No evidence of excessive cancer screening in female noncarriers from BRCA1/2 mutation—positive families

S. Guedaoura PhD,†‡ S. Pelletier MSP,† W.D. Foulkes MD PhD,‡§ P. Hamet MD PhD,‖# J. Simard PhD,‡‡ N. Wong MSC,§ Z. El Haffaf MD,‖** J. Chiquette MD,†††† and M. Dorval PhD†††

ABSTRACT

Background  In families with a proven BRCA1/2 mutation, women not carrying the familial mutation should follow the cancer screening recommendations applying to women in the general population. In the present study, we evaluated the cancer screening practices of unaffected noncarriers from families with a proven BRCA mutation, and we assessed the role of family history in their screening practices.

Methods  Self-report data were provided retrospectively by 220 unaffected female noncarriers for periods of up to 10 years (mean: 4.3 years) since disclosure of their BRCA1/2 genetic test result. A ratio for the annual frequency of breast and ovarian cancer screening exams (mammography, breast ultrasonography, breast magnetic resonance imaging, transvaginal or pelvic ultrasound, cancer antigen 125 testing) was calculated as number of screening exams divided by the number of years in the individual observation period.

Results  The annual average for mammography exams was 0.15, 0.4, 0.56, and 0.71 in women 30–39, 40–49, 50–59, and 60–69 years of age respectively. The uptake of other breast and ovarian cancer screening exams was very low. Mammography and breast ultrasonography and magnetic resonance imaging were generally more frequent among participants with at least 1 first-degree relative affected by breast cancer.

Conclusions  In most noncarriers, screening practices are consistent with the guidelines concerning women in the general population. When noncarriers adopt screening behaviours that are different from those that would be expected for average-risk women, those behaviours are influenced by their familial cancer history.

Impact  Decision tools might help female noncarriers to be involved in their follow-up in accordance with their genetic status and their family history, while taking into account the benefits and disadvantages of cancer screening.

Key Words  BRCA genes, true noncarriers, cancer screening practices, familial cancer history, cohort studies

INTRODUCTION

In families with a proven BRCA1/2 mutation, most women who do not carry the familial mutation (“true negatives”) can be reassured that they are no longer considered at high risk for breast and ovarian cancer1–5. For that reason, such women should be encouraged to adopt the cancer screening practices recommended for women of their age in the general population1–5. In Canada, each province operates an organized breast screening program with its own guidelines6. At the time of the present study, the Quebec Breast Cancer Screening Program recommended that women 50–69 years of age undergo breast screening mammography every 2 years7.

Nevertheless, some controversy still surrounds the magnitude of the residual cancer risk in noncarriers based on risk factors other than BRCA1 and BRCA2 mutations—especially a significant familial cancer history, which is considered to be among the most important risk factors for breast and ovarian cancer1–12. Some studies have postulated a higher risk for noncarriers than for similarly-aged women in the general population. A modest
elevation, doubling the risk, in true-negative family members in BRCA-positive families cannot be excluded\textsuperscript{2,4,13}. Being neither massive nor trivial, such an elevation can be cause for caution with respect to the optimistic claim that noncarriers sustain no clinically relevant excess risk burden. Some authors have therefore suggested that noncarriers from BRCA-positive families should consider continued screening\textsuperscript{14–19}.

Information about cancer screening practices among noncarriers from BRCA1/2 mutation-positive families is limited and inconsistent; whether those women follow general population guidelines for cancer screening is still uncertain. Recent studies reported that some noncarriers “overuse” breast and ovarian cancer screening after genetic testing\textsuperscript{20–24}; others reported fewer screening practices\textsuperscript{25–27}. Familial cancer history has been suggested as a major factor that could influence use of cancer screening in this population\textsuperscript{21–24}, but to our knowledge, no study has yet evaluated that hypothesis in real-world conditions. The objectives of the present study were therefore twofold:

- Describe the breast and ovarian cancer screening practices of noncarriers from BRCA1/2 mutation-positive families.
- Assess the role of family history in the cancer screening practices of noncarriers from BRCA1/2 mutation-positive families.

