BMJ Open

Disentangling the determinants of interest and willingness to pay for breast cancer susceptibility testing in the general population: A cross-sectional Web-based survey

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016662
Article Type:	Research
Date Submitted by the Author:	03-Mar-2017
Complete List of Authors:	Blouin-Bougie, Jolyane; Université Laval, Management Amara, Nabil; Université Laval, Management Bouchard, Karine; Université Laval- Centre de recherche du CHU de Québec, Centre des maladies du sein Deschênes -Fabia Simard, Jacques; Université Laval- Centre de recherche du CHU de Québec, Medicine Dorval, Michel; Université Laval- Centre de recherche du CHU de Québec, Pharmacie
Primary Subject Heading:	Genetics and genomics
Secondary Subject Heading:	Oncology, Public health, Health services research
Keywords:	Interest, Willingness-to-pay, Breast cancer susceptibility testing, Women of the general population

Title

Disentangling the determinants of interest and willingness to pay for breast cancer susceptibility testing in the general population: A cross-sectional Web-based survey

Authors & Affiliation

1. Jolyane Blouin-Bougie, PhD Candidate
(Corresponding author)
Department of management, Université Laval
2325, rue de la Terrasse, Pavillon Palasis-Prince, 1516
Québec, QC (Canada) G1V 0A6
(418) 656-2131 # 1379
Jolyane.blouin-bougie@fsa.ulaval.ca

2. Nabil Amara, PhD
Department of management, Université Laval
2325, rue de la Terrasse, Pavillon Palasis-Prince, 1519
Québec, QC (Canada) G1V 0A6
(418) 656-2131 # 4382
Nabil.amara@fsa.ulaval.ca

3. Karine Bouchard, MSc
Centre des maladies du sein Deschênes-Fabia
Centre de recherche du CHU de Québec-Université Laval
Hôpital du Saint-Sacrement, 1050, chemin Sainte-Foy
Québec, QC (Canada) G1S 4L8
(418) 525-4444 # 82721
Karine.Bouchard@crchudequebec.ulaval.ca

4. Jacques Simard, PhD
Faculty of Medecine, Université Laval
Centre de recherche du CHU de Québec-Université Laval
2705, boulevard Laurier, R4-4787
Québec, QC (Canada) G1K 7P4
(418) 654-2264
Jacques.Simard@crchul.ulaval.ca

5. Michel Dorval, PhD
Faculty of Pharmacy, Université Laval
Centre de recherche du CHU de Québec-Université Laval
Hôpital du Saint-Sacrement, 1050, chemin Sainte-Foy
Québec (Canada) G1S 4L8
(418) 682-8047
michel.dorval@pha.ulaval.ca

Key Words
Interest; Willingness-to-pay; Breast cancer susceptibility testing; Women of the general population

Abbreviations
BC = Breast cancer; BCST = Breast cancer susceptibility testing; PM = Personalized medicine; WTP = Willingness-to-pay

Words count
4602 (excluding title page, abstract, references, figures and tables)

Abstract

Objectives: To identify common and specific individual factors of women of the general population that favour or impede interest and willingness-to-pay (WTP) for breast cancer susceptibility testing (BCST), and to hierarchize these factors according to their impact on these two phenomena. The underlying assumption is that interest is a prerequisite of WTP.

Design and Methods: This study used a self-administered cross-sectional web-based questionnaire that included scenarios about the availability of a new genetic test for breast cancer.

Participants: French-speaking women of the general population of Québec (Canada), aged between 35 and 69, were identified from Web-based panel (2410 meet the selection criteria, 1160 were reached, and 1031 have completed the survey).

Measures: The outcomes are the level of interest and the WTP for BCST. Three categories of individual factors identified in the literature were used as potential explanatory factors, i.e., demographic, clinical, and psychosocial.

Results: Descriptive statistics indicated that the great majority of the women are interested in BCST (90%). Among those interested, more than half of them are willing-to-pay for such a test (57%). The regression model also pointed out to several factors associated with both outcomes (e.g., age, familial income, family history, locus of control (powerful others), or numeracy). Marginal effects estimates were also used to highlight most impactful factors on each outcome (*interest*: anxiety (.409), loci of control-powerful others (0.441) and chance (-.244), family history (.357); *WTP*: locus of control-powerful others (.283), family history (.208), familial income (-.154)).

Conclusion: The results of this study provide a proxy of the readiness of the women of the general population to use and to collectively pay for BCST. They also offer insights for developing inclusive and specific strategies to foster informed decision-making, and guide the services offered by health organizations corresponding to women's preferences and needs.

Strengths and limitations of this study

- In spite of a good response rate and a relatively large sample size, self-reported data like those used in this study are subject to social desirability bias.
- This study proposes a conceptually-driven two-step regression model allowing to test several explanatory factors of interest and WTP for genetic testing for which mixed findings have been reported in previous studies.
- To the extent of our knowledge, this study is the first to use marginal effects in the context of interest and WTP for cancer susceptibility testing in order to hierarchize the impact of various factors on those two outcomes.
- While this scenario-based study allowed to measure the degree of interest and level of WTP of a genetic test that is very likely to be offered to a wide range of women in the general population, it might have overestimated the level of interest and the real sum paid out-of-pocket in a realistic situation.

Introduction

Personalized medicine (PM) is an important growing area of research,[1] a significant driving economic sector,[eg. 2 3] and a promising avenue to improve the delivery of health care services.[4 5] One major aspect of PM is the utilization of genetic tests for which two main finalities are pursued: one is preventive, the other is curative.[6] The former relates to the assessment of the baseline risk or the susceptibility of an individual to develop a disease, and the surveillance or screening strategies that aim to detect a disease as early as possible. The latter instead refers to the clinical progression phase of a disease, i.e., the diagnosis, the prognosis, and the treatment. This distinction is essential as this paper focuses on the preventive part of PM: it assesses individual factors that impact on the interest and the value attributed by women of the general population (and not ill patients) to breast cancer susceptibility testing (BCST) in order to get insights on the readiness of this target population for the integration and the utilization of genetic information for BC prevention. BCST aims to identify women at risk of developing BC for a suitable offer of risk-management strategies that would be adapted to women's risk level and preferences (e.g., type of screening - mammograms or MRI - or consideration of prophylactic interventions - mastectomy or chemoprevention).[6-8]

Why does BCST matter? Firstly, BC is one of the leading causes of death of women all around the world,[9] and reduction of the burden of this disease is among the health care priorities of many developed countries, as demonstrated by their ongoing national BC screening programs.[10 11] Secondly, the case of BC is especially promising regarding PM development,[12 13] notably because BCST is used in highly-specialized clinics[14 15] since the commercialization of the BRCA1/2 mutation carrier test in the mid-90's.[16] This confers a well-established experience in managing the genetic risk of BC on which to build for the expansion of genetic services in the general population.[17] Thirdly, several genes and polymorphisms (SNPs) are now known as BC susceptibility risk factors and can be detected in women who are healthy.[18 19] Given that some of them are associated with greater risks than others, stratifying women's BC risk is viewed as a promising opportunity to adapt BC screening programs for maximizing benefits and minimizing drawbacks in the general population and the health care systems.[12 17 20] Fourthly, private companies already provide some BC genetic tests directly to consumers (DTC)[21 22] in overriding the

necessity of health care professionals' assessment and support.[8 23 24] This raises a lot of concerns, markedly regarding the test results' understanding and their implications for the consumers (e.g., worries, risk of discrimination, repercussions on family members, etc.).[6 21 23]

However, are end-users or consumers (women) interested in BCST? Are women willing to pay for genetic tests to possibly strictly get informational input on their risk of developing such a disease as BC? Even if the classic cost-effectiveness framework assesses these outcomes in association with actionable health care measures (i.e., provide guidance for treatment decisions), yet recent literature shows that the answer is positive. It may reduce uncertainty, offer some reassurance, guide life or family planning decisions, and may be useful to other family members.[25-28] How and why women value BCST is less clear, but these are imperative questions for decision-makers and managers involved in the development of PM or the improvement of BC preventive services.

Background

During the last decades, the number of publications on the valuation of health care technologies has gradually increased. One of the standard economic measures used and recognized to offer enough tractability to assess how people value or prefer health information, goods or services is the willingness-to-pay (WTP).[28-31] It is defined as "the maximum amount of money an individual could pay for the health improvement and still consider himself or herself better off".[25]

In this respect, a recent literature review has drawn useful conclusions on WPT for diagnostic technologies, mentioning that genetic tests are among the most studied.[25] The body of empirical evidence regarding WTP for genetic testing in this review is however discussed as an integrative part of the larger one on diagnostic technologies valuation literature, and this includes various types of genetic tests -more specifications on the type of genetic tests are available in *The Genetic Home Reference of the U.S. National Library of Medicine* at https://ghr.nlm.nih.gov/primer/testing/uses- but also imaging and physical exams.[25] Furthermore, it underlines that a great variability seems to exist regarding populations (patients, general population, family members, etc.) and health conditions studied when estimating WTP values, whilst conclusions on WTP for diagnostic technologies were drawn from a panoply of health conditions and populations.[25] Although these elements advocate for more focus on the type of genetic test used for a

particular purpose, disease or population, it provides relevant avenues to explore the peculiarities of BCST for women of the general population.

