Genetics in Medicine (2025) 27, 101453

ELSEVIER

Genetics in Medicine
An Official Journal of the ACMG

www.journals.elsevier.com/genetics-in-medicine

ARTICLE

Psychological and emotional impacts of communicating breast cancer risk using multifactorial assessment with polygenic risk score: Findings from PERSPECTIVE I&I

Laurence Lambert-Côté[1], Annie Turgeon[1], Kristina M. Blackmore[2], Amy Chang[2], Antonis C. Antoniou[3], Kathleen A. Bell[2], Mireille J.M. Broeders[4], Jennifer D. Brooks[5], Tim Carver[3], Sue-Ling Chang[1], Jocelyne Chiquette[1,6,7], Éric Demers[1], Douglas F. Easton[3], Andrea Eisen[2,8], Laurence Eloy[9,10], D. Gareth R. Evans[11], Samantha Fienberg[2], Yann Joly[12], Raymond H. Kim[2,13], Bartha M. Knoppers[12], Corinne Labeau-Caouette[1], Johanne Lessard[10], Aisha Lofters[14], Hermann Nabi[1,15,16], Jean-Sébastien Paquette[7], Nora Pashayan[3], Amanda J. Sheppard[2,5], Tracy L. Stockley[13,17,18], Meghan J. Walker[2,5], Anna M. Chiarelli[2,5], Jacques Simard[1,19], Michel Dorval[1,16,20,*]

ARTICLE INFO

Article history:
Received 26 November 2024
Received in revised form
23 April 2025
Accepted 23 April 2025
Available online 10 May 2025

Keywords:
Breast cancer screening
Polygenic risk score
Psychosocial issues
Risk communication
Risk stratification

ABSTRACT

Purpose: To examine the psychological and emotional outcomes of personalized breast cancer risk communication up to 1 year after disclosure in a risk-stratified breast screening preimplementation study (Personalized Risk Assessment for Prevention and Early Detection of Breast Cancer: Integration and Implementation).

Methods: Among 3753 females aged 40 to 69, unaffected by breast cancer, with a prior mammogram, and who underwent multifactorial risk assessment to estimate their 10-year breast cancer risk, 2734 completed follow-up questionnaires up to 1 year after risk communication: 78.5% were at average risk, 16.5% at higher than average risk, and 5.0% at high risk. The impact of risk communication on breast cancer worry and psychological distress and factors associated with decisional regret were examined.

Results: Breast cancer worry and psychological distress scores remained low after risk communication and at 1 year follow-up. Up to 1 year after disclosure, small significant differences in breast cancer worry were observed between risk levels. Decisional regret was very low 1 year after risk communication. Lower levels of decisional regret were significantly associated with some factors, including higher satisfaction with the information received.

Conclusion: This study suggests that personalized breast cancer risk communication has low negative psychological and emotional effects and highlights the importance of the information received for implementing this approach at population level.

The Article Publishing Charge (APC) for this article was paid through institutional agreement with Université Laval.

Anna M. Chiarelli, Jacques Simard, and Michel Dorval contributed equally to this work.

*Correspondence and requests for materials should be addressed to Michel Dorval, CHU de Québec-Université Laval Research Center, 1050 chemin Sainte-Foy, Quebec City, QC, Canada G1S 4L8. *Email address:* michel.dorval@crchudequebec.ulaval.ca

Affiliations are at the end of the document.

doi: https://doi.org/10.1016/j.gim.2025.101453

Introduction

Population-based breast screening programs have been implemented in many countries and have been associated with significant reductions in breast cancer mortality.[1] Risk-stratified breast cancer screening using multifactorial risk assessment, including a polygenic risk score (PRS), is increasingly regarded as an alternative to the current age-based screening.[2-6] This approach has the potential to improve the benefit-to-harm ratio and the cost-effectiveness of screening programs by tailoring screening recommendations to individual risk.[7,8] Personalized Risk Assessment for Prevention and Early Detection of Breast Cancer: Integration and Implementation (PERSPECTIVE I&I) is an ongoing Canadian project that seeks to improve personalized risk assessment, to inform the development of cost-effective risk-based approaches for prevention and early detection of breast cancer, and to determine optimal implementation approaches within the Canadian health care system.[5,9]

Various issues need to be considered when implementing a personalized risk-based breast cancer screening at the population level.[5,6] An important consideration is the potential negative impacts of risk assessment and communication on individuals. Current literature on monogenic (eg, *BRCA*) and polygenic testing (eg, PRS) in cancer genetic clinic settings indicates no evidence of clinically significant long-term adverse psychological outcomes or substantial decisional regret.[10,11] In contrast, population-level multifactorial risk assessment adds complexity by encompassing multiple risk factors, which requires a more nuanced interpretation of risk. This complexity may contribute to increased uncertainty or anxiety because it underscores the intricate interplay of lifestyle, environmental, and genetic factors in determining risk and potentially overwhelming individuals with respect to the actions they can take to mitigate it. Consequently, the psychological impacts of risk communication derived from previous studies on monogenic or polygenic testing may not be directly applicable to multifactorial risk evaluations.

Previous studies in the United States[12] and England[13,14] have evaluated the psychological impact of providing women with breast cancer risk estimates using multifactorial risk assessment. These studies have shown that personalized breast cancer risk communication has a modest impact on breast cancer worry and anxiety and is unlikely to have adverse consequences in this respect.[12-14] Of these, only the Predicting-Risk-Of-Cancer-At-Screening (PROCAS-2) study (Breast Cancer Predict) involved women with different levels of risk (high, moderate, average, and below average) but included only a highly selected subsample of the study population.[14] The studies only followed participants for up to 6 months; therefore, they did not provide a longer-term perspective. Additionally, they did not measure decisional regret, which is important to consider when implementing a risk-based screening approach in existing screening programs because it could affect future engagement.

This study evaluated the psychological and emotional outcomes of breast cancer risk communication up to 1 year after disclosure in a real-word setting using the PERSPECTIVE I&I prospective cohort study. The study aimed to test the hypothesis that women identified as high risk would experience higher levels of breast cancer worry and psychological distress compared with those at average risk in the short term, with no clinically significant differences anticipated between the groups after 1 year. It also explored which factors, beyond risk levels, are associated with higher decisional regret 1 year after risk communication. Finally, it explored the emotional dimension of learning about breast cancer risk level 1 year after risk disclosure.

Materials and Methods

Context

This research was conducted as part of the Canadian PERSPECTIVE I&I project fully described elsewhere.[5,9] Briefly, participants completed an entry questionnaire that inquired about their family history of cancer, as well as lifestyle and hormonal risk factors. Participants also provided a saliva sample from which DNA was extracted and tested to calculate a PRS with 295 single nucleotide polymorphisms (SNPs) based on the 313-SNP breast cancer PRS previously identified.[15,16] Participants were not screened for pathogenic variants in monogenic cancer susceptibility genes (eg, *BRCA1*, *BRCA2*, *PALB2*, *CHEK2*, and *ATM*). Mammographic density was obtained from the screening mammogram report. The 10-year absolute risk of having breast cancer was calculated using the multifactorial CanRisk prediction tool, which integrates all collected risk factors, including family history, PRS, lifestyle and hormonal factors, and breast density.[17] Risk estimates were stratified into 3 categories using age-dependent absolute risk thresholds: average (<15%,), higher than average (15 to <25%), and high (≥25%), which correspond to a breast cancer remaining lifetime risk from ages 30 to 80 years.[18] The PRS and the risk assessment tool (CanRisk) were primarily developed using individuals of European ancestry, which resulted in less accurate performance across all

ethnicities. For ethical reasons and to ensure equity, we did not exclude participants based on ethnicity. Instead, we included a disclaimer in the consent form, noting that the risk estimate provided might be less precise for certain groups.

