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ORIGINAL REPORT

Effectiveness of Screening With Annual Magnetic Resonance Imaging and Mammography: Results of the Initial Screen From the Ontario High Risk Breast Screening Program

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Terms in blue are defined in the glossary, found at the end of this article and online at www.jco.org.

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ABSTRACT

Purpose
The Ontario Breast Screening Program expanded in July 2011 to screen women age 30 to 69 years at high risk for breast cancer with annual magnetic resonance imaging (MRI) and digital mammography. To the best of our knowledge, this is the first organized screening program for women at high risk for breast cancer.

Patients and Methods
Performance measures after assessment were compared with screening results for 2,207 women with initial screening examinations. The following criteria were used to determine eligibility: known mutation in *BRCA1*, *BRCA2*, or other gene predisposing to a markedly increased risk of breast cancer, untested first-degree relative of a gene mutation carrier, family history consistent with hereditary breast cancer syndrome and estimated personal lifetime breast cancer risk ≥ 25%, or radiation therapy to the chest (before age 30 years and at least 8 years previously).

Results
The recall rate was significantly higher among women who had abnormal MRI alone (15.1%; 95% CI, 13.8% to 16.4%) compared with mammogram alone (6.4%; 95% CI, 5.5% to 7.3%). Of the 35 breast cancers detected (16.3 per 1,000; 95% CI, 11.2 to 22.2), none were detected by mammogram alone, 23 (65.7%) were detected by MRI alone (10.7 per 1,000; 95% CI, 6.7 to 15.8), and 25 (71%) were detected among women who were known gene mutation carriers (30.8 per 1,000, 95% CI, 19.4 to 43.7). The positive predictive value was highest for detection based on mammogram and MRI (12.4%; 95% CI, 7.3% to 19.3%).

Conclusion
Screening with annual MRI combined with mammography has the potential to be effectively implemented into an organized breast screening program for women at high risk for breast cancer. This could be considered an important management option for known *BRCA* gene mutation carriers.

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INTRODUCTION

Among Canadian women, breast cancer is the leading incident cancer and second leading cause of cancer death.[1] Women with a family history of breast cancer are at increased risk compared with the general population, with greater risk according to the number, closeness, and (younger) age of the affected relative(s).[2-4] Approximately 5% of breast cancer diagnoses are thought to be due to an inherited predisposition, resulting directly from one or more gene mutations inherited from a parent.[5] The two most common high-risk cancer-predisposing genes are *BRCA1* and *BRCA2* (hereafter *BRCA1/2*). Although the estimated prevalence in the general population is low (0.11% and 0.12%, respectively),[6,7] carriers have an estimated 40% to 87% lifetime risk of developing breast cancer.[8-11] The only other comparable risk group is women who have undergone therapeutic chest radiation (eg, for lymphoma) before age 30 years.[12]

International collaborative groups have presented guidelines for managing women at high risk for breast cancer, often based on experts' opinion.[13-18] Preventive options for women at high risk for breast cancer include risk-reducing mastectomy, salpingo-oophorectomy, or use of tamoxifen. The majority of women at high risk for breast cancer

decline risk-reducing mastectomy[19,20] and require screening starting no later than age 30 years.

Recent evidence from prospective cohort studies suggests that women at high risk for breast cancer on the basis of their family history or genetic testing, including *BRCA1/2* mutation carriers, benefit strongly from breast cancer screening that includes magnetic resonance imaging (MRI) of the breast in addition to mammography.[21-28] A systematic review of these studies found the sensitivity of mammography (13% to 40%) is much lower than the sensitivity of MRI (71% to 100%).[29] A recent review of the literature suggested that the combination of MRI and mammography performed annually was the optimal imaging regimen for screening high-risk women for breast cancer.[30] International breast cancer screening guidelines, developed by the American Cancer Society[31] and the United Kingdom,[32] have since recommended annual breast MRI with or without mammography for identified *BRCA1/2* mutation carriers, untested first-degree relatives of *BRCA* mutation carriers, and women identified as having a 20% to 30% or greater lifetime risk of developing breast cancer. Cancer Care Ontario's (CCO's) Program in Evidence-Based Care similarly recommended combined annual MRI screening with mammography for women age 30 to 69 years at high risk for breast cancer.[33,34]

The Ontario Breast Screening Program (OBSP) has operated since 1990 to deliver a population-based breast cancer screening program of biennial mammography for unaffected women age 50 to 74 years[35] and was expanded in July 2011 to screen women age 30 to 69 years at high risk for breast cancer (including those with a previous history of breast cancer) with annual MRI screening in addition to digital mammography. The objective of this study was to evaluate screening performance measures among women screened in the first year of the OBSP High Risk Screening Program.