Indeed, it notably underlines three main categories of factors potentially associated with WTP for diagnostic technologies: the individual level, the disease level and recently, the test level.[25] The first included the socio-demographic (e.g., age, ethnicity, income) and psychological characteristics (e.g., risk perception, optimism) of an individual. The disease level encompasses the seriousness of the disorder, prior test results, and family history. The test level refers to the tests' accuracy. Moreover, it stresses that previous study results did not allow to understand how preferences and WTP values vary according to individual factors, nor tried to present the magnitude of their impact on the valuation of genetic tests. For that reason, this paper deepens a hierarchization of individual factors associated with WPT for BSCT.

Further literature screening also shows that authors agreed on the existence of a certain association between WTP and interest.[21 32-34] However, there is no consensus about which one influenced the other. Indeed, some authors contended that WTP explains interest in genetic testing because the cost might be an indicator of individuals' interest in genetic testing.[21] In contrast, other authors advocated that interest is a predictor of WTP.[32 33] Bosompra and his colleagues, for example, found that the likelihood of being tested and preferences toward genetic tests are crucial to explain WTP as it is an antecedent of the acceptable amount of money a person could consent to pay to get the test.[32] As a consequence of this lack of agreement, interest and WTP for genetic testing were often considered independently in previous studies[eg. 30 35] or interest was used as a proxy for WTP.[eg. 34] In this paper, interest is considered as a prerequisite of WTP; it proposes a two-step model where WTP is conditional on interest.

The adoption of this theoretical position leads to explore studies on interest in genetic testing. The literature revealed that similar explanatory factors to those exposed for WTP have been used to assess genetic testing intentions (e.g., interest, likelihood) and behaviours (e.g., uptake, utilization, decision).[26] They are classified in two broad categories: subjective (disease and test-related factors) and objective factors (demographics and health background factors).[26] As for the WTP literature, this classification has been drawn from various types of genetic tests intended for different purposes, diseases, and populations.

In order to deal with the absence of an established theoretical background, a list of recurrent individual variables empirically tested as explanatory factors of WTP and of interest in cancer susceptibility testing was identified in the literature. The variables were thereafter classified in three categories: demographic, medical, and psychosocial, enabling to recognize more easily those associated with both outcome measures. The literature overview is well detailed in Appendix 1. It highlights general definitions and main conclusions for each factor, presents the main justification for the exclusion of some of them from the empirical exercise performed in this study, and outlines ambiguous results from previous studies on cancer susceptibility testing.

The method used to disentangle individual factors that impact on interest and WTP for BCST among women of the general population, and then to hierarchize these factors according to both outcome measures, is presented in the following section.

Methods

Sample

The target population was made up of French-speaking women of the general population aged between 35 to 69 of the province of Québec in Canada. The sample was selected from an internet panel maintained by a survey firm and weighted for age, regions, and education level according to Statistics Canada census profiles.[36] The sample size was calculated prior to data collection with a margin of error of 3% and at a 95% confidence interval.

Survey

A cross-sectional web-based survey developed from a literature review on genetic risk communication was used for this study. Respondents were asked to focus on their: general health state, BC clinical history and risk factors, level of literacy and numeracy regarding various ways of presenting BC risk, interest and opinions toward the use of BCST, ways to react toward various life events, general psychological health state, and demographic characteristics. Most of the items were measured on a 5 or 6-point Likert scale. The questionnaire was pre-tested with eligible women in February 2012.

Data collection

The questionnaire was adapted for a Web platform and a survey link was sent by the firm to a sample of 2410 women in March 2012. Three prize draws were offered to the participants: one of $3000 and two of $1000. Overall, 1160 women were reached. Among them, 40 clicked the questionnaire's link after the data collection period, 81 did not complete the questionnaire, and 8 cancelled their panel subscription. The survey generated 1031 usable questionnaires for a net response rate of 43%. Several prior studies on interest and willingness to pay for genetic testing obtained comparable response rates.[e.g.31 37 38]

Measures

Detailed information regarding operational measures of outcomes and explanatory factors, including coding and main references, is presented in Appendix 2. Factors relate to 1) demographic, 2) medical, and 3) psychosocial factors. Moreover, all clinical information needed to estimate the BC life-time risk of the respondents according to the Gail Model parameters was collected for descriptive purposes.[39]

Some potential factors underlined in the literature were not included in the analysis for methodological concerns such as distribution of respondents or theoretical redundancy. However, no variables were removed from the models on the basis of low statistical significance because they were assumed to be of theoretical interest and expected to have some effect on women's interest and WTP for BCST.

Chosen measures were assessed with validated scales or in accordance with the scientific literature. The constructs with multiple-item scales (i.e., loci of control, monitoring, and anxiety) were evaluated with a principal components factor analysis; the unidimensionality criterion was satisfied. Cronbach's alpha (α) shows that items forming each of them are reliable. Finally, reported tolerance statistic values are all higher than 0.2 (Appendix 1); there is no multicollinearity concerns.[40]

Statistical analysis

According to the assumption adopted in this study, a two-step approach was used to investigate: 1) women's interest in BCST that may allow more frequent screening if their risk level is higher than the one of the general population and then, for those interested, and 2) women's level of WTP for this genetic

test. This approach corresponds to sample-selected outcomes that refer to the situation where responses to a variable (Y) are conditional on a variable (Z). In this case, WTP is conditional on interest (INTER). So, women who responded, in the first step, '*Not at all interested*' in BCST were discarded from the second analysis, i.e., the model on WTP.

The dependent variable in each step is modeled as an ordered logit model.[41 42] This type of model uses an intermediate continuous variable Y^* (qualifications made by women regarding the dependent variable: INTER or WTP) in a latent regression with a set of independent variables X_i. The range of the unobserved Y related to INTER and WTP is subdivided, respectively, in five (1= *Not interested at all* to 5= *Extremely interested*) and three (1= *0$*, 2= *1 to 100$,* 3= *101$ and more*) adjacent intervals representing the classes of an observed variable, Z.

Therefore, the ordered logit models assume that the respondent constructs an index (Y^*) by weighting the various factors influencing, respectively, the level of interest and of WTP for BCST. For each dependent variable (INTER and WTP), the outcome of respondent *i* is represented by the latent index:

$$Y_i^* = \beta_1 X_{1i} + \ldots\ldots\ldots\ldots + \beta_k X_{ki} + \varepsilon_i = \beta X + \varepsilon$$

Where:

Y_i^* = the value of the index to the observation *i*

X = a vector of independent variables

β = the vector of parameters to be estimated

ε = the error term

The β coefficients inform on the signs and significance of the explanatory variables, but do not take into account the scope of these coefficients.[43] In order to assess the magnitude of their impact on interest and WTP for BCST, the marginal effects of the significant independent variables were ascertained with LIMDEP version 8.0 Econometrics Software Package.[44] This enables a hierarchization of these variables, which could be useful in targeting for intervention the most influential factors.

Moreover, a *post-hoc* power analysis with the statistical program G*power 3.1 was conducted to assess the appropriate sample size for statistical analysis to be performed, and the possibility of committing a Type I or II errors.[45 46] When using an alpha of 0.05, a power level of 0.90, and an odd ratio of 1.42, the minimal sample size was to be 479 respondents. Given this results, our sample was sufficiently large to meet these data considerations, i.e. the number of valid cases included in sample-selected regression model (n = 635 [INTER model]; n = 544 [WPT model]) is higher than what is required to detect a "true" effect when it exists.

Results

Descriptive statistics

As shown in Table 2, the sample is mostly composed of white educated women, in a civil union, and living in a large urban area (> 100 000 inhabitants). Descriptive statistics also revealed that 89% of the respondents are interested in BSCT that may allow more frequent screening, and 57% are willing to pay a certain amount of money to get the test. Moreover, most of the respondents overestimate their personal BC life-time risk (mean = 33.05%; SD = 22.25%) and the one of women in the general population (Figure 1). However, according to the Gail Model parameters,[39] approximately 85% of the respondents have less than 15% of BC life-time risk.

[Table 1 and Figure 1]

Ordered logit regressions

The results of the estimation of the two ordered logit models are presented in Table 3. The computation of the measures of goodness of fit of the two models leads to conclude that they are well behaved. This is indicated by the thresholds in increasing order ($\alpha_1<\alpha_2<\alpha_3$) and the Chi-squared statistics that are much larger than the critical value (step 1- INTER: χ^2 (21) = 65.861; p < .000; step 2- WTP: χ^2 (21) = 60.961; p < .000). In addition, the «predictive power» of the model appears to be acceptable (50.23%, and 53.31%, respectively, for INTER and WTP regressions). The Nagelkerke R^2 (Pseudo- R^2), which is not directly comparable to the R^2 derived in conventional OLS regression,[41] varies between .104 and .120. This is acceptable for models with qualitative dependent variables.