All participants received a personalized risk letter that included their risk level and proposed screening action plan. This document was accessible via a secured web portal or sent by mail. Screening action plans were based on risk level, age and provincial breast screening guidelines (Supplemental Table 1).[5] For women aged 40 to 49 who are estimated to be at average risk, no mammography screening is recommended, whereas women aged 50 to 69 should be screened every 2 years by mammography. Women estimated to be at higher-than-average risk (40-69 years) in Quebec are recommended to undergo screening every 1 to 2 years, whereas in Ontario, they are encouraged to discuss screening options with their primary care provider (40-49 years) or undergo annual screening with mammogram (50-69 years). Finally, it is proposed that all women (40-69 years) estimated to be at high risk undergo annual screening with both a mammogram and magnetic resonance imaging. Women identified as high risk were contacted by a health care professional (nurse or genetic counselor) to disclose their risk level and/or for further counseling about their risk level and screening action plan.

The study was approved by the Ethics Research Committees of the CHU de Québec-Université Laval (MP-20-2020-4670), McGill University (A12-B65-18A), University of Toronto (00036881), Grand River Hospital (2020-0709), McMaster University (11468), St. Michael's Hospital (19-220), Sunnybrook Health Sciences Centre (2255), University Health Network (19-5340), and Queens University (6030732 EPID-712-20). Informed consent was obtained from all participants involved in the study.

Participants

The PERSPECTIVE I&I project recruited females aged 40 to 69 years who had at least 1 previous mammogram. Those who had been diagnosed with breast, ovarian, or pancreatic cancer, had a mastectomy, had genetic counseling and/or genetic testing for breast cancer, or had received chest radiotherapy treatments before the age of 30 were ineligible. For this study, participants from the PERSPECTIVE I&I cohort who had a risk calculated and communicated to them and who completed all 3 questionnaires were included. Participants were excluded if they reported a breast cancer diagnosis in 1 of the follow-up questionnaires.

Data collection

Data from the 3 questionnaires were used: (1) the entry questionnaire (before risk assessment: July 2019-December 2021); (2) the follow-up questionnaire (at the time of risk communication: March 2020-October 2022); and (3) the 1-year follow-up questionnaire (1 year after risk communication: April 2021-August 2023). The questionnaires were administered in both English (Ontario) and French (Quebec).

Measures

Questions used to measure the emotional outcome of knowing their risk level, breast cancer worry, psychological distress, and decisional regret are shown in Supplemental Questionnaire 1.

Breast cancer worry

Breast cancer worry was assessed using 5 questions adapted from the Lerman Breast Cancer Worry Scale[19] used in previous studies.[12,20] Participants were asked about how often in the past month they had any thoughts, worries, or feelings of distress about their risk of developing breast cancer and how often their thoughts affected their mood and daily activities. The breast cancer worry score ranged from 5 to 20, a higher score indicating more frequent thoughts or greater worry about breast cancer risk. Data from all 3 questionnaires were used for this analysis.

Psychological distress

Psychological distress was assessed using the Kessler Psychological Distress Scale (K10), which consists of 10 questions about emotional states experienced in the past 30 days.[21,22] The psychological distress score ranged from 0 to 40, a higher score indicating a higher level of psychological distress. Data from all 3 questionnaires were used for this analysis.

Regret after the decision to know the level of risk

Regret after the decision to know the level of risk was assessed using the decision regret scale,[23] a validated 5-item scale with scores ranging from 0 to 100. A score of 0 indicated no regret, whereas a score of 100 meant great decisional regret. Data from the 1-year follow-up questionnaire were used for this analysis.

Information on follow-up with the health care providers, the intention to follow the screening action plan, and satisfaction with the information received

Information on follow-up with the health care providers (HCPs), the intention to follow the screening action plan, and satisfaction with the information received was also collected 1 year after risk communication. Participants were asked if they had discussed their risk level with their HCP. If they had, shared decision making on the proposed screening action plan was measured from the participant's perspective using 4 items from the Shared Decision-Making Questionnaire.[24] Each item was measured using a 5-point scale with scores ranging from 4 to 20. The participants also indicated

if they had chosen to follow the proposed screening action plan. Satisfaction with the information received was assessed using an adaptation of a previously published scale.[14,25] The satisfaction score ranged from 5 to 20, with higher scores indicating higher satisfaction. All of these questions are shown in Supplemental Questionnaire 2.

Emotional outcomes of knowing risk level

Emotional outcomes of knowing risk level were assessed using 2 questions evaluating the extent to which learning their breast cancer risk level was a relief or was upsetting for them.[26] Data from the 1-year follow-up questionnaire were used for this analysis.

Sociodemographic and health information

Sociodemographic and health information included the participant's province and age group at risk assessment. Variables obtained from the entry questionnaire included the country of birth, ethnic or cultural origin, marital status, highest level of education, employment status, and perceived general health. These variable definitions were derived from Canadian census questionnaires. Using Statistics Canada's definition, we categorized individuals as visible or nonvisible minorities, based on their ethnic or cultural origins. Visible minorities, as defined by the Employment Equity Act, include groups such as South Asian, Chinese, Black, Filipino, Arab, Latin American, Southeast Asian, West Asian, Korean, and Japanese.[27] This definition was used to align with Canadian terminology at the time of the study and to ensure reliable, robust estimates, given that population groups other than White were relatively small in our sample.[9]

Other self-reported covariates included personal history of breast cancer, number of previous mammograms, age at first mammogram, mammogram screening frequency, and perceived lifetime breast cancer risk.

Data analysis

To evaluate the impact of risk communication on breast cancer worry and psychological distress, we used a generalized linear model with an identity link and normal distribution and generalized estimating equations to account for correlation over time. Analyses were adjusted for potential confounding variables (age group, province, education, visible minority status, family history of breast cancer, perceived risk, and worry about breast cancer). Province was considered as a potential confounding variable to account for different recruitment methods used in each province (recruitment through population-based invitations within the provincial screening program vs convenience sampling). These methods resulted in variations in age groups, sociodemographic, risk factors, and risk level distribution, as previously reported.[9] Participants with missing values for at least 1 of the 3 measurement points or adjustment variables were excluded from the analyses. To assess factors associated with decisional regret 1 year after risk communication, we computed adjusted mean scores and 95% confidence intervals using a generalized linear model with a log link and a Poisson working model in univariable and multivariable models.[28] Model-robust variances were obtained with sandwich estimators to account for the larger variance of Poisson variables compared with binomial variables.[29] A stepwise covariate selection method was used for the multivariable model. In addition, the following variables were systematically included in the multivariable model: age group at risk assessment (40-49, 50-59, and 60-70), province, and the interaction term between the for risk levels and the family history. Additional information on data analysis is described in the Supplemental Data Analysis. Statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc).

Results

Among the 4477 participants recruited in the PERSPECTIVE I&I project, 3714 had their risk level calculated and disclosed. All 3 questionnaires were sent to 3672 participants, of whom 2734 (74.5%) completed them all (Supplemental Figure 1). Of these, 2147 (78.5%) were at average risk, 450 (16.5%) were at higher than average risk, and 137 (5.0%) were at high risk. The follow-up questionnaire was completed on average within 1 month after risk communication (mean = 25 days, SD = 36 days), whereas the 1-year follow-up questionnaire was completed on average 13 months after risk communication (mean = 395 days, SD = 47 days).

Given that approximately a quarter of the initial study participants were excluded because of missing data over the course of the study, we examined whether attrition was related to the main study outcomes or other participant characteristics. Participants included in the analyses did not differ materially from those excluded in terms of baseline psychological distress (mean scores: 5.74 vs 5.43), breast cancer-related worries (mean scores: 6.65 vs 6.85), and age (means: 57.6 vs 58.6). However, the proportion of participants excluded from the analyses was higher among those recruited in Ontario (35%) compared with Quebec (15%) and slightly different by risk level (average risk = 26%, higher than average risk = 22%, and high risk = 15%).

The majority of participants determined to be at high risk were under the age of 60 (n = 137, 81.0%), had a first degree family history of breast cancer (n = 32, 64.2%), and were mainly from the province of Quebec (n = 105, 76.6%) (Table 1).

