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Young women's decision-making and experience of using tamoxifen to reduce *BRCA1/2* breast cancer risk: a qualitative study

Running title: Young women's decision-making about tamoxifen

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Abstract

Objective: Tamoxifen has been demonstrated to reduce breast cancer risk in high-risk, premenopausal women. Yet, very few young women with hereditary breast and ovarian cancer syndrome in Australia use tamoxifen despite this being a less invasive option compared to risk-reducing mastectomy. This study aims to examine young women's decision-making about and experience of taking tamoxifen to reduce their breast cancer risk.

Methods: Young women with a *BRCA1/2* mutation participated in semi-structured qualitative interviews, recruited mainly from a metropolitan clinical genetics service. Data were analysed using an inductive, team-based approach to thematic analysis.

Results: Forty interviews with women aged 20-40 years with a *BRCA1/2* mutation were conducted. Eleven women could not recall discussing tamoxifen with their healthcare provider or were too young to commence cancer risk management. Twenty-three women chose not to use tamoxifen because it is contraindicated for pregnancy or because it did not offer immediate and great enough risk reduction compared to bilateral risk-reducing mastectomy. Six women who were definite about not wanting to have children during the following five-year period chose to use tamoxifen, and most experienced none or transient side effects.

Conclusions: Decision-making about tamoxifen was nuanced and informed by considerations characteristic of young adulthood, especially childbearing. Therefore, clinical discussions about tamoxifen with young women with a *BRCA1/2* mutation must include consideration of their reproductive plans.

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Introduction

Women who have inherited a *BRCA1* or *BRCA2* mutation (*BRCA1/2* mutation) have a 69-72% lifetime risk of breast cancer and 17-44% lifetime risk of ovarian cancer.[1] This risk of breast cancer can be managed with breast screening or reduced using medication or surgery.[2,3] For premenopausal women with a *BRCA1/2* mutation, tamoxifen taken daily and continuously for five years has been demonstrated to reduce ER-positive breast cancer risk by 44% over 10 years,[4] with ER-positive breast cancer accounting for 19% and 84% of diagnoses in premenopausal women with a *BRCA1* or *BRCA2* mutation, respectively.[5] In contrast, the surgical option of bilateral prophylactic mastectomy offers a more substantial risk reduction of 90-95%,[2] but can require multiple surgeries if reconstruction is chosen and social and psychological implications are commonly experienced.[6,7] While tamoxifen has been offered to high-risk women in Australia for longer than two decades (see Box 1) and offers a less invasive method of risk reduction than breast surgery, very few high-risk women choose tamoxifen to reduce their risk of breast cancer.[8,9]

Unaffected women with a *BRCA1/2* mutation are recommended to commence these cancer risk management and/or reduction strategies during their young adulthood.[10,11] This formative life stage, characterised by identity exploration, formation of life-long relationships, childbearing and rearing, and career development,[10,11] has been shown to be significantly impacted by increased breast cancer risks and risk management choices.[12-14] Each of these choices impacts experiences that characterise young womanhood. Choosing bilateral prophylactic mastectomy means breastfeeding is not an option for any future children. In contrast, tamoxifen is a teratogen and therefore incompatible with pregnancy and it also reduces the efficacy of hormonal forms of contraception.[15]

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The low uptake of tamoxifen, and chemoprevention in general, by high-risk women has created cause for consternation, internationally.[16-18] Research has established that physicians in the US, UK, and Australia experience barriers to prescribing tamoxifen to high-risk women, including lack of awareness or education about risk management, lack of time, and concerns about efficacy or affordability.[19-24] Multiple systematic reviews have demonstrated that chemoprevention uptake (16.3% [95% CI 13.6-19.0] overall) and adherence by high-risk women is significantly lower in clinical settings compared to trials.[25-27] Further, concern that even when offered, women may not be making an informed decision about tamoxifen has resulted in the development of decision-aids.[28-30]

Research to date of women's experiences and decision-making about tamoxifen is largely drawn from populations of women at increased risk of breast cancer defined by risk prediction models and who are premenopausal but generally past childbearing age.[31] Younger women with a *BRCA1/2* mutation are notably absent, resulting in a critical shortfall in empirical evidence describing their decision-making and experience of using tamoxifen.[18] There is a growing population of women accessing predictive genetic testing from at least 18 years of age, if not in their early 20's, for a known familial *BRCA1/2* mutation. Those who test positive are often offered tamoxifen once they commence cancer risk management and so understanding their experiences of this offer, their decision-making, and experience of taking tamoxifen will offer insight into why this medication is so rarely chosen to reduce breast cancer risk.[18] Therefore, this study aims to examine the decision-making and experience of young women with a *BRCA1/2* mutation of using tamoxifen as a risk reducing medication.