**METHODS**

**Participants**

Participants were recruited from four cancer genetics clinics in the province of Quebec, in Montreal (\(n = 3\)) and Quebec City (\(n = 1\)). Eligible participants were female noncarriers from BRCA1/2 mutation-positive families tested in the clinics who received their genetic test result between 1 January 2002 and 31 December 2011, and who had not to that point been affected by breast or ovarian cancer. Women who were more than 75 years of age at recruitment or more than 70 years of age at disclosure of their test result were ineligible. The study was approved by the institutional ethics review boards of the participating institutions, and all participants signed an informed consent form.

**Data Collection**

In this cross-sectional study, participants were asked to report their yearly uptake of all screening examinations for breast cancer [mammography, breast ultrasonography, breast magnetic resonance imaging (MRI)] and ovarian cancer [pelvic or transvaginal ultrasonography, test for serum cancer antigen 125 (CA125)] from the disclosure of their BRCA1/2 test result to 31 December 2012. The period for which participants reported data was therefore different for each individual. That period was called the “individual observation period.” The data for that period were retrospectively collected using a self-administered questionnaire (“screening history diary”) developed specifically for the study.

Based on the event history calendar approach\textsuperscript{28}, the diary included a timeline grid into which participants were encouraged to write significant personal life events that occurred during their individual observation period and that they could later use as cues to help them recall their breast and ovarian examinations. The participants received a suggestion that they use the timeline as a reference when recording, on similarly designed grids (one for each type of examination), the breast and ovarian examinations that they received during their individual observation period. Precise instructions and separate sections were provided to favour the most accurate possible distinction between screening exams and exams scheduled for diagnosis purposes. The diary was extensively pretested before use in the study. Telephone support from research personnel was available for participants needing help to complete the questionnaire.

Familial cancer history was collected about breast and ovarian cancers in first- and second-degree relatives, on both the maternal and the paternal sides. Cancer risk perception was separately assessed for breast and ovarian cancers using one item (“How would you rate your chance of developing breast [ovarian] cancer?”) rated on a 5-point scale ranging from 1 (“very low”) to 5 (“very high”).\textsuperscript{29} The response options “very low,” “moderately low,” and “neither high nor low” were grouped and designated as “low–moderate cancer-risk perception”; “moderately high” and “very high” were grouped and designated as “high cancer-risk perception.”

**Analyses**

The breast and ovarian cancer screening practices since genetic testing are described on an annual basis, by age stratum (<30 years, 30–39 years, 40–49 years, 50–59 years, 60–69 years). The annual screening frequency for each screening examination was calculated as a ratio: number of screening exams divided by the number of years in the individual observation period. For example, a participant who had 3 mammography exams during a 6-year observation period would have a ratio of 0.5—that is, an average of 1 mammography exam every 2 years. A ratio of 0.67 would represent an average of 2 mammography exams over a period of 3 years. Undergoing mammography at less than 40 years of age or more than once every 2 years, and any use of breast ultrasonography, MRI, transvaginal ultrasonography, or CA125 testing were defined as an “excessive” screening practice compared with the Canadian cancer screening recommendations for women in the general population\textsuperscript{30,31}.

Associations of cancer screening practices with the variables of interest were analyzed using univariate (chi-square or Fisher exact test) and multivariate models (binary or polytomous logistic regression), overall and by age stratum. Odds ratios (ORs) with their 95% confidence intervals (CIs) were used to report the associations. Explicative variables considered included family history of breast and ovarian cancer in first-degree relatives (\(\geq 1\) vs. 0), education level (with vs. without college degree), follow-up by a family doctor or a gynecologist (yes vs. no), mutation status (BRCA1 vs. BRCA2), and cancer risk perception (high vs. low–moderate). Two potentially confounding and modifying variables were also considered in the multivariate models: length of the individual observation period (1–2 years, 3–4 years, or \(\geq 5\) years), and the cancer
genetics clinic at which the participant was tested (Centre hospitalier universitaire de Québec, Hôpital du Saint-Sacrement; Centre hospitalier de l’université de Montréal, Hôtel-Dieu de Montréal; Sir Mortimer B. Davis Jewish General Hospital; McGill University Health Centre, Montreal General Hospital). The potential confounding effects of those variables were assessed by comparing the crude and adjusted models. In the study, the proportion of missing values was less than 10% for all explicative variables considered in the models. To take into account the potential effect of missing values, sensitivity analyses were performed with and without the missing values; the results were not materially affected. The results reported here are based on a pairwise deletion approach for treating missing values. All significance levels are two-sided ($p = 0.05$). Statistical analyses were performed using the SAS software application (version 9.4: SAS Institute, Cary, NC, U.S.A.).

