Variation in Rates of Uptake of Preventive Options in BRCA1 and BRCA2 Mutation Carriers Across Canada

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Abstract:

Background: Women with a BRCA1 or BRCA2 mutation have several options available for cancer prevention, including prophylactic surgery, chemoprevention, and screening. In this study, we report on actual preventive practices in women with and without breast cancer, and we examine differences according to geographic area within Canada and ethnicity.

Methods: Canadian women with a BRCA1 or BRCA2 mutation were followed after genetic testing and questioned regarding preventive practices. Women reported on uptake of prophylactic mastectomy, prophylactic oophorectomy, tamoxifen/raloxifene usage, and screening practices. Analyses of uptake were done for all of the options. A sub-analysis was done according to geographic area within Canada where genetic testing was provided.

Results: 675 women were included in the study. Follow-up questionnaires were completed after a mean of 4.0 years (range 1.6 – 8.9 years). Of the 344 women without breast cancer, 72 (21%) had a prophylactic bilateral mastectomy. 365 women (54%) had a bilateral prophylactic oophorectomy. Seventeen women (6%) took tamoxifen and twelve women (4%) reported taking raloxifene. For the women without breast cancer, 46% of the women had not undertaken any cancer prevention option (mastectomy, oophorectomy, or tamoxifen/raloxifene). Thirty-nine percent of women from Ontario and 34% of women from Western Canada had not elected for any preventive option. Sixty-two percent of women from Quebec had not undertaken any preventive procedure. Conclusion: Significant differences in uptake of preventive options by women with a BRCA1 or BRCA2 mutation were observed within Canada. Future research should be help to explain why these differences exist.

Introduction

Women with a BRCA1 or BRCA2 mutation have a lifetime risk of developing breast cancer between 45% and 87% (1, 2)). By identifying women at high-risk of developing cancer and adopting appropriate intervention strategies, it is anticipated that cases of cancer will be prevented. Ultimately, the value of genetic testing for BRCA1 and BRCA2 depends on the uptake of effective cancer prevention options. There are several preventive options available, with varying levels of effectiveness. Prophylactic mastectomy offers the greatest reduction in breast cancer risk (approximately 95%) (3) . Prophylactic oophorectomy prior to the age of 40 in women with a BRCA1 or BRCA2 mutation is associated with a 50% risk reduction of breast cancer (4). Tamoxifen has been shown to reduce breast cancer risk by 50% in women at high-risk of developing breast cancer (5). The evidence in favor of tamoxifen for primary prevention in BRCA1/2 carriers is based on the prevention of contralateral breast cancer (6).

Previous research that has examined uptake rates of various preventive options among BRCA1 and BRCA2 carriers is limited. However there are suggestions that the uptake of preventive procedures differs significantly according to country (7-11). Differences in uptake rates are likely due to many factors, including patient preferences, physician preferences, and access to care. In this study, we present data on a Canadian cohort of BRCA1 and BRCA2 carriers who were followed systematically from the time of genetic testing. We report on preventive practices in women with and without breast cancer, and examine differences in uptake rates according to geographic area within Canada and/or ethnicity of the population studied.

**Methods**

# Study Population

Eligible subjects were drawn from a database of carriers of deleterious mutations in either the BRCA1 or the BRCA2 gene. These women have been assessed for genetic risk at twelve centers across Canada and were found to carry a BRCA1 or BRCA2 mutation. All study subjects provided written informed consent for genetic testing. The study has been approved by the ethics committees of all participating centres. In most cases, testing was offered initially to women who were affected either by breast or ovarian cancer. When a mutation in either the BRCA1 or BRCA2 gene was found in a proband or in her relative, testing was offered to other at-risk women in her family. However, in some cases (fewer than 10% of total) an affected woman in the family was not available for study and an unaffected woman was the first member of the family to be tested. Mutation detection was performed using a range of techniques, but in all nucleotide sequences were confirmed with direct sequencing of genomic DNA. A woman was eligible for the study when the molecular analysis established that she was a mutation carrier. We studied both unaffected and affected women with breast cancer.

Subjects were eligible for this study if they were a resident of Canada and received genetic testing at a Canadian genetics center, were known to be a BRCA1 or BRCA2 mutation carrier, were between 25 and 80 years old, and had no previous history of cancer, other than breast cancer. Subjects who were diagnosed with breast cancer during the follow-up period were excluded. Subjects had at least 18 months of follow-up after genetic testing and were alive at the date of follow-up.