Breast cancer worry and psychological distress

The adjusted mean breast cancer worry and psychological distress scores before, at, and up to 1 year after risk communication are presented in Figures 1 and 2, respectively. Overall, the adjusted mean scores of breast cancer

Table 1 Sociodemographic and health characteristics of 2734 participants who completed the 3 questionnaires

	Risk Level							
	Average Risk		Higher Than Average Risk		High Risk		Total	
	$n = 2147$		$n = 450$		$n = 137$		$n = 2734$	
Characteristics	*n*	(%)[a]	*n*	(%)[a]	*n*	(%)[a]	*n*	(%)[a]
Age at risk assessment (y)								
Mean (SD)	58.3	(7.1)	55.9	(7.2)	52.1	(7.5)	57.6	(7.3)
40-49	272	(12.7)	90	(20.0)	54	(39.4)	416	(15.2)
50-59	849	(39.5)	192	(42.7)	57	(41.6)	1098	(40.2)
60-70	1026	(47.8)	168	(37.3)	26	(19.0)	1220	(44.6)
Province								
Ontario	1101	(51.3)	190	(42.2)	32	(23.4)	1323	(48.4)
Quebec	1046	(48.7)	260	(57.8)	105	(76.6)	1411	(51.6)
Born in Canada								
Yes	1895	(88.6)	396	(88.4)	120	(88.2)	2411	(88.5)
No	244	(11.4)	52	(11.6)	16	(11.8)	312	(11.5)
Missing	8		2		1		11	
Visible minority								
Not a visible minority	2009	(95.6)	409	(92.3)	126	(94.0)	2544	(95.0)
Visible minority	93	(4.4)	34	(7.7)	8	(6.0)	135	(5.0)
Don't know/prefer not to answer/missing	45		7		3		55	
Highest level of education								
Below university bachelor's degree	1049	(49.2)	212	(47.2)	47	(34.6)	1308	(48.1)
University bachelor's degree or above	1085	(50.8)	237	(52.8)	89	(65.4)	1411	(51.9)
Prefer not to answer/missing	13		1		1		15	
Marital status								
Married/common law	1638	(76.7)	336	(75.5)	103	(75.7)	2077	(76.5)
Single/widowed/ divorced/ separated	497	(23.3)	109	(24.5)	33	(24.3)	639	(23.5)
Prefer not to answer/missing	12		5		1		18	
Employment status								
Employed	1252	(58.5)	286	(63.6)	106	(77.4)	1644	(60.3)
Retired/not employed	888	(41.5)	164	(36.4)	31	(22.6)	1083	(39.7)
Prefer not to answer/missing	7		0		0		7	
Family history of breast cancer								
First- and second degree	124	(5.8)	91	(20.2)	56	(40.9)	271	(9.9)
First degree only	264	(12.3)	97	(21.6)	32	(23.3)	393	(14.4)
Second degree only	544	(25.3)	132	(29.3)	30	(21.9)	706	(25.8)
None	1215	(56.6)	130	(28.9)	19	(13.9)	1364	(49.9)
Number of previous mammograms								
1	173	(11.5)	42	(13.0)	16	(15.4)	231	(11.9)
2-10	1109	(73.7)	225	(69.4)	72	(69.2)	1406	(72.8)
11-20	173	(11.5)	45	(13.9)	15	(14.4)	233	(12.1)
>20	49	(3.3)	12	(3.7)	1	(1.0)	62	(3.2)
Don't know/missing	643		126		33		802	
Age at first mammogram								
<40	300	(19.9)	99	(30.4)	46	(45.1)	445	(23.0)
40-49	614	(40.7)	146	(44.8)	42	(41.2)	802	(41.4)
≥50	595	(39.4)	81	(24.8)	14	(13.7)	690	(35.6)
Don't know/missing[b]	638		124		35		797	
Mammogram screening frequency before risk assessment								
Every year or less	413	(19.3)	149	(33.4)	60	(44.1)	622	(22.8)
Every 2 or 3 years	1446	(67.6)	233	(52.2)	51	(37.5)	1730	(63.6)
Do not have regular mammograms/had only 1 mammogram	281	(13.1)	64	(14.4)	25	(18.4)	370	(13.6)

(continued)

Table 1 Continued

Characteristics	Risk Level: Average Risk n = 2147		Higher Than Average Risk n = 450		High Risk n = 137		Total n = 2734	
	n	(%)[a]	*n*	(%)[a]	*n*	(%)[a]	*n*	(%)[a]
Don't know/missing	7		4		1		12	
Perceived lifetime breast cancer risk before risk assessment								
Much lower than others	117	(5.7)	10	(2.4)	5	(3.7)	132	(5.0)
Lower than others	474	(23.1)	67	(15.8)	18	(13.2)	559	(21.4)
The same as others	1051	(51.3)	180	(42.4)	37	(27.2)	1268	(48.6)
Higher than others	390	(19.0)	153	(36.1)	65	(47.8)	608	(23.3)
Much higher than others	19	(0.9)	14	(3.3)	11	(8.1)	44	(1.7)
Don't know/missing	96		26		1		123	
Overall health before risk assessment								
Excellent/very good	1443	(67.4)	311	(69.3)	110	(80.3)	1864	(68.3)
Good	606	(28.3)	118	(26.3)	21	(15.3)	745	(27.3)
Fair/poor	93	(4.3)	20	(4.4)	6	(4.4)	119	(4.4)
Don't know/missing	5		1		0		6	

[a]Percentage excludes missing/prefer not to answer/don't know.
[b]Includes those whose age at first mammogram was <20 years ($n = 8$).

worry and psychological distress were low and remained so throughout the follow-up period, reaching a maximum of 7.1 out of a total score of 20 and 6.3 out of 40, respectively, at risk communication. The changes observed for these outcomes were small, with changes of less than 1 unit on the measurement scales.

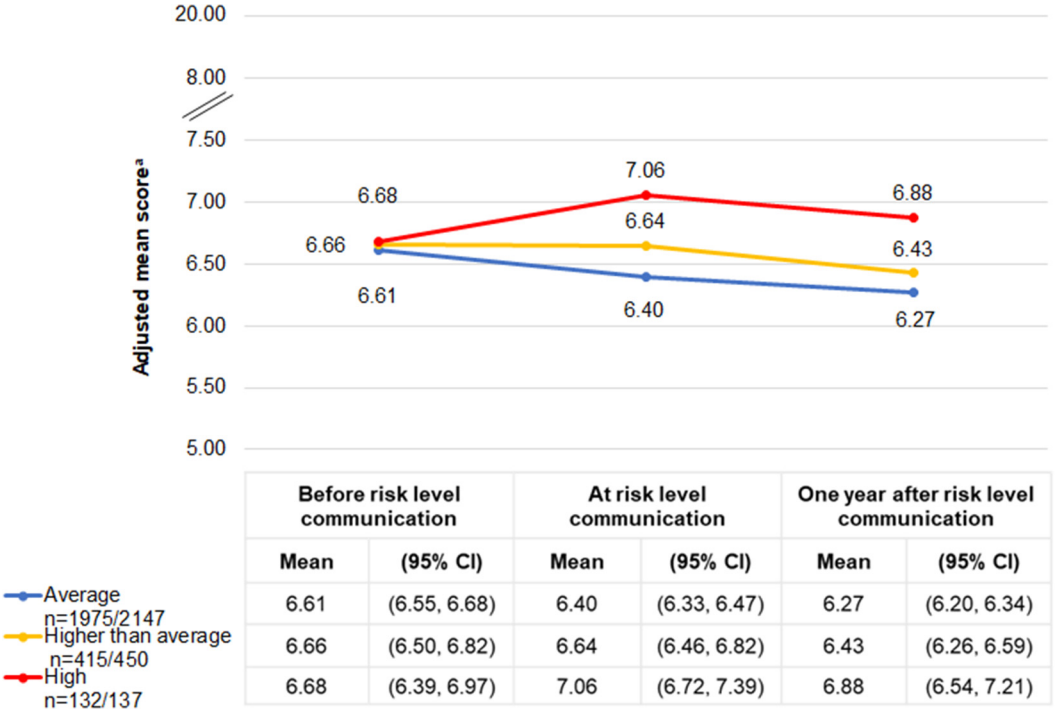
Adjusted mean breast cancer worry scores decreased slightly, although statistically significantly, at risk communication in the average-risk group ($P < .0001$) and increased slightly in the high-risk group ($P = .030$) (Table 2). Worry about breast cancer decreased significantly between the period before risk assessment and 1 year after risk communication, both in the average-risk ($P < .0001$) and higher-than-average-risk ($P = .008$) groups, whereas no significant change was observed in the high-risk group ($P = .211$). Higher levels of breast cancer worry were observed among the high-risk group compared with the average- and higher-than-average-risk groups at risk communication and 1 year later, as well as in the trend observed before risk communication up to 1 year after disclosure (all P values < 0.05).

