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# Effect of Referral for Genetic Counseling on Genetic Testing and Surgical Prevention in Women at High Risk for Ovarian Cancer-Results from a Randomized Controlled Trial

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## Abstract

**Background—**Guidelines recommend genetic counseling and testing for women with a pedigree suggestive of an inherited susceptibility for ovarian cancer. We evaluated the effect of referral to genetic counseling on genetic testing and prophylactic oophorectomy via a randomized controlled trial.

**Methods—**Data from an electronic mammography reporting system identified 12,919 women with a pedigree including breast cancer, of whom 625 were identified as high risk for inherited susceptibility to ovarian cancer using a risk assessment questionnaire. Of these, 458 women provided informed consent and were randomized 1:1 to intervention consisting of a genetic counseling referral (n=228) or standard clinical care (n=230).

**Results—**Participants were predominantly aged 45 to 65; 30% and 20% reported a personal history of breast cancer or a family history of ovarian cancer, respectively. Eighty-five percent of women in the intervention group participated in a genetic counseling session. Genetic testing was reported by 74 (33%) and 20 (9%) women in the intervention and control arms ($p<0.005$)

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respectively. Five women in the intervention arm and two women in the control arm were identified as germline mutation carriers. Ten women in the intervention arm and three women in the control arm underwent prophylactic BSO ($p<0.05$).

**Conclusion—**Routine referral of women at high risk for ovarian cancer to genetic counseling promotes genetic testing and prophylactic surgery. Our findings from a randomized controlled trial demonstrate the value of implementing strategies targeting women at high risk for ovarian cancer to ensure they are offered access to recommended care.

### Keywords

Ovarian cancer; Surgical prevention; Genetic counseling; Referral and Consultation; Risk Assessment and Genetic Testing

## Introduction

Risk reducing salpingo-oophorectomy (RRSO) is an established epithelial ovarian cancer prevention strategy that reduces incidence dramatically in women at high genetic risk for the disease [1,2]. A meta-analysis that included 10 studies demonstrated that RRSO reduces future risk of EOC in high-risk women by >80% [3]. RRSO is recommended for all women with *BRCA1/2* mutations between the ages of 35 and 40 once childbearing is complete[4]; it is also recommended around the age of menopause in women with mutations in DNA mismatch repair genes associated with hereditary non-polyposis colon cancer (Lynch Syndrome) [5-7].

Uptake of RRSO is low, perhaps because high-risk women are either unaware of their risk [8] or perceive it inaccurately [9-11]. Genetic counseling and genetic testing are important steps in assessing a woman's risk accurately [12] and identifying risk management strategies including RRSO [13]. Evidence suggests that genetic counseling and testing services are under utilized [14]. Manual chart review has been proposed to identify candidates for genetic counseling referral [15], but it is costly relative to an automated search. Electronic family history data collection has been described [16], but not evaluated for hereditary breast-ovarian cancer syndrome families to our knowledge.

We conducted a randomized controlled trial to test whether a strategy using electronic medical records and questionnaires to systematic identify high-risk women for referral to genetic counseling could improve the uptake of risk-appropriate medical behaviors, including genetic testing and RRSO, compared to routine clinical care. We identified 458 women at high-risk for ovarian cancer who provided informed consent and were randomized 1:1 to genetic counseling referral (n=228) or standard clinical care (n=230).

## Materials and Methods

### Participant identification and recruitment

Electronic medical records were used to identify women who were potentially at high risk for carrying a deleterious cancer-predisposing gene mutation. We used routinely collected, self-reported family and medical history data stored in a Mammography Reporting System© (MRS) database to identify women with a personal or family history of breast cancer who

had a mammogram during a 28-month window between January 2006 and April 2008 at three Swedish Medical Center (SMC) facilities in Seattle, Washington. SMC is a large community-based hospital system that provides mammography screening to over 60,000 women in King County, Washington annually. We identified 12,919 women aged 35-80 reporting a personal or family history of breast cancer, no personal history of ovarian cancer, and no prior history of bilateral salpingo-oophorectomy (BSO). Each woman was mailed a study packet including an introductory letter from a SMC provider, a three-page Screening Questionnaire (SQ), and a consent form for future contact by study investigators. The letter explained that she was identified based on prior participation in mammography at SMC facilities, asked her to fill out and return the SQ, and offered her potential participation in cancer prevention research. The SQ assessed personal and family cancer history information that was not available in the MRS database.

