


5-2016

# Factors Influencing Uptake of Risk-Reducing Salpingo-Oophorectomy by BRCA1 and BRCA2 Mutation Carriers

Victoria E. Breen

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FACTORS INFLUENCING UPTAKE OF RISK-REDUCING SALPINGO-  
OOPHORECTOMY BY *BRCA1* AND *BRCA2* MUTATION CARRIERS

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OOPHORECTOMY BY *BRCA1* AND *BRCA2* MUTATION CARRIERS

A

THESIS

Presented to the Faculty of  
The University of Texas  
Health Science Center at Houston  
and  
The University of Texas  
MD Anderson Cancer Center  
Graduate School of Biomedical Sciences  
in Partial Fulfillment

of the Requirements

for the Degree of

MASTER OF SCIENCE

by

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May, 2016

FACTORS INFLUENCING UPTAKE OF RISK-REDUCING SALPINGO-  
OOPHORECTOMY BY *BRCA1* AND *BRCA2* MUTATION CARRIERS

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Germline mutations in the *BRCA1* and *BRCA2* genes are associated with significantly increased risks for ovarian cancer. The National Comprehensive Cancer Network (NCCN) currently recommends that female BRCA mutation carriers undergo risk-reducing salpingo-oophorectomy (RRSO) after age 35; however, not all women elect this option. The purpose of this study was to prospectively survey women with BRCA mutations currently undergoing ovarian cancer screening about their intention to have an RRSO and the various factors influencing their decision. Of the 26 women who completed our survey, 26 (100%, CI: 86.8-100) plan to undergo an RRSO in their lifetime. The average woman reported 6.7 motivations and 2.9 barriers to RRSO, indicating that in our population women tend to have more reasons for electing, rather than avoiding, this surgery. We further found that while most women appeared to share the same motivations for surgery, they often had unique barriers that were not common to others. The most important reasons in favor of surgery included a desire to reduce one's risk for ovarian cancer and live longer for family members. The most important barrier to RRSO was fear of the symptoms related to menopause. We believe these results will assist healthcare providers when discussing the option of RRSO with BRCA mutation carriers undergoing ovarian cancer screening.

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## INTRODUCTION

Hereditary breast and ovarian cancer (HBOC) syndrome due to germline mutations in the *BRCA1* or *BRCA2* genes accounts for approximately 10% of all cases of ovarian cancer. The average lifetime risk of ovarian cancer is up to 45% with a *BRCA1* mutation and up to 25% with a *BRCA2* mutation, compared with a 1.7% lifetime risk for the general population [1]. These risks are especially concerning given that the vast majority (>79%) of these malignancies are detected at an advanced stage and the 5-year survival rate after diagnosis is only 45% (data from SEER 18 2005-2011). The National Comprehensive Cancer Network (NCCN) currently recommends that women with HBOC undergo risk-reducing salpingo-oophorectomy (RRSO) prior to natural menopause to reduce the risk of ovarian cancer by 85-90% and also decrease overall cancer-related mortality [2-4]. Despite the effectiveness of RRSO, uptake of surgery by mutation carriers is not universal, with estimates suggesting that in the United States approximately 25-35% of carriers do not elect surgery and remain at elevated risk [5, 6]. While ovarian cancer screening options are available, including pelvic examination, serum CA-125 analysis, and transvaginal ultrasound, these procedures are not significantly effective at detecting an early stage malignancy or reducing ovarian cancer related mortality [7].

A number of quantitative and qualitative research studies have investigated factors associated with the uptake of RRSO by women with HBOC. The most commonly reported sociodemographic variables include older age, particularly  $\geq 40$ -years [8], and parity [8-10]. Researchers have also investigated the influence of personal and family history of cancer on decision making, but findings have been inconsistent. Women with a personal history of breast cancer may have a preference for RRSO over screening [11-13]; however, not all evidence supports this [14, 15]. It is similarly unclear if family history of breast or ovarian cancer significantly affects uptake of RRSO, with some quantitative studies suggesting an association



[8, 16], while others do not [17, 18]. One qualitative study noted that experiencing a family member die from breast or ovarian cancer heavily influenced the uptake of risk reducing surgeries, including RRSO [19].

Additional investigations have sought to determine the psychosocial factors that influence decision making, particularly perceived cancer risk and cancer-related anxiety. Numerous studies have concluded that women with HBOC have a higher perceived cancer risk and this significantly impacts their decisions about RRSO [14-16, 20]. Similar evidence also supports that women with high levels of cancer-related anxiety are more likely to opt for this surgery [5, 21] as a means of alleviating these distressing feelings [22]. Interestingly, two large studies have found no evidence of a relationship between anxiety and uptake of RRSO [9, 18], so its true impact remains unclear. Personal values, such as wanting to gain more control over one's cancer risk, as well as a sense of obligation to stay healthy for other family members have also been cited as important factors for women considering RRSO [18, 19]. Finally, limited research has investigated how the concepts of body image, femininity and self-identity affect decision-making; however, available studies suggest that these may be relevant barriers to surgery [20, 23, 24].

An important consideration for women undergoing RRSO is the immediate onset of early menopause with the potential for adverse sexual outcomes and increased risks for multiple health problems. Compared to women who enter menopause naturally, women with surgically-induced menopause may have more severe vasomotor symptoms, as well as a higher frequency of dyspareunia (pain during intercourse) and reduced sexual satisfaction [25]. Multiple studies have also linked early-onset menopause to an increased risk for cardiovascular disease [26], osteoporosis [27], and an overall increased risk of mortality [28]. Despite the well-documented risks of early-menopause, the effects of this information on mutation carriers' decisions have

not been well established. A handful of qualitative studies have reported that at-risk women perceive the onset of menopausal symptoms as a major limitation of the surgery [10, 24, 29, 30], but additional research is needed to determine how these concerns compare to other factors women consider when deciding about RRSO.