RESULTS

Of the 347 eligible women identified, 286 agreed to participate (82%), of whom 220 (63%) completed and returned their questionnaire (Table 1). Two thirds of participants had at least 2 first- or second-degree relatives affected by breast cancer, and almost half had a familial ovarian cancer history. Few ($n = 17$) had a familial history of ovarian cancer only. The participants belonged to families with BRCA1 or BRCA2 familial mutations in similar proportions.

Half the participants retrospectively provided information for a period of 5 years or more. Most received regular follow-up, either by a family doctor (91%) or a gynecologist (46%); 42% were followed by both. Only 4% of the women ($n = 9$) were not followed by any physician. Most participants (84%) reported that their doctors were aware of their genetic status. More than three quarters of the women perceived their breast cancer risk (79%) and ovarian cancer risk (76%) as low–moderate.

Overall, 65% of participants had undergone at least 1 screening mammography exam since receiving their genetic test result (Table i). Slightly more than one third of the participants had undergone more than 1 mammography exam every 2 years. Mammography use started from about the age of 30 and increased progressively by participant age (Table i). On average, respondents 50 years of age and older had undergone a mammography exam slightly more often than once every 2 years, with more than a quarter of that subpopulation undergoing mammography annually. However, 11% of participants in that age group had not undergone mammography since disclosure of their genetic screening test result. In women 40–49 years of age, 21% had undergone mammography once annually. One quarter of women 30–39 years of age had undergone mammography at least once since their genetic testing, and 10% had undergone mammography once annually.

The uptake of the other breast and ovarian cancer screening exams was very low. With respect to breast cancer screening exams, participants 40–49 years of age were the ones who most frequently attended breast ultrasonography exams (19%); those 30–39 years of age were the ones who most frequently attended breast MRI exams (12%). With respect to ovarian cancer screening, little variation in

| TABLE I | Selected characteristics of the study participants |
|----------|---------------------------------------------|
| **Characteristic** | **Value** |
| Patients ($n$) | 220 |
| Mean age (years) | 44.9±12.2 |
| Age group at disclosure [$n$ (%)] | |
| <30 Years | 28 (13) |
| 30–39 Years | 46 (21) |
| 40–49 Years | 57 (26) |
| 50–59 Years | 58 (26) |
| 60–69 Years | 31 (14) |
| Education [$n$ (%)] | |
| Without university degree | 108 (49) |
| With university degree | 112 (51) |
| Genetics clinic [$n$ (%)] | |
| CHU de Québec, Hôpital du Saint-Sacrement | 36 (16) |
| CHUM, Hôtel-Dieu de Montréal | 71 (32) |
| Sir Mortimer B. Davis Jewish General Hospital | 72 (33) |
| MUHC, Montreal General Hospital | 41 (19) |
| Breast cancer history [$n$ (%)] | |
| First-degree relatives | | |
| 0 | 88 (40) |
| 1 | 74 (34) |
| $\geq$2 | 58 (26) |
| First- or second-degree relatives | | |
| 0 | 28 (13) |
| 1 | 46 (21) |
| $\geq$2 | 146 (66) |
| Ovarian cancer history [$n$ (%)] | |
| First-degree relatives | | |
| 0 | 167 (76) |
| $\geq$1 | 53 (24) |
| First- or second-degree relatives | | |
| 0 | 121 (55) |
| $\geq$1 | 99 (45) |
| BRCA mutations statusa [$n$ (%)] | |
| BRCA1 | 114 (52) |
| BRCA2 | 106 (48) |
| Individual observation period | |
| Duration group [$n$ (%)] | |
| 1–2 Years | 60 (27) |
| 3–4 Years | 52 (24) |
| $\geq$5 Years | 108 (49) |
| Mean duration (years) | 4.9±2.7 |

a Two participants from families positive for BRCA1 and BRCA2 mutations.