### Participant eligibility assessment and enrollment

Based on 2,797 responses to the SQ, 1,114 potentially eligible women were mailed a self-administered Baseline Questionnaire (BQ) to confirm eligibility. The BQ assessed detailed family history, history of genetic testing, deleterious mutations identified by testing, use of breast and ovarian cancer screening services, current and prior use of oral contraception and menopausal hormone therapy, tubal sterilization, past gynecologic surgery including surgical indication and reproductive and menstrual history. Women were considered risk-eligible for the trial if they met pedigree criteria similar to those of the 2013 guidelines of the National Comprehensive Cancer Network (NCCN) [17] for referral to a genetic counselor. Personal history of triple negative breast cancer, family history of non-breast and non-ovarian cancers, and cancers in 3rd degree relatives were not specifically included. To ensure that all high-risk women retaining their ovaries were included, we did not exclude women reporting a deleterious mutation in *BRCA1, BRCA2*, genes related to Lynch syndrome *(MLH1, PMS2, MSH2, MSH6*), or *TP53*. We also included women with 1) a first or second-degree relative positive for Lynch Syndrome; 2) Ashkenazi Jewish ancestry with any family history of breast cancer among first or second-degree relatives; and 3) personal history, or a first-degree relative, or multiple second-degree relatives with breast cancer diagnosed before age 50. Women were ineligible if they 1) had a history of prior ovarian cancer or BSO; 2) had tested negative for a previously identified family germline mutation; 3) were unable or unwilling to provide informed consent; or 4) could not identify a primary care physician to receive reports from the genetic counselor. Women were not excluded based on prior genetic counseling or testing.

Of the 1,114 women contacted, 667 returned the BQ; 625 were confirmed to be eligible and invited to participate in an enrollment visit. Women were not provided individualized risk assessment information or more general information about ovarian cancer risk factors at the enrollment visit, but they were told that women with a personal history of breast cancer, or a family history of breast or ovarian cancer, may be at increased risk for developing ovarian or breast cancer. They were also informed that the purpose of the study was to evaluate the effects of referral for genetic counseling on medical decision-making related to cancer and cancer risk among women at increased risk for cancer. Interested women were asked to provide informed consent for randomization and study-related medical record review, and

informed that any costs associated with genetic testing during the study would be the responsibility of the participant and her insurance company. All study procedures were reviewed and approved by the Human Subjects Institutional Review Boards of the Fred Hutchinson Cancer Research Center and Swedish Medical Center in Seattle, WA, and conformed to the ethical guidelines of the 1975 Declaration of Helsinki and Belmont Report. The trial was registered on http://www.clinicaltrials.gov. (Trial #NCT01851109). Of 625 eligible women, 458 provided informed consent and were enrolled between July 2008 and December 2009.

## Sample size

In the Ovarian Cancer Early Detection screening cohort [18], we had observed a 1% annual rate of RRSO among high-risk women receiving standard care. The trial was powered to detect a 4.5× increase in the rate of RRSO over two years from 2% in the control arm to 9% in the intervention arm. Target enrollment for the trial was 300 women per arm, yielding over 90% power to detect a difference of 7% in rate of RRSO.

## Randomization

At enrollment, participants were randomized (by computer) 1:1 to an intervention arm (n=228) or a control arm (n=230) using a simple random allocation sequence provided by a statistician who was not involved in the collection of outcomes. Participants allocated to the intervention arm were invited to participate in a genetic counseling session as detailed below. Control arm women received routine care as directed by their primary health care provider, with no study-related intervention except follow-up outcome assessments. The study did not provide personalized risk assessment information, general information about ovarian cancer risk factors, or advice regarding ovarian cancer risk, to control-arm participants.

