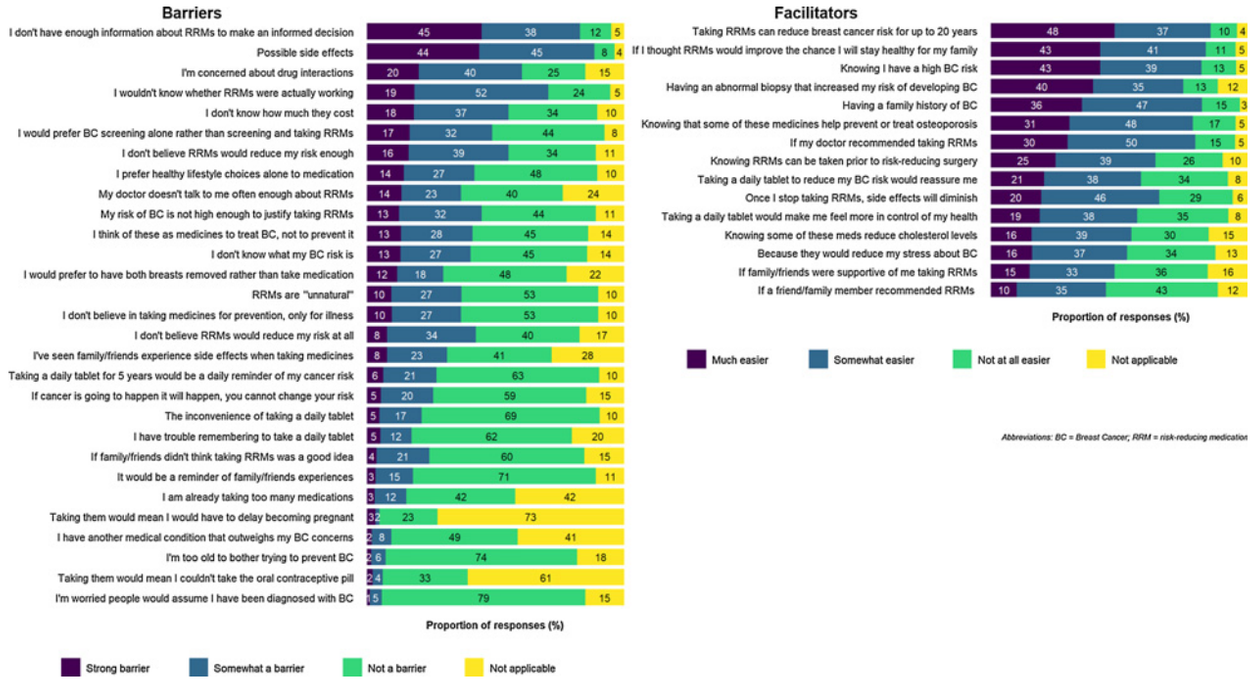

Figure 2.

Strength of individual barriers and facilitators to risk-reducing medication for kConFab women (n = 715). Charts show the percentage of kConFab women who identified each barrier or facilitator to risk-reducing medication use as strong, somewhat, not a barrier/facilitator and not applicable. RRM, risk-reducing medication; BC, breast cancer.

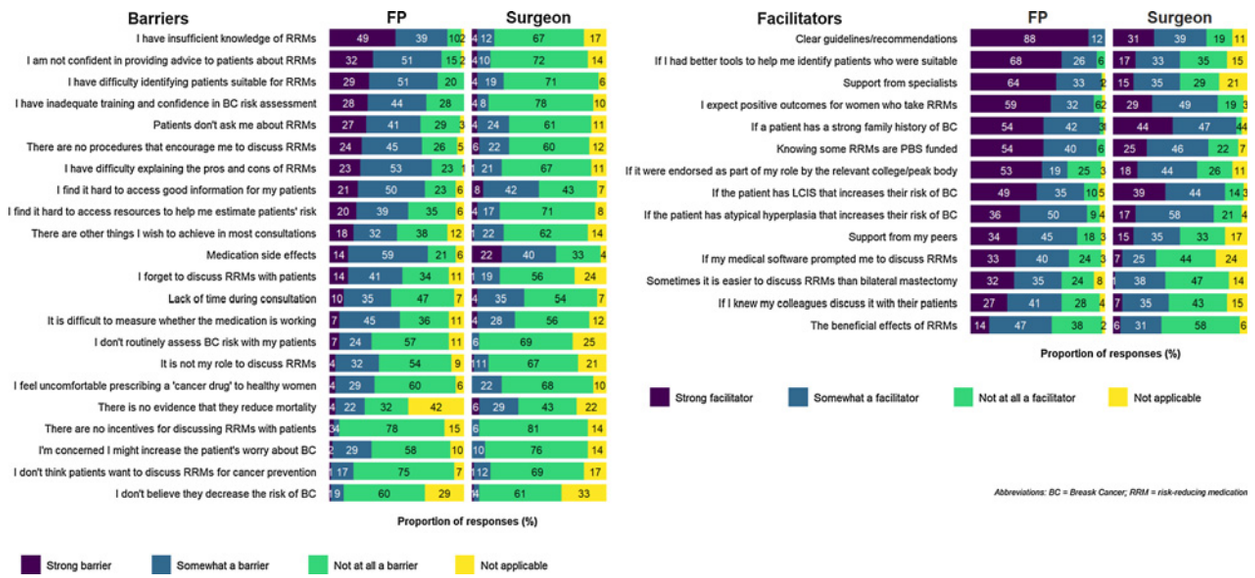

Figure 3.