Women were grouped according to geographic area. Women who received genetic testing at the BC Cancer Agency (Vancouver) (n=67), in Edmonton (n=20), in Saskatoon (n=8), and in Winnipeg (n=15) were classified as from Western Canada. Women from Ontario received genetic testing and counseling either at Sunnybrook Health Sciences Centre (n=40), Women’s College Hospital (Toronto) (n=139), the Toronto General Hospital (n=50), the London Regional Cancer Centre (n=56), or the Hamilton Regional Cancer Centre (n=30). Women from Quebec received genetic testing and counseling at Hotel-Dieu Hospital (Montreal) (n=165), or the Montreal General Hospital (Montreal) (n=82). Three women from Halifax were included in the overall analysis, but were not included in the geographic sub-analysis (due to the small number). Subjects were divided by ethnicity into Jewish, French Canadian, and other.

# Procedures

All subjects completed a baseline questionnaire at the time of genetic testing, which assessed cancer history, and past use of cancer prevention options and screening tests. Follow-up questionnaires were administered by telephone or by mail. Questions assessed uptake of cancer preventive options, including prophylactic surgery (mastectomy or oophorectomy), chemoprevention (tamoxifen/raloxifene), and/or breast MRI.

Statistical Analysis

Chi-square test was used to compare frequencies of categorical variables, such as different preventive options among regions, and ANOVA was used to compare the mean values of continuous variables among different regions. All Statistical tests were done by statistical software SAS version 9.1.3, SAS Institute, Inc., Cary, NC, USA.

**Results**

1054 women with a BRCA1 or BRCA2 mutation were identified for this study. Of these, 328 women were ineligible (12 women were less than 25 years, 10 women were greater than 80 years, 105 women were deceased at follow-up, 111 women had ovarian cancer, 15 women were followed for less than 18 months, 52 women were diagnosed with breast cancer during the follow-up period, and 23 women resided outside of Canada); 29 women refused to complete the follow-up questionnaire; and 22 women were lost to follow-up. 675 women were included in the study. Follow-up questionnaires were completed a mean of 4.0 years after genetic testing (range 1.6 – 8.9 years). 110 women received genetic testing and counseling in Western Canada (from four centres), 315 women in Ontario (from five centres), 247 women in Quebec (from two centres) and three from Halifax. 331 women (49%) had a previous diagnosis of breast cancer and 334 (51%) women had no previous breast cancer. Characteristics of the subjects are presented in Table 1. The mean age of the subjects at time of genetic testing was 47 years (range 25 to 79 years) and the mean age at follow-up was 51 years (range 28-82 years). There were no statistical differences in mean ages at time of genetic testing according to geographic area (p=0.39), but there were differences in ethnicity (p<10-4) (Table 1).

***Prophylactic Mastectomy***

Of the 344 women without breast cancer, 72 (21%) had a prophylactic bilateral mastectomy (Table 2). The majority of these women (74%) had their surgery after receiving their genetic test result. The other nineteen women (26%) had prophylactic mastectomy prior to genetic testing, based on their family history alone. All 72 prophylactic mastectomies were performed before the age of 60 (range 26-58). Women from western Canada had the highest rate of prophylactic mastectomy (46%) compared to 22% of women from Ontario, and 8.4% of women from Quebec (Table 5). Across Canada, 8.7% of French Canadians had prophylactic mastectomy compared to 24.6% of Ashkenazi Jewish women and 26.9% of women of other ethnicities (Table 7).

## Prophylactic Oophorectomy

365 women (54%) had a bilateral prophylactic oophorectomy. 217 of these women (59%) had the surgery after receiving genetic test result (Table 3). We were not able to distinguish between oophorectomies that were done for cancer prophylaxis or for other reasons. More women with a history of breast cancer had a prophylactic oophorectomy (60%) than women without breast cancer (48%)(p=0.002). Women from western Canada were the most likely to have prophylactic oophorectomy (67%) followed by women from Ontario (61%) (Table 5). Women from Quebec were the least likely to have prophylactic oophorectomy (39%). Across Canada, 34% of French Canadians had prophylactic oophorectomy compared to 66% of Ashkenazi Jewish women and 63% of women of other ethnicities (Table 7).