Psychological distress increased slightly, although statistically significantly, at risk level communication in the average ($P < .0001$) and higher-than-average-risk ($P = .036$) groups (Table 2). No significant difference was noted between risk levels for psychological distress at risk communication and 1 year later, as well as in the trend observed before risk communication up to 1 year post-disclosure.

No statistically significant difference by risk level was observed for breast cancer worry and psychological distress, except for a slight increase in psychological distress over time in Ontario's average-risk group compared with Quebec's ($P = .008$) (Supplemental Table 2). A sensitivity analysis was conducted, including the 925 excluded participants, and the results remained virtually unchanged.

Factors associated with decisional regret

Decisional regret 1 year after risk level communication was low, with a mean regret score of 10.9 out of 100 (SD = 13.5, median = 5.0), with 46.8% of participants reporting no regret at all about their decision (score = 0). Factors associated with decisional regret 1 year after risk level communication are presented in Table 3. In the multivariable analysis, for those at high risk, having a family history of breast cancer was associated with a higher decisional regret score than for participants at average risk with no family history ($P = .001$). In contrast, the absence of family history for women at higher than average risk was associated with a higher decisional regret ($P = .003$). Women who perceived their breast cancer risk as much higher/higher than others before risk assessment had a lower decisional regret score than those who perceived their risk as the same as others ($P < .0001$). Decisional regret was higher among members of visible minorities ($P = .041$). Of participants who decided to follow the proposed screening action plan, those who reported changes in their usual screening experienced less regret 1 year after risk disclosure than those who reported no change in their usual screening ($P = .009$). Participants who felt relief after risk disclosure had lower



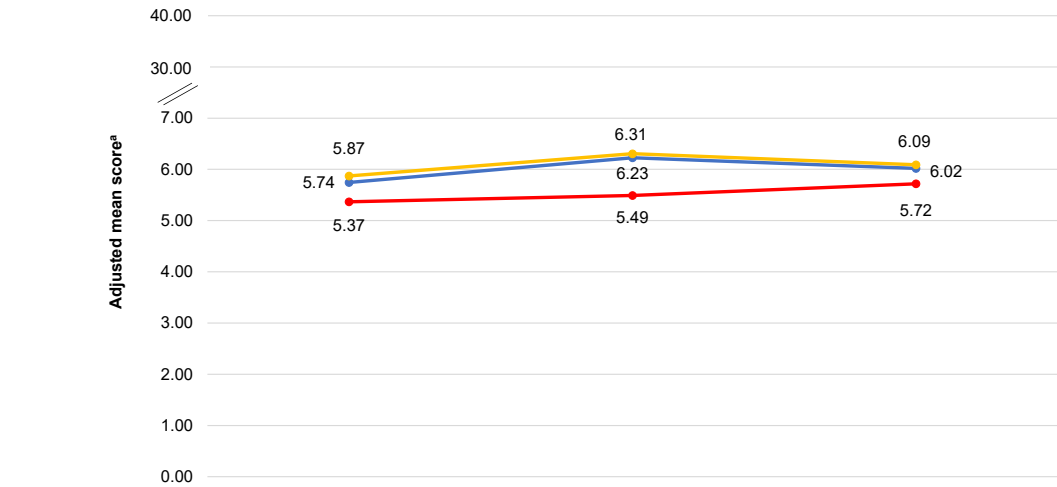
	Before risk level communication		At risk level communication		One year after risk level communication	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Average n=1975/2147	6.61	(6.55, 6.68)	6.40	(6.33, 6.47)	6.27	(6.20, 6.34)
Higher than average n=415/450	6.66	(6.50, 6.82)	6.64	(6.46, 6.82)	6.43	(6.26, 6.59)
High n=132/137	6.68	(6.39, 6.97)	7.06	(6.72, 7.39)	6.88	(6.54, 7.21)

Figure 1 **Adjusted mean score for breast cancer worry before and after risk communication by risk level ($n = 2522$).** [a]Adjusted for age group, province, education, visible minority status, family history of breast cancer, perceived risk, and psychological distress.

decisional regret scores than those who had no relief at all ($P < .0001$). Finally, a higher satisfaction score with the information received was associated with a lower decisional regret score ($P < .0001$).

Emotional outcome of knowing risk level

1 year after risk communication, most participants reported some degree of relief about knowing their breast cancer risk



	Before risk communication		At risk communication		One year after risk communication	
	Mean	(95% CI)	Mean	(95% CI)	Mean	(95% CI)
Average n=1938/2147	5.74	(5.54, 5.95)	6.23	(5.99, 6.46)	6.02	(5.78, 6.26)
Higher than average n=406/450	5.87	(5.38, 6.36)	6.31	(5.79, 6.82)	6.09	(5.55, 6.63)
High n=132/137	5.37	(4.51, 6.23)	5.49	(4.66, 6.32)	5.72	(4.87, 6.57)

Figure 2 **Adjusted mean score for psychological distress before and after risk communication by risk level ($n = 2476$).** [a]Adjusted for age group, province, education, visible minority status, family history of breast cancer, perceived risk, and worry about breast cancer.

Table 2 Differences in adjusted mean score for breast cancer worry and psychological distress over time by risk level

Variable	Time	Risk Level	Adjusted Mean[a]	(95% CI)	*P* value
Breast cancer worry (n = 2522)	At risk vs before risk communication	Average	−0.21	(−0.28 to −0.15)	<.0001
		Higher than average	−0.01	(−0.18 to 0.15)	.859
		High	0.38	(0.04-0.71)	.030
	1 year after risk vs at risk communication	Average	−0.13	(−0.19 to −0.07)	<.0001
		Higher than average	−0.22	(−0.38 to −0.06)	.008
		High	−0.18	(−0.52 to 0.16)	.296
	At risk communication	Average vs higher than average	−0.24	(−0.44 to −0.05)	.015
		Average vs high	−0.66	(−1.00 to −0.31)	<.001
		Higher than average vs high	−0.41	(−0.79 to −0.04)	.032
	1 year after risk communication	Average vs higher than average	−0.16	(−0.34 to 0.02)	.086
		Average vs high	−0.61	(−0.96 to −0.27)	.001
		Higher than average vs high	−0.45	(−0.82 to −0.08)	.017
	Before risk up to 1 year after risk communication	Average	−0.17	(−0.21 to −0.14)	<.0001
		Higher than average	−0.12	(−0.20 to −0.03)	.008
		High	0.10	(−0.06 to 0.25)	.211
		Average vs higher than average	−0.06	(−0.15 to 0.04)	.228
		Average vs high	−0.27	(−0.43 to −0.12)	.001
		Higher than average vs high	−0.21	(−0.39 to −0.04)	.017
Psychological distress (n = 2476)	At risk vs before risk communication	Average	0.48	(0.30-0.67)	<.0001
		Higher than average	0.43	(0.03-0.84)	.036
		High	0.12	(−0.58 to 0.83)	.729
	1 year after risk vs at risk communication	Average	−0.21	(−0.40 to −0.02)	.030
		Higher than average	−0.22	(−0.67 to 0.23)	.340
		High	0.23	(−0.48 to 0.93)	.527
	At risk communication	Average vs higher than average	−0.08	(−0.65 to 0.50)	.787
		Average vs high	0.74	(−0.14 to 1.61)	.100
		Higher than average vs high	0.82	(−0.15 to 1.78)	.099
	1 year after risk communication	Average vs higher than average	−0.07	(−0.67 to 0.53)	.820
		Average vs high	0.30	(−0.59 to 1.19)	.509
		Higher than average vs high	0.37	(−0.63 to 1.37)	.468
	Before risk up to 1 year after risk communication	Average	0.14	(0.04 to 0.24)	.007
		Higher than average	0.11	(−0.13 to 0.35)	.376
		High	0.18	(−0.23 to 0.58)	.396
		Average vs higher than average	0.03	(−0.23 to 0.29)	.827
		Average vs high	−0.04	(−0.46 to 0.38)	.856
		Higher than average vs high	−0.07	(−0.54 to 0.40)	.779

[a]Adjusted for age group, province, education, visible minority, family history of breast cancer, perceived risk and worry about breast cancer, or psychological distress.

level (79.9%) and were not upset at all (81.4%) (Figure 3). Regardless of their family history of breast cancer, fewer participants at higher than average risk and at high risk were relieved (all P values < .005), and more participants were upset compared with women at average risk without a family history of breast cancer (all P values < .0001) (Supplemental Table 3).