## Intervention

Women allocated to the intervention arm were invited to participate in a standard clinical genetic counseling session at no cost. A typical session lasted approximately one hour and included a face-to face consultation with a certified genetic counselor. Counseling included review of the lifetime risk of breast and ovarian cancer for all women, an individualized discussion tailored to the participant's personal medical and family history, and determination of the need for genetic testing for the participant and/or her affected relative. Advantages and disadvantages of genetic testing were reviewed. Testing was usually arranged by the genetic counselor who tracked results and performed follow up for the proband and subsequently reviewed test results with the participant. Testing included selected analysis for mutations in *BRCA1/2* and Lynch syndrome genes based on clinical indications. *BRCA* testing included screening for large scale rearrangements when indicated. Multi-gene panel tests which combine *BRCA* and Lynch gene testing with a range of other cancer pre-disposing genes into a single test based on a next generation sequencing platform were not available during the study period. The genetic counselor provided the patient's primary care provider with a summary of the counseling session, results of genetic testing if performed, and clinical options for risk management. For each intervention-arm participant, the genetic counselor documented 1) her attendance at a visit, 2) any recommendation made

for mutation testing for her or her affected relative, 3) review with her of any genetic test results, and 4) any referral to a gynecologic oncologist or other provider to discuss RRSO.

### Follow up

To ensure unbiased ascertainment of pelvic surgery during the study period, medical charts were reviewed by an abstractor who was blinded to study arm of the participant. In addition, questionnaires administered one and two years post-enrollment were used to obtain self-reported follow-up information regarding genetic testing and pelvic surgery. Mailed follow up questionnaires were completed by 215 (94.3%) and 225 (97.8%) women in the intervention and control arms respectively. Women were asked to provide information regarding any pelvic surgery including bilateral or unilateral salpingo-oophorectomy performed for any indication as well as RRSO procedures for ovarian cancer prevention. Data abstraction was complete for all participants in 07/2013.

### Outcomes ascertainment

Medical records from all participants identified through chart review to have had pelvic surgery were reviewed by the study nurse to ascertain the clinical indication for surgery, whether or not the surgery resulted in BSO, and the clinical indication for removing the ovaries and fallopian tubes. The study nurse, blinded to study arm of the participant, reviewed the pre-operative assessment by the surgeon, the operative note, and the pathology report. To further ensure lack of bias in ascertainment of outcomes, de-identified abstracted information for all instances of BSO was reviewed by the study gynecologic oncologist to classify all identified BSO procedures as either prophylactic or performed for other reasons. The procedure was considered prophylactic if either 1) the primary indication for pelvic surgery was RRSO, or 2) pelvic surgery was performed to treat a benign condition and the ovaries and fallopian tubes were removed solely to prevent cancer due to family history suggesting inherited susceptibility. BSO was considered *not* to be prophylactic if it was performed to treat any type of cancer or if there was any suspicion of ovarian cancer.

### Analysis

Baseline characteristics of women were reported by study arm. The hypothesis of interest was tested using intent-to-treat proportional hazards analysis based on the assigned treatment at the time of randomization, comparing the rates of RRSO between women in the intervention and control arms. Observations were censored at 2 years post-enrollment (n=421), at the last available follow up (n=19), or at the time of BSO for non-prophylactic indications (n=5). Two-year cumulative incidence curves were generated and the Log-rank test was used to test significance of the difference in rates (hazards) of RRSO by study arm. All tests were two-tailed. Statistical analyses were performed using R software (Version 3.1.0; The R Foundation for Statistical Computing, Seattle, WA). Cumulative incidence curves and the Log-rank test were calculated using the Survival package for R [19].

## Results

Recruitment, enrollment and study outcomes by trial arm are shown in Figure 1. A total of 12,919 women with a family or personal history of breast cancer were identified from

electronic mammography records and mailed an eligibility SQ. Five hundred fifty-two SQ mailings were returned to the study center with no forwarding address. Of the remaining 12,367 SQ mailings, 2797 were completed and returned for an overall response rate of 23%. Of the 2797 SQ respondents, 1683 did not meet the study inclusion criteria. The remaining 1114 SQ respondents were invited to complete the BQ. Of BQ mailings sent, 30 were returned to the study center with no forwarding address, 417 were not returned, 42 were completed by women who were found to be ineligible based on their responses, and 625 were completed by apparently eligible women who were sent an invitation to attend an enrollment visit. Of these 625, one woman could not be contacted, 129 did not attend the clinic visit, and 37 were identified as ineligible during the enrollment interview. The remaining 458 women were enrolled in the trial. Randomization resulted in 228 and 230 women allocated to the intervention and control arms respectively. Mean (standard deviation) follow-up time was 3.4 (0.9) and 3.5 (0.7) years in the intervention and control arms, respectively (p-value = 0.92, Log-Rank test).