The purpose of this study was to prospectively survey women with BRCA mutations currently undergoing ovarian cancer screening about their future intentions to elect or avoid RRSO. Simultaneously, we also investigated the various factors that are influencing this decision. The novelty of our design is that we had participants rank their influences, thereby allowing us to elucidate the relative importance of each within a woman's decision making process. Our analysis included both a chart review for sociodemographic and clinical variables, as well as a questionnaire that evaluated psychosocial factors, and other previously reported influences, such as onset of menopause, femininity/identity, quality of life concerns, perception of ovarian cancer screening, and family history. In doing so we hoped to better identify the most important motivations and barriers to women who are considering this surgery in the context of an ovarian cancer screening program.

## **METHODS**

### *Study population*

All participants were recruited from the University of Texas MD Anderson Cancer Center, Gynecologic Oncology High-Risk Screening Clinic. Eligibility criteria included women 35-years or older with a confirmed pathogenic mutation in the *BRCA1* or *BRCA2* genes who were undergoing ovarian cancer screening. Women had to have at least 1 ovary *in situ*. Potential participants were excluded if they had a personal history of ovarian cancer, RRSO, or if they were not fluent in both verbal and written English.

### *Data collection*

Eligible women were approached by a research study member during their visit to the high-risk Gynecologic Oncology screening clinic. Each woman was given a verbal overview of the study and then asked about her desire to participate. If a woman expressed interest in the study she was provided an informed consent document to review and sign, which was then collected by the research study member. Each woman was also given a copy of the signed consent document for her own records. Following informed consent, all sociodemographic, and clinical data were obtained through a review of the electronic medical record. Each woman also provided her preferred email and was subsequently sent a link to a confidential survey administered through the REDCap (Research Electronic Data Capture) web-based survey application. Approval for this study was obtained from the Institutional Review Board (IRB) of The University of Texas MD Anderson Cancer Center.

### *Demographic and clinical information*

A review of each woman's medical record was performed to gather demographic and clinical information. This included date of birth, ethnicity, race, religion, health insurance, highest level of education achieved, marital status, employment, date of genetic testing results, *BRCA1* and *BRCA2* mutation status, personal cancer history, menstrual status, gravidity, parity, age at parity, history of contraception use, fertility treatment, hormone replacement therapy (HRT), breast cancer screening, mastectomy history, Tamoxifen use, date of first gynecologic screening at MD Anderson, total number of gynecologic screening visits at MD Anderson, and outcomes of gynecologic screening, such as transvaginal ultrasound and CA-125 results.

### *Cancer risk perceptions*

Three items were adapted from Gurmankin Levy et al. [31] to measure women's perceptions of their ovarian cancer risk. Women indicated their numerical risk for ovarian cancer on a scale of 0% to 100% with 10 digit intervals. 0% corresponded to no risk for cancer and 100% corresponded to a certainty of developing cancer. In addition, women were asked to rate their risk for developing cancer on a Likert-type scale with answers including, very low, moderately low, neither high nor low, moderately high, or very high. For the final question women reported how their risk compares to the average woman's risk with options including much lower than, a little lower than, the same as, a little higher than, or much higher than the average woman's risk.

### *Cancer-specific worry*

We assessed cancer worry using the Lerman cancer worry scale adapted for ovarian cancer [32]. This consisted of 3 Likert-style questions measuring how often women think about ovarian cancer, if these thoughts have affected their mood, and if these thoughts have interfered with their daily activities. Scores can range from 3 to 12 with higher scores indicating a higher level of worry.

### *Anxiety*

The State-Trait Anxiety Inventory (STAI) Form Y was used to evaluate anxiety in our population [33]. This tool includes 40 questions that measure either state (i.e. temporary), and trait (i.e. inherent) anxiety. All questions are Likert-style with a 4 point scale, and higher scores correspond to higher levels of anxiety.

### *Intent for RRSO*

Women were asked to report if and when they plan to have an RRSO. Possible answer choices included: age 35-40, age 41-45, age 46-50, after age 50, after menopause, or never.

### *Factors influencing decision making*

To identify factors influencing decision making regarding RRSO women were given a list of 17 factors that may be motivating their desire to have surgery and a separate list of 24 factors that may be discouraging them from having surgery. Women were allowed to select all factors that were applicable to them, and there was an additional “other” option in which they could record their own factor if it was not already provided. Factors provided in the survey were based on a literature review of surgical decision-making and/or clinical experience of the authors. After selecting relevant factors, women were asked to choose the 5 most important factors for each category (motivating and discouraging) and rank these in an order of 1 to 5 with 1 being the most important for their decision making and 5 being the least important. If a participant initially selected less than 5 factors she was asked to rank these from 1 through the number she selected. She could also choose not to rank any of her selections. A weighted scoring algorithm was used to compare the various factors based on women’s rankings. A rank of 1 was given 5 points, 2 was 4 points, 3 was 3 points, 4 was 2 points and 5 was 1 point. The total score for each factor was then used for comparisons.

### *Data analysis*

Analysis of demographic and clinical information, as well as all survey variables consisted of measures of central tendency and descriptive statistics. An exact binomial confidence interval

Demographic	Number of Participants	Percentage (%)
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was used for the proportion of women who self-reported a desire to have an RRSO in their lifetime.