CHU/M = Centre hospitalier de l’Université (de Montréal); MUHC = McGill University Health Centre.
uptake was observed from about the age of 30 for pelvic or transvaginal ultrasonography and from about the age of 40 for CA125 testing. Younger participants underwent very few screening exams.

The use of mammography, breast ultrasonography, and MRI was generally more frequent among respondents with at least 1 first-degree relative affected by breast cancer than among those without such a relative (Table III). The use of pelvic or transvaginal ultrasonography and CA125 testing was also more frequent among women who had at least 1 first-degree relative affected by ovarian cancer than among those without such a relative.

In participants 40–49 years, undergoing mammography more often than once every 2 years was more frequent among women reporting a high cancer risk perception than among those reporting a low–moderate cancer risk perception for breast cancer development (63% vs. 26%; or: 12.0; 95% CI: 1 to 148.1). In addition, slightly more ovarian cancer screening exams were attended by noncarriers from BRCA1 mutation-positive families (18% and 12% respectively for pelvic or transvaginal ultrasonography and CA125 testing) than by noncarriers from BRCA2 mutation-positive families (15% and 8% respectively); however, those differences were not statistically significant.

### DISCUSSION AND CONCLUSIONS

The present study is the first to describe actual breast and ovarian cancer screening behaviours among BRCA1/2 mutation-negative women in real-world conditions and over a lengthy period (self-reported data could be provided for periods up to 10 years). On the whole, the findings do not show as many “excessive” practices as reported in previous studies, most of which were carried out among research cohorts. Screening practices by our participants were, for the most part, consistent with the guidelines established for women in the general population. Breast cancer screening consisted primarily of mammography, and it targeted women from about the age of 40, and mostly those 50 years of age and older. Moreover, when participants used screening exams not recommended for women in the general population or at frequencies higher than advisable, those practices were, in most cases, related to a family history of breast or ovarian cancer.

### TABLE II

| Screening practice and frequency | Age group |
|--------------------------------|-----------|
|                                | 18–29 Years (n=28) | 30–39 Years (n=58) | 40–49 Years (n=78) | 50–59 Years (n=84) | 60–69 Years (n=51) | Overall (n=220) |
| Mean study length per woman (years) | 3.3±2.1 | 3.5±1.9 | 3.9±2.2 | 3.9±2.2 | 3.9±2.1 | 4.9±2.7 |

### Breast cancer screening

| Mammmography frequency [n (%)] | 18–29 Years (n=28) | 30–39 Years (n=58) | 40–49 Years (n=78) | 50–59 Years (n=84) | 60–69 Years (n=51) | Overall (n=220) |
|-------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|
| Never                         | 28 (100)          | 43 (74.1)         | 30 (38.5)         | 14 (16.7)         | 1 (2)             | 76 (34.5)       |
| Less than once every 2 years  | 0 (0)             | 6 (10.3)          | 16 (20.5)         | 14 (16.7)         | 7 (13.7)          | 41 (18.6)       |
| Once every 2 years            | 0 (0)             | 2 (3.5)           | 8 (10.3)          | 17 (20.2)         | 10 (19.6)         | 29 (13.2)       |
| More than once every 2 years  | 0 (0)             | 1 (1.7)           | 8 (10.3)          | 16 (19.1)         | 15 (29.4)         | 41 (18.6)       |
| Annual                        | 0 (0)             | 6 (10.3)          | 16 (20.5)         | 23 (27.4)         | 18 (35.3)         | 33 (15)         |
| Average annual exams          | 0±0               | 0.15±0.32         | 0.4±0.39          | 0.56±0.35         | 0.71±0.26         | 0.41±0.37       |