Median age at enrollment was 54.1 and 51.8 years in the intervention and control arms respectively; 71 (31.1%) intervention-arm, and 65 (28.3%) control-arm, participants had a personal history of breast cancer. Clinical characteristics of participants at the time of enrollment are reported in Table 1; with the exception of minor variation in age distribution, they did not differ by study arm. Participants were predominantly Caucasian, college-educated, parous, and never smokers. About 18% reported being of Ashkenazi Jewish descent. Two-thirds were between the ages of 45 and 65. About 77% had used hormonal contraception and 26% reported having used menopausal hormone therapy. Approximately 30% had a personal history of breast cancer and 20% reported at least one relative with ovarian cancer. About 10% had undergone hysterectomy and 12% reported tubal ligation. Roughly 15% had prior mutation testing with 2 women in each arm reporting having a *BRCA* mutation.

Compliance with the intervention was 85%: per study records, 194 of 228 women in the intervention arm attended a trial-sponsored genetic counseling session. Use of genetic testing services during the study period was significantly higher among women in the intervention arm. Of 228 and 230 women allocated to the intervention and control arms respectively, 74 (32%) and 20 (9%) respectively reported having undergone genetic testing after the start of the trial ($p<0.005$). Five women in the intervention arm were identified as germline mutation carriers (4 *BRCA*, 1 *MLH1*) compared to 2 women with germline mutations (both *BRCA*) in the control arm.

Thirteen women (10 in the intervention arm and 3 in the control arm) underwent RRSO within two years of enrollment (Table 2). Blinded medical record review confirmed that in all 13 cases EOC prevention was the primary indication for removal of ovaries and fallopian tubes. The majority had no abnormalities found, and most also underwent hysterectomy. The median time to RRSO was 11 months in the intervention arm and 21 months in the control arm. The two-year incidence of RRSO was more than 3-fold higher in the intervention arm compared to the control arm (4.4% vs. 1.3%, respectively, from Kaplan-Meier estimates). Figure 2 presents the cumulative probability of RRSO in each of the study arms. The

hazards ratio was 3.44 (95% CI (Wald): 0.95 - 12.49) and the p-value for the Log-Rank test for the comparison of RRSO by study arm was 0.046.

Characteristics of all 18 participants who underwent any BSO procedure within 24 months of enrollment are described in Table 2. Among the 13 women having RRSO only three (all in the intervention arm) were under the age of 50. Six of the 13 women had a germline mutation including five women in the intervention arm and one in the control arm.

Four women including three in the intervention arm and one in the control arm underwent RRSO despite genetic test results that were negative for known deleterious mutations. All four had a personal history of breast cancer and at least one first or second-degree family member with breast cancer. Two of the four also had a family member with ovarian cancer including one with both breast and ovarian cancer. All were age 45 or older at the time of RRSO.

Three women (including two in the intervention arm and one in the control arm) opted for RRSO without prior genetic testing, including one who had RRSO in the context of surgery for pelvic relaxation. Two had a personal history of premenopausal breast cancer as well as family members with breast cancer. The woman without a personal history of breast cancer had a first-degree relative who was diagnosed with both breast and ovarian cancer.

The remaining five women had BSO for reasons other than risk reduction. One woman in each arm received BSO as treatment for breast cancer, another woman in each arm had BSO to address symptoms or test results that were suspicious for ovarian cancer, and one woman in the intervention arm underwent BSO as part of therapy for endometrial cancer.

## Discussion

Results of this efficacy trial suggest that, compared to routine care, a strategy that includes systematic identification and referral to genetic counseling of high-risk women promotes genetic testing and prophylactic surgery to prevent ovarian cancer. In an intent-to-treat analysis, high-risk women offered genetic counseling underwent both genetic testing and RRSO at about 3.5 times the rate of women receiving routine care within a two-year follow-up period. The background genetic testing rate in control group of 9% over 2 years women confirms prior reports that many high-risk women do not receive guideline recommended care [20]. Fewer than 20% of eligible women reported having had genetic counseling, and most women (> 75%) were unaware of their elevated risk for ovarian cancer[8]. Among those that enrolled in the study, roughly 20% reported having a first or second-degree relative with ovarian cancer and therefore meet current guidelines for genetic testing[4].