Discussion

In this study, which evaluated the impact of communicating personal breast cancer risk levels up to 1 year after risk disclosure, there was no evidence of major adverse impact on breast cancer worry and psychological distress. Overall, most participants were somewhat relieved and not upset at all to learn about their breast cancer risk level, but this varied depending on their risk levels. Decisional regret 1 year after risk level communication was low, and almost half of the participants expressed no regret at all. Certain characteristics were associated with lower levels of decisional regret, including perceiving lifetime risk before risk communication as much higher or higher than others, willingness to follow proposed screening action plan with changes to usual breast screening, degree of relief after risk disclosure, and higher satisfaction with the information received. Inversely, decisional regret was higher among members of visible minorities.

In the multivariable analysis, for those at high risk, having a family history of breast cancer was associated with a higher decisional regret score than for participants at average risk with no family history (P = .001). In contrast, the absence of family history for women at higher-than-average risk was associated with a higher decisional regret (P = .003).

Table 3 Factors associated with decisional regret mean scores 1 year after risk level communication

		Univariate			Multivariate		
Characteristics	*n*	Mean Score	(SE)	*P* Value[a]	Adjusted Mean Score	(SE)	*P* Value[a]
Total (SD)	2638	10.93	(13.46)				
Risk Level							
Average	2066	10.26	(0.29)				
Higher than average	437	13.46	(0.64)	<.0001			
High	135	12.95	(1.15)	.024			
Age group at risk assessment (y)							
40-49	410	9.88	(0.66)	.085	9.38	(0.68)	.113
50-59	1064	11.22	(0.41)		10.64	(0.39)	
60-70	1164	11.03	(0.39)	.732	10.49	(0.39)	.787
Family history of breast cancer							
No	1309	11.05	(0.37)				
Yes	1329	10.81	(0.37)	.636			
Risk level and family history							
Average risk without FHx	1164	10.43	(0.39)		9.94	(0.41)	
Average risk with FHx	902	10.04	(0.45)	.505	10.05	(0.44)	.865
Higher than average risk without FHx	126	16.50	(1.19)	<.0001	13.87	(1.25)	.003
Higher than average risk with FHx	311	12.23	(0.76)	.036	9.98	(0.80)	.972
High risk without FHx	19	12.89	(3.07)	.426	11.28	(2.98)	.657
High risk with FHx	116	12.96	(1.24)	.052	14.60	(1.40)	.001
Province							
Ontario	1257	10.92	(0.38)		9.79	(0.39)	
Quebec	1381	10.93	(0.36)	.989	10.87	(0.36)	.058
Highest level of education							
Below bachelor's degree	1253	11.37	(0.38)				
Bachelor's degree or above	1372	10.51	(0.36)	.103			
Marital status							
Single/widowed/ divorced/ separated	617	10.80	(0.54)				
Married/common law	2004	10.91	(0.30)	.859			
Employment status							
Employed	1592	10.82	(0.34)				
Retired/not employed	1040	11.09	(0.42)	.610			
Visible minority group membership							
Not a visible minority	2461	10.60	(0.27)		10.26	(0.25)	
Visible minority	125	15.65	(1.19)	<.0001	12.89	(1.26)	.041
Perceived lifetime breast cancer risk before risk assessment							
Much lower/lower than others	664	11.44	(0.52)	.526	11.51	(0.51)	.298
The same as others	1225	11.03	(0.38)		10.87	(0.36)	
Much higher/higher than others	639	9.75	(0.53)	.051	8.23	(0.54)	<.0001
Age at first mammogram							
<50	1208	10.49	(0.39)	.294			
≥50	666	11.17	(0.52)				
Don't know/missing[b]	764	11.41	(0.49)	.736			
Mammogram screening frequency before risk assessment							
Every year or less	596	11.56	(0.55)	.270			
Every 2 or 3 years	1665	10.85	(0.33)				
Do not have regular mammograms/ had only one mammogram	365	10.22	(0.70)	.413			
Overall health				.542			
Excellent/very good	1801	10.79	(0.32)	.631			
Good	713	11.07	(0.50)				
Fair/poor	118	12.13	(1.24)	.429			

(continued)

Table 3 Continued

Characteristics	*n*	Univariate Mean Score	(SE)	*P* Value[a]	Multivariate Adjusted Mean Score	(SE)	*P* Value[a]
Risk level discussed with HCP							
Yes	1860	11.01	(0.31)				
No	758	10.83	(0.49)	.749			
Decision-making score	735	0.46[c]	(0.13)	<.001			
Decision to follow breast screening action plan							
Yes, there were no changes to my usual screening	1739	10.04	(0.32)		10.49	(0.31)	
Yes, will follow changes to my usual screening	413	10.08	(0.65)	.958	8.52	(0.66)	.009
No, will not follow screening action plan/health care professional has not recommended it/due to COVID-19	187	14.44	(0.97)	<.0001	11.86	(0.94)	.170
Don't know	262	15.14	(0.82)	<.0001	11.59	(0.85)	.227
Degree of relief after risk disclosure							
No relief at all	504	15.41	(0.58)		13.47	(0.63)	
Slight/moderate/considerable relief	1999	9.38	(0.29)	<.0001	9.59	(0.29)	<.0001
Degree of upset after risk disclosure							
Not upset at all	2083	9.88	(0.29)				
Slightly/moderately/very upset	472	14.05	(0.60)	<.0001			
Satisfaction with the information received	2612	1.40[c]	(0.08)	<.0001	−1.31[a]	(0.08)	<.0001
Psychological distress before risk assessment	2636	0.12[c]	(0.05)	.024			
Breast cancer worry before risk assessment	2632	0.42[c]	(0.15)	.005			

FHx, Family history of breast cancer; *HCP*, health care professional.
[a]*P* value of the mean difference.
[b]Includes those whose age at first mammogram was <20 years ($n = 8$).
[c]Estimate from the linear regression.

Our study showed that the emotional outcomes after risk communication and breast cancer worry changed in line with the risk levels provided. For instance, regardless of family history, being identified at higher-than-average or high risk was associated with experiencing less relief and being more upset 1 year after risk disclosure. Higher levels of breast cancer worry were observed over time in the high-risk group compared with the average- and higher-than-average-risk groups. This is consistent with findings from the PROCAS 2 study (Breast Cancer Predict), in which breast cancer worry changed in line with the risk levels provided (high, moderate, average, and below average) 6 months after risk disclosure.[14] Despite statistically significant differences between risk groups in our study, the differences observed on the breast cancer worry scale were very small and unlikely to be clinically significant. Therefore, our findings suggest that concerns that risk stratification would produce adverse psychological effects through increased breast cancer worry or anxiety are not supported, even for individuals identified at high risk. This is consistent with previous studies indicating that communicating risk levels may have no or limited effect on breast cancer anxiety, far from reaching clinical levels.[12-14] However, it should be kept in mind that even small individual differences, even if not significant enough to be considered pathological, can have meaningful effects when aggregated across a population.