### Breast ultrasonography [n (%)]

| Breast ultrasonography [n (%)] | 18–29 Years (n=28) | 30–39 Years (n=58) | 40–49 Years (n=78) | 50–59 Years (n=84) | 60–69 Years (n=51) | Overall (n=220) |
|-------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|
| Never                         | 26 (92.9)         | 51 (87.9)         | 63 (80.8)         | 74 (88.1)         | 48 (94.1)         | 186 (84.5)      |
| At least once during observation period | 2 (7.1)         | 7 (12.1)          | 15 (19.2)         | 10 (11.9)         | 3 (5.9)           | 34 (15.5)       |
| Average annual exams          | 0.03±0.13         | 0.05±0.15         | 0.09±0.22         | 0.06±0.2          | 0.04±0.2          | 0.07±0.19       |

### Breast magnetic resonance imaging [n (%)]

| Breast magnetic resonance imaging [n (%)] | 18–29 Years (n=28) | 30–39 Years (n=58) | 40–49 Years (n=78) | 50–59 Years (n=84) | 60–69 Years (n=51) | Overall (n=220) |
|-------------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|
| Never                                     | 27 (96.4)         | 51 (87.9)         | 75 (96.2)         | 77 (91.7)         | 49 (96.1)         | 202 (91.8)      |
| At least once during observation period   | 1 (3.6)           | 7 (12.1)          | 3 (3.8)           | 7 (8.3)           | 2 (3.9)           | 18 (8.2)        |
| Average annual exams                      | 0.02±0.13         | 0.06±0.19         | 0.01±0.07         | 0.05±0.18         | 0.04±0.2          | 0.04±0.17       |

### Ovarian cancer screening

| Pelvic or transvaginal ultrasonography [n (%)] | 18–29 Years (n=28) | 30–39 Years (n=58) | 40–49 Years (n=78) | 50–59 Years (n=84) | 60–69 Years (n=51) | Overall (n=220) |
|-----------------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|
| Never                                         | 27 (96.4)         | 52 (89.7)         | 68 (87.2)         | 71 (84.5)         | 42 (82.4)         | 184 (83.6)      |
| At least once during observation period       | 1 (3.6)           | 6 (10.3)          | 10 (12.8)         | 13 (15.5)         | 9 (17.6)          | 36 (16.4)       |
| Average annual exams                          | 0.01±0.06         | 0.04±0.15         | 0.09±0.27         | 0.08±0.22         | 0.07±0.19         | 0.07±0.2        |

| Cancer antigen 125 [n (%)]                   | 18–29 Years (n=28) | 30–39 Years (n=58) | 40–49 Years (n=78) | 50–59 Years (n=84) | 60–69 Years (n=51) | Overall (n=220) |
|----------------------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-----------------|
| Never                                        | 28 (100)          | 57 (98.3)         | 68 (87.2)         | 74 (88.1)         | 44 (86.3)         | 198 (90)        |
| At least once during observation period      | 0 (0)             | 1 (1.7)           | 10 (12.8)         | 10 (11.9)         | 7 (13.7)          | 22 (10)         |
| Average annual exams                         | 0±0               | 0.02±0.13         | 0.07±0.23         | 0.08±0.25         | 0.07±0.2          | 0.06±0.2        |
A positive association between the use of more mammography than recommended and a family history of breast cancer in first-degree relatives was found in participants 30–39 years of age and 50–69 years of age. Those results accord with assumptions suggesting that screening behaviours by noncarriers can be strongly influenced by their family history of cancer. Although the mechanism by which family history influences screening behaviours in noncarriers remains unknown, those women—or their physicians—might have asked for or prescribed mammography earlier or more often than expected. Other factors such as cancer risk perception might play a role in the effect of family history on screening practices. Indeed, some authors suggest that an overestimation of cancer risk, increased pessimism, and feelings of self-vulnerability can be involved in the decision made by noncarriers less than 40 years of age to ask for more screening measures.