[Table 2]

Common explanatory of interest and WTP

For all two models, the results suggest that having a BC family history compared to those without, a locus of control highly attributed to powerful others, being widowed, separated or divorced rather than being married or in a union, and a perception of health status as good instead of excellent or very good, are all significantly associated with a higher interest and higher WTP for BCST.

Conversely, having a high numeracy score compared to a low numeracy score, a familial income less than 55 000$ comparatively to a familial income of 75 000$ and more, and being aged under 50 rather than being aged 50 and over, are all significantly associated with a lower interest and lower WTP for BCST. The variables biopsy, parity, and education appeared to have no impact on either interest nor WTP for BCST.

Regarding marginal effects, the coefficients show that the BC family history, the familial income, and the locus of control- powerful others are the common explanatory variables that have the highest impact on the women's interest and WTP for BCST.

Specific factors associated to interest for BCST

Furthermore, there are several explanatory variables that are significantly associated only with interest for BCST. Indeed, being a high monitor compared to a low monitor, and having a higher perceived risk of BC are significantly associated with a higher interest, whilst being highly optimistic rather than being poorly optimistic, and having a locus of control highly attributed to chance are significantly associated with a lower interest for BCST.

More specifically, the locus of control -powerful others, the level of anxiety, and the BC family history stand with the highest marginal impact values, respectively of .441, .409, and .357. For the two former continuous variables, this implies that a positive relative change of 10% on these factors increases the level of women's interest for BCST by 4.41% and 4.09%. For the categorical variable, it means that

interest for BCST is 35.7% greater among women with a family history of BC comparatively to those without.

Most impactful factors on WTP for BCST

For the WTP model, variables with the highest marginal effects are the locus of control- powerful others (marginal effect = .283), the BC family history (marginal effect = .208), and the familial income (marginal effect = -.154, -.103 and -.079). These coefficients indicate that for a positive relative change of 10% on the score of the locus of control- powerful others, women's WTP for BCST would increase by 2.83%. This also means that WTP for BCST is 20.8% greater among women with a family history compared to those without, and is as much as 15.4% lower among women with a familial income of less than 75 000$ compared to those who have a familial income of 75 000$ and more.

Discussion

This study investigated the common and specific individual factors associated to interest and WTP for BCST that may allow more frequent screening if the BC risk level is higher than the one of the general population. Overall, women's age, familial income, marital status, and family history are significantly associated with both interest and WTP for BCST. Optimism, monitoring, external loci of control (powerful others and chance), anxiety, numeracy, perceived risk, and health status have a significant impact on women's interest for BCST, but one locus of control (powerful others), numeracy, and perceived health status remained significant for explaining WTP for such a test. Moreover, the estimation of the marginal effects indicates that factors which impacted the most on interest for BCST are anxiety, loci of control-powerful others and chance, and family history. The locus of control- powerful others, the BC family history, and the familial income have a greater impact regarding WTP for BCST.

Our findings might be considered as representative of French-speaking women aged between 35 and 69 living in Québec (Canada), but should be cautiously extrapolated to other similar or neighbouring populations. Moreover, while we try to avoid as much as possible sources of bias, readers are advised to consider results in light of some limitations. First, self-reported data like those used in this study are subject to a social desirability bias. Second, a hypothetical scenario was used in this study and so

reported results on the degree of interest and level of WTP should not be taken as an objective uptake measure of testing, but as a measure of intention.[21 26 31] Other studies have also demonstrated that revealed measures of WTP overestimate the real sum paid out-of-pocket in a realistic situation.[28 47] Finally, as this paper only focused on individual factors, future studies should investigate other potential factors associated to interest and WTP, like those at the organizational, social or environmental level, and clearly distinguish the type of genetic test assessed. Future research should nevertheless more explicitly ground the explanatory factors in theoretical frameworks.

Potential implications

The present findings provide a reasonable proxy of the readiness of the general population to get genetically tested for BC susceptibility and the amount its individual expect to be acceptable to pay for such services in private settings. In a publicly-funded health care system as in Canada, these results provide insights on the willingness of the general population to collectively pay for BSCT. They may also provide insights on their degree of openness toward a new co-payment method for such a test or may support the setting of insurance co-payments, if any, in some situations.[25 30] As the results show, the majority of the women are interested in BCST (~90%) and, among them, more than half are willing to pay a certain amount of money for such a test, and this in spite of living in a province with a publicly-funded health care system. Nonetheless, some women are not willing to pay (24%) or do not put themselves forward on the survey item assessing their WTP for BCST (18% of missing data). This suggests that the women of Québec have mitigated enthusiasm toward BSCT if they have to pay for it, which is consistent with previous studies.[38]

Furthermore, the results suggest that many psychosocial factors are important factors associated to women's interest and WTP for BCST. It is worth mentioning, firstly, that women's interest and WTP for BCST should be analyzed in light of another important finding: women greatly overestimated both their personal lifetime risk of developing BC and the one of women in the general population. This could result in a biased level of interest and WTP for BSCT. Indeed, the higher the women's BC risk perceptions are, the higher their level of interest in BCST is. In addition, as reported by other studies,[21 38] more anxious, less optimistic women and those with poor numeracy skills are more interested in BCST and thus, will

probably more extensively use such services. These facts lead, as others proposed,[eg. 21 26 32] to reiterate the necessity to put a stronger emphasis on popular education, and to develop educational material toward genetics and the notion of risk to ensure that the choice of getting tested for BC susceptibility is made following an informed decision-making process, and based on more objective and realistic risk perceptions of BC. For instance, explaining to women how family history impacts on their risk among other risk factors, stating clearly the prevalence and risk of BC from a genetic point of view, or clarifying the benefits and consequences of being tested for BC susceptibility might improve women's awareness and knowledge toward BCST, may reduce anxiety or worries about BC risk or even motivate some of them to seek out more information about their BC risk. Interventions improving knowledge and awareness, as well as fostering objective BC risk evaluation, have the potential to improve ethical and informed decision-making, but may also slightly decrease interest and WTP for BCST.[26 32 33]

Moreover, one of the most impactful factors on women's interest and WTP is the external health locus of control-powerful others. It implies that a woman who believes that others she considers as experts to be largely responsible for her health is more interested and willing to pay for BCST. This result suggests that health care providers' recommendations, public health or for-profit organizations' communication campaigns or marketing strategies might have an impact on some women's interest and WTP for BCST. Beyond that, private companies' DTC advertising efforts may take advantage of actual consumers' emotional concerns or knowledge deficit in genetics.[24 38] These companies should thus be «fully encouraged» to incorporate adapted modes of communication and provide personalized risk counselling to consumers, instead of their current approach of "one-size-fits-all".[24] On the other hand, interventions designed to improve women's empowerment toward their breast health and BC prevention also have the potential to reduce their interest and WTP for BSCT.

The findings of this study may also help health organizations, either private or public, to better define the range of service offerings. Indeed, to have the pulse of the end-users is an important element which could allow to adjust service delivery modalities to public or consumers' preferences and needs.[32 33] For instance, following results discussed previously on perceived risk, numeracy, anxiety or optimism, it seems that reassurance, support, and education as provided in highly specialized services of genetic

counselling are important elements to be adapted for public health care settings - such in the case of the implementation of a BC risk stratification program - and to be provided by private companies selling BC genetic tests DTC in order to minimize drawbacks for consumers (e.g., anxiety, miscomprehensions, etc.).[24 32 38]

Finally, study results related to some medical and demographic factors could provide insightful paths of action for developing strategies targeting specific sub-groups of women in the population. First, women with a BC family history are at greater risk of BC, and are more interested and willing to pay for BCST. Thus, they may value and get more benefits from such testing than those without family history, but providers must ensure that their interest and willingness to take the test is based on an informed decision instead of the results of biased self-estimations of BC risk. This notably suggests that continuing to sensitize and educate primary care providers in BC family history-taking and BSCT may be relevant as they are the professionals seen on a regular basis or who are the most accessible to women of the general population. Second, paying more attention to young women (35 to 49 years old) in clinical encounters could be a winning strategy. It might contribute to the demystification of the notion of risk and the genetic component of BC into the next generation of women who will be likely invited into BC stratification programs. Furthermore, familial and genetic BC are often developed at a younger age than the sporadic form of BC.[48] So, this could allow to discuss and to recommend early risk management strategies to young women at greater risk of BC who are less interested and attribute less value to BSCT. Lastly, considering that the study's results indicate that interest and WTP for BCST increased with income, which was also pointed out by previous studies on genetic testing,[30 32] interventions designed for women from lower-resourced neighbourhoods or targeting physicians with a large panel of women with low income could prevent some inequalities in the uptake of BCST.