***Tamoxifen/Raloxifene***

Tamoxifen and raloxifene usage was examined for women without breast cancer but with both breasts intact (ie. no prophylactic mastectomy). Seventeen women (6%) took tamoxifen and twelve women (4%) reported having taken raloxifene (Table 4). Women from Ontario were the most likely to take one of the two chemopreventive drugs (16%). Four percent of women from Quebec and 13% of women from Western Canada took one of the two drugs (Table 5). Across Canada, 3.2% of French Canadians took tamoxifen or raloxifene, compared to 16.3% of Ashkenazi Jewish women and 14.1% of women of other ethnicities (Table 7).

***No Preventive Option***

For the women without breast cancer, 46% of the women had chosen no cancer prevention option (mastectomy, oophorectomy, or tamoxifen/raloxifene). Thirty-nine percent of women from Ontario and 34% of women from Western Canada had not elected for any preventive option. Sixty-two percent of women from Quebec had not undertaken any preventive procedure.

***MRI and Mammography***

Of the 272 women without breast cancer and without prophylactic bilateral mastectomy, data were available on 241 women regarding MRI usage. One hundred and four women (43%) had had an MRI for screening for breast cancer. The majority of these women (96%) were below the age of 60. There were differences in uptake according to geographic region; 62% of women from Ontario (81 of 131 women) had had an MRI, compared to 14% of women from Quebec (15 of 109 women) and 27% of women from Western Canada (8 of 30 women) (Table 5). Within Quebec, there was a significant difference in uptake of MRI by ethnicity. In Quebec, French Canadian women were less likely to have had an MRI compared to women of other ethnicities (5.4% vs. 50.0%; p <10-4).

In contrast, the majority of women without breast cancer had mammography (96%). Most of these women (86%) began mammography screening prior to genetic testing, however, 14% of the women had their first mammogram after receiving the genetic test result. Uptake rates were similar according to geographic area. 99% of women from Ontario, 93% of women from western Canada, and 93% of women from Quebec reported undergoing mammography.

**Interpretation**

This is the first study to report on the rates of uptake of various cancer preventive options among Canadian women with a BRCA1 or BRCA2 mutation. Overall, the uptake rates of various preventive modalities were similar to those reported in other countries, however, there were dramatic differences across the country. Approximately two-thirds of women from Quebec had elected no preventive option, compared to approximately one-third of women from Western Canada and Ontario.

The greatest differences in uptake rates were observed with prophylactic mastectomy. Women from Western Canada had the highest uptake of prophylactic mastectomy (46%), followed by women from Ontario (22%), and Quebec (8%). These rates are comparable to those that have previously been reported(8) (9) (11) (12). Uptake of prophylactic mastectomy has ranged from 3% in the United States to 54% (11) in the Netherlands (9). We expect to see these numbers rise in with the increasing acceptance of subcutaneous mastectomy for prophylaxis (13).

We also observed pronounced differences in rates of uptake of prophylactic oophorectomy. Sixty-seven percent of women from Western Canada and 61% of women from Ontario had preventive oophorectomy. Again, fewer women from Quebec elected to have this preventive surgery (39%). Previous international research has also suggested that there are differences in uptake of prophylactic oophorectomy(8, 11, 14). Uptake of prophylactic oophorectomy in BRCA1 and BRCA2 mutation carriers has ranged from 13% in the United States (11) to 64% in the Netherlands (14).

The effectiveness of tamoxifen for primary prevention of breast cancer in BRCA1 carriers is not yet proven. However, tamoxifen has been shown to reduce the risk of contralateral breast cancer by 50% (6, 15). We previously surveyed women with a BRCA1 or BRCA2 mutation regarding tamoxifen usage (16). Only 12% of this sample had taken tamoxifen for breast cancer prevention, with the main reason for not taking the drug being fear of side-effects. Patient reluctance to take tamoxifen has also been documented in three major trials of tamoxifen as a chemopreventive agent (these women were on average at a much lower risk of developing breast caner than *BRCA* carriers). Each of these trials demonstrated a significant rate of attrition (5, 17, 18), which was, in part, attributable to patient reluctance to take tamoxifen. After the release of the NSABP1 Trial results (5) which demonstrated a significant breast cancer risk reduction associated with tamoxifen, high-risk women were offered tamoxifen for breast cancer prevention on a clinical basis. Port et al. described that there was still a reluctance to take tamoxifen for breast cancer prevention, despite the proven effectiveness of the drug (19). Recent data from the STAR trial also suggests that raloxifene is effective in preventing breast cancer in high-risk post-menopausal women and is associated with fewer side-effects. These new findings may lead to an increase in the uptake of chemoprevention in BRCA1 and BRCA2 carriers