It remains difficult to make any statement about the screening behaviours of participants 40–49 years of age. At the time during which the participants in the present study were surveyed, Canadian recommendations did not support the inclusion of mammography screening in, or its exclusion from, the periodic health examination for women 40–49 years of age. However, the last guidelines for Canada (published in 2011) recommend against routine breast screening for that age group. In other countries, and especially in the United States, current screening guidelines concerning women 40–49 years of age also lack clarity. Various organizations disagree about whether population-based mammography should begin at the age of 40 or 50 years, and controversies about the issue can be seen in both the medical literature and the mass media. According to the most recent U.S. recommendations applicable to women in the general population, mammography use before the age of 50 should be an individual decision that takes into account the patient's background and her values and preferences with respect to the advantages and drawbacks associated with the exam. However, in light of the novel finding of the younger age of proven noncarriers at diagnosis of breast cancer, some guidelines indicate that screening at 40 years of age rather than later could be warranted based on the statistically and clinically relevant risk in those women. Consequently, even though the findings in our study indicate that nearly 2 of 3 participants in their 40s underwent mammography every 2 years on average, that frequency cannot be considered "excessive," as reported by other studies carried out in women in that age group.

Furthermore, 11% of participants 50 years of age and older had undergone no mammography exams since the disclosure of their genetic test result. Given that about 80% of those women perceived their own risk of breast cancer to be low, they might have been falsely reassured by the result of their genetic test and could have become less vigilant about screening.

Very few studies have focused on the use of breast ultrasonography and MRI by BRCA1/2 mutation-negative women. The findings of the present study indicate that, compared with mammography, such exams are rarely used—which is not surprising, given they are not recommended for women in the general population. The use of those breast cancer screening measures by some participants is also associated with a family history

### TABLE III

| Screening practice | Breast cancer | First-degree family history | Ovarian cancer |
|-------------------|--------------|-----------------------------|---------------|
|                   | 0 Tests [n (%)] | ≥1 Test [n (%)] | ORa 95% CI | 0 Tests [n (%)] | ≥1 Test [n (%)] | ORa 95% CI |
| Mammography, 30–39 years (<1 since test result) | 2 (8) | 13 (38) | 5.4 | 1 to 28.2 | 13 (27) | 2 (22) | 0.8 | 0.1 to 4.3 |
| Mammography, 40–49 years (>1 since test result) | 8 (24) | 16 (36) | 2.6 | 0.9 to 8 | 19 (31) | 5 (31) | 1.1 | 0.3 to 4 |
| Mammography, 50–69 years (>1 every 2 years) | 12 (33) | 47 (60) | 5.8 | 1.4 to 25 | 41 (50) | 18 (55) | 1 | 0.3 to 3.6 |
| Breast ultrasonography (>1 since test result) | 6 (7) | 28 (21) | 4.1 | 1.3 to 12.6 | 24 (14) | 10 (19) | 1.4 | 0.6 to 3.1 |
| Breast magnetic resonance imaging (>1 since test result) | 1 (1) | 17 (13) | 12.6 | 1.1 to 146.6 | 14 (8) | 4 (8) | 0.9 | 0.3 to 2.8 |
| Pelvic or transvaginal ultrasonography (>1 since test result) | 9 (10) | 27 (20) | 2.3 | 1 to 5 | 20 (12) | 16 (30) | 2.9 | 1.1 to 7.5 |
| Cancer antigen 125 (>1 since test result) | 8 (9) | 14 (11) | 1.2 | 0.5 to 3 | 9 (5) | 13 (25) | 7.3 | 2.6 to 20.9 |

a Adjusted for length of individual observation period, recruitment setting, and age at genetic test result disclosure (years). OR = odds ratio; CI = confidence interval.
of breast cancer. Ovarian cancer screening is also not recommended for women in the general population\(^{56,57}\) because of the sparse evidence-based results about its efficacy and the high number of false-positive and false-negative results generated\(^{56,58}\). As expected, most participants did not undergo screening tests for ovarian cancer. Only a small proportion underwent pelvic or transvaginal ultrasonography and CA125 testing, and that at very low frequencies. Contrary to reports emerging from earlier studies\(^{22–24,55}\), no screening overuse is evident in the present study. Our findings also suggest that use of screening exams is highly related to a family history of ovarian cancer. Because \(BRCA1\) mutations confer a higher risk of ovarian cancer than \(BRCA2\) mutations do\(^{59,60}\), it might be expected that more ovarian cancer screening exams would be performed in noncarriers from \(BRCA1\) mutation–positive families, but that assumption was not confirmed.