Conclusion

This study disentangles common and specific individual determinants of interest and WTP for BSCT according to women of the general population of Québec (Canada). Overall, the results provide a proxy of the readiness of the general population to pay for BCST. It also presents insights for developing inclusive and specific strategies that could support women's informed decision-making toward BCST and the range

of service offerings by health organizations with regards to this test. For managers and decision-makers involved in BC prevention, thinking to adjust or to extend BC genetic services and desiring to adapt it to public preferences and needs, this study highlights two ways of proceeding that could be profitable from a social and economic point of view. The first is to develop interventions targeting the whole population, such as health promotion campaigns, by focusing on the psychosocial factors, given the number of significant factors explaining interest and WTP for BCST. The second is to tailor interventions to particular sub-populations by considering the most impactful factors associated to interest and WTP for BCST, such as family history backgrounds or strata of familial income.

References

1. Khoury MJ, Coates RJ, Fennell ML, et al. Multilevel research and the challenges of implementing genomic medicine. *JNCI Monographs* 2012;2012(44):112-20.
2. Health Leaders Media - a division of HCPro Inc. In collaboration with Price Water House Cooper. The Impact of Personalized Medicine Today Massachusetts, United-States2010 [Available from: www.healthleadersmedia.com/breakthroughs.
3. Schleidgen S, Klingler C, Bertram T, et al. What is personalized medicine: sharpening a vague term based on a systematic literature review. *BMC Med Ethics* 2013;14(1):55.
4. Welch BM, Kawamoto K. Clinical decision support for genetically guided personalized medicine: a systematic review. *J Am Med Inform Assoc* 2013;20(2):388-400.
5. Diamandis M, White NMA, Yousef GM. Personalized Medicine: Marking a New Epoch in Cancer Patient Management. *Mol Cancer Res* 2010;8:1175-87. doi: doi: 10.1158/1541-7786.MCR-10-0264
6. Ginsburg GS, Willard HF. Genomic and personalized medicine: foundations and applications. *Translational research* 2009;154(6):277-87.
7. Amara N, Blouin-Bougie J, Jbilou J, et al. The knowledge value-chain of genetic counseling for breast cancer: an empirical assessment of prediction and communication processes. *Fam Cancer* 2016;15(1):1-17. doi: 10.1007/s10689-015-9835-7
8. O'Daniel J. The Prospect of Genome-guided Preventive Medicine: A Need and Opportunity for Genetic Counselors. *Journal of genetic counseling* 2010;19(4):315-27. doi: 10.1007/s10897-010-9302-4
9. International Agency for Reseach on Cancer - World Health Organanization. Cancer Incidence in Five Continents Vol. X. IARC Scientific Publication No 164. Lyon, France, 2014:1365 pp.
10. Onega T, Beaber EF, Sprague BL, et al. Breast cancer screening in an era of personalized regimens: A conceptual model and National Cancer Institute initiative for risk - based and preference - based approaches at a population level. *Cancer* 2014;120(19):2955-64.
11. Gail MH. Personalized estimates of breast cancer risk in clinical practice and public health. *Stat Med* 2011;30(10):1090-104. doi: 10.1002/sim.4187
12. Burton H, Jackson C, Abubakar I. The impact of genomics on public health practice. *Br Med Bull* 2014;112(1):37-46.
13. Chowdhury S, Dent T, Pashayan N, et al. Incorporating genomics into breast and prostate cancer screening: assessing the implications. *Genet Med* 2013;15(6):423-32.
14. Howell A, Astley S, Warwick J, et al. Prevention of breast cancer in the context of a national breast screening programme. *J Intern Med* 2012;271(4):321-30. doi: 10.1111/j.1365-2796.2012.02525.x
15. Foulkes WD, Knoppers BM, Turnbull C. Population genetic testing for cancer susceptibility: founder mutations to genomes. *Nat Rev Clin Oncol* 2016;13(1):41-54. doi: 10.1038/nrclinonc.2015.173
16. Parthasarathy S. Architectures of Genetic Medicine: Comparing Genetic Testing for Breast Cancer in the USA and the UK. *Social Studies of Science* 2005;35(1):5-40. doi: 10.1177/0306312705047172
17. Howe R, Miron-Shatz T, Hanoch Y, et al. Personalized Medicine Through SNP Testing for Breast Cancer Risk: Clinical Implementation. *Journal of Genetic Counseling* 2015;24(5):744-51. doi: 10.1007/s10897-014-9803-7
18. Evans DG, Howell A. Can the breast screening appointment be used to provide risk assessment and prevention advice? *Breast Cancer Res* 2015;17(1):84-84 1p. doi: 10.1186/s13058-015-0595-y
19. Couch FJ, Nathanson KL, Offit K. Two decades after BRCA: setting paradigms in personalized cancer care and prevention. *Science (New York, NY)* 2014;343(6178):1466-70. doi: 10.1126/science.1251827
20. Eccles SA, Aboagye EO, Ali S, et al. Critical research gaps and translational priorities for the successful prevention and treatment of breast cancer. *Breast Cancer Research* 2013;15(5):1-37. doi: 10.1186/bcr3493
21. Graves K, Peshkin B, Luta G, et al. Interest in genetic testing for modest changes in breast cancer risk: implications for SNP testing. *Public Health Genomics* 2011;14(3):178.
22. Goldsmith L, Jackson L, O'Connor A, et al. Direct-to-consumer genomic testing: systematic review of the literature on user perspectives. *European Journal of Human Genetics* 2012;20(8):811-16.
23. Zimmern RL, Khoury MJ. The impact of genomics on public health practice: the case for change. *Public Health Genomics* 2012;15(3-4):118-24.
24. Bellcross CA, Page PZ, Meaney-Delman D. Direct-to-consumer personal genome testing and cancer risk prediction. *The Cancer Journal* 2012;18(4):293-302.
25. Lin P-J, Cangelosi MJ, Lee DW, et al. Willingness to pay for diagnostic technologies: a review of the contingent valuation literature. *Value In Health* 2013;16(5):797-805.
26. Sweeny K, Ghane A, Legg AM, et al. Predictors of Genetic Testing Decisions: A Systematic Review and Critique of the Literature. *Journal of Genetic Counseling* 2014;23(3):263-88. doi: 10.1007/s10897-014-9712-9
27. Kopits IM, Chen C, Roberts JS, et al. Willingness to pay for genetic testing for Alzheimer's disease: a measure of personal utility. *Genetic testing and molecular biomarkers* 2011;15(12):871-75.
28. Neumann PJ, Cohen JT, Hammitt JK, et al. Willingness - to - pay for predictive tests with no immediate treatment implications: a survey of US residents. *Health economics* 2012;21(3):238-51.
29. Blumenschein K, Blomquist GC, Johannesson M, et al. Eliciting Willingness to Pay Without Bias: Evidence from a Field Experiment*. *The Economic Journal* 2008;118(525):114-37. doi: 10.1111/j.1468-0297.2007.02106.x
30. Kilambi V, Johnson FR, González JM, et al. Valuations of Genetic Test Information for Treatable Conditions: The Case of Colorectal Cancer Screening. *Value in Health* 2014;17(8):838-45.
31. Lacour RA, Daniels MS, Westin SN, et al. What women with ovarian cancer think and know about genetic testing. *Gynecologic Oncology*;111(1):132-36. doi: 10.1016/j.ygyno.2008.06.016
32. Bosompra K, Ashikaga T, Flynn BS, et al. Psychosocial factors associated with the public's willingness to pay for genetic testing for cancer risk: a structural equations model. *Health Education Research* 2001;16(2):157-72.
33. Matro JM, Ruth KJ, Wong Y-N, et al. Cost sharing and hereditary cancer risk: Predictors of willingness-to-pay for genetic testing. *Journal of genetic counseling* 2014;23(6):1002-11.