Compliance with the genetic counseling referral was good at 85%, possibly in part because it was offered at no cost during the trial. About 1/3 of women in the intervention arm had genetic testing, a rate that is consistent with other studies that report between 26% and 55% of breast cancer family members attending high-risk clinics opt for testing [21,22]. Costs have been reported as an obstacle to *BRCA* testing [23]. In our study insurance coverage was verified before the testing was performed. Insurers' guidelines varied and some insurers covered testing for affected women only. Full price of the genetic test was about $3000 but

cost was a deterrent to only a few women because out-of-pocket costs seldom exceeded $200. The recommendation that an affected family member be tested to definitively interpret results was a barrier for some unaffected women as an affected family member was not always available for testing. Targeting other factors associated with the decision to proceed with genetic testing such as age, personal cancer history, race and psychosocial issues [23-26] may improve genetic testing rates.

The rate of RRSO in the intervention arm was increased more than 3-fold ($p<0.05$). Five of the ten intervention arm women who underwent RRSO had a deleterious mutation at the time of the procedure. The benefits of RRSO for mutation carriers are well documented. The role of RRSO in women without a documented mutation is less clear. Women who test negative for a mutation segregating in the family are not at increased risk. However not all cancer families are explained by the known susceptibility genes and many women choose to forgo genetic testing. Since this study was conducted, several new ovarian cancer susceptibility genes have been identified including RAD51D, RAD51C, BRIP1, PALB2 and BARD1 [27-29]; clinical testing for mutations in some of these genes is now available. Recent guideline updates now include a recommendation that BRIP1, RAD51 and RAD51C mutation carriers consider RRSO[4].

The 2-year follow-up period of the study is consistent with other studies evaluating procedure choice in high-risk women, but some women may have undergone RRSO outside of this follow-up interval. Studies suggest that most women who opt for RRSO undergo the procedure shortly after learning the results of genetic testing. For example, in a cohort study of 272 BRCA mutation carriers the median time from receiving genetic test results to surgery in patients undergoing RRSO was 123 days with an Inter-quartile range (IQR) of 56-331 days [30]. In a separate cohort of 244 mutation carriers, the median time to RRSO was .75 years (IQR .41 to 2.10)[31] Consistent with this data, the median time from enrollment to RRSO in our study was 11 months and 21 months in the intervention and control arms respectively. Intervention-arm women were offered genetic counseling immediately after study enrollment. The delay in time to RRSO in control-arm women may reflect in part the additional time it took for women receiving usual care to be referred to genetic counseling and/or learn about their risk.

Data available to us electronically were intended for assessment of breast cancer risk and as an aid in interpretation of mammography results. Consequently additional steps were required to identify women at high genetic risk for ovarian cancer. Overall it was necessary to contact 12,919 women to identify 625 potentially eligible women for this study, largely because of incomplete risk assessment at the time of mammography. A more comprehensive risk assessment tool that includes questions about ovarian cancer family history would simplify the identification of women at high risk for both ovarian and breast cancer. It is not known how many mammography facilities in the U.S. do comprehensive cancer risk assessment at the time of mammography, or to what extent electronic data are available for this purpose.

In summary, our results from a randomized controlled trial demonstrate that risk-appropriate use of genetic testing and surgical prevention strategies can be enhanced by systematic

identification and referral of women at high risk for a deleterious genetic mutation to a genetic counselor. The approach has public health potential to reduce ovarian cancer incidence in women at greatest risk. These findings motivate action to design and implement efficient strategies to ensure that high-risk women are identified and offered access to currently available and recommended care[13].