PATIENTS AND METHODS

Program Design

On the basis of recommendations from the CCO Program in Evidence-Based Care[33,34] and the Ontario Health Technology Advisory Committee,[36] CCO engaged an expert panel to design a screening program for women at high risk for breast cancer. The OBSP High Risk Screening Program was implemented in 28 screening centers across the province to provide access to annual breast MRI screening with digital mammography for eligible women. The expert panel recommended four groups of women deemed to be at high risk for developing breast cancer: (1) women with a known deleterious mutation in *BRCA1/2* or other gene predisposing to a markedly increased breast cancer risk, (2) untested first-degree relatives of a carrier of such a gene mutation, (3) women with a family history consistent with hereditary breast cancer syndrome and estimated personal lifetime risk of breast cancer $\geq 25\%$, and (4) women who had radiation therapy to the chest (before age 30 years and at least 8 years previously). Although the original Ontario guideline[33,34] did not include women with prior chest irradiation in their recommendations because of the lack of data on MRI screening, the expert panel opted to include this group because of their high risk of breast cancer.[12]

Women in one of the high-risk eligibility groups are eligible for the OBSP High Risk Screening Program if they are 30 to 69 years of age and asymptomatic. Women were not excluded if they had a prior history of breast cancer and/or other cancers (eg, ovarian), had breast implants, or had had a unilateral mastectomy or other breast surgery, as long as they still had palpable breast tissue. Women were ineligible if they had had a bilateral mastectomy.

A clinical pathway was developed by the OBSP expert panel. Women referred by their physician to the program were assigned to one of two categories. If there was prior knowledge that the woman met one of the high-risk criteria she was automatically enrolled and was eligible for screening. Otherwise, the woman was registered in the program but was first referred for genetic assessment to determine her eligibility. These women were assessed as having a $\geq 25\%$ personal lifetime risk of breast cancer according to the International Breast Cancer Intervention Study (IBIS)[37] or Breast and Ovarian Analysis of Disease Incidence of Carrier Estimation Algorithm (BOADICEA)[38] models. All outcomes of genetic assessments were communicated to the OBSP High Risk Screening Centre. Before the first round of screening, women were assessed for any potential contraindications to MRI or reasons why their screening should be delayed. If MRI was contraindicated, the woman was scheduled for a screening breast ultrasound. Observational screening studies have shown that ultrasound rarely found cancers missed by MRI (but many cancers missed by ultrasound were found by MRI). However, ultrasound found many cancers missed by mammography, with an overall sensitivity similar to that of mammography.[21,26,27]

All OBSP High Risk Screening Centres provide digital mammography consisting of standard craniocaudal and mediolateral oblique views performed by certified mammography technologists. Quality assurance for the equipment met or exceeded that specified by the Canadian Association of Radiologists' Mammography Accreditation Program, which also provides accreditation for all OBSP radiologists and technologists. All centers conducted MRI-guided biopsy on site or had a partnership with a facility that could perform biopsies and were affiliated with an OBSP Breast Assessment Site to facilitate referral of women with abnormal screens. The following were minimum MRI standards: 1.5 Tesla, injection contrast gadolinium (0.1 to 0.2 mmol/kg), and a dedicated breast coil with bilateral axial or sagittal acquisition. The largest imaging matrix within the acquisition window is used with an in-plane pixel size of 0.5×0.5 mm to 1×1 mm and a through plane pixel size of 1 to 3 mm.

The majority of eligible women (90.7%) were screened with MRI within 30 days of their mammogram. Radiologists were aware of the mammogram results before interpreting the MRI studies.