During follow-up, no significant difference was observed between risk levels for psychological distress. Levels of psychological distress in this study (Mean K10 score = 5.7/40, SD = 5.1) were also comparable to those observed in the Canadian general population (Mean K10 score = 5.4/40, SD = 5.5).[30] Decisional regret 1 year after risk level communication was also very low in our study (Mean = 10.9/100, SD = 13.5, Median = 5.0). This is similar to the decisional regret observed among women who received their breast cancer PRS (Mean = 9.3/100, SD = 15.1).[11] Our study shows that decisional regret 1 year after risk communication among women aged 40 to 49 does not differ from that in women aged 50 to 59. This is an encouraging result for potentially including participants 40 to 49 in screening programs, a target many jurisdictions are moving toward.

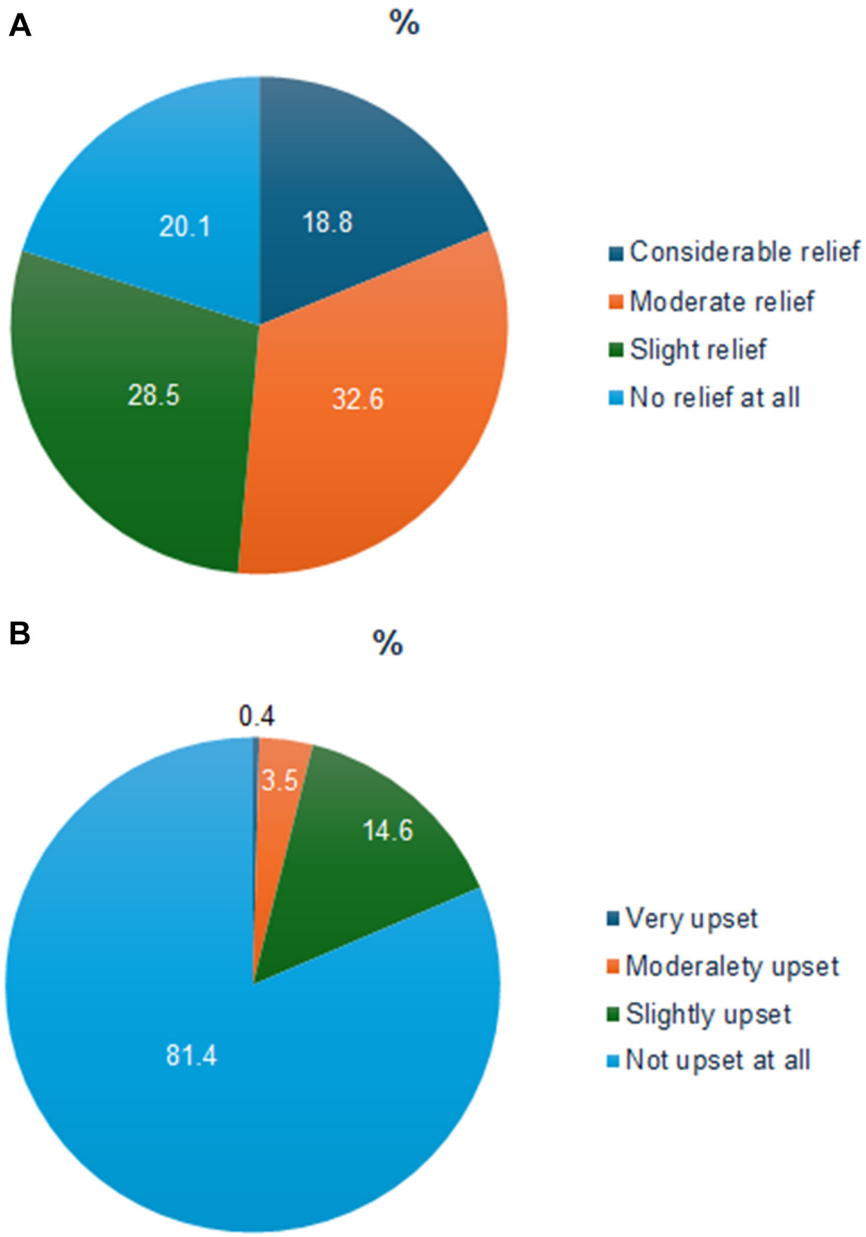


Figure 3 Emotional impacts from learning breast cancer risk level 1 year after risk communication ($n = 2734$). A. Excludes don't know/missing data ($n = 153$). B. Excludes don't know/missing data ($n = 98$).

Study strengths and limitations

This study has several strengths. First, the participation rate in both follow-up questionnaires was excellent, resulting in a large sample size. Second, our study assessed the impacts across all 3 risk levels, which is crucial for understanding how risk communication may affect diverse risk groups. If implemented at the population level, risk-stratified breast cancer screening will be available to all eligible individuals, with screening frequency and modalities tailored according to each woman's risk category. Third, our study assessed decisional regret, an important factor to consider when implementing a risk-based screening approach within existing screening programs because it may affect future engagement. Fourth, participants were followed up to 1 year after risk disclosure, providing a longer-term perspective on the impact of risk level communication compared with other studies at a population level.

The results should be interpreted with consideration of the potential limitations. First, approximately 15% of our cohort was 40 to 49 years of age and had a mammogram. Therefore, they may have already known/suspected that they had an increased risk of breast cancer because this age group was not targeted by either province's breast screening program at the time of the study. Second, compared with the Canadian census, a greater proportion of PERSPECTIVE

I&I participants were not visible minorities and had a higher educational attainment.[9] Third, in Quebec, participants were also required to have a primary HCP to whom the risk letter was systematically sent. According to a 2022 survey, it is estimated that more than 1 in 5 Canadians do not have a family physician or nurse practitioner they see regularly.[31] Consequently, access to information and guidance about the personalized screening action plan, as well as referral for recommended screening exams, would be a key issue at the population level. Fourth, the indicators used in this study are specific indicators that do not take into account all aspects related to the psychological and emotional outcomes. For all of these reasons, it is likely that the psychological and emotional burden maybe greater in the general population.

Considerations for implementation

Our results underline the importance of having risk communication strategies that consider the specific emotional needs of individuals, particularly those who will be identified at higher levels of risk. Risk communication should also include comprehensive and clear information tools for participants. In this study, higher satisfaction with the received information was associated with a lower decisional regret score 1 year after risk disclosure. A systematic review reported that lower satisfaction with the information provided was significantly associated with greater regret about health decisions in some studies,[32] which is consistent with our findings. This systematic review also reported that belonging to a minority race/ethnicity was associated with decisional regret, consistent with our study results.[32] Having culturally appropriate breast screening information at the population level is crucial for improving health outcomes, reducing disparities, and reducing decisional regret.

In this study, participants who perceived their risk as "much higher/higher than others" before risk assessment experienced less decisional regret than those who perceived their risk as "the same as other," which suggests that risk perception before risk assessment could be an important factor in determining future reactions of individuals after risk communication. As highlighted in a systematic review of qualitative research, women have preconceptions and expectations about their breast cancer risk before receiving a clinical risk estimate.[33] The results could inform participants that their risk is lower than expected or validate their risk appraisals. In the first case, this is consistent with our findings that feeling relieved in some way after risk communication is associated with less regret about the decision. In the latter, confirming a higher risk could be advantageous, potentially allowing access to more frequent mammograms or magnetic resonance images. This is in line with our findings, which indicate that changes to the screening action plan were associated with less decisional regret. Screening for high-penetrance pathogenic variants in susceptibility genes, such as *BRCA1*, *BRCA2*, and *PALB2*, was not performed in our study. This could have increased decisional regret among some women. Greater decisional regret was observed in our study among high-risk women with a family history of breast cancer.