## RESULTS

### *Demographic characteristics*

35 women were invited to participate in this study and all agreed to sign the informed consent documents. 27 of the 35 women completed the online survey, giving us an initial response rate of 77%. One participant's results were excluded from analysis because she completed the survey after having a RRSO so our final assessment consisted of 26 women (74% of those consented). The demographic characteristics of these women are summarized in **Table 1**. The average age of our population was 43.9 years with a range of 35-66 years. The majority of women (17, 65%) were white, married (21, 81%), had at least some college education (20, 77%) and were employed (19, 73%). All women surveyed had health insurance, with private plans being the most common (21, 81%). Regarding mutation status, 12 (46%) women had a *BRCA1* mutation and 14 (54%) had a *BRCA2* mutation. The average age at disclosure of genetic testing results was 42.5 years with a range of 29-66 years, and 14 (56%) had their genetic testing coordinated through MD Anderson. 15 women (57%) had a personal history of cancer, all of which had breast cancer, and of those 15, 10 were actively undergoing treatment at the time of survey completion.

<b>Age</b>		
Median (Range)	42 (35-66) years	
Mean	43.9 years	
<b>Race</b>		
African America	4/26	15
American Indian	1/26	4
Asian	3/26	12
White	17/26	65
Hispanic	5/26	19
Unknown	1/26	4
<b>Education</b>		
High school	4/26	15
Some college/ associates degree	7/26	27
Bachelor's or advanced degree	13/26	50
Unknown	2/26	8
<b>Religion</b>		
Christian	15/26	58
Other	5/26	19
None or not reported	6/26	23
<b>Marital Status</b>		
Married	21/26	81
Divorced	1/26	4
Single	4/26	15
<b>Employment</b>		
Employed	19/26	73
Unemployed	7/26	27
<b>Insurance</b>		
Private	21/26	81
Medicaid	4/26	15
Medicare	1/26	4
<b>BRCA1 mutation</b>	12/26	46
<b>BRCA2 mutation</b>	14/26	54
<b>Age at BRCA results</b>		
Mean (Range)	42.5 (29-66) years	
<b>Genetic testing through MD Anderson</b>	14/26	56
<b>Personal History of Cancer</b>	15/26	57
Breast cancer	15/15	100
Currently undergoing cancer treatment	10/26	38

**Table 1: Demographic characteristics of survey participants, (N = 26)**

### *Gynecologic and breast history*

Information regarding women's gynecologic and breast history is summarized in **Table 2**. A little over half (58%) of women were premenopausal and the majority (81%) were parous. 4 of the 26 women (15%) had a previous hysterectomy, 7 (27%) had a tubal ligation, and 13 (50%) used oral contraceptives with an average use of 9.5 years. For women who received their genetic testing through MD Anderson, the average time between disclosure of BRCA results and the first documented visit for high-risk gynecologic screening was 4 months, with a range of 0-13 months. The majority of women, regardless of where they had their genetic testing, had been followed for less than 1 year in the MD Anderson screening clinic at the time of survey completion. More specifically, the mean length of follow up was 12.9 months and ranged from 0 to 82 months. Of the 26 women in our study, 1 (4%) had a previous abnormal CA-125 screening result at MD Anderson and no one had an abnormal transvaginal ultrasound. Regarding breast history, 20 women (77%) were also followed in the MD Anderson Breast Screening Clinic with the mean length of follow up being 29.1 months (range 0-218 months). 15 women (58%) had a previous mastectomy (bilateral or unilateral) and 3 (12%) used Tamoxifen.

### *Cancer risk perceptions*

When women were asked to indicate their numerical lifetime risk in units of 10 (range 0-100) all recorded at least a 10% risk with 22 women (85%) choosing a risk of 50% or higher. The most commonly chosen risks were 50% or 60% with 6 women selecting each of these categories. 5 additional women selected 70%, 2 selected 80%, 2 selected 90%, and 1 selected 100%. None of the women selected 30% or 40% as a risk number. Type of *BRCA* mutation did not appear to influence numerical risk perception. When asked about their qualitative risk perceptions, the majority of women (22, 85%) indicated that their lifetime risk for developing



ovarian cancer is “moderately high” or “very high”. 3 (11%) considered their risk to be “neither high nor low”, and 1 woman (4%) categorized her risk as “moderately low”. When asked how their risk compares to the average woman, 25 women (96%) stated that their risk is higher than the average. 1 woman (4%) recorded her risk as a “little lower” than the average woman’s.

#### *Cancer worry and anxiety*

Cancer-related worry was measured using the Lerman cancer worry scale adapted for ovarian cancer. Our mean score was 5.04 out of 12 with a range of 3-11. We also measured women’s anxiety using the STAI and found that the mean trait anxiety score was 35.6 with a range of 21-57. The previously published trait anxiety mean for women ages 19-39 is 36.5, for ages 40-49 is 35.03 and for ages 50-69 is 31.79 [33].

#### *Intent for RRSO*

All 26 women (100% CI: 86.8-100) reported an intention to have an RRSO during their lifetime (**Figure 1**). The majority of women (21, 81%) wanted to have surgery prior to age 50, 5 reported “after age 50”, and no one indicated “after menopause”. The most commonly reported timing for both *BRCA1* and *BRCA2* mutation carriers was age 41-45. All but 3 women with a *BRCA1* mutation plan to have an RRSO before age 45, and all but 2 *BRCA2* carriers desire the surgery before age 50.