Study Population

A cohort was identified from 6,863 women age 30 to 69 referred to the OBSP High Risk Screening Program from July 1, 2011, to June 30, 2012, and observed until March 20, 2013 (Fig 1). Of these women, 964 (14.0%) were previously known to meet one of the high-risk eligibility criteria and were referred directly for screening; 5,899 women (86.0%) were referred for genetic assessment to determine their eligibility. Of the 5,201 women who completed genetic counseling and/or testing, 1,629 (31.3%) were considered eligible. Of the 2,593 women eligible for screening, 234 declined, deferred, died, planned a bilateral mastectomy, or had an MRI outside of the program and were excluded from analysis. The study cohort consisted of the remaining 2,359 women. Of the women screened, 19.3% had a previous MRI and mammogram, and 33.6% had a previous mammogram only before attending the OBSP High Risk Screening Program. However, because the reasons for (diagnostic or screening) and results of the tests are unknown, all results are reported by initial program screen only.

Data Collection

The data used for this study consisted of routine information collected for all women screened within the OBSP High Risk Screening Program from CCO's Integrated Client Management System. The Requisition for High Risk Screening Form included data on method of referral into the program, high-risk criteria, history suggestive of hereditary breast cancer, and medical history. For women referred for genetic assessment, the Genetics Report Form collected data on high-risk criteria, eligibility for screening, and whether women declined testing. For women screened, data from the OBSP Screening Report included age at screening, number of previous screens, and radiologist findings by modality. For women diagnosed with primary invasive breast cancer or ductal carcinoma in situ (DCIS) after screening, pathologic confirmation was obtained through record linkage with the Ontario Cancer Registry. Women participating in the OBSP were asked to sign an Authorization for the Release of Personal Health Information, which specified that their screening data would be used for evaluation, and they were asked to give written consent

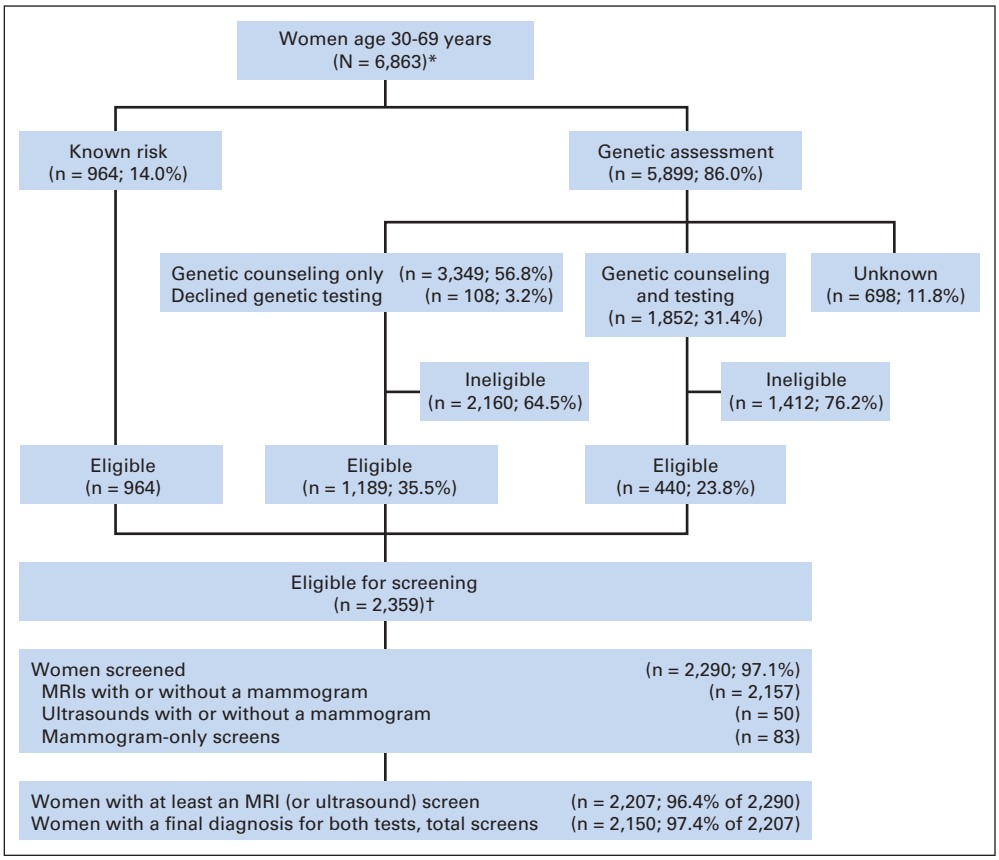

Fig 1. Participation and screening outcomes in the Ontario High Risk Breast Screening Program (July 1, 2011, through June 30, 2012). (*) Follow-up of women who registered between July 1, 2011, and June 30, 2012, was through March 20, 2013. (†) Two hundred thirty-four women were excluded (declined, deferred, died, planned bilateral mastectomy, or had external magnetic resonance imaging [MRI] during first year of the program).