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Methods

This study was approved by the Peter MacCallum Cancer Centre Human Research Ethics Committee (protocol 14/91_L, 14th July 2014). This study was conducted in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

Research design

A qualitative approach using semi-structured interviews was used to collect data. Australian women were invited to participate if they were a) aged 18-40 years; and b) diagnosed with a *BRCA1/2* mutation at least 12 months prior to recruitment. Women were excluded if they had a prior diagnosis of cancer; not fluent in English; or diagnosed with a psychiatric disorder. Purposive recruitment was conducted using the Familial Cancer Centre clinical database at the Peter MacCallum Cancer Centre and followed a stratified sampling strategy to ensure an even spread across four age categories (18-25 years; 26-30 years; 31-35 years; and 36-40 years) to systematically capture the experience of living with a *BRCA1/2* mutation across young adulthood from 18-40 years. Ninety-three potential participants were mailed an invitation letter and interviews were organized with those who expressed interest. The National Breast Cancer Foundation also disseminated information about the study to their membership and some participants disseminated information about the study to their support groups hosted on social media platforms.

Data collection

Interviews were conducted by the first author either in-person or via telephone depending on participants' location and preference. The interviews were facilitated using an interview guide designed to explore cancer risk perception; use and experience of risk management

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strategies; impact of carrier status and risk management strategies on intimate relationships, reproductive decision-making, and childbearing and rearing; family communication; and experiences of support and unmet support needs. This paper reports on the decision-making and experience of using tamoxifen as risk management. Interviews were audio-recorded with informed consent, transcribed verbatim and de-identified with participant-assigned pseudonyms. Transcripts were uploaded into NVivo 11 (QSR International) for data management and analysis.

Data analysis

Thematic analysis was undertaken using an iterative process where transcripts were read and reread to allow constant comparison within and between transcripts.[32] Transcripts were inductively coded for ideas, categories and concepts, which were then grouped into themes.[33] Preliminary coding was completed by LEF for all transcripts, and co-investigators coded three transcripts each (MAY, RFS, and LK) to ensure reliability of coding and to develop a coding framework. Core themes relating to risk management strategies with a sub-code specifically capturing data about the decision-making and experience of using tamoxifen were identified by the team. LEF then coded all transcripts, adapting codebook definitions until additional interviews did not modify existing or add new dimensions to codes (i.e., thematic saturation).[34]

Results

Forty interviews were conducted with women from August 2014 to September 2015 (Table 1), indicating a response rate of 43% based only on the invitation letters mailed to eligible participants from the Familial Cancer Centre clinical database. Twenty-one interviews were

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conducted in-person and 19 via telephone; interviews were on average 63 minutes in length (range 42-107 mins). At the time of the interview, five women (12%) were yet to commence any breast cancer risk management (Table 2). Of the 35 women engaged in breast cancer risk management, five (12%) were taking tamoxifen concurrently while breast screening, and a sixth woman had taken tamoxifen for six months before ceasing the medication. Six women (15%) could not recall ever being offered tamoxifen and the remainder recalled being offered tamoxifen but declined to use this medication.

Four themes were identified describing key and contextual factors that informed women's decision-making about tamoxifen, as well as, the experiences of those who had taken the medication. These themes were derived from the experiences and decision-making of the 23 (58%) women who had been offered but declined tamoxifen and the 6 (15%) who had ever used tamoxifen. The themes are 1) "Maintaining reproductive choice"; 2) "Running risks: comparing tamoxifen with breast surgery"; 3) "Too many drawbacks"; and 4) "From some to none: Experiencing a spectrum of side-effects".