The superiority of MRI over mammography in BRCA1 and BRCA2 mutation carriers in detecting small breast cancers is becoming evident (20-22). For many women, screening is more acceptable than either preventive surgery or chemoprevention. We anticipated that if women were not having prophylactic mastectomy that the rates of MRI usage would be high. In Ontario this was the case, with 72% of women without prophylactic mastectomy having MRI for screening. This rate was lower in Western Canada (27%), and in Quebec (16%). The women in Quebec had the lowest uptake of all of the preventive options, and also had the lowest uptake of MRI screening.

Our results, and those of others, suggest that there are wide variations in uptake of preventive options in BRCA1 and BRCA2 mutation carriers. It is not clear why, but differences may be due to various factors, including; 1) cultural differences influencing patient preferences; 2) health care professionals’ acceptance and recommendation of the procedures; and/or 3) access (including cost and availability). This question will be the subject of future research.

Our study subjects were women who have been found to carry a BRCA1 or BRCA2 mutation at one of 12 specialized genetic counseling centers across Canada between 1995 and 2003. Although ours is a relatively large sample (675 women), it may not be representative of all women who have received a positive genetic test result in Canada. Canadian women may have undergone genetic testing in centers other than the ones included here and we do not have any information on their cancer prevention. Furthermore, the patients were tested on average, seven years ago, and patterns of practice have evolved since 1999. We believe that genetic services are now better integrated with surgical care and that physician attitudes may have changed with regards to specific preventive measures. It is our intention to repeat this survey in five years time in order to evaluate trends in clinical practice.

Health care professionals’ acceptance and recommendations clearly influence uptake. There is evidence that physicians have differing opinions on the various preventive options available to women with a BRCA1 or BRCA2 mutation. In Maryland, USA, surgeons were surveyed about prophylactic mastectomy. A greater proportion of plastic surgeons (84.6%) than general surgeons (47.0%) or gynecologists (38.3%) agreed that bilateral prophylactic mastectomy has a role in the care of high-risk women (23). In France, only 11% of French physicians found it acceptable to propose prophylactic mastectomy to women with a *BRCA* mutation (24). Peshkin et al. (25) surveyed physicians regarding recommendations for tamoxifen for primary breast cancer prevention. The physicians were more likely to recommend tamoxifen to BRCA2 carriers (73%) than to BRCA1 carriers (57%) (p<0.0001). The authors concluded that physicians were not convinced of the benefits of tamoxifen in BRCA1 and BRCA2 mutation carriers. Although this research did not examine the uptake of the preventive options by women based on their physicians preference, it is expected that the physicians would influence patient choices.

Other authors have examined the differences in uptake of preventive options in various countries (26). Women from Canada (Quebec), France and Great Britain were surveyed about their medical decisions related to BRCA1 and BRCA2 mutation testing. Bouchard et al. found differences in the uptake of preventive procedures in three countries. They attributed these to cultural differences and to differences in the information that was provided during the counseling session. Differences in provider information may explain the differences that we observed across Canada. When we compared uptake of preventive options among French Canadians in different centres, we observed that uptake was associated more with centre where genetic testing was provided, and not on French ethnicity alone (Table 6).

Access to services may also contribute to the observed differences. This is a likely contributor for the difference in uptake of MRI across Canada. To date, screening MRI is offered on a research basis, and is not widely available as a clinical service. Women with access to the research studies are more likely to have MRI for screening. The differences in tamoxifen uptake may also be due to access issues, including cost. Currently, tamoxifen costs approximately twenty-five dollars per month. Some women may not have drug coverage and therefore may not be able to afford this drug.

The differences in surgical uptake are probably not due to differences in access issues across the country. Canadian women have coverage for prophylactic surgeries, including breast reconstruction, without cost. This would not be the case in the United States, and differences in uptake of preventive procedures have been attributed to financial constraints. Schwartz et al (27) attributed the low rate of prophylactic oophorectomy to constrained financial resources of the women in the study.