regarding the release to the OBSP of results of further tests following an abnormal screening examination. All women gave written approval except for three who were excluded from the follow-up analysis. Research ethics approval was not required for this study, because it fell into the category of quality assurance as specified by the University of Toronto Research Ethics Office.

Performance Measures

The performance measure definitions used for this study were primarily those adopted by the Canadian Breast Cancer Screening Initiative[39] and the Breast Imaging Reporting and Data System (BI-RADS) Manual, Fourth Edition.[40] The unit for all analyses was the initial program screening examination, and the primary outcome of interest was screen-detected breast cancer. The recall rate was defined as the percentage of women referred for immediate further testing because of an abnormal screening result. Positive predictive value (PPV) was defined as the proportion of women with an abnormal screening result (PPV_1) or proportion of women who had a biopsy (PPV_3) with complete follow-up, found to have breast cancer after diagnostic work-up. A probably benign assessment after work-up with 6-month follow-up was classified as test negative. The cancer detection rate was defined as invasive or DCIS breast cancers detected per 1,000 initial screening examinations.

Screening result was examined in three mutually exclusive groups with screening abnormalities. "Mammography alone" refers to women with an abnormal mammogram result and a normal MRI (or ultrasound) result. "MRI (or ultrasound) alone" refers to women with an abnormal MRI (or ultrasound) result and a normal mammogram result. "MRI (or ultrasound) and mammography" refers to women with an abnormal MRI (or ultrasound) and abnormal mammogram result.

Statistical Analysis

Performance measures and approximate 95% CIs calculated for binomial proportions were measured for all women screened with a final diagnosis after recommended work-up and/or biopsy stratified by screening result. Cancer detection rates were further stratified by tumor type (invasive or DCIS), age at diagnosis (< 50 or ≥ 50 years) and by two of the risk groups (known carrier of a gene mutation or family history with a cumulative lifetime breast cancer risk $\geq 25\%$). We did not examine the cancer detection rate among women with prior chest irradiation because of small numbers ($n = 2$). Breast density was collected as a binary variable; therefore, mammographic density by using the standard BI-RADS classification was not examined. Performance measures were compared by using χ^2 statistics. All analyses were conducted by using SAS version 9.2 (SAS Institute, Cary, NC). A two-tailed 5% significance level was used for statistical tests.

RESULTS

Of the 2,359 women eligible for screening, 2,290 (97.1%) were screened. Of the women screened, 2,157 (94.2%) had an MRI, 50 (2.2%) had an ultrasound with or without a mammogram, and 83 (3.6%) had a mammogram only. Women screened with only a mammogram were excluded from further analyses. The final sample consisted of 2,150 women screened with a final diagnosis (Fig 1). Overall, the majority of women enrolled onto the OBSP High Risk Screening Program were younger than 50 years of age (72.1%; Table 1). Among the 906 women known to be at high risk for breast cancer, 62.4% were known gene mutation carriers, and 20.4% had a family history consistent with hereditary breast cancer and an estimated lifetime breast cancer risk of $\geq 25\%$. In contrast, among the 1,453 women who were referred for genetic assessment to determine their eligibility, the majority (76.3%) had a family history consistent with hereditary breast cancer and an estimated lifetime breast cancer risk of $\geq 25\%$. There were 226 women (9.9%) who had been diagnosed with breast

Table 1. Characteristics of Eligible Women by Referral Method, Age, Risk Criteria, and Prior Breast Cancers