For the present study, we considered selection, information, and confusion biases, which we tried, as far as possible, to alleviate. The participation rate (63%) is more than acceptable given the duration of the individual observation periods, which reached 10 years for some participants. As in other studies, the sample is rather well-educated, but the education level is probably quite representative of the female population attending cancer genetics clinics. Furthermore, the fact that this study was performed in the four main cancer genetics clinics in the province of Quebec might have fostered the representativeness of the sample.

Screening practices were assessed based on self-report data, which might be considered a limitation. Given the scope of this study, the use of administrative data was not the method of choice, because only mammography data would have been available for the entire study period\(^{61}\). Moreover, it was important to distinguish tests for screening purposes from tests for diagnostic purposes, which is challenging to accomplish using administrative data. We addressed that concern by developing the “screening history diary,” which provided the women with specific instructions to help them to classify screening and diagnostic exams with the most precision possible. Earlier studies did not make that distinction.

Based on the history calendar approach, the “screening history diary” also seeks to minimize recall difficulties by inciting participants to use flexible indicators responsive to their individual situation\(^{62}\). Nevertheless, self-report of cancer screening practices is not the most accurate way to determine cancer screening rates. Such reports are subject to memory bias, which generally overestimates exam frequency. That bias has been confirmed in a meta-analysis of thirty-seven studies\(^{63}\) and cross-confirmed in numerous other studies\(^{64–67}\), including even after \(BRCA1/2\) testing\(^{68}\). More recently, a Canadian Community Health Survey of Ontarians, pooling from 5 additional provincial-level health databases, found that the report-to-record ratio was persistently greater than 1, indicative of significant over-reporting\(^{69}\). Despite the fact that our data concerning the frequency of cancer screening are most likely overestimated, the yearly averages of screening exams as self-reported here remain within the expected screening boundaries for women in the general population, which is reassuring in the face of the potential for “excessive” cancer screening in female noncarriers from \(BRCA1/2\) mutation–positive families.

Finally, data were adjusted for a number of potentially confounding variables, but residual confounding remains possible.

In the absence of specific guidelines for breast and ovarian cancer screening for female noncarriers from \(BRCA1/2\) mutation–positive families, family history, single nucleotide polymorphisms, and other genetic variants could be used to better estimate risk and create tailored follow-up for these women. The potential for increased risk in some noncarriers makes it difficult to draw conclusions about possible “excessive” screening practices in this population group, because a higher test ratio could actually be the expression of the need for some women to be provided with individualized management. With that potential in mind, it would be relevant to develop decision-making tools that would allow noncarriers to participate in their follow-up, taking into account the benefits and disadvantages of breast and ovarian cancer screening.

In coming years, advances in genomics should be translated into more and more accurate cancer risk estimates for noncarriers. As has been the case for mutation-positive women, further studies will be needed to foster the development of interventions and tools that will allow for the optimal use of screening strategies by \(BRCA1/2\) mutation–negative women in accordance with their genetic status and family history.

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**CONFLICT OF INTEREST DISCLOSURES**

We have read and understood Current Oncology’s policy on disclosing conflicts of interest, and we declare that we have none.

**AUTHOR AFFILIATIONS**

1. Faculté de pharmacie, Université Laval, Québec; 1Centre de recherche du CHU de Québec-Université Laval, Québec; 1Department of Human Genetics and Oncology, McGill University, Montreal; 2Sir Mortimer B. Davis Jewish General Hospital, Montreal; 3Faculté de médecine, Université de Montréal, Montréal; 4Service de médecine génétique, CHUM, Montréal; 5Faculté de médecine, Université Laval, Québec; and 7Centre des maladies du sein Deschênes–Fabia, CHU de Québec–Université Laval, Québec.

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