34. Ries NM, Hyde-Lay R, Caulfield T. Willingness to pay for genetic testing: a study of attitudes in a Canadian population. *Public Health Genomics* 2010;13(5):292-300. doi: 10.1159/000253120
35. Lacour RA, Daniels MS, Westin SN, et al. What women with ovarian cancer think and know about genetic testing. *Gynecologic oncology* 2008;111(1):132-6. doi: 10.1016/j.ygyno.2008.06.016 [published Online First: 2008/08/08]
36. Statistics Canada. Enquête sur la santé dans les collectivités canadiennes (ESSC), 2010:417pp.
37. Neumann PJ, Hammitt JK, Mueller C, et al. Public attitudes about genetic testing for Alzheimer's disease. *Health Affairs* 2001;20(5):252-64.
38. Miron-Shatz T, Hanoch Y, Doniger GM, et al. Subjective but not objective numeracy influences willingness to pay for BRCA1/2 genetic testing. *Judgment and Decision Making* 2014;9(2):152-58.
39. Gail MH, Brinton LA, Byar DP, et al. Projecting Individualized Probabilities of Developing Breast Cancer for White Females Who Are Being Examined Annually. *Journal of the National Cancer Institute* 1989;81(24):1879-86. doi: 10.1093/jnci/81.24.1879
40. Field A. Discovering statistics using IBM SPSS statistics: Sage 2013.
41. Aldrich JH, Nelson FD. Linear probability, logit, and probit models: Sage 1984.
42. Amara N, Ouimet M, Landry R. New evidence on instrumental, conceptual, and symbolic utilization of university research in government agencies. *Science Communication* 2004;26(1):75-106.
43. Landry R, Amara N, Lamari M. Does social capital determine innovation? To what extent? *Technological forecasting and social change* 2002;69(7):681-701.
44. Greene WH. LIMDEP: Version 8.0: Econometric Modeling Guide: Econometric Software 2002.
45. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behav Res Methods* 2009;41(4):1149-60.
46. Portney LG, Watkins MP. Foundations of clinical research: applications to practice. 3rd ed. Philadelphia, USA: FA Davis Co. 2015.
47. Cookson R. Willingness to pay methods in health care: a sceptical view. *Health economics* 2003;12(11):891-94.
48. Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *American journal of human genetics* 1995;56(1):265.
49. Bunn JY, Bosompra K, Ashikaga T, et al. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. *Preventive medicine* 2002;34(6):567-77.
50. Bottorff JL, Ratner PA, Balneaves LG, et al. Women's interest in genetic testing for breast cancer risk the influence of sociodemographics and knowledge. *Cancer Epidemiology Biomarkers & Prevention* 2002;11(1):89-95.
51. Biesecker BB, Ishibe N, Hadley DW, et al. Psychosocial factors predicting BRCA1/BRCA2 testing decisions in members of hereditary breast and ovarian cancer families. *American Journal of Medical Genetics* 2000;93(4):257-63.
52. Sanderson SC, O'Neill SC, Bastian L, et al. What can interest tell us about uptake of genetic testing? Intention and behavior amongst smokers related to patients with lung cancer. *Public Health Genomics* 2009;13(2):116-24.
53. Petersen GM, Larkin E, Codori A-M, et al. Attitudes toward Colon Cancer Gene Testing: Survey of Relatives of Colon Cancer Patients. *Cancer Epidemiology Biomarkers & Prevention* 1999;8(4):337-44.
54. Bosompra K, Flynn BS, Ashikaga T, et al. Likelihood of undergoing genetic testing for cancer risk: a population-based study. *Preventive Medicine* 2000;30(2):155-66.
55. Kinney AY, Croyle RT, Dudley WN, et al. Knowledge, attitudes, and interest in breast-ovarian cancer gene testing: a survey of a large African-American kindred with a BRCA1 mutation. *Preventive medicine* 2001;33(6):543-51.
56. Aizer AA, Chen M-H, McCarthy EP, et al. Marital Status and Survival in Patients With Cancer. *Journal of Clinical Oncology* 2013;31(31):3869-76. doi: 10.1200/jco.2013.49.6489
57. Dawood SS, Lei X, Dent R, et al. Impact of marital status on prognostic outcome of women with breast cancer. *J Clin Oncol (Meeting Abstracts)* 2014;32(15_suppl):594-.
58. Braithwaite D, Sutton S, Steggles N. Intention to participate in predictive genetic testing for hereditary cancer: the role of attitude toward uncertainty. *Psychology and Health* 2002;17(6):761-72.
59. Welkenhuysen M, Evers-Kiebooms G, Decruyenaere M, et al. A community based study on intentions regarding predictive testing for hereditary breast cancer. *Journal of medical genetics* 2001;38(8):540-47.
60. National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP). The Breast Cancer Risk Assessment Tool 3.0. In: U.S. Department of Health and Human Services, ed., 2011.
61. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. *Journal of personality and social psychology* 1994;67(6):1063.
62. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. *Journal of personality and social psychology* 1987;52(2):345.
63. Nordin K, Björk J, Berglund G. Factors influencing intention to obtain a genetic test for a hereditary disease in an affected group and in the general public. *Preventive medicine* 2004;39(6):1107-14.
64. Malcarne VL, Fernandez S, Flores L. Factorial validity of the multidimensional health locus of control scales for three American ethnic groups. *Journal of Health Psychology* 2005;10(5):657-67.
65. Cameron LD, Reeve J. Risk perceptions, worry, and attitudes about genetic testing for breast cancer susceptibility. *Psychology & Health* 2006;21(2):211-30.
66. Reitz F, Barth J, Bengel J. Predictive value of breast cancer cognitions and attitudes toward genetic testing on women's interest in genetic testing for breast cancer risk. *GMS Psycho-Social Medicine* 2004;1:Doc03.
67. KESSLER R, nbsp, C., et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine* 2002;32(06):959-76. doi: doi:10.1017/S0033291702006074
68. Schwartz LM, Woloshin S, Black WC, et al. The Role of Numeracy in Understanding the Benefit of Screening Mammography. *Annals of Internal Medicine* 1997;127(11):966-72. doi: 10.7326/0003-4819-127-11-199712010-00003
69. Trottier C, Mageau G, Trudel P, et al. Validation de la version canadienne-française du Life Orientation Test-Revised. *Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement* 2008;40(4):238.
70. Levy AG, Shea J, Williams SV, et al. Measuring perceptions of breast cancer risk. *Cancer Epidemiology Biomarkers & Prevention* 2006;15(10):1893-98.

71. French translation and validation of the Miller Behavioral Style Scale. INTERNATIONAL JOURNAL OF PSYCHOLOGY; 1996. PSYCHOLOGY PRESS 27 CHURCH RD, HOVE, EAST SUSSEX, ENGLAND BN3 2FA.
72. Talbot F, Nouwen A, Gauthier J. Is Health Locus of Control a 3 - factor or a 2 - factor construct? *Journal of clinical psychology* 1996;52(5):559-68.
73. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological medicine* 2002;32(06):959-76.

Acknowledgement/Funding sources

This research was supported by the Canadian Institutes of Health Research as a part of the CIHR Team in Familial Risks of Breast Cancer Grant (CRN-8752-1). The Government of Canada through Genome Canada and the Canadian Institutes of Health Research (GPH-129344), the *Ministère de l'Économie, de la Science et de l'Innovation* du Québec through Genome Québec, the Québec Breast Cancer Foundation for the PERSPECTIVE project also funded this study.

Conflict of interest: All authors declare no conflicts of interest in this paper.

Contributors: All authors were responsible for the project design. MD and KB were in charge of the survey development and the data collection, while JBB and NA have made all the data analysis and have drafted the preliminary version of the manuscript. All authors contributed to results interpretation and agreed on the final version of this article before submission.

Data sharing statement: No additional data are available.

Appendix 1. Literature overview on interest and willingness to pay for cancer susceptibility testing (CST)