Characteristic	Known Risk (n = 906)		Genetic Assessment (n = 1,453)		Total (N = 2,359)	
	No.	%	No.	%	No.	%
Age, years*						
30-39	216	23.8	543	37.4	759	32.2
40-49	339	37.4	602	41.4	941	39.9
50-59	249	27.5	251	17.3	500	21.2
60-69	102	11.3	57	3.9	159	6.7
Risk criteria*†						
Known carrier	565	62.4	313	21.5	878	37.3
Family history and ≥ 25% risk	185	20.4	1,108	76.3	1,293	54.8
Untested first-degree relative	31	3.4	32	2.2	63	2.7
Chest radiation	125	13.8	0	0.0	125	5.3
Prior breast cancer*						
No	780	86.4	1,281	92.6	2,061	90.1
Yes	123	13.6	103	7.4	226	9.9
No. unknown	3		69		72	
Time since prior breast cancer, years*‡						
< 5	31	26.1	66	66.0	97	44.3
≥ 5 and < 10	43	36.1	15	15.0	58	26.5
≥ 10	45	37.8	19	19.0	64	29.2
No. unknown (client not yet screened)	4		3		7	

*Significant difference ($P < .001$) in distribution of factors between known risk and genetic assessment.
†If a woman met more than one risk criterion, the following hierarchy was selected to classify the woman: known carrier, family history and ≥ 25% risk, untested first-degree relative, chest radiation.
‡Time from diagnosis date to date of first screen among women with prior breast cancer in Ontario High Risk Breast Screening Program.

cancer before their first screen in the program. Significantly more women who were known to be at high risk had a prior breast cancer (13.6%) compared with women who required genetic assessment (7.4%; $P < .001$).

Of the 2,150 women screened with a final diagnosis, 554 (25.8%) had an abnormal screen result, and 197 (9.2%) had a biopsy (Table 2). Recalls occurred significantly more often because of an abnormal MRI alone (15.1%; 95% CI, 13.8% to 16.4%; $P < .001$) compared with an

Table 2. Recall Rates, Cancer Detection Rates (per 1,000 initial screening examinations), and PPVs by Screening Result for Women Screened in the OBSP High Risk Screening Program (N = 2,207)

Measure	Screening Result											
	Overall			Abnormal Mammogram Alone*			Abnormal MRI (or ultrasound†) Alone			Abnormal Mammogram and MRI (or ultrasound†)*		
	No.	Rate (%)	95% CI	No.	Rate (%)	95% CI	No.	Rate (%)	95% CI	No.	Rate (%)	95% CI
Screening examinations												
All women	2,207			2,133			2,207			2,133		
Women with a final diagnosis	2,150			2,082			2,150			2,082		
Abnormal screening examinations	554			133			324			97		
Recall rate		25.8	24.2 to 27.4		6.4	5.5 to 7.3		15.1	13.8 to 16.4‡		4.7	3.9 to 5.5§
Biopsies	197			15			136			46		
Cancers detected	35			0			23			12		
Cancer detection rate		16.3	11.2 to 22.2	0				10.7	6.7 to 15.8‡		5.8	3.0 to 10.0‡
PPV_1		6.3	4.7 to 8.3	0				7.1	4.9 to 9.9‖		12.4	7.3 to 19.3‡
PPV_3		17.8	13.4 to 22.9	0				16.9	11.8 to 23.1		26.1	15.8 to 38.8

Abbreviations: MRI, magnetic resonance imaging; OBSP, Ontario Breast Screening Program; PPV, positive predictive value; PPV_1, the proportion of women with an abnormal screening result; PPV_3, proportion of women who had a biopsy.
*Excluding screens that were MRI (or ultrasound) only.
†Fifty women were screened with a screening ultrasound and not a screening MRI, four had an abnormal screening result, and one invasive cancer was detected by ultrasound alone.
‡$P < .001$, comparison group, mammogram alone.
§$P = .02$, comparison group, mammogram alone.
‖$P = .002$, comparison group, mammogram alone.