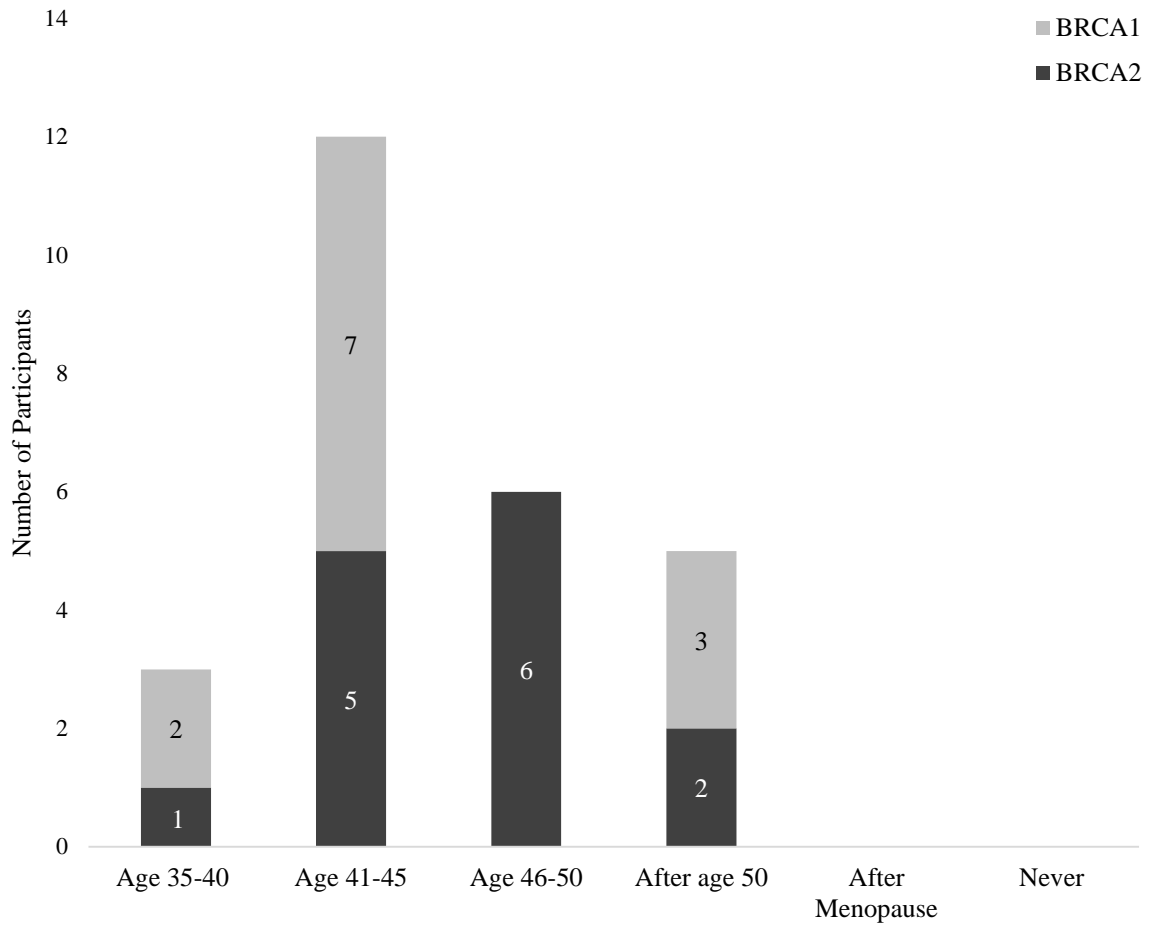
<b>Gynecologic History</b>	<b>Number of Participants</b>	<b>Percentage (%)</b>
Premenopausal	15/26	58
Post-menopausal	11/26	42
Parity		
Parous	21/26	81
Mean age at parity (Range)	22.6 (15-33) years	
History of hysterectomy	4/26	15
History of tubal ligation	7/26	27
Oral contraceptive use	13/26	50
Average time between BRCA results and 1 <sup>st</sup> gynecologic screening visit (Range) <sup>a</sup>	4.0 (1-13) months	
Followed for less than 1 year in screening clinic	17/26	65
Mean length of follow up in ovarian screening clinic (Range)	12.9 (0-82) months	
Abnormal CA-125 result(s)	1/26	4
Abnormal TVUS result(s)	0/26	0
<b>Breast History</b>		
Followed in breast screening clinic	20/26	77
Mean follow-up in breast screening clinic	29.1 months	
Any Mastectomy	15/26	58
Bilateral risk-reducing mastectomy	5/26	19
Bilateral mastectomy for treatment	2/26	8
Unilateral risk-reducing mastectomy <sup>b</sup>	6/26	23
Unilateral mastectomy for treatment	8/26	31
Tamoxifen use	3/26	12
Mean length of use	9.3 months	

**Table 2: Gynecologic and breast history of survey participants**

RRSO = Risk-reducing salpingo-oophorectomy.

<sup>a</sup> Only calculated for women who received BRCA genetic testing through MD Anderson

<sup>b</sup> All occurred simultaneously with mastectomy for cancer treatment



**Figure 1: BRCA mutation carriers' intended timing for RRSO**

Women were asked to indicate if and when they plan to have an RRSO in their lifetime. The answers for each category were further divided by *BRCA1* and *BRCA2* mutation status.

RRSO = Risk-reducing salpingo-oophorectomy.