Explanatory factors		Outcome measures †		Definitions of factors, description of previous study results, and precisions
		Interest for CST	WTP for CST	
Socio-demographic factors	Age*	Age: NEG[32] POS [49-51] NS[21 52 30 53 54] Younger age: POS [55]	Age: NS [21 32] NEG[33 28]	Definition: Age of either patients or individuals of the general population ∝ Link between age and interest or WTP for CST are still equivocal. ∝ Systematic reviews conclusions: studies having assessed association between age and interest toward genetic tests proposed globally mixed findings and mostly inconsistent effects[26]; WTP values for dx tests can be positively influenced by older age.[25] ∝ Age is an important element of women's BC risk assessment: aging is associated with BC, but familial and genetic BC are often developed at a younger age than sporadic forms of BC.[48]
	Ethnicity	Race: NS [21 30 31 53]	Race: NS[21 31] Race: NS[33] Ashkenazi decent: NS[38]	Definition: Person's race or cultural traits relevant to particular group ∝ According to the literature on CST, race seems to not have any effect on interest and WTP. ∝ Systematic reviews conclusions: These variables have not been discussed for interest; WTP values for dx tests are positively influenced by a majority race or ethnicity, especially white Americans.[25] ∝ Some populations or groups of a particular biological background are at greater risk of BC (e.g., French-Canadian, Ashkenazi, Islanders). *N.B. The sample does not present sufficient variation in terms of ethnicity backgrounds (95% of White women) to be included in the statistical exercise.*
	Marital Status*	Marital status: NS[21 30 55] NEG[51]	Marital status: NS[21 33]	Definition: Person's legal marital status (e.g., common law, single, divorced…) ∝ According to the literature on CST, marital status seems to not have an effect on interest and WTP. ∝ Systematic reviews conclusions: Relationship between interest and marital status is supported by equivocal findings.[26] ∝ As genetic tests results might have important implications for family-planning decisions, it seems logical that marital status could influence genetic testing decisions.[26] This variable was also proved to be of great importance in cancer care. It has recently been demonstrated that unmarried persons were at a higher risk for cancer, undertreatment and death from cancer. [56 57]
	Education level*	Education: NS[21 31 53 55 58] Year of education: NEG[50]	Education: NEG.[28] POS.[31 33] NS.[21]	Definition: Person's highest completed degree or diploma. ∝ Link between education level and interest or WTP for CST is still equivocal. ∝ Systematic reviews conclusions: Interest toward genetic tests is inconsistent across studies.[26] WTP values are generally positively associated with education for dx tests.[25]
	Employment status/ primary activities	Employment: POS [30] NS [21 58]	Employment: NS [21 33]	Definition: Person's primary activities of a diary day; it can correspond to employment status for paid work (part- or full-time), but also to unpaid work such as study, housework, social support, volunteering, etc. ∝ Link between employment and interest or WTP for CST seems not significant. ∝ Systematic reviews conclusions: Few studies have assessed the link between employment and interest for genetic testing. Mixed findings are reported. [26]
	Income*	Household income: NS[21 53 55] POS.[30]	Household income: NS.[21 28 33]	Definition: Combined gross income of all members of a household. ∝ Link between income and interest or WTP for CST seems to not be significant. ∝ Systematic reviews conclusions: Associations of interest for genetic testing and income are inconsistent,[26] but WTP values for dx tests are generally positively associated with incomes. [25]
	Household size	Household size: POS.[30]	NA	Definition: Number of persons residing in a private household. ∝ There is insufficient information regarding household size and interest or WTP for CST. *N.B. This concept is partly assessed by marital status and parity for many respondents. It was eliminated.*
	SES	Socio-economic status: NEG[32 49] NS[54]	Socio-economic status: POS.[32]	Definition: SES is a concept that reflects more broadly familial resources, including education, employment, goods and revenues. ∝ There is insufficient information regarding SES and interest or WTP for CST. *N.B. As this concept is a mix of other retrieved sociodemographic characteristics in the literature, it has been discarded from the statistical models to avoid theoretical redundancy.*

Medical factors	Past medical exams/results*	Previous examination: MA[53] Timing of the most recent biopsy NS[21] Prior history of cancer: POS[55 50]	Personal breast cancer history: NS[21] Personal history of GI cancer: NS[33] Personal history of any cancer: NS[33]	Definition: Prior test results or health exams of an individual linked to the evaluated health condition. ∝ According to the literature on CST, past medical exams or results could have an impact on interest while they seem to not have an effect on WTP. ∝ Systematic reviews conclusions: It is not clear whether WTP values for dx tests were associated with past medical exams and results.[25] *N.B. Biopsy was used as a measure of past exam in the present study.*
	Children/ Parity*	Children: NS[30] POS[59]	NA	Definition: Woman having/giving birth to at least one child. ∝ Parity/parental status was insufficiently assessed for CST. ∝ Systematic reviews conclusions: Relationship between interest for genetic testing and parental status is still equivocal. [26] ∝ Nulliparty (never having given birth) is a risk factor as parity is a protective factor of BC. [60]
	Family history*	FDR had cancer: NEG[32] NS[21 53 58] POS[49 58 50] BC in family: POS[59 54] Number of first-degree relatives: POS [55]	FDR had cancer: NEG[32 33 53] NS[21 38] Family member tested positive: NS[38]	Definition: People who have one or more relatives (1st to 3rd degree) who have had a cancer dx. ∝ Family history seems to be associated with interest for CST while more evidence is needed for WTP for such a test. ∝ Systematic reviews conclusions: Generally, positive family history is associated with interest in genetic testing[26] and WTP for dx tests technologies.[25] ∝ Family history is an important risk factor of BC.[60]
Psychosocial factors	Optimism*/ Pessimism	Optimism NEG [32] POS[49 51] Pessimism: POS[49 54 32] (Depressive sx: POS[55])	Optimism: NEG[32] Pessimism : NS[32]	Definition: Person's tendency to have positive (optimists) or negative (pessimists) expectancies about their future (e.g., events, acts).[61] ∝ Mixed findings were reported regarding association between optimism/pessimism and interest for genetic testing and more research is needed for WTP in the context of CST. ∝ Systematic reviews conclusions: Person having a more positive outlook, highly optimistic or low in depression sx was more interested in genetic testing even if some mixed findings were reported for BC. [26] ∝ This construct is often measured with the Life Orientation Scale. [61]
	Monitoring*	Seek information: NS [49] Information seeking: NS[32] Preference for medical information: NS[54]	Information seeking: NEG[32]	Definition: Coping style based on personal information preferences about an event: information seekers are considered as high monitors and information avoiders are considered as low monitors. [26 62] ∝ In the context of CST, retrieved studies indicate that being an information seeker is not associated with interest for genetic testing. ∝ Systematic reviews conclusions: High monitors have more interest in genetic testing even if mixed findings are reported for some cancers. [26] ∝ This construct is often measured with the Miller Behavioral Style Scale. [62]
	Perceived control*	Perceived control: NS[63 58]POS[63] God Locus of Health control: NS[55]	Risk tolerance: NEG [28] Perceived control: POS [33]	Definition: Person's perception of his own ability to manage his health/disease risk. ∝ More research is needed toward perceived health control and interest as well as WTP for CST, but retrieved studies seem to indicate that it could have an impact on both outcome measures. ∝ Systematic reviews conclusions: Greater perceived control over the management and prevention of a disease is associated with interest for genetic testing. [26] For some disease without controllable risk factors, WTP values are higher.[25] ∝ This construct could be measured with the Multidimensional Health Locus of Control Scales.[64]
	Worries/ (Anxiety*)	Concerns about developing cancer: POS[53] Cancer worries: POS[21] NS[65] Intrusions-Worries: POS[66] Fears: NEG[66] Uncertainty: POS[58]	Worry about positive results: POS[33] NS[38] Cancer worries: POS[21]	Definition: Personal emotional aspects of risk for a specific health condition. [26] ∝ Worries toward cancer are generally associated with interest and WTP for CST. However, measures used by authors varied considerably. ∝ Systematic reviews conclusions: Mixed findings were reported regarding interest for genetic testing and disease-specific worries even if studies tend to support a positive association between those concepts. [26] *N.B. As this concept is related to disease-specific perceived risk [26] a scale of general psychological distress was used to measure respondents' level of anxiety. The K-6 was used.* [67]

Numeracy*	Understanding risk information: NS[21] Objective numeracy: NS[38] Subjective numeracy: POS[38]	Understanding risk information: NEG[21]	Definition: Person's ability to understand quantitative information and manipulate basic probability and numerical concepts.[68] ∝ There is insufficient information regarding numeracy and interest in CST. Mixed findings for WTP for CST are reported. It is important to note however the variation of the operationalization used to measure the concept of numeracy. ∝ Systematic reviews conclusions: this concept was not reported.
Knowledge	Genetic knowledge: NS[21 55 66] Knowledge of genetic test: POS [50] Awareness: NS[54]	Genetic knowledge: NS[21] Knowledge & awareness: NS[33]	Definition: Generally concerned about what a person knows about genetic risk or genetic test for a particular disease. ∝ Systematic reviews conclusions: Mixed findings were reported regarding its association with interest toward genetic testing. *N.B. This concept was not included in the statistical model as it was too correlated with perceived risk.*
General health*	Current health: NS [53] Health Behaviors:	NA	Definition: Perception of own actual health state. ∝ There is insufficient evidence regarding perceived health status and interest or WTP for CST. ∝ Systematic reviews conclusions: Few studies have assessed the relationship between general health and interest in genetic testing; equivocal results are reported.[26] More health conscious people are likely to accept higher WTP values.[25]
Perceived risk of BC*	Perceived susceptibility POS[32 49 54] Perception of risk: MA[53] Absolute perceived risk: NS[21] Comparative perceived risk: NS[21] Numeric perceived risk: NS[21] Perceived risk: NS[65 58] POS [55] Perceived vulnerability: POS[66]	Prior risk: NS[28] Perceived susceptibility: POS[32] Perceived susceptibility: NS[38] Perceived risk of having the mutation: POS[38] Absolute perceived risk: NS[21] Comparative perceived risk: NS [21 33] Numeric perceived risk: NS[21]	Definition: Generally, the person's estimation of his own likelihood of developing the disease in a specific time frame. ∝ Link between risk perception and interest or WTP for CST is still equivocal. ∝ Systematic reviews conclusions: In general, perceived risk is associated with an increased interest for genetic testing, but inconsistent findings were reported for some hereditary conditions. [26] Increased WTP values for dx tests were associated with higher risk perception.[25]

† NS.: association not significant; MA.: Marginally significant association; NEG.: negative association; POS.: positive association.
* Variables conserved in the regression models.