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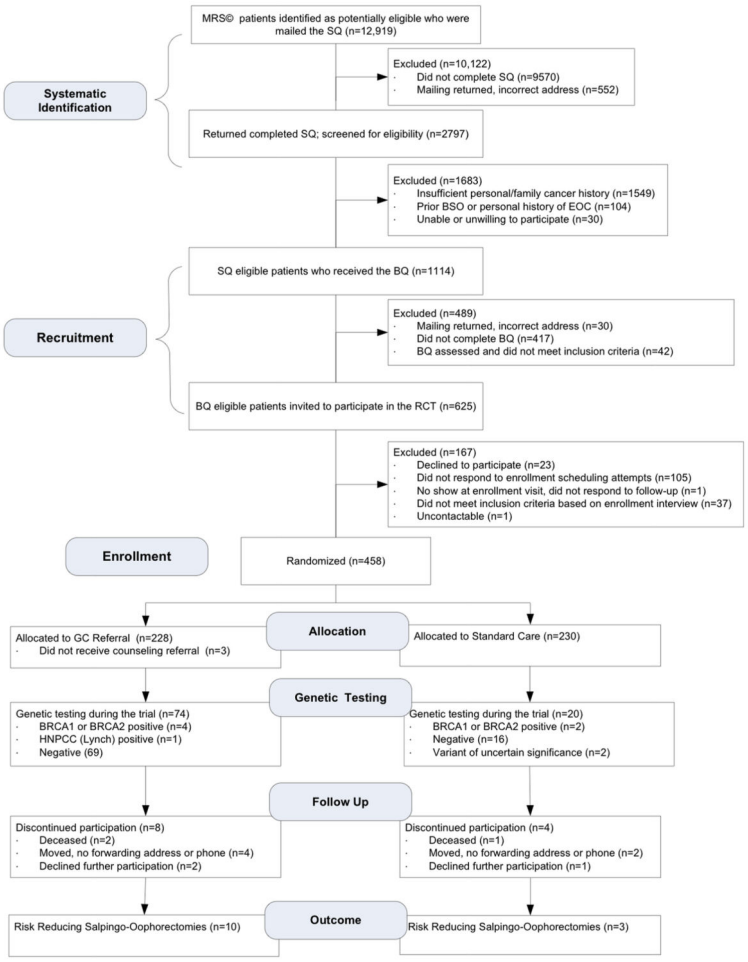