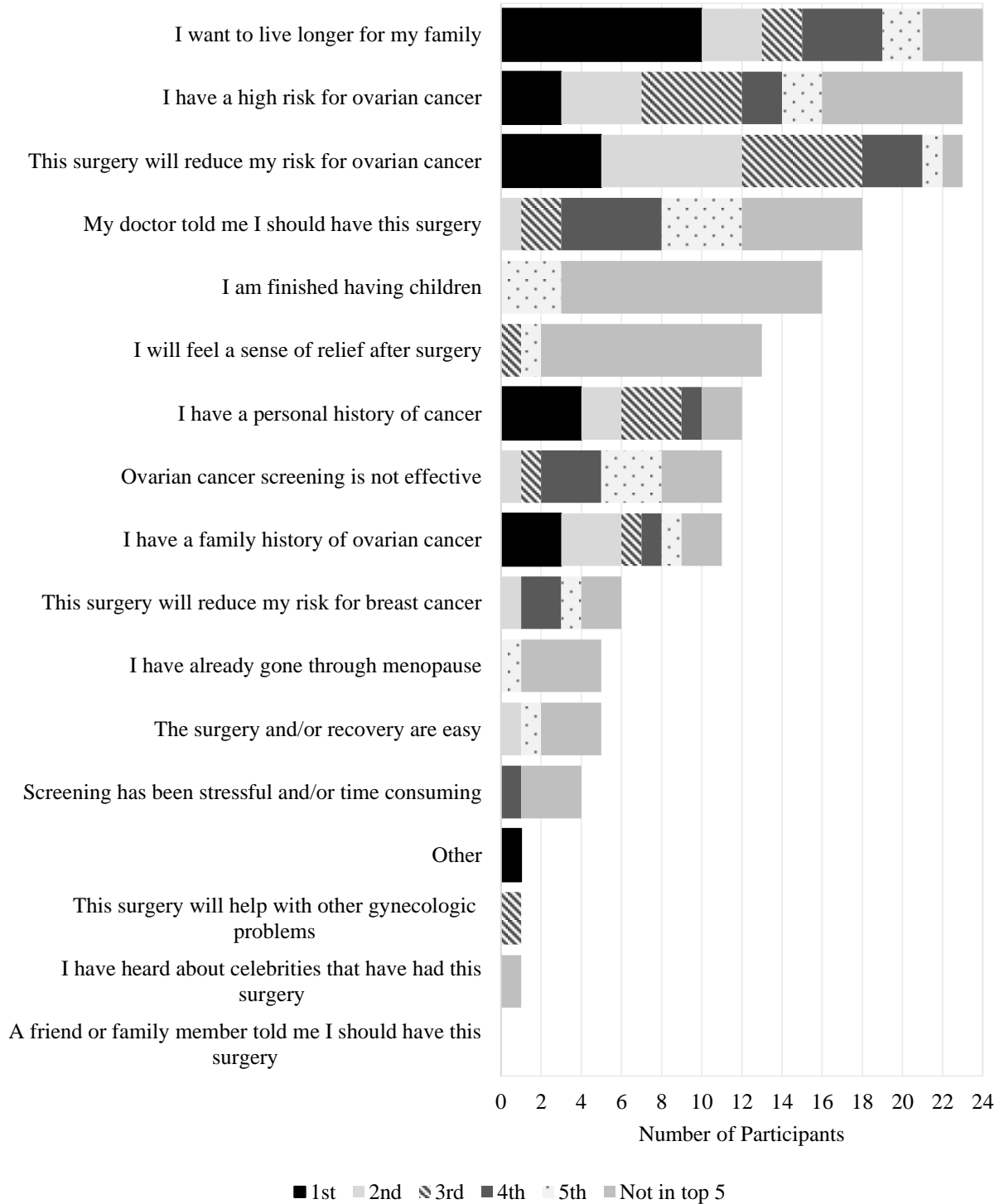
### *Motivations for RRSO*

**Figure 2** summarizes the reported factors motivating women to have an RRSO. Of the 17 provided answers, including one free response option “other”, 16 were selected by at least one woman as influencing her decision making. On average each woman indicated 6.7 unique motivations (range: 1-9) and the most commonly selected answer (n=24) was “I want to live longer for my family”. Women were also asked to rank their top 5 selected motivations and from this 6 different factors were identified as the 1<sup>st</sup> or “most important” motivation for RRSO by 1 or more women. The most common 1<sup>st</sup> motivation was “I want to live longer for my family” (n=10), followed by “This surgery will reduce my risk for ovarian cancer” (n=5). A weighted ranking scoring algorithm was then used to identify the overall most important motivations for our population (**Table 3**). This analysis determined that the 5 most important motivations included: 1) I want to live longer for my family, 2) This surgery will reduce my risk for ovarian cancer, 3) I have a high risk for ovarian cancer, 4) I have a personal history of cancer, 5) I have a family history of ovarian cancer.

### *Barriers to RRSO*

Information regarding women’s reported barriers to RRSO is presented in **Figure 3**. Women were provided with 24 possible answers, including one free response option “other”, and of those, 20 were selected. The average number of barriers reported per woman was 2.9, with a range of 0-8. The most commonly selected barrier was “I am worried about the symptoms of menopause (e.g. hot flashes or night sweats) (n=11). When participants were asked to rank their top 5 reasons to delay or avoid RRSO, 11 unique barriers were recorded, with the most common 1<sup>st</sup> reason being “I am currently completing treatment for another type of cancer” (n=6). Because RRSO is almost always contraindicated during cancer treatment, we

corrected this bias by removing all women who were currently undergoing cancer treatment from the weighted scoring analysis for barriers to surgery. After reanalyzing the data and applying the scoring algorithm the 5 most important barriers included: 1) I am worried about menopause symptoms (e.g. hot flashes and night sweats), 2) I do not have time for the surgery and/or recovery, 3) I am worried about the menopause-associated sexual problems (e.g. loss of sexual drive and vaginal dryness), 4) I am afraid of the surgery and/or recovery, 5) I plan to have the surgery when I am older (**Table 3**).