Appendix 2. Operational definitions* of variables and descriptive statistics †

Variables	Main reference	Measure, items and coding (final model)		Mean (SD)	*n* (%)	Tolerance
Outcomes						
Interest [INTER]	Adapted from the study of Graves et al.[21]	Scenario Imagine that a new genetic test for breast cancer (BC) risk evaluation is available on the market. This test could inform on your personal risk level to develop BC. It could be possibly used to adapt BC screening tests frequency to your risk (more frequent screening if your risk is higher than that of the general population).	To what extent would you be interested in this test if it could allow you to get more frequent BC screening tests? 5 point-Likert scale coded as 1 if not interested at all 2 if somewhat interested- 5 if extremely interested (for step 2) Sys miss	3,48 (1,19)	1016 93 (9,0) 923 (89,5) 15 (1,5)	-
Willingness to pay [WTP]			How much would you be willing to pay for this test? Ordinal scale recoded as 1 if do not want to pay; 2 if between 1$ and 100$ 3 if 101$ and more Sys miss	1,97 (0,74)	840 250 (24,2) 362 (35,1) 228 (22,1) 191 (18,5)	-
Factors						
Age [AGE]	Statistics Canada, ESCC-2010[36]	Data available from firms' panel. Continuous variable recoded as dichotomous 1 if 50 to 69 years old[§] 0 if 35 to 49 years old Sys miss		50,32 (9,24)	528 (51,2) 503 (48,8) 0	.844
Familial income [INC1] [INC2] [INC3] [INC4]		Check the answer that best described the gross income measure (before tax) of your household. Ordinal scale recoded as 1 if income less than 25 000$; 0 if else 1 if income between 25 000$ and 54 999$; 0 if else 1 if income between 55 000$ and 74 999$; 0 if else 1 if income between 75 000$ and more; 0 if else Sys miss		-	98 (9,5) 267 (25,9) 187 (18,1) 299 (29,0) 180 (17,15)	.656 .620 .713 Ref.
Marital status [WDS] [SING] [MARUN]		What is your current marital status? Nominal variable recoded as 1 if widowed, divorced or separated; 0 if else 1 if single; 0 if else 1 if married or common-law; 0 if else Sys miss		-	186 (18,0) 152 (25,7) 689 (66,8) 4 (0,4)	.831 .764 Ref.
Education [EDUC1] [EDUC2] [EDUC3]		Data available from firms' panel. Ordinal variable recoded as dichotomous 1 if no diploma or secondary school diploma; 0 if else 1 if college or CEGEP diploma; 0 if else 1 if university degree; 0 if else Sys miss		-	399 (38,7) 265 (35,6) 367 (35,6) 0	.666 .742 Ref.
Biopsy [BIOPSY]	Adapted from the Breast Cancer Risk Assessment Tool of the NICE[60]	Have you ever had a breast biopsy or puncture? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	117 (11,3) 943 (91,5) 31 (3,0)	.916
Parity [PARITY]		Have you ever given birth to a child? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	820 (79,5) 211 (20,5) 0	.849

Familial history [FAMHIS]		How many women of your family's first degree relatives (FDR) ever had breast cancer? Ordinal variable coded as dichotomous 1 if 1 or more FDR 0 if no family history Sys miss	- 	 146 (14,2) 869 (84,4) 16 (1,6)	 .873
Optimism [OPTIMS]	Validated French Canadian version of the Life Orientation Test –Revised [69]	I'm always optimistic about my future. 5-point agreement Likert scale recoded as dichotomous 1 if agree or strongly agree; 0 if else Sys miss	 	 172 (16,7) 845 (82,0) 14 (1,4)	 .861
Perceived health status [FAIRBAD] [GOOD] [EXVER]	Statistics Canada, ESCC-2010[36]	In general, would you say that your health is … 5-point Likert scale recoded as 1 if bad or fair; 0 if else 1 if good; 0 if else 1 if very good or excellent; 0 if else	 	 83 (8,1) 387 (37,5) 561 (54,4)	 .773 .823 Ref.
Numeracy [NUM]	Adapted from the numeracy test of Schawartz et al.[68]	Score of 3 items: total number of correct answers [range 0-3] a- Familiarity with probability: "Imagine that we flip a fair coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips? ____times out of 1,000." b- Conversion of percentage to proportion: "In a lottery, the chance of winning a $10 prize is 1%. What is your best guess about how many people would win a $10 prize if 1000 people each buy a single ticket? person(s) out of 1,000." c- Conversion of proportion to percentage: "In a prize draw, the chance of winning a car is 1 in 1,000. What is the percentage of winning tickets?____%." Sys miss	1,6 (1,0) 	1031 0	
Perceived risk [RISK]	Adapted from Levy et al.[70]	What do you think your chance is of developing breast cancer in your lifetime? Continuous variables were 0% means "not at all likely" and 100% means "definitely likely" Nb of cases Sys miss	 33,05 (22,2) 	 784 (76,0) 247 (24,0)	 .836
Monitoring [MO_MBSS]	Validated French Canadian version of the MBSS[71]	8 items of monitoring for 2 scenarios (dentist: α = .696; sales: α = .720). Score coded as 0 if < or = 23 (low monitoring) 1 if > or = 23 (high monitoring) Sys miss	 	 558 (54,1) 467 (45,3) 6 (0,6)	 .921
Health locus of control [PHLC] [IHLC] [CHLC]	Validated French Canadian version of the MHLC[72 64]	3 scales (total of 9 items) for 3 types of locus of control (powerful others: α = .615; internal: α = .686; chance: α = .736). Weighted mean of a 6-point agreement Likert scale Powerful others Sys miss Internal Sys miss Chance Sys miss	 4,15 (1,08) 5,00 (0,87) 2,66 (1,32) 	 1027 4 1026 5 1021 10	 .869 .911 .908
Anxiety [ANX_K6]	Validated psychological distress scale used by ESCC-2010 [36 73]	6 items of non-specific psychological distress (α = .831). Weighted mean of a 5-point frequency Likert scale Nb of cases Sys miss	4,09 (0,63) 	 1031 0	.795

* Items were initially in French as the survey was administered to a French speaking population. They are freely translated for comprehension purposes in this article.

† All missing data, including options "do not want to answer" or "don't know" were coded as missing system data ("sys miss"). Descriptive statistics are presented for the initial model, i.e., the Interest outcome measure.

§ This age group corresponds to eligible women to the PQDCS, the national breast cancer screening program in Québec (Canada).

Table 1. Demographic characteristics of the sample*

Respondents' characteristics	*n* = 1031 (%)
Age	
35 to 49 years old	503 (48,8)
50 to 69 years old	528 (51,2)
Sys miss	0
Ethnicity	
White	977 (94,8)
Other	54 (5,2)
Sys miss	0
Marital status	
Widowed, divorced or separated	186 (18,1)
Single	152 (14,7)
Married or common-law	689 (66,9)
Sys miss	4 (0,4)
Education	
No diploma or secondary school	399 (38,7)
College or CEGEP diploma	265 (35,6)
University degree	367 (35,6)
Sys miss	0
Employment	
Full time	573 (55,6)
Part time	138 (13,4)
Retired	180 (17,5)
Student	15 (1,5)
Unemployed/not working	111 (10,8)
Sys miss	14 (1,4)
Household size	
1	135 (13,1)
2	403 (39,1)
3	192 (18,6)
4	181 (17,6)
5+	102 (9,9)
Sys miss	18 (1,7)
Location area	
Rural	146 (142,0)
Small urban	138 (13,4)
Medium urban	95 (9,2)
Large urban	636 (61,7)
Sys miss	16 (1,6)
Objective risk of BC†	
< 15%	878 (85,2)
= ou > 15%	122 (11,8)
Sys miss	31 (3,0)
Perceived personal risk	
< or =15%	229 (22,2)
15% >	555 (53,8)
Sys miss	247 (24,0)
Interest	
Not interested	93 (9,0)
Somewhat interested	113 (11,0)
Moderately interested	221 (21,4)
Very interested	389 (37,7)
Extremely interested	200 (19,4)
Sys miss	15 (1,5)
Willingness-to-pay	
Do not want to pay	250 (24,2)
Between $1-$100	362 (35,1)
Between $101-$250	153 (14,8)
Between $251-$500	59 (5,7)
Between $501-$1000	13 (1,3)
Over 1000$	3 (0,3)
Sys miss	191 (18,5)

* Sys miss category is the sum of the system missing data, and the option of answers «do not know» and «do not want to answer»

† Calculated with the Gail model parameters (available online: http://www.cancer.gov/bcrisktool/)