Maintaining reproductive choice

Women's reproductive intentions were critical in their decision to reduce their breast cancer risk using tamoxifen. The teratogenic effects of tamoxifen posed a barrier for many women if they were considering reproduction in the following five-year period, and they were unwilling to compromise any opportunity to bear children during this fertile stage of life. Moreover, they wanted to maintain their reproductive freedom, which they interpreted to mean being able to choose to conceive at any time during the following five-year period, without having to consider the latent toxicity of tamoxifen. These women prioritised their fertility and any

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future childbearing opportunities over reducing their breast cancer risk using a medication that is incompatible with pregnancy.

> *I sort of shut it [tamoxifen] out pretty quickly because I thought, "well I don't know how that's going to go down with starting a family as well. I don't know if you can be on that and be trying to conceive." So, it was, a lot of our decisions were based around, yeah, family and trying to have babies… (Beatrix, 30 years)*

Some women who were not partnered at the time of the interview and wanted to form an intimate relationship prior to having children were equally as unwilling to take tamoxifen. These women wished to safeguard their opportunity to have children once they met their future partner without any potential intrusion or delay in conception that they perceived they might encounter if they took tamoxifen.

> *…if you want to have children you need to stop it [tamoxifen] a certain amount of time before … and I just thought, "you know what, I'm just not going to play around with that sort of thing." I'm 31 and I don't have a partner [chuckles], I need all the help I can get [laughs]. (Yasmin, 31 years)*

Other women did not have definitive plans to have children within the following five-year period and were uncertain about childbearing during this time. However, within the context of recalling their decision about tamoxifen, their uncertainty about whether they would be childbearing in the following five years lead to a cautious dismissal of using tamoxifen. As Emma (26 years) explains: "*I'm unsure what the next sort of five years holds for me in terms of family and whatnot, [so] it's [tamoxifen] probably something that I wouldn't take."* Kathryn (24 years), offered this view:

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… that's when I started thinking about, like, well I don't know when I'm going to want to have kids. I know it's not any time soon, but you know, what if that [tamoxifen] interrupts that, is there any point starting to take it and then stopping?

The few who chose to use tamoxifen to reduce their breast cancer risk were confident they did not want to have any children in the following five-year period. Some of these women described not being ready to have children, which provided a window of opportunity to use chemoprevention to reduce their breast cancer risk.

…kids were never something that I wanted to have young. … I'm glad that I started [tamoxifen] at the age that I started in terms of being younger, and I think it would have been a big consideration … had I started when I was say 30 or something. But [at] 25 to 30 … like kids never would have been in the plan between those ages, so it's been fine. (Kiera, 25 years)

Others who had completed their childbearing and had no intention to have any more children also chose tamoxifen. As Hannah (36 years) described: *"We're happy with two [children], so that's why I started the medication"*. For these women, tamoxifen was an interim measure; a way of reducing their breast cancer risk and deferring their decision about risk-reducing breast surgery to the future.

[Risk-reducing breast surgery is] really not for me at the moment, so I've decided to go on tamoxifen. (Ineka, 39 years)

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Running risks: Comparing tamoxifen with breast surgery

A key element of women's decision-making about taking tamoxifen centred on their desire to reduce their risk of breast cancer. For some women, like Rosie (26 years), taking tamoxifen to moderately reduce their breast cancer risk was better than doing nothing: *"It can reduce the risk up to half, so half the risk is better than … [having] all the risk."*

Counter-intuitively, many women who wanted to reduce their breast cancer risk were reticent to commit to the greatest risk-reducing option available to them: a bilateral risk-reducing mastectomy. Many risk-averse women taking tamoxifen were avoidant of a bilateral risk-reducing mastectomy because of the magnitude of the procedure. Risk-reducing medication was, therefore, a more acceptable alternative for some, enabling them to take action and reduce their breast cancer risk without resorting to a drastic surgical procedure.

> *…having something like a mastectomy, I couldn't do it now. When I spoke to the doctors I was sort of like, "oh yeah, that probably seems like a wise idea", and then I spoke to one of my friends who's a doctor and she's like, "No, it's actually really invasive, and they've got to cut away like all of your breast tissue", and I was like "oh OK, that's kind of a bigger deal than I'd really thought. (Kiera, 25 years)*

In contrast, many other women were unsatisfied by the moderate risk reduction offered by tamoxifen in comparison to bilateral risk-reducing mastectomy. These women often described that: *"tamoxifen was the one that you took which reduced your chances, but it didn't reduce them enough"* (Belinda, 40 years). Other women described themselves as being strongly risk-averse and felt the residual cancer risk remaining despite long-term engagement

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with tamoxifen was intolerable. Their preferred outcome by taking action to reduce breast cancer risk was to reduce it completely.