**Figure 2: Reported motivations for RRSO**

Women were asked to select any factors that were motivating them to have an RRSO. Following this, women were given the opportunity to rank their selections from 1 to 5 with 1 being the most important to their decision making and 5 being the least important. RRSO = Risk-reducing salpingo-oophorectomy.

**Weighted Score**

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**Motivations**

I want to live longer for my family	78
This surgery will reduce my risk for ovarian cancer	78
I have a high risk for ovarian cancer	52
I have a personal history of cancer	39
I have a family history of ovarian cancer	33

**Barriers**

I am worried about menopause symptoms (e.g. hot flashes and night sweats)	37
I am currently completing treatment for another type of cancer	33
I do not have time for the surgery and/or recovery	17
I am worried about menopause-associated sexual problems (e.g. loss of sex drive and vaginal dryness)	17
I am afraid of the surgery and/or the recovery	16

**Barriers**

**(corrected for current cancer treatment)**

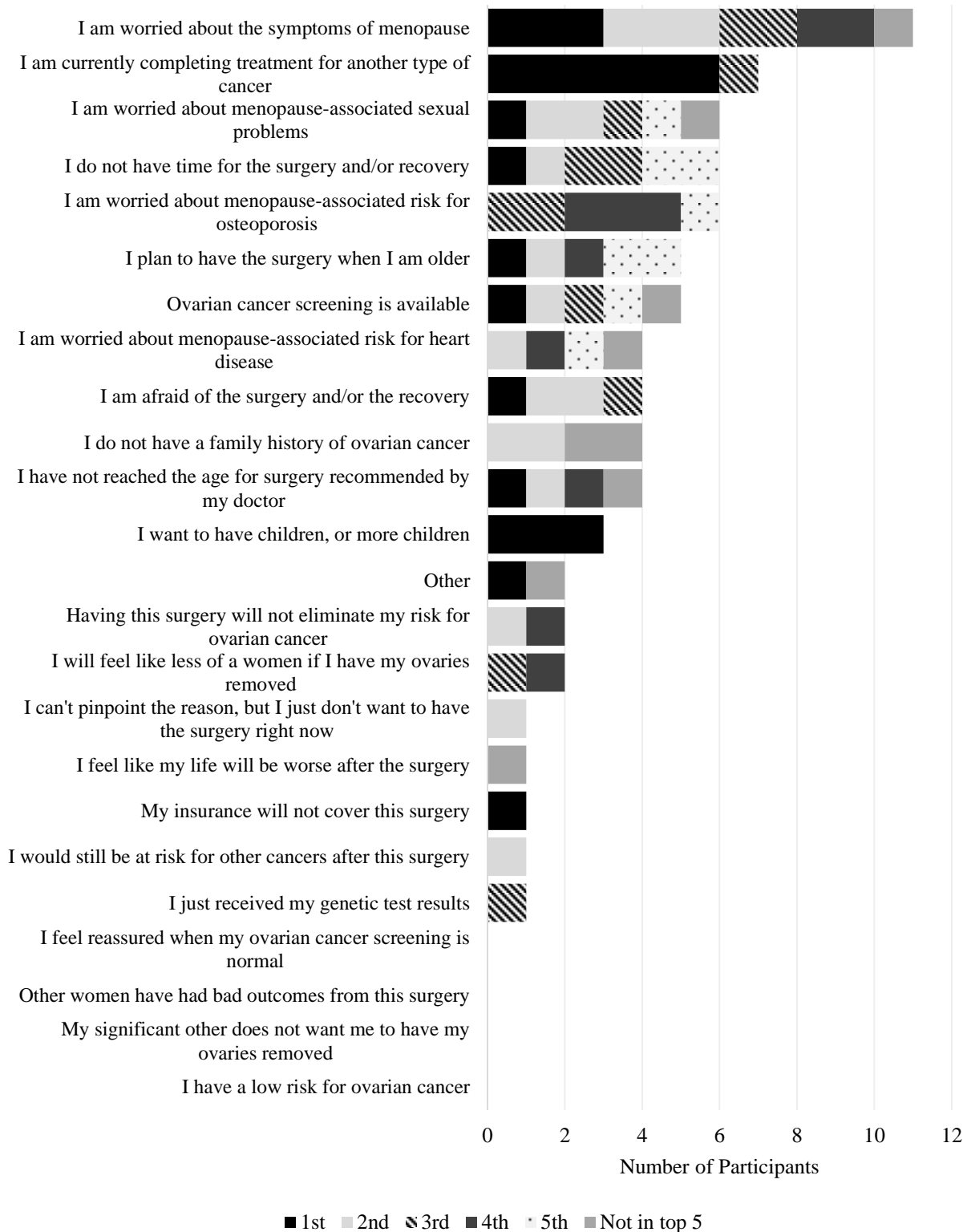
I am worried about menopause symptoms (e.g. hot flashes and night sweats)	32
I do not have time for the surgery and/or recovery	13
I am worried about menopause-associated sexual problems (e.g. loss of sex drive and vaginal dryness)	13
I am afraid of the surgery and/or the recovery	12
I plan to have the surgery when I am older	15

---

**Table 3: Weighted scores for the top 5 motivations and barriers to RRSO**

Women were asked to separately rank the 5 most important motivations for and barriers to RRSO from 1-5. 1 was considered the most important motivation or barrier and 5 was the least important. A weighted scoring algorithm was used for comparisons. A rank of 1 was given 5 points, 2 was 4 points, 3 was 3 points, 4 was 2 points and 5 was 1 point. The total scores for the top 5 answers for each category are summarized here. Analysis of the barriers was corrected for women currently undergoing cancer treatment because RRSO is contraindicated.