**Figure 1. Flow diagram of participants at each phase of the study**

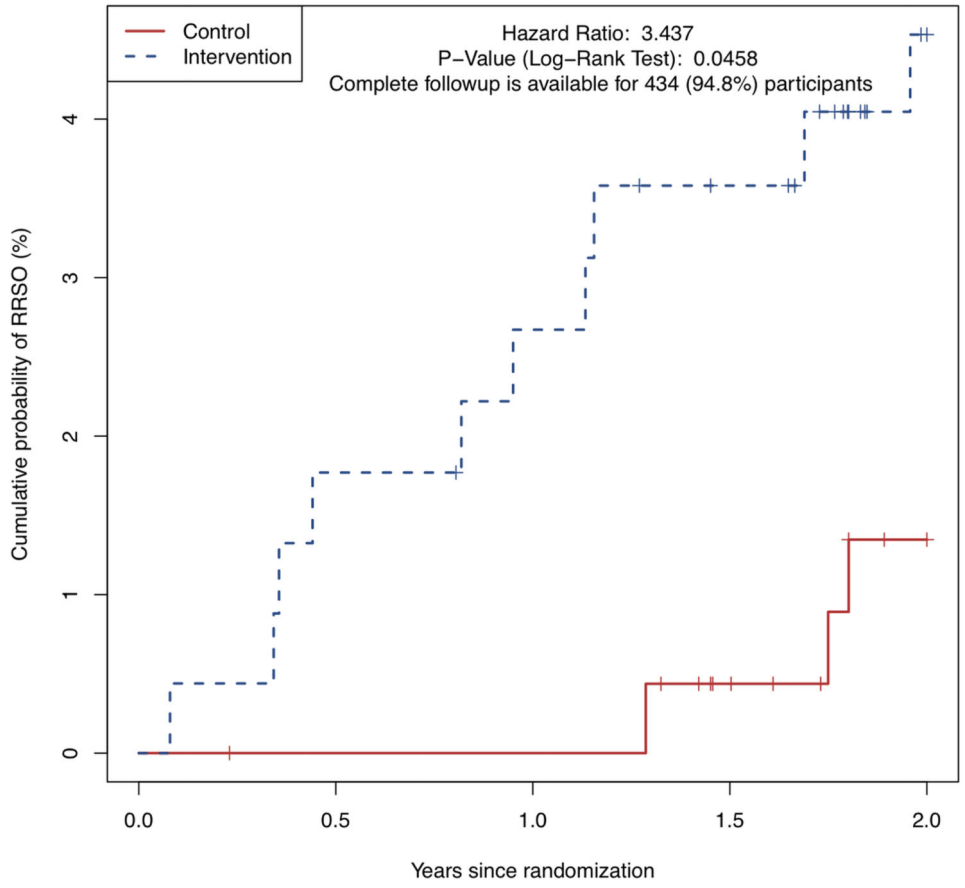


**Figure 2. Cumulative incidence curves illustrating time to prophylactic bilateral salpingo-oophorectomy from randomization by study arm**

## Table 1
### Baseline characteristics of trial participants by study arm

| Category | Variable / Value | Control Arm | Intervention Arm |
|---|---|---|---|
| Sample Size | | 230 | 228 |
| Age | Mean (SD) | 53 (10) | 54 (10) |
| Age (Categorical) | 35 ≤ age ≤ 44 | 43 (18.7%) | 43 (18.9%) |
| | 45 ≤ age ≤ 54 | 109 (47.4%) | 86 (37.7%) |
| | 55 ≤ age ≤ 64 | 47 (20.4%) | 72 (31.6%) |
| | 65 ≤ age < 90 | 31 (13.5%) | 27 (11.8%) |
| BMI ($kg/m^2$) | Mean (SD) | 23 (5) | 23 (5) |
| Race * | Black or African American | 3 (1.3%) | 0 (0.0%) |
| | White or Caucasian | 163 (70.7%) | 152 (66.7%) |
| | Asian | 8 (3.5%) | 10 (4.4) |
| | Other | 2 (0.9%) | 1 (0.4%) |
| Ashkenazi Jewish Ethnicity * | Yes | 36 (15.7%) | 34 (14.9%) |
| | No | 157 (68.3%) | 153(67.1) |
| Education * | Some high school | 0 (0.0%) | 1 (0.4%) |
| | High school graduate or GED | 5 (2.2%) | 9 (3.9%) |
| | Some college or technical school | 45 (19.6%) | 37 (16.2%) |
| | Graduated college or beyond | 178 (77.4%) | 177 (77.6%) |
| Smoking | Prior Smoker | 66 (28.7%) | 79 (34.6%) |
| | Current Smoker | 12 (5.2%) | 9 (3.9%) |
| | Never Smoker | 152 (66.1%) | 140 (61.4%) |
| Hysterectomy * | Yes | 18 (7.9%) | 26 (11.4%) |
| | No | 210 (91.3%) | 198 (86.8%) |
| Tubal Ligation * | Yes | 24 (10.4%) | 29 (12.7%) |
| | No | 205 (89.1%) | 197 (86.4%) |
| Hormonal Contraception | Used for < 1 year | 26 (11.3%) | 24 (10.5%) |
| | Used for ≥ 1 year | 152 (66.1%) | 149 (65.4%) |
| | Never Used | 52 (22.6%) | 55 (24.1%) |
| Menopausal Hormone Therapy * | Used for < 1 year | 17 (7.4%) | 21 (9.2%) |
| | Used for ≥ 1 year | 34 (14.8%) | 35 (15.4%) |
| | Never Used | 154 (67.0%) | 150 (65.7%) |
| Parity | Nulliparous | 81 (35.2%) | 81 (35.5%) |
| | Parous | 149 (64.8%) | 147 (64.5%) |
| Mammogram (every two years) | Yes | 229 (99.6%) | 227 (99.6%) |
| | No | 1 (0.4%) | 1 (0.4%) |
| Ultrasound of Ovaries * (every two years) | Yes | 74 (32.2%) | 90 (39.5%) |
| | No | 146 (63.5%) | 133 (58.3%) |
| Prior Genetic Testing * | Yes | 37 (16.1%) | 31 (13.6%) |