Strength of individual barriers and facilitators to risk-reducing medication for family physicians (n = 96) and breast surgeons (n = 72). Charts show the percentage of clinicians who identified each barrier or facilitator to risk-reducing medication use as strong, somewhat, not a barrier/facilitator and not applicable. BC, breast cancer; RRM, risk-reducing medication.

standards (16). Women in our study may have had greater exposure to information about risk-reducing medication due to their involvement in kConFab, so use of this efficacious prevention intervention could be lower still in other Australian women at increased risk of breast cancer. This study is unique in assessing the views of both women and their clinicians regarding risk-reducing medication. The response rate was high compared with some other survey studies (20); however, the views of nonresponders may differ from those reported here. Regardless, this study has identified several important factors that influence the use of risk-reducing medication, and the behavioral domains in which they operate.

Deficiencies in the "knowledge" domain for both clinicians and women were a prominent barrier to risk-reducing medication use. Unexpectedly, 25% of women in this study perceived their breast cancer risk as low (1%) or average (24%), and this important subset of our study sample is unlikely to have considered use of risk-reducing medication. The reasons for their inappropriately low risk perception are unclear and require further research. Consistent with other studies (34), half of kConFab women and a third of their family physicians had never heard of risk-reducing medication, thus expecting those clinicians to prescribe risk-reducing medication, and women to ask for them, is unrealistic. The potential reasons why a large number of women were unaware of risk-reducing medication was not addressed by this study but would be important to address in future research. Only half of breast surgeons felt very confident in providing information on risk-reducing medications. A clear framework is required in order to improve knowledge, and consequently uptake, of risk-reducing medication. Application of the COM-B behavior change wheel (27) suggests that interventions focused on education, training, and enablement (**Table 1**) may be effective. Risk-reducing medications are all off patent; thus, no commercial incentive exists for pharmaceutical companies to educate clinicians or women about these older generic prevention medicines. In Australia, peak bodies, policymakers, and consumer organizations such as The Royal Australian College of General Practitioners, Cancer Australia, Breast Cancer Network Australia, and BreastSurgANZ could take on this role.

Breast cancer risk assessment is encouraged in Australian primary care guidelines (35). Family physicians identified barriers and facilitators within the domains of "environmental context and resources" (difficulty selecting suitable patients and need for better tools to identify suitable patients) and "skills" (inadequate confidence in breast cancer risk assessment). This is consistent with previous research demonstrating that family physicians lack confidence in personalized medicine, knowledge of risk, and risk perception (36). These findings point to environmental restructuring interventions, such as development of national guidelines mandating routine breast cancer risk assessment, and incorporating prompts into family physician software to assess breast cancer risk and to discuss risk-reducing medication if criteria are met (which has been shown to be effective in other health promotion settings (37)). They also point to the importance of training to impart skills to clinicians in breast cancer risk assessment. Active education strategies such as workshops focusing on assessment and discussion of breast cancer risk and appropriate risk-reducing strategies may improve family physician confidence in discussing risk-reducing medication. Tools to enhance informed decision-making about risk-reducing medication, which present the benefits and potential harms of these medications, could support discussions in primary care (38). Use of iPrevent (an Australian online breast cancer risk assessment and risk management decision support tool for women and clinicians that is endorsed by Cancer Australia; https://www.canceraustralia.gov.au/affected-cancer/check-your-cancer-risk-online) may improve breast cancer risk assessment in primary care and provide easy-to-access, personalized information on the benefits of risk-reducing medication (32, 33, 39). For women, a public campaign around knowing your breast cancer risk and available interventions may increase awareness of risk-reducing medication. Breast cancer screening programs may provide a convenient platform to roll out education about risk-reducing medication. It has been demonstrated in a large study embedded in a screening program in the Manchester area of the UK, that the majority of women want to know their breast cancer risk, and that providing personalized risk information in this setting does not cause psychological harms (40), and results in engagement in prevention programs (41). One Australian state, Western Australia, has mandated that women receive information on their mammographic density from the free breast cancer screening program (similar to several jurisdictions in the United States), but a personalized risk estimate is not provided, nor is this linked to specific prevention information or programs.

Abnormal breast biopsy was identified as a strong facilitator to clinicians to discuss or prescribe risk-reducing medication. Atypical hyperplasia and lobular carcinoma *in situ* are associated with a significant increase in breast cancer risk, and risk-reducing medication reduces risk of invasive breast cancer in these conditions (6, 11, 42). Women with atypical hyperplasia have low uptake of risk-reducing medication and often underestimate their breast cancer risk (43). Environmental restructuring with mandated routine discussion of women with atypical hyperplasia or lobular carcinoma *in situ* at multidisciplinary meetings, after their surgery or biopsy, could help prompt consideration of risk-reducing medication. Automatic prompts in clinician software may also be helpful.