Table 3. Cancer Detection Rates (per 1,000 initial screening examinations) by Screening Result, Detection Type, Age Group, and Risk Group for Women Screened in the OBSP High Risk Screening Program

	Screening Result*											
	Overall				Abnormal MRI (or ultrasound†) Alone				Abnormal Mammogram and MRI (or ultrasound†)			
Measure	Cancers	Screens	Cancer Detection Rate‡	95% CI	Cancers	Screens	Cancer Detection Rate	95% CI	Cancers	Screens‡	Cancer Detection Rate	95% CI
Overall	35	2,150	16.3	11.2 to 22.2	23	2,150	10.7	6.7 to 15.8	12	2,082	5.8	3.0 to 10.0
Tumor type												
Invasive	27	2,150	12.6	8.2 to 18.0	17	2,150	7.9	4.6 to 12.5	10	2,082	4.8	2.3 to 8.8
DCIS	8	2,150	3.7§	1.6 to 7.3	6	2,150	2.8	1.0 to 6.1	2	2,082	1.0	0.1 to 3.5
Age group, years												
< 50	20	1,506	13.3	8.0 to 20.2	13	1,506	8.6	4.6 to 14.6	7	1,465	4.8	1.9 to 9.8
≥ 50	15	644	23.3	12.8 to 37.3	10	644	15.5	7.4 to 27.9	5	617	8.1	2.6 to 18.7
Risk group‖¶												
Known carrier	25	813	30.8	19.4 to 43.7	15	813	18.5	10.2 to 29.7	10	789	12.7	6.0 to 22.9
Family history and ≥ 25% risk	8	1,158	6.9#	3.0 to 13.5	6	1,158	5.2	1.9 to 11.2	2	1,117	1.8	0.2 to 6.4

Abbreviations: DCIS, ductal carcinoma in situ; MRI, magnetic resonance imaging; OBSP, Ontario Breast Screening Program.
*No cancers were detected by mammography alone.
†Fifty women were screened with a screening ultrasound and not a screening MRI, four had an abnormal screening result, and one invasive cancer was detected by ultrasound alone.
‡Excluding screens that were MRI (or ultrasound) alone.
§$P = .001$, comparison group, invasive tumors.
‖If a woman met more than one risk criterion, the following hierarchy was selected to classify the woman: known carrier, family history and ≥ 25% risk, untested first-degree relative, chest radiation.
¶Two cancers were detected among women whose only risk factor was chest radiation therapy.
#$P < .001$, comparison group, known carriers.

abnormal mammogram and MRI (4.7%; 95% CI, 3.9% to 5.5%), or an abnormal mammogram alone (6.4%; 95% CI, 5.5% to 7.3%).

Of the 35 breast cancers detected, none were detected by a mammogram alone, 23 were detected by MRI alone (10.7 per 1,000; 95% CI, 6.7 to 15.8), and 12 were detected by both modalities (5.8 per 1,000; 95% CI, 3.0 to 10.0; Table 2). PPV_1 and PPV_3 were higher, although not significantly, for detection based on mammogram and MRI (12.4% [95% CI, 7.3% to 19.3%] and 26.1% [95% CI, 15.8% to 38.8%], respectively) compared with MRI alone (7.1% [95% CI, 4.9% to 9.9%] and 16.9% [95% CI, 11.8% to 23.1%], respectively).

Overall, the cancer detection rate was significantly higher for invasive cancers (12.6 per 1,000; 95% CI, 8.2 to 18.0) compared with DCIS (3.7 per 1,000; 95% CI, 1.6 to 7.3; $P = .001$; Table 3). Cancer detection rates were higher, although not significantly, among women age ≥ 50 years (23.3 per 1,000; 95% CI, 12.8 to 37.3) compared with women younger than age 50 years (13.3 per 1,000; 95% CI, 8.0 to 20.2) and significantly higher among those who were known gene mutation carriers (30.8 per 1,000; 95% CI, 19.4 to 43.7) compared with those with a family history plus an estimated lifetime cancer risk of ≥ 25% (6.9 per 1,000; 95% CI, 3.0 to 13.5; $P < .001$).

DISCUSSION

The first-year results suggest that the OBSP High Risk Screening Program is achieving the expected improved performance based on the high cancer detection rate (16.3 per 1,000) provided by the addition of MRI to mammography. Although the cancer detection rate in high-risk women without a known mutation (6.9 per 1,000) was significantly lower than that for the known mutation carriers, it was higher than the detection rate for the OBSP average-risk screening program (4.9 per 1,000 for full-field digital mammography[41]), indicating that the criteria for determining high-risk screening eligibility are appropriate.