How individuals would be recruited for breast cancer risk-stratified screening at the population level could have an impact on emotional outcomes after risk communication. Participants from Quebec reported being less relieved from learning their risk level than participants from Ontario, which could be partially explained by the difference in the recruitment method. Ontario's sample was recruited via a population-based mail invitation approach from the provincial screening program, whereas Quebec participants were convenience-sampled, and interested women registered on our study website. With this latter approach, it is likely that individuals with stronger contributory risk factors participated. For example, Quebec participants were much more likely than Ontario participants to have a family history of breast cancer (first and/or second degree).[9] Seeking validation of being at high risk may have motivated some women to participate in the study, as previously observed in other studies.[33] Motivations and expectations to enroll in a risk-stratified study could lead to different emotional outcomes, which should be considered when implementing such an approach within a screening program.

In conclusion, our observations suggest that there is no evidence of major adverse psychological outcomes associated with personalized breast cancer risk communication. It also highlights some considerations for implementing a risk-stratified breast cancer screening approach at the population level. Further research should examine the other implications of risk stratification, particularly how women and their HCPs can use information on risk level and the associated screening action plan to make informed decisions about breast cancer screening, as well as the clinical outcomes. It will be essential to assess the readiness of healthcare organizations and determine the best approaches for implementation.

Data Availability

Parts of the material underlying this article are based on data and information provided by Ontario Health (Cancer Care Ontario). Ontario Health is prohibited from making the data used in this research publicly accessible if they include potentially identifiable personal health information and/or personal information as defined in Ontario law, specifically the Personal Health Information Protection Act and the Freedom of Information and Protection of Privacy Act. Upon request, data deidentified to a level suitable for public release may be provided. A subset of the Quebec participants have consented to sharing their data in the context of future research. Deidentified data from these participants are available upon request to the principal investigator

of the PERSPECTIVE I&I project (jacques.simard@crchudequebec.ulaval.ca). For the other subset of Quebec participants, data cannot be shared because of consent form constraints. No personally identifiable information will be shared.

Acknowledgments

The authors thank and acknowledge the PERSPECTIVE I&I Activity 3 Project Team (alphabetical): Lucie Amyot, Gabriel Couture, Gratien Dalpé, Martine Dumont, Clarissa Encisa, Hortense Galois, Palmira Granados, Julie Lapointe, Emmanuelle Lévesque, Cynthia MBuya-Bienge, Penny Soucy, Rosemary Sousa, and Lara Tardif-Michaud; collaborators and health professionals: Nathalie Bolduc, Vivianne Freitas, and Kardi Kennedy; Ontario Health: Andrea Mackesy and Emma Sabo; and PULSAR and Université Laval: Kevin Arseneault, François Breton, Anne-Sylvie Chenat, Marie-Noëlle Guillemette, Marie-Andrée Levesque, Jean-Philippe Lévesque, and Sylvain Parent.

Funding

This work was supported by the Government of Canada through Genome Canada (grant #: 13529), the Canadian Institutes of Health Research (grant #: 155865), the Ministère de l'Économie et de l'Innovation du Québec through Génome Québec, the Quebec Breast Cancer Foundation, the CHU de Québec Foundation, the CHU de Québec-Université Laval Research Center, and the Ontario Ministry of Research and Innovation through the Ontario Research Fund. Antonis C. Antoniou and Tim Carver are supported by Cancer Research UK grant: PPRPGM-Nov20\100002.

Author Contributions

Conceptualization: A.C.A., J.D.B., J.C., D.F.E., A.E., L.E., Y.J., B.M.K., H.N., N.P., M.J.W., A.M.C., J.S., M.D.; Formal Analysis: L.L.-C., A.T., E.D., A.M.C., J.S., M.D.; Funding Acquisition: A.M.C, J.S.; Investigation: L.L.-C., A.T., K.M.B., A.C., A.C.A., T.C., S.-L.C., D.F.E., C.L.C., J.L.; Project Administration: L.L.-C., A.T., K.M.B., A.C.; Resources: L.L.-C., A.T., K.M.B., A.C., K.A.B., J.C., A.E., S.F., R.H.K., J.L., A.L., J.-S.P., A.J.S., T.L.S., A.M.C., J.S., M.D.; Writing-original draft: L.L.-C., A.T., K.M.B., A.C., A.C.A., K.A.B., M.J.M.B., J.D.B., T.C., S.-L.C.; J.C., E.D., D.F.E., A.E., L.E., D.G.R.E., S.F.,Y.J., R.H.K., B.M.K., C.L.-C., J.L., A.L., H.N., J.-S.P., N.P., A.J.S., T.L.S., M.J.W., A.M.C., J.S., M.D.; Writing-review and editing: L.L.-C., A.T., K.M.B., A.C., A.C.A., K.A.B., M.J.M.B., J.D.B., T.C., S.-L.C.; J.C., E.D., D.F.E., A.E., L.E., D.G.R.E., S.F.,Y.J., R.H.K., B.M.K., C.L.-C., J.L., A.L., H.N., J.-S.P., N.P., A.J.S., T.L.S., M.J.W., A.M.C., J.S., M.D.

Ethics Declaration

The study was approved by the Ethics Research Committees of the CHU de Québec-Université Laval (MP-20-2020-4670), McGill University (A12-B65-18A), University of Toronto (00036881), Grand River Hospital (2020-0709), McMaster University (11468), St. Michael's Hospital (19-220), Sunnybrook Health Sciences Centre (2255), University Health Network (19-5340), and Queens University (6030732 EPID-712-20). Informed consent was obtained from all participants involved in the study.

Conflict of Interest

Antonis C. Antoniou, Tim Carver, and Douglas F. Easton are creators of BOADICEA, which has been licensed to Cambridge Enterprise (University of Cambridge). The funders had no role in the design of the study; collection, analyses or interpretation of data; writing of the manuscript; or decision to publish the results. All other authors declare no conflicts of interest.

Additional Information

The online version of this article (https://doi.org/10.1016/j.gim.2025.101453) contains supplemental material, which is available to authorized users.

Affiliations

[1]CHU de Québec-Université Laval Research Center, Quebec City, QC, Canada; [2]Ontario Health, Toronto, ON, Canada; [3]Centre for Cancer Genetic Epidemiology, Department of Public Health and Primary Care, University of Cambridge, Cambridge, United Kingdom; [4]IQ Health Science Department, Radboud university medical center, Nijmegen, The Netherlands; [5]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada; [6]Centre des maladies du sein, CHU de Québec-Université laval, Quebec City, QC, Canada; [7]Department of Family Medicine and Emergency Medicine, Faculty of Medicine, Université Laval, Quebec City, QC, Canada; [8]Sunnybrook Health Science Centre, Toronto, ON, Canada; [9]Programme québécois de cancérologie, Ministère de la Santé et des Services sociaux, Quebec City, QC, Canada; [10]Centre intégré de santé et de services sociaux de Lanaudière, Joliette, QC, Canada; [11]Department of Medical Genetics and Cancer Epidemiology, The University of Manchester, Manchester, United Kingdom; [12]Centre of Genomics and Policy, McGill University, Montreal, QC, Canada; [13]Princess Margaret Cancer Centre, Toronto, ON, Canada; [14]Canada Women's College Research Institute, Toronto,

ON, Canada; [15]Department of Social and Preventive Medicine, Faculty of Medicine, Université Laval, Quebec City, QC, Canada; [16]Université Laval Cancer Research Center, Quebec City, QC, Canada; [17]Division of Clinical Laboratory Genetics, University Health Network, Toronto, ON, Canada; [18]Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada; [19]Department of Molecular Medicine, Faculty of Medicine, Université Laval, Quebec City, QC, Canada; [20]Faculty of Pharmacy, Université Laval, Quebec City, QC, Canada