This research study is the first to describe the significant differences in uptake of preventive options by women with a BRCA1 or BRCA2 mutation who have received genetic testing in different areas of one country. The differences cannot be explained by differing health care systems because all of the women in this study have similar access to health care (with the exception of MRI) and therefore no woman would be denied any of the preventive procedures because of lack of health insurance (Canada has universal health care). We have speculated that the differences exist because of various reasons, including 1) cultural differences across Canada; 2) health care professionals’ acceptance and recommendation of the procedures; and/or 3) access (including cost and availability). In this study we could not ascertain the specific reason for the discrepancies across Canada, but future research will address this important question.

Table 1. Subject Characteristics by Geographic Region

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Characteristic | Ontario  N=315  # (%) | Quebec  N=247  #(%) | Western Canada  N=110  #(%) | All  N=675  #(%) | P-valuea |
| Mutation  BRCA1  BRCA2  BRCA1+2 | 190(60.3)  123(39.1)  2(0.6) | 132(53.4)  110(44.5)  5(2.0) | 70(63.6)  40(36.4)  0(0.0) | 384(58.4)  274(40.6)  7(1.0) | 0.12 |
| Mean Year of Birth  (range) | 1952.7  (1917-1976) | 1951.5  (1922-1972) | 1954.4  (1921-1976) | 1952.5  (1917-1976) | 0.08 |
| Mean age at Genetic Testing  (range) | 47.0  (25-79) | 47.3  (25-77) | 45.6  (25-76) | 46.9  (25-79) | 0.39 |
| Mean age at Breast Cancer Diagnosis  (range) | 148(47.0)  42.4  (24-70) | 128(51.8)  42.3  (27-75) | 54(49.1)  42.3  (24-70) | 331(49.0)  42.41  (24-75) | 1.00 |
| Mean Year of Genetic Testing  (range) | 1999.7  (1995.5-2003.9) | 1998.8  (1994.9-2003.7) | 2000.0  (1995.3-2002.5) | 1999.4  (1994.9-2003.9) | <10-4 |
| Mean years of follow-up  (range) | 3.84  (1.59-8.95) | 4.20  (1.70-8.03) | 3.89  (1.57-8.86) | 3.97  (1.57-8.95) | 0.06 |
| Ethnicity  French Canadian  Jewish  Other | 32(10.2)  61(19.4)  222(70.5) | 184(74.5)  43(17.4)  20(8.1) | 5(4.6)  12(10.9)  93(84.6) | 221(32.7)  116(17.2)  338(50.1) | <10-4 |

a ANOVA for differences in mean values between the three regions; chi-square test for the differences in frequency distributions of the three regions

Table 2. Prophylactic Mastectomy For Women Without Breast Cancer

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Age (Years) | Number (%) | No Prophylactic Mastectomy | Prophylactic Mastectomy | Prophylactic Mastectomy Timing | |
| Before Genetic Testing | After Genetic Testing |
| 25 to 35  36 to 60  61 to 70  >70 | 67(19.5)  246(71.5)  18(5.2)  13(3.8) | 51  190  18  13 | 16(23.9)  56(22.8)  0  0 | 3  16  0  0 | 13  40  0  0 |
| Total | 344(100.0) | 272(79.1) | 72(20.9) | 19(5.5) | 53(15.4) |

Table 3. Prophylactic Oophorectomy by Breast Cancer Status

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Age (years) | Number  (%) | No Prophylactic Oophorectomy | Prophylactic Oophorectomy  (%) | Prophylactic Oophorectomy Timing | |
| Before Genetic Testing | After Genetic Testing |
| All Women 25 to 35  36 to 40  41 to 60  61 to 70  >70 | 83(12.3)  127(18.8)  377(55.9)  56(8.3)  32(4.7) | 64  70  136  23  17 | 19(22.9)  57(44.9)  241(63.9)  33(58.9)  15(46.9) | 2  12  95  26  13 | 17  25  146  7  2 |
| Total | 675  (100.0) | 310  (45.9) | 365  (54.1) | 148  (21.9) | 217  (32.2) |
| No BreastCancer 25 to 35  36 to 40  41 to 60  61 to 70  >70 | 67(19.5)  80(23.3)  166(48.3)  18(5.2)  13(3.8) | 53  47  62  5  10 | 14(20.9)  33(41.3)  104(62.7)  13(72.2)  3(23.1) | 2  6  40  10  2 | 12  27  64  3  1 |
| Total | 344  (100.0) | 177  (51.5) | 167  (48.6) | 60  (17.4) | 107  (31.1) |
| BreastCancer 25 to 35  36 to 40  41 to 60  61 to 70  >70 | 16(4.8)  47(14.2)  211(63.8)  38(11.5)  19(5.3) | 11  23  74  18  7 | 5(31.5)  24(51.1)  137(64.9)  20(52.6)  12(63.2) | 0  6  55  16  11 | 5  18  82  4  1 |
| Total | 331  (100.0) | 133  (40.2) | 198  (59.8) | 88  (26.6) | 110  (33.3) |