Our cancer detection rate for MRI alone (10.7 per 1,000) is similar to the cancer detection rate reported by other prospective cohort studies on the basis of cancers referred by a positive MRI alone, ranging from 8.2 to 15.9 per 1,000.[21-26] These single-center and multicenter studies used various methodologies, including criteria for eligibility; therefore, the results may not be directly comparable to results from this study.

As expected, we observed a higher cancer detection rate among women older than age 50 years compared with those younger than age 50. We also found the highest cancer detection (30.8 per 1,000) among women who were known gene mutation carriers. Two other studies compared detection rates by risk profiles and similarly found greater cancer detection for mutation carriers compared with those with a personal history of breast cancer and those with a cumulative lifetime risk of 15% to 49%.[22,24] Data on prognostic features of cancers and 1-year follow-up of women with normal screening test results on both mammogram and MRI screening to determine whether they have an interval cancer is incomplete at this time. A future study will examine the pathology of screen-detected cancers, test sensitivity, and interval cancer rate. On the basis of previous studies,[42,43] we expect that breast cancers detected by MRI alone will have more favorable prognostic features compared with those detected by mammography alone.

All of the breast cancers in our study were detected by MRI either alone or with mammography. Recent screening guidelines published by the National Institute for Health and Care Excellence[32] recommend considering or not offering mammography along with annual MRI for women age 30 to 39 years at high risk for breast cancer with no personal history of breast cancer. In future rounds of screening, we plan to further examine the number of breast cancers detected by mammography alone. There may be subgroups of women for whom mammography can be omitted, sparing them unnecessary radiation.

PPV_1 and PPV_3 were higher for cancer detection based on both MRI and mammography compared with MRI alone. A lower PPV for MRI alone is acceptable because with mammography alone, two thirds of the cancers would be missed. Other studies found similar[44] or lower[27] PPVs for cancer detection based on MRI and mammography compared with MRI alone. These studies differed from ours in their method of recruitment[44] or number of screening rounds.[27]

Being recalled for an abnormal screening result causes patients stress and anxiety and comes at a significant cost to the health care system.[45] Recalls occurred significantly more often as a result of an abnormal MRI alone (15.1%) compared with mammography alone (6.4%), which is consistent with prospective studies from the United States[25] and the United Kingdom,[23] which have recall rates ranging from 1.9% to 3.9% for referrals based on abnormal mammography alone and 8.2% to 10.7% for referrals based on MRI alone. However, it is expected that the recall rate will likely be significantly lower in future rounds of screening when there is a baseline MRI for comparison and when the centers gain more experience. Recalls resulting from an abnormal MRI and mammogram occurred slightly less often (4.7%) compared with an abnormal mammogram alone (6.4%).

To the best of our knowledge, this is the first organized clinical screening program for women at high risk for breast cancer. The most significant aspect of this new program is that women age 30 to 69 years at high risk for breast cancer across Ontario are being screened with the combination of MRI and mammography. The collection of data from individual screening allows performance to be monitored, which facilitates the provision of high-quality care. Moreover, the prospective collection of data on this large population of high-risk women will help resolve many of the yet unanswered questions about high-risk screening, including the need for mammography, the adequacy of annual MRI for women younger than age 40 (the age at which MRI may safely be discontinued), and the benefit of MRI for screening women with a history of chest radiation.

This evaluation study demonstrates that screening with annual MRI and mammography for high-risk women has the potential to be effectively implemented within an organized screening program. In particular, screening with annual MRI could be considered an important management option for women who are known *BRCA* gene mutation carriers.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

AUTHOR CONTRIBUTIONS

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Manuscript writing: All authors
Final approval of manuscript: All authors

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GLOSSARY TERMS

***BRCA1*:** a tumor suppressor gene known to play a role in repairing DNA breaks. Mutations in this gene are associated with increased risks of developing breast or ovarian cancer.

***BRCA2*:** a tumor suppressor gene whose protein product is involved in repairing chromosomal damage. Although structurally different from *BRCA1*, *BRCA2* has cellular functions similar to *BRCA1*. *BRCA2* binds to RAD51 to fix DNA breaks caused by irradiation and other environmental agents. Also known as the breast cancer 2 early onset gene.

magnetic resonance imaging: a procedure in which radio waves and a powerful magnet linked to a computer are used to create detailed pictures of areas inside the body. These pictures can show the difference between normal and diseased tissue.