References

1. Dibden A, Offman J, Duffy SW, Gabe R. Worldwide review and meta-analysis of cohort studies measuring the effect of mammography screening programmes on incidence-based breast cancer mortality. *Cancers (Basel)*. 2020;12(4):976. http://doi.org/10.3390/cancers12040976
2. Esserman LJ, WISDOM Study, Investigators Athena. The WISDOM Study: breaking the deadlock in the breast cancer screening debate. *npj Breast Cancer*. 2017;3:34. http://doi.org/10.1038/s41523-017-0035-5
3. Roux A, Cholerton R, Sicsic J, et al. Study protocol comparing the ethical, psychological and socio-economic impact of personalised breast cancer screening to that of standard screening in the "My Personal Breast Screening" (MyPeBS) randomised clinical trial. *BMC Cancer*. 2022;22(1):507. http://doi.org/10.1186/s12885-022-09484-6
4. Evans DG, Astley S, Stavrinos P, et al. Improvement in Risk Prediction, Early Detection and Prevention of Breast Cancer in the NHS Breast Screening Programme and Family History Clinics: a Dual Cohort Study. *Programme Grants Appl Res*. 2016;4(11):1-210. http://doi.org/10.3310/pgfar04110
5. Brooks JD, Nabi HH, Andrulis IL, et al. Personalized risk assessment for prevention and early detection of breast cancer: integration and implementation (PERSPECTIVE I&I). *J Pers Med*. 2021;11(6):511. http://doi.org/10.3390/jpm11060511
6. Pashayan N, Antoniou AC, Ivanus U, et al. Personalized early detection and prevention of breast cancer: ENVISION consensus statement. *Nat Rev Clin Oncol*. 2020;17(11):687-705. http://doi.org/10.1038/s41571-020-0388-9
7. Pashayan N, Morris S, Gilbert FJ, Pharoah PDP. Cost-effectiveness and benefit-to-harm ratio of risk-stratified screening for breast cancer: a life-table model. *JAMA Oncol*. 2018;4(11):1504-1510. http://doi.org/10.1001/jamaoncol.2018.1901
8. Van den Broek JJ, Schechter CB, Van Ravesteyn NT, et al. Personalizing breast cancer screening based on polygenic risk and family history. *J Natl Cancer Inst*. 2021;113(4):434-442. http://doi.org/10.1093/jnci/djaa127
9. Walker MJ, Blackmore KM, Chang A, et al. Implementing multifactorial risk assessment with polygenic risk scores for personalized breast cancer screening in the population setting: challenges and opportunities. *Cancers*. 2024;16(11):2116. http://doi.org/10.3390/cancers16112116
10. Ringwald J, Wochnowski C, Bosse K, et al. Psychological distress, anxiety, and depression of cancer-affected BRCA1/2 mutation carriers: a systematic review. *J Genet Couns*. 2016;25(5):880-891. http://doi.org/10.1007/s10897-016-9949-6
11. Yanes T, Meiser B, Kaur R, et al. Breast cancer polygenic risk scores: a 12-month prospective study of patient reported outcomes and risk management behavior. *Genet Med*. 2021;23(12):2316-2323. http://doi.org/10.1038/s41436-021-01288-6
12. Xie Z, Wenger N, Stanton AL, et al. Risk estimation, anxiety, and breast cancer worry in women at risk for breast cancer: a single-arm trial of personalized risk communication. *Psycho-Oncology*. 2019;28(11):2226-2232. http://doi.org/10.1002/pon.5211
13. French DP, Southworth J, Howell A, et al. Psychological impact of providing women with personalised 10-year breast cancer risk estimates. *Br J Cancer*. 2018;118(12):1648-1657. http://doi.org/10.1038/s41416-018-0069-y
14. French DP, McWilliams L, Bowers S, et al. Psychological impact of risk-stratified screening as part of the NHS Breast Screening Programme: multi-site non-randomised comparison of BC-Predict versus usual screening (NCT04359420). *Br J Cancer*. 2023;128(8):1548-1558. http://doi.org/10.1038/s41416-023-02156-7
15. Mavaddat N, Michailidou K, Dennis J, et al. Polygenic risk scores for prediction of breast cancer and breast cancer subtypes. *Am J Hum Genet*. 2019;104(1):21-34. http://doi.org/10.1016/j.ajhg.2018.11.002
16. Mavaddat N, Ficorella L, Carver T, et al. Incorporating alternative polygenic risk scores into the BOADICEA breast cancer risk prediction model. *Cancer Epidemiol Biomarkers Prev*. 2023;32(3):422-427. http://doi.org/10.1158/1055-9965.EPI-22-0756
17. Carver T, Hartley S, Lee A, et al. CanRisk tool-A web interface for the prediction of breast and ovarian cancer risk and the likelihood of carrying genetic pathogenic variants. *Cancer Epidemiol Biomarkers Prev*. 2021;30(3):469-473. http://doi.org/10.1158/1055-9965.EPI-20-1319
18. Pashayan N, Antoniou AC, Lee A, et al. Should age-dependent absolute risk thresholds be used for risk stratification in risk-stratified breast cancer screening? *J Pers Med*. 2021;11(9):916. http://doi.org/10.3390/jpm11090916
19. Lerman C, Trock B, Rimer BK, Jepson C, Brody D, Boyce A. Psychological side effects of breast cancer screening. *Health Psychol*. 1991;10(4):259-267. http://doi.org/10.1037//0278-6133.10.4.259
20. Andersen MR, Smith R, Meischke H, Bowen D, Urban N. Breast cancer worry and mammography use by women with and without a family history in a population-based sample. *Cancer Epidemiol Biomarkers Prev*. 2003;12(4):314-320.
21. Kessler RC, Barker PR, Colpe LJ, et al. Screening for serious mental illness in the general population. *Arch Gen Psychiatry*. 2003;60(2):184-189. http://doi.org/10.1001/archpsyc.60.2.184
22. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychol Med*. 2002;32(6):959-976. http://doi.org/10.1017/s0033291702006074
23. Brehaut JC, O'Connor AM, Wood TJ, et al. Validation of a decision regret scale. *Med Decis Making*. 2003;23(4):281-292. http://doi.org/10.1177/0272989X03256005
24. Kriston L, Scholl I, Hölzel L, Simon D, Loh A, Härter M. The 9-item shared decision making questionnaire (SDM-Q-9). Development and psychometric properties in a primary care sample. *Patient Educ Couns*. 2010;80(1):94-99. http://doi.org/10.1016/j.pec.2009.09.034
25. French DP, Maissi E, Marteau TM. Psychological costs of inadequate cervical smear test results. *Br J Cancer*. 2004;91(11):1887-1892. http://doi.org/10.1038/sj.bjc.6602224
26. Dorval M, Gauthier G, Maunsell E, et al. No evidence of false reassurance among women with an inconclusive BRCA1/2 genetic test result. *Cancer Epidemiol Biomarkers Prev*. 2005;14(12):2862-2867. http://doi.org/10.1158/1055-9965.EPI-05-0512
27. Visible Minority and Population Group reference guide, census of population. Statistics Canada. Accessed October 16, 2023. https://www12.statcan.gc.ca/census-recensement/2021/ref/dict/index-eng.cfm
28. Lumley T, Kronmal R, Ma S. Relative risk regression in medical research: models, contrasts, estimators, and algorithms. UW Biostatistics Working Paper Series Working. https://biostats.bepress.com/uwbiostat/paper293/
29. Spiegelman D, Hertzmark E. Easy SAS calculations for risk or prevalence ratios and differences. *Am J Epidemiol*. 2005;162(3):199-200. http://doi.org/10.1093/aje/kwi188

30. Shen Y. Mental health and labor supply: evidence from Canada. *SSM Popul Health*. 2023;22:101414. http://doi.org/10.1016/j.ssmph.2023.101414
31. Duong D, Vogel L. National survey highlights worsening primary care access. *CMAJ*. 2023;195(16):E592-E593. http://doi.org/10.1503/cmaj.1096049
32. Becerra Pérez MM, Menear M, Brehaut JC, Légaré F. Extent and predictors of decision regret about health care decisions: a systematic review. *Med Decis Making*. 2016;36(6):777-790. http://doi.org/10.1177/0272989X16636113
33. Woof VG, Howell A, McWilliams L, Gareth Evans D, French DP. How do women who are informed that they are at increased risk of breast cancer appraise their risk? A systematic review of qualitative research. *Br J Cancer*. 2022;127(11):1916-1924. http://doi.org/10.1038/s41416-022-01944-x