Consistent with previous research, the strongest barrier to risk-reducing medication identified by women and breast surgeons was side effects (18, 22). Seeing family and friends experience side effects from similar medications was also a strong barrier. In our familial breast cancer cohort setting, these experiences are likely to have been in relatives receiving these medications for cancer treatment. Experience of side effects differs when used for breast cancer treatment compared with prevention, because side effects of endocrine therapies

are often confused with chemotherapy toxicities (22). This needs to be carefully outlined when discussing options to prevent overestimation of side effects. Fear of side effects in our study was mainly focused on endometrial cancer and venous thromboembolism. Aromatase inhibitors and raloxifene do not increase endometrial cancer risk, and tamoxifen only increases it in postmenopausal women where the risk is approximately 1 in 250 over 5 years (resolving on completion; ref. 44). Most (62%) women in our study who ranked endometrial cancer risk as most important to them were under the age 50 years, despite tamoxifen conferring no increased risk of endometrial cancer in premenopausal women; this emphasizes the importance of personalized discussions and education to address these misconceptions. Aromatase inhibitors do not increase incidence of venous thromboembolism, and in women on tamoxifen or raloxifene, the absolute risk is generally small (1 in 250 over 5 years of use; ref. 44).

The nocebo effect has the potential to influence patient acceptability of treatments and compliance (45). This is supported by the IBIS prevention trials, which demonstrated similar rates of adverse reactions in both intervention and placebo groups (3, 6). For example in the IBIS II trial, 57% of those in the intervention arm and 49% in the placebo arm experienced vasomotor symptoms, suggesting that only about 1 woman in 12 will experience these symptoms due to risk-reducing medication. Online tools, such as iPrevent (32), can help clinicians provide personalized estimates of the absolute risk reduction, as well as the absolute risk of serious side effects with risk-reducing medication. Considering a short trial of therapy to assess side-effect profile, before a 5-year course, may be a useful approach (2). Low-dose tamoxifen (5 mg daily for 3 years) may be a useful alternative for women who do experience side effects on the standard dose (11). Behavioral change theory (27) also points to incentivization as a possible strategy to address barriers that operate in the Theoretical Domains Framework "beliefs about consequences" domain, as does concern about side effects of risk-reducing medication. Highlighting the potential beneficial effects of risk-reducing medication may be important. Over half of women in our study identified that reduction in cholesterol and the potential prevention of osteoporosis would make it easier to take risk-reducing medication.

It is important to note that for a small number of women we were unable to identify the barriers and facilitators to risk-reducing medication, indicating that there may be other barriers and facilitators that we did not elucidate.

Despite many lacking awareness and confidence, the majority of family physicians (75%) viewed initial discussion of risk-reducing medication as part of their role. Fewer (31%) felt that writing the first prescription was appropriate but 98% were happy to provide ongoing prescriptions. This is consistent with other studies (46) but is potentially a major hurdle, as optimal implementation of risk-reducing medication may require family physicians to prescribe the first dose.

Reducing breast cancer incidence requires a clear strategy that incorporates routine breast cancer risk assessment with implementation of evidence-based risk reduction strategies, including risk-reducing medication. We have identified a significant knowledge and resource gap for both women and clinicians. Application of a behavioral change model suggests that both an individual and a system-based approach, including interventions in education, training, incentivization, and environmental restructuring, could be instrumental in increasing uptake of risk-reducing medication.

Authors' Disclosures

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Authors' Contributions

C. Macdonald: Conceptualization, data curation, formal analysis, validation, investigation, methodology, writing–original draft, writing–review, and editing. **C.M. Saunders:** Conceptualization, supervision, investigation, visualization, writing–review, and editing. **L.A. Keogh:** Conceptualization, data curation, formal analysis, supervision, investigation, visualization, writing–review, and editing. **M. Hunter:** Data curation, software, formal analysis, investigation, and methodology. **D. Mazza:** Conceptualization, supervision, visualization, methodology, writing–review, and editing. **S.-A. McLachlan:** Conceptualization, supervision, writing–review, and editing. **S.C. Jones:** Conceptualization, supervision, writing–review, and editing. **S. Nesci:** Resources, data curation, software, funding acquisition, project administration, writing–review, and editing. **M.L. Friedlander:** Conceptualization, visualization, writing–review, and editing. **J.L. Hopper:** Conceptualization, validation, methodology, writing–review, and editing. **J.D. Emery:** Conceptualization, supervision, methodology, writing–review, and editing. **M. Hickey:** Conceptualization, visualization, writing–review, and editing. **R.L. Milne:** Conceptualization, resources, software, formal analysis, investigation, methodology, writing–review, and editing. **K.-A. Phillips:** Conceptualization, resources, data curation, formal analysis, supervision, funding acquisition, validation, investigation, visualization, project administration, writing–review, and editing.

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