Table 4. Tamoxifen and Raloxifene

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Age | Number  (%) | No Chemopreventive Drug | Tamoxifen | Raloxifene | Either Tamoxifen or Raloxifene |
| 25 to 35  36 to 60  61 to 70  >70 | 51(18.7)  190(69.9)  18(6.6)  13(4.8) | 51  166  13  13 | 0  14(7.4)  3(16.7)  0 | 0  10(5.3)  2(11.1)  0 | 0  24(12.6)  5(2.8)  0 |
| Total | 272(100.0) | 236(89.3) | 17(6.3) | 12(4.4) | 29(10.7) |

Table 5. Preventive Option by Geographic Area

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Western Canada | Ontario | Quebec | P-value |
| Prophylactic Mastectomy1  N=342 | 26(46.4%) | 36(21.6%) | 10(8.4%) | 8.3x10-9 |
| Prophylactic  Oophorectomy2  N=672 | 74(67.3%) | 193(61.3%) | 96(38.9%) | 1.0x10-9 |
| Tamoxifen or Raloxifene3  N=270 | 4(13.3%) | 21(16.0%) | 4(3.7) | 0.008 |
| MRI3  N=270  No  Yes  Miss | 22(73.3)  8(26.7)  0(0.0%) | 32(24.4%)  81(61.8%)  18(13.7%) | 81(74.3%)  15(13.8%)  13(11.9%) | <10-10\* |

1: For subjects without breast cancer;

2: For all subjects in the 3 regions;

3: For subjects with no prophylactic mastectomy and no breast cancer ;

\*: missing data not included in the test;

Table 6. Preventive Option by ethnicity

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | French Canadian  (Hotel-Dieu) | Other French Canadian | Other Ethnicities | P-value |
| Prophylactic Mastectomy1  N=344 | 1 (1.3%) | 8(27.6%) | 63(26.3%) | 2x10-6 |
| Prophylactic Oophorectomy2  N=675 | 38(23.6%) | 38(63.3%) | 289(63.7%) | <10-10 |
| Tamoxifen or Raloxifene3  N=272 | 2(2.7%) | 1(4.8%) | 26(14.7%) | 0.01 |
| MRI3  N=272  No  Yes  Miss | 67(90.5)  1(1.4)  6(8.1%) | 6(28.6%)  10(47.6%)  5(23.8%) | 64(36.2%)  93(52.5%)  20(11.3%) | <10-10\* |

1: For subjects without breast cancer;

2: For all subjects;

3: For subjects with no prophylactic mastectomy and no breast cancer;

\*: Missing data not included in the test;

Table 7. Preventive Option by ethnicity

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | French Canadian | Jewish | Other | P-value |
| Prophylactic Mastectomy1  N=344 | 9 (8.7%) | 16(24.6%) | 47(26.9%) | 0.001 |
| Prophylactic Oophorectomy2  N=675 | 76(34.4%) | 76(65.5%) | 213(63.0%) | <10-10 |
| Tamoxifen or Raloxifene3  N=272 | 3(3.2%) | 8(16.3%) | 18(14.1%) | 0.01 |
| MRI3  N=272  No  Yes  Miss | 73(76.8%)  11(11.6%)  11(11.6%) | 12(24.5%)  30(61.2%)  7(14.3%) | 52(40.6%)  63(49.2%)  13(10.2%) | <10-10\* |

1: For subjects without breast cancer;

2: For all subjects;

3: For subjects with no prophylactic mastectomy and no breast cancer;

\*: Missing data not included in the test;

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