> *I guess I'm an all or nothing kind of person, and I don't like running risks, I'm just not a risk taker [...] if screening and tamoxifen were the better option rather than a preventative mastectomy, I would have done it. (Beatrix, 30 years)*

Other women described that their enthusiastic attitude towards a quick and efficient reduction in their breast cancer risk meant tamoxifen was not a suitable risk-reducing option; the length of time required to adhere to the medication (5 years) was too long a period of time to enact their risk reduction. In contrast to tamoxifen, bilateral risk-reducing mastectomy offered a method to "*deal with"* their breast cancer risk and then *"get on with it"* (Madeline, 29 years).

> *I'm pretty gung-ho, I want to get in and deal with the issue and get it done. (Amelia, 25 years)*
>
> *I wasn't interested [in tamoxifen] […] I know with surgery, you do that, and even though it's massive it brings your chances right down, and then that's it, you're done. It's a one off, one thing, done. (Melanie, 36 years)*

Too many drawbacks

Many of the women who declined tamoxifen were concerned about the side effects and did not want to have to *"deal with"* (Claire, 31 years) them while managing their breast cancer risk.

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I actually got the script, but then I never got it filled because I sort of went away and looked into the side effects and all the other things and just went, "hmm, I don't know that I really want to do that either." (Fione, 38 years)

Diana was concerned specifically about the potential side effect of weight gain if she took tamoxifen. She had completed childbearing and was trying to lose weight to be waitlisted for bilateral mastectomy. The potential for tamoxifen to work against her weight loss efforts meant Diana ruled it out as an interim option to surgery.

The reason I've not gone down that path is because in one breath they say if I want my [breast] surgery I need to lose weight. Side effect is it [Tamoxifen] makes you put on weight, and it's hard to lose weight. (Diana, 35 years)

Other women described they held negative attitudes to taking medication in general: "I *don't like drugs at the best of times"* (Cecilia, 39 years). This was especially reinforced because they were healthy young women who were not sick and only took medication when they were unwell:

I just don't feel that I'm sick, and I just don't feel that I should be taking a drug that I'm assuming has its own side effects, or its own risks, or you know like I'm putting it in my body for what reason. I don't feel that I need to do that at this point … it [Tamoxifen] just doesn't resonate with me at this stage, or align with my values. (Shoshana, 26 years)

A number of women also held concerns that evidence was not yet available regarding the efficacy of tamoxifen, interpreting the outcome of current research on tamoxifen as

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chemoprevention as optimistic: "*they're hoping that it's going to help you, but it hasn't been long enough as a preventative*" (Cecilia, 39 years). Others were concerned about the lack of women their age included in clinical trials testing the efficacy of tamoxifen in preventing breast cancer.

> *I just couldn't find enough information for someone my age, and whether it's worth it or not … I think a few of the studies I read were more for people in like their mid-30s […] I don't know if there's been any trials done on someone my age. (Kathryn, 24 years)*

From some to none: Experiencing a spectrum of side-effects

Most of the six women who took tamoxifen experienced various side effects, described as *"chemo"*-like symptoms, including "*mood swings", "hot flushes", "hair loss"* (Ineka, 39 years). Another participant experienced gastric symptoms including nausea and anorexia, as well as, pain in her legs.

> *… shit side effects … it makes me feel sick … pains in my legs … I wasn't hungry for like four weeks straight. (Rosie, 26 years)*

Umi (26 years) experienced discomfort of having itchy skin after commencing tamoxifen and without having any alternative aetiology or physical evidence of causation, she attributed it to the medication.

> *[I had] itching sensation on my legs or on my arms, or on my stomach, but there's no rash, I just feel tingly. (Umi, 26 years)*

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One participant described her surprise at experiencing no symptoms after commencing tamoxifen, despite her preparedness for side effects:

> *I was pretty nervous about the side effects. I haven't experienced any at all ... oh maybe like a slightly heavier period, but that's like really minor. So I was pretty surprised that I didn't experience any. I thought I'd get like night sweats or something like that, but I didn't at all. So it was initially a factor, but it's really kind of fallen by the wayside in terms of something that I care about. (Kiera, 25 years)*

For all bar one of the participants who took tamoxifen, the experience of side effects were transient and did not significantly impact their quality of life, or deter them from adhering to the medication and continuing with the prescribed course. However, for Vivian (34 years) the side-effects she experienced of *"repeated thrush episodes, like constantly for about six months"* significantly impacted her quality of life until she ceased taking tamoxifen.