RRSO = Risk-reducing salpingo-oophorectomy.



**Figure 3: Reported barriers to RRSO**

Women were asked to select any factors that would delay or prevent them from having an RRSO. Following this women were asked to rank their selections from 1 to 5 with 1 being the most important factor to their decision making and 5 being the least important.

RRSO = Risk-reducing salpingo-oophorectomy.



## DISCUSSION

Currently, the NCCN recommends RRSO as the primary ovarian cancer management option for women with HBOC over the age of 35. Despite its ability to reduce ovarian cancer risk and potentially breast cancer risk, not all women with a BRCA mutation elect RRSO. A number of past research studies, both qualitative and quantitative, have identified a variety of factors that may influence a women's decision to undergo or avoid surgery; however, to our knowledge no study to date has asked women to rank the relative importance of these factors. For this reason, we prospectively investigated the surgical intentions of women with BRCA mutations currently undergoing ovarian cancer screening, as well as their most important motivations and barriers to RRSO. The strength of our study design is that we captured women within their decision making process at the ages most relevant to RRSO.

Overall 74% of women completed our survey indicating that the results likely represent the population of women attending our screening clinic and may be generalizable to women in other screening clinics. Based on the responses, all 26 women (100% CI: 86.8-100) intended to have an RRSO during their lifetime. While few previous studies have measured BRCA mutation carriers' surgical intentions, rather than uptake, a study by Tiller et al. in Australia found that 68% of women planned to have an RRSO after a positive genetic testing result [14]. Our estimate could be higher due to the fact that women attending a screening clinic may be more inclined towards RRSO than the average woman with HBOC. Additionally, our results suggest that all of the women surveyed were using screening as a temporary option until their future surgery, rather than a replacement for RRSO. Of note, 5 women (19%) listed the availability of screening as a reason to delay or avoid RRSO. This result is concerning given that screening is not an effective management option for ovarian cancer, and we encourage healthcare providers to continually emphasize this to their patients. A limited number of studies

have investigated the process by which women with HBOC transition from intending to have surgery to actually undergoing the procedure; however, evidence suggests that women with BRCA mutations prefer a shared decision making process with their health care provider [14, 34]. An interesting follow-up to this study would be to re-contact women who reported an intent for RRSO to measure the actual rate of surgical uptake and elucidate how this decision was finalized.

Regarding the specific timing for RRSO, most women with a *BRCA1* mutation reported a plan to have an RRSO prior to age 45, while many of those with a *BRCA2* mutation reported timing up to age 50. Both of these timing preferences are within 5 years of the current NCCN management guidelines that recommend RRSO between ages 35-40 for women with a *BRCA1* mutation and between ages 40-45 for those with a *BRCA2* mutation. Notably, the majority of women with a BRCA1 mutation who indicated age 40-45 were already over the age of 40 when they received their genetic testing results, which likely explains their timing. As well, because a large portion of women were undergoing cancer treatment, surgery may not have been possible within the recommended timeline. 5 women in our population did report a desire to have an RRSO after age 50; however, all of these women were  $\geq 50$ -years-old (range: 50-66) at the time of survey, and 4 of the 5 received their genetic testing results after age 50. Again, the RRSO timing for these women is more likely explained by the age at which they received their mutation results, rather than a deviation from current guidelines. Importantly, we also found that none of the women indicated a desire to wait until after menopause, which is consistent with the NCCN guidelines for reducing breast cancer risk. Overall these results emphasize that women within a screening clinic intend to have an RRSO at an age that is consistent with, or close to those recommended by the NCCN.

We next investigated the factors motivating women to pursue an RRSO. 16 of the 17 possible motivations were selected by our participants, indicating that a variety of factors encourage women to elect surgery. Further, the average number of motivations selected by each woman was 6.9, highlighting that even for an individual there are multiple reasons she may opt for an RRSO. Of note, more than half of the selected factors were chosen by >40% of women and the 3 most common answers were chosen by  $\geq 88\%$ . This indicates that most motivations were shared across the women in this study, and suggests that within the context of a high-risk screening program women identify multiple similar reasons to elect RRSO. Additional studies are needed to determine if this finding holds true for BRCA mutation carriers in other high-risk screening programs and those who do not elect screening.

Based on the weighted ranking analysis the most important motivations for women in our population included a desire to reduce one's ovarian cancer risk, and a desire to live longer for family members. Previous literature has demonstrated an association between cancer risk perception and uptake of RRSO [14] and one study has even cited "wanting to reduce ovarian cancer risk" as the most important influence on RRSO decision making [15]. This motivation agrees with women's answers regarding risk perceptions, as the vast majority of them reported a higher than average perceived risk for ovarian cancer. We also measured cancer worry using the Lerman cancer worry scale and found that the mean score of 5.03 out of 12 (range 3-11) was similar to previously reported values for women with BRCA mutations [21, 35] and corresponds to a moderate level of worry [35]. This supports the influence of ovarian cancer risk and the desire for risk reduction through RRSO in women with HBOC.

Besides wanting to reduce their ovarian cancer risk women were also very motivated by a will to live longer for family members. While the weighted score for this motivation was the same as risk reduction, wanting to live longer for family members was the most commonly

selected motivation and the most commonly reported 1<sup>st</sup> motivation among women. Few studies have previously investigated how the idea of family responsibilities or obligations influence RRSO; however, Hallowell, 1998 noted that all of her 41 study participants felt compelled to understand and reduce their cancer risks so that they could better care for their family. This finding is important because most conversations about RRSO are centered on the patient's individual outcomes (e.g. personal cancer risk reduction), while our data suggest that the discussion should additionally focus on how having surgery will benefit other family members and may increase a woman's time with them.