| Category | Variable / Value | Control Arm | Intervention Arm |
|---|---|---|---|
| | No | 192 (83.5%) | 195 (85.5%) |
| *BRCA1/2* Mutation * | Yes | 2 (0.9%) | 2 (0.9%) |
| | No | 3 (1.3%) | 0 (0.0%) |
| | Unknown | 32 (13.9%) | 29 (12.7) |
| Mutations in First and Second-Degree Relatives * | *BRCA1/2* | 10 (4.3%) | 4 (1.8%) |
| | Deleterious Mutation | 5 (2.2%) | 3 (1.3%) |
| | Variant of Unknown Significance | 5 (2.2%) | 1 (0.4%) |
| | Unknown | 210 (91.3%) | 211 (92.5%) |
| Personal History of Cancer * | Breast Cancer | 58 (25.2%) | 65 (28.5%) |
| | Other Cancer | 27 (11.7%) | 23 (10.1%) |
| | Breast and Other Cancer | 7 (3.0%) | 6 (2.6%) |
| | None | 138 (60.0%) | 134 (58.8%) |
| No. of Relatives with Ovarian Cancer ** | 0 | 179 (77.8%) | 183 (80.7%) |
| | 1 | 42 (18.3%) | 37 (16.2%) |
| | 2 | 7 (3.0%) | 5 (2.2%) |
| | 3+ | 2 (0.9%) | 2 (0.9%) |
| No. of Female Relatives with Breast Cancer ** | 0 | 28 (12.2%) | 29 (12.7%) |
| | 1 | 98 (42.6%) | 96 (42.1%) |
| | 2 | 60 (26.1%) | 59 (25.9%) |
| | 3+ | 44 (19.1%) | 44 (19.3%) |

* Numbers do not add to study arm total due to missing data

** Counts include first and second-degree relatives

**Table 2**

**Bilateral Salpingo-Oophorectomy (BSO) procedures performed during the study period**

| Age at time of BSO procedure (years) | Genetic testing result | Months from enrollment to BSO procedure | Uterus removed at time of BSO | Indication for BSO based on medical record review | Personal and family cancer history in women electing RRSO without documented mutation* |
|---|---|---|---|---|---|
| **RRSO procedures** | | | | | |
| **Control Arm (n=3)** | | | | | |
| 45-54 | mBRCA2 | 21 | No | EOC prevention | |
| 55-64 | negative | 16 | Yes | EOC prevention | PHx BrCA: 2nd degree relative- BrCA and EOC |
| 55-64 | not tested | 22 | Yes | EOC prevention | PHx PreM BrCA; 2nd degree relative - BrCA |
| **Intervention Arm (n=10)** | | | | | |
| 55-64 | mBRCA1 | 4 | Yes | EOC prevention | |
| 55-64 | mBRCA2 | 10 | Yes | EOC prevention | |
| 45-54 | mBRCA2 | 14 | Yes | EOC prevention | |
| 65-74 | mMLH1 | 5 | Yes | EOC prevention | |
| 35-44 | mBRCA2 | 1 | Yes | EOC prevention | |
| 45-54 | negative | 21 | No | EOC prevention** | PHx PreM BrCA; three 1st degree relatives diagnosed with unspecified cancers |
| 45-54 | negative | 14 | No | EOC prevention | PHx PreM BrCA; 1st degree relative- BrCA, Ashkenazi Jewish ancestry |
| 55-64 | negative | 12 | No | EOC prevention | PHx PreM BrCA; two 2nd degree relatives- BrCA; 2nd degree relative- EOC |
| 55-64 | not tested | 4 | No | EOC prevention | PHx PreM BrCA; 1st degree relative and two 2nd degree relatives BrCA; 2n degree relative- EOC |
| 55-64 | not tested | 24 | Yes | EOC prevention** | PHx Other Cancer; 1st degree relative- BrCa and EOC |
| **Other indications for BSO** | | | | | |
| **Control Arm (n=2)** | | | | | |
| 45-54 | Variant of uncertain significance | 3 | No | Breast cancer treatment | |
| 65-74 | not tested | 16 | No | Suspected ovarian cancer | |
| **Intervention Arm (n=3)** | | | | | |
| 45-54 | negative | 15 | Yes | Breast cancer treatment | |
| 65-74 | negative | 18 | Yes | Suspected ovarian cancer | |
| 45-54 | negative | 10 | Yes | Endometrial cancer | |

* pHx=personal history, BrCA=breast cancer diagnosis, PreM=pre-menopausal, EOC=epithelial ovarian cancer

** BSO was performed opportunistically during pelvic surgery for a benign condition