Taking tamoxifen also provided psychological benefit with some participants describing the medication as a *"safety blanket"* (Umi, 26 years), where adhering to tamoxifen provided some security and comfort that they were acting to reduce their breast cancer risk.

> *I felt a lot better about everything while I was taking it. (Vivian, 34 years)*

Discussion

This is the first study to examine the decision-making of young women aged 20 to 40 years with a *BRCA1/2* mutation who were offered tamoxifen to reduce their risk of breast cancer in a routine clinical setting. Few young women in this study chose to use tamoxifen to reduce their breast cancer risk, which is similar to other cohorts of high-risk women who were

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offered tamoxifen in trial settings.[27] These young women's decision-making about tamoxifen was frequently driven by their reproductive intentions or desire to protect their ability to conceive in case they wanted to have children in the following five years. Many of the young women who wanted to reduce their breast cancer risk chose not to use tamoxifen because it did not offer enough reduction in terms of quantity or immediacy.

There have been a number of mixed-methods studies that provide some context to decision-making about tamoxifen by women more generally who are at increased risk of breast cancer (moderate and high-risk).[31,35,36] These studies consistently record that one of the reasons women declined tamoxifen was due to concerns about side-effects.[31,35,36] This is concordant with the findings of this study as a reason for declining tamoxifen, however, it was not as prominent as participants' preference to maintain their reproductive choice. Declining tamoxifen due to the intention to conceive was also cited by Skandarajah et al. (2017) describing 15% (25/168) of women attending the risk management clinic at the Royal Melbourne Hospital, Australia, who had preventive endocrine therapy discussed with them.[35] Nevertheless, the heterogenous samples of these studies were not described in enough detail to identify the perspectives of women with a *BRCA1/2* mutation or these women were not included in the qualitative data collection at all, and participants were older on average than the young women in this study.[31,35,36]

It is perhaps unsurprising that most young women with a *BRCA1/2* mutation are averse to using tamoxifen. As a medication with teratogenic effects and incompatibility with hormonal forms of contraception,[37] tamoxifen clashes with fundamental decisions and experiences characteristic of young womanhood: fertility management, pregnancy, and childbearing.

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Women of reproductive age already experience a myriad of contradictions when contracepting (e.g., how to contracept in ways that are compatible with their lifestyle and reproductive values);[38] therefore, offering young women tamoxifen may further complicate their fertility management by restricting them to non-hormonal forms of contraception.

Young women with a *BRCA1/2* mutation have been described as experiencing a 'compressed family life cycle', perceiving the need have children at a younger maternal age and closer together to ensure they complete their childbearing prior to the recommended ages to have ovarian cancer risk-reducing surgery.[39-41] Offering tamoxifen further highlights the tension between childbearing and risk reduction through the need to find a five-year window where childbearing is not a consideration. Furthermore, the immediacy and quantity of risk reduction was also an important factor for young women in this study when comparing bilateral risk-reducing mastectomy and tamoxifen. Consistent with prior research, these findings suggest women who choose breast surgery have a lower tolerance for ambiguity.[42] Young women's impatience with the more subtle and lengthy risk reduction offered by tamoxifen also speaks to the sense of urgency some may feel to undertake the developmental tasks of young adulthood. They may not perceive there to be time available to take a medication over a five-year period while developing their career, forming intimate relationships, and family planning. Therefore, having surgery to reduce breast cancer risk has a dual role: it reduces breast cancer risk immediately and, theoretically, does not impose any restriction on moving on to other important life events, especially childbearing.[43,44]

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Study limitations

The primary limitation of this study is the source of the participants. The majority of women who participated were recruited from a metropolitan, cancer-specialist hospital in Australia. These women are enrolled in a cancer risk management clinic staffed by genetics and oncological specialists who offer annual review specifically for high-risk women. Therefore, many women in this study have access to the latest evidenced-based information provided by specialised genetics and oncology health professionals and have theoretically been offered and made an informed choice about their breast cancer risk management options. This may contrast to other women with a *BRCA1/2* mutation who do not have access to this type of multidisciplinary care and may not have a choice about the type of risk management they can use, due to geographical barriers or less well-resourced provision of health services. In order to address this limitation, this research is continuing using an online survey recruiting young women with a *BRCA1/2* mutation nationally in Australia. The survey content has been purpose-designed based on the interview results and aims to collect data from a geographically diverse group of women.