Personal history of any cancer and family history of ovarian cancer were the 4<sup>th</sup> and 5<sup>th</sup> most important motivations for RRSO. In our population all of the women who selected personal history of cancer had a history of breast cancer, which has been cited by multiple studies as a significant influence on RRSO [12, 13]. Moreover, given that this group comprised 57% of our study population it is not surprising that a history of cancer was among the most important factors. Past literature has been more conflicted over the influence of family history of ovarian cancer on RRSO [8, 17, 36]; however, our study supports a strong influence. Of note, we did not record the number of family members with ovarian cancer or their degree of relationship, and thus could not determine if either of these variables impact women's responses. Regardless, we encourage healthcare providers to always consider a woman's personal and family history of cancer when discussing RRSO.

In addition to motivations, we also investigated the barriers that women perceive to RRSO. Of the 24 provided reasons one might delay or avoid surgery 20 were selected, emphasizing that much like the motivations, there are a range of barriers influencing women in our population. However, unlike for the motivations, the average number of barriers per woman was 2.9. Despite the lower average number per women, 11 separate barriers were chosen as

women's 1<sup>st</sup> or "most important". Moreover, 9 of the 26 women (35%) only reported 1 barrier and of those 9, 6 (66%) regarded it as their most important reason to delay or avoid RRSO. It appears that the majority of women have a few, but very important barriers that may not be universal for other BRCA mutation carriers. This novel finding suggests that when counseling about RRSO it is imperative to elicit the barrier(s) that are influencing each specific woman, as responses are likely to vary between individuals.

For the barriers that were shared between women we performed a weighted ranking analysis after correcting for women currently completing breast cancer treatment. This analysis revealed that the fear of menopausal symptoms (e.g. hot flashes and night sweats) was the most important barrier to women in our study. Importantly, when we looked specifically at the 15 premenopausal women, 10 of them (66%) had selected this barrier. 1 postmenopausal woman also chose this barrier. Moreover, worry about menopause-related sexual problems (e.g. loss of libido and vaginal dryness) was tied for the second most important barrier, indicating that women were concerned about multiple issues related to menopause. These are notable findings given that past literature has conflicted regarding the influence of surgically induced menopause on RRSO decision making [10, 19, 20, 24, 29, 37]. Our study clearly demonstrates that among premenopausal women, the onset of menopause is one of, if not the most important barrier to RRSO and healthcare providers should incorporate this into their discussion, if they do not already. This is especially relevant given the recent evidence that prophylactic salpingectomy with delayed oophorectomy (PSDO) may provide an attractive alternative for BRCA carriers who are interested in avoiding early menopause [38, 39]. Future clinical trials are needed to assess the impact of PSDO on ovarian cancer risk and quality of life in BRCA mutation carriers.

Other important barriers to RRSO included not having time for the surgery, fear of the surgical risks, and planning to have the surgery at an older age. Brain et al., 2004 previously

reported that taking time off work for an RRSO and the subsequent recovery was one of the greatest perceived obstacles to women [10]. Given that the majority of women who completed our survey are employed, this concern could be particularly relevant to them. Regarding the desire to have surgery at an older age, all of the women who selected this barrier were either on the early side of the recommended age spectrum, or were younger than the NCCN recommended ages. More specifically, 2 *BRCA1* carriers (ages 35 and 36) were just within the recommended timing for RRSO (age 35-40) while the 3 *BRCA2* carriers (ages 36, 37, and 37) were younger than the prescribed age for RRSO with a *BRCA2* mutation (age 40-45). This finding could highlight that some women may prefer to delay surgery till the latest recommended age. As well, some healthcare providers might support, or even encourage this preference given that the risk for ovarian cancer is 2-3% by age 40 in *BRCA1* carriers and 2-3% by age 50 in *BRCA2* carriers [40, 41]. For this reason, clinicians should inquire about a woman's specific timing preferences even within the recommended age ranges.

One of the most consistently published barriers to RRSO is parity. In our population we did not find this to be one of the top 5 barriers; however, the majority of women in our study were parous and nearly half were postmenopausal. Many of the previous studies that evaluated the influence of parity did so in populations that included women under the age of 35, and may have been less likely to have completed childbearing. Our data suggests that for women who are within the NCCN recommended ages for RRSO the desire for children (or more children) may not be as common. We did find that when a desire for children was reported (n=3) it was always considered the most important barrier to RRSO, which is consistent with past studies [8, 9, 20]. From this we infer that while fewer women age 35 or older may want to have children, it is likely to be the most important barrier to RRSO if they do.

There are several limitations to our study. First we had a lower number of participants so the generalizations that can be drawn from our data may be limited. Moreover, all participants were recruited from the same MD Anderson screening clinic and the majority of respondents were white and well-educated. With this in mind, our results may not be representative of minority or lesser-educated women with BRCA mutations. As well, our population could be more motivated to address their ovarian cancer risk than others given their willingness to come for ovarian cancer screening every 6 months.

In conclusion, through this prospective survey of surgical decision making in women with BRCA mutations we found that 100% intend to pursue an RRSO. The majority of women were similarly motivated by their desire to reduce their ovarian cancer risk, as well as live longer for their family. We determined that most women have a few unique barriers to surgery and this is important to keep in mind when counseling about RRSO. The most important barrier to our population was the fear of menopause, especially in premenopausal women. Future studies are needed to confirm the findings of this study in more diverse HBOC populations, particularly the influence of menopause on decision making. However, our results may be helpful to healthcare members providing surgical counseling in the context of a high-risk ovarian cancer screening clinic.

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