Practice Implications

The findings from this study can inform clinical discussions with young women about cancer risk management and facilitate decision-making. Using these findings to inform clinical interactions may not increase the uptake of tamoxifen *per se*, but may improve medical specialists' understanding of women's decision-making about tamoxifen thereby facilitating a more nuanced discussion about the pros and cons of using tamoxifen.[45,46] Irrespective of young women's choice of breast cancer risk management, they should always be the

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beneficiaries of full and frank discussions with well-informed health professionals about their breast cancer risk management options.

Conclusion

In conclusion, this study has elucidated and described the nuanced and complex decision-making process that young women with a *BRCA1/2* mutation undergo when considering using tamoxifen to reduce their breast cancer risk. Few young women with a *BRCA1/2* mutation chose to use tamoxifen, primarily because the teratogenic effect interferes with women's family planning, regardless of whether they are partnered. Nevertheless, tamoxifen offered an option to women who wished to reduce their risk of breast cancer but who were averse to the magnitude of breast surgery. For those who took this medication, the side effects were minimal or tolerable for most with only one woman ceasing tamoxifen due to the insufferable experience. While this medication has poor uptake, it remains important for women to be offered all breast cancer risk management options during their young adulthood to ensure they can choose the method that fits best with their own personal beliefs and circumstances.

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Conflict of interest statement

The authors declare they have no conflict of interest

Data availability statement

The author elects to not share data

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Table 1. Participant description

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Boxes

Box 1. Prescription of tamoxifen in Australia and cancer risk management

Tamoxifen was first approved by the Australian Therapeutic Goods Administration (TGA) in 1991 and listed on the Pharmaceutical Benefits Scheme (PBS) for the adjuvant treatment of breast cancer.[47] In 1998, the Food and Drug Administration (FDA) in the USA approved the use of tamoxifen for primary prevention of breast cancer.[48] By the late-1990's in Australia, clinicians in Familial Cancer Centres were discussing tamoxifen with high-risk women for breast cancer risk reduction.[49] Prescription of tamoxifen was off-label as it was being used outside of the TGA-registered indication and cost $0.2-$1 (AUD) per day.[38] By 2011, Cancer Australia guidelines recommended tamoxifen be considered for women with a BRCA1/2 mutation.[50] In 2016, tamoxifen was included on the PBS for primary prevention of breast cancer for women at moderate to high risk of breast cancer.[48] There are no Australian age-related guidelines regarding the prescription of tamoxifen for primary prevention. However, Australia women with a BRCA1/2 mutation are recommended to commence cancer risk management by 30 years of age.[51]

The Peter MacCallum Cancer Centre in Melbourne located in the State of Victoria, Australia, runs a cancer risk management clinic for women at high-risk of breast cancer. Women with a BRCA1/2 mutation can attend this multidisciplinary clinic annually for their breast screening and discussion about risk-reducing medication and surgery. Women with a BRCA1/2 mutation are recommended to attend this clinic from 30 years of age. However, for some women, family history or personal preference results in their attendance from 25 years of age. Similar clinics are conducted at other public hospitals in Australia with a clinical genetics department with women allowed to commence from 30 years of age.

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Tables

Table 1. Participant description

		n (%)	mean (SD)
Response rate		40/93 (43)	
Age at interview (years)	18-25	9 (23)	30.5 (5.4)
	26-30	11 (27)	
	31-35	11 (27)	
	36-40	9 (23)	
Gene mutation	BRCA1	18 (45)	
	BRCA2	22 (55)	
Partnered		32 (80)	
Time since genetic testing (years)	range	1-12	4 (3.0)
No. of children	0	23 (58)	
	≥ 1	17 (42)	

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Table 2. Breast cancer risk management strategies

	n (%)
None (yet to commence)	5 (12)
Breast screening only	19 (48)
Tamoxifen (and screening)	5 (12)
Bilateral risk-reducing mastectomy	11 (28)

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