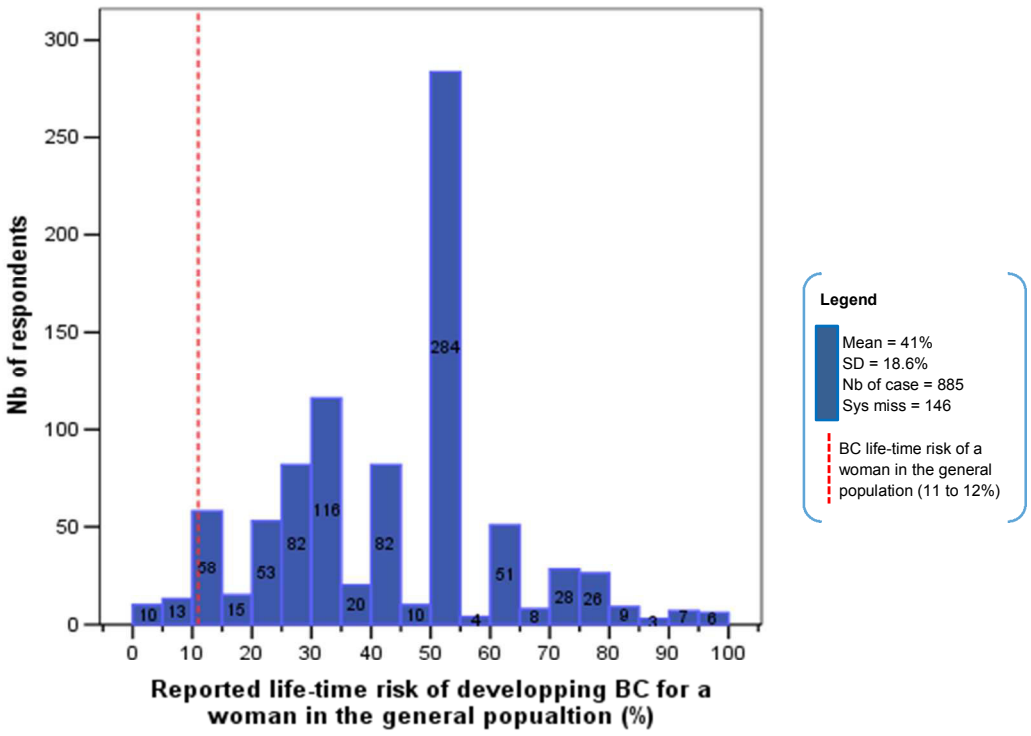
Table 2. Estimated ordered logit models of factors affecting women's interest and willingness-to-pay (WTP) for breast cancer susceptibility testing (BCST) allowing more frequent screening

	STEP 1		STEP 2	
	Outcome INTEREST [INTER] [1= Not interested at all to 5= Extremely interested]		**Outcome WILLINGNESS-TO-PAY** [WTP] [1= 0$; 2= 1 to 100$; 3=101$ and more]	
Explanatory factors	Coefficients (β)	Marginal effect†	Coefficients (β)	Marginal effect†
Sociodemographic factors				
Age [AGE]	-.215*	-.054	-.555***	-.058
Familial income				
∝ Less than 25 000$ [INC1]	-.667***	-.101	-2.081***	-.154
∝ 25 000$ to 54 999$ [INC2]	-.510***	-.098	-1.083***	-.103
∝ 55 000$ to 74 999$ [INC3]	-.074	---	-.762***	-.079
∝ 75 000$ and more [INC4]	*Benchmark*		*Benchmark*	
Marital status				
∝ Widowed-Separated-Divorced [WSD]	.284*	.027	.381*	.038
∝ Single [SING]	.184	---	.201	---
∝ Married or in union [MARUN]	*Benchmark*		*Benchmark*	
Education				
∝ No diploma or secondary school diploma [EDUC1]	-.074	---	-.168	---
∝ College or CEGEP diploma [EDUC2]	-.218	---	-.004	---
∝ University diploma or degree [EDUC3]	*Benchmark*		*Benchmark*	
Medical factors				
Biopsy [BIOPSY]	-.213	---	-.358	---
Parity [PARITY]	.060	---	.131	---
Familial history [FAMHIS]	.319**	.357	.396**	.208
Psychological factors				
Optimism [OPTIMS]	-.299*	-.045	.122	---
Monitoring [MO_MBSS]	.464***	.054	.115	---
Health locus of control				
∝ Powerful others [PHLC]	.266***	.441	.211***	.283
∝ Internal [IHLC]	-.040	---	-.103	---
∝ Chance [CHLC]	-.190***	-.244	-.050	---
Anxiety [ANX_K6]	.332***	.409	.213	---
Numeracy [NUM]	-.421***	-.055	-.304*	-.094
Perceived risk of BC [RISK]	.070***	.092	-.002	---
Perceived health status				
∝ Good [GOOD]	.285**	.047	.513***	.035
∝ Fair-Bad [FAIRBAD]	.428	---	.378	---
∝ Excellent -Very good [EXVER]	*Benchmark*		*Benchmark*	
Ancillary parameters				
Threshold 1	-1.434		-2.346	
Threshold 2	-.248		-.153	
Threshold 3	.962			
Threshold 4	2.728			
Number of cases	635		544	
Likelihood Ratio (*df* = 21)	65.861		60.961	
Nagelkerke R^2 (Pseudo R^2)	.104		.120	
Percentage of correct predictions	50.23%		53.31%	

*; ** and *** indicate that variable is significant at 10%, 5% and 1%, respectively.

†For continuous variables, values of marginal effect represent the variation in percentage on the outcome for 1% positive relative change in the corresponding explanatory factor, whilst for categorical variables, marginal effect values indicate the variation in percentage on the outcome if the sub-sample of respondents would share the same characteristic of those of the reference category.

Figure 1 Reported breast cancer life-time risk for a woman of the general population according to the sample of respondents



STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

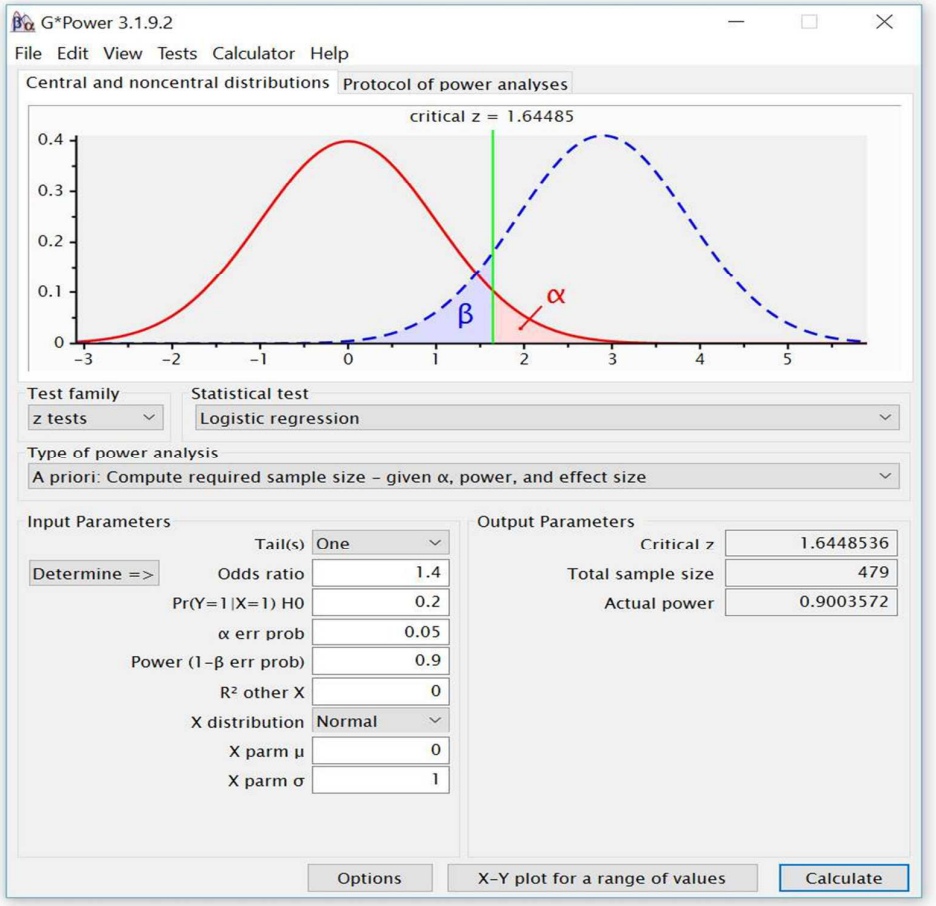
Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6 (4-6)
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6-7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6-7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-6 + Table 1
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Appendix 1
Bias	9	Describe any efforts to address potential sources of bias	6-7 and 9
Study size	10	Explain how the study size was arrived at	7 + Appendix 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Appendix 1
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	Appendix 1
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7 + Table 3

		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9 + Table 2
		(b) Indicate number of participants with missing data for each variable of interest	Appendix 1
Outcome data	15*	Report numbers of outcome events or summary measures	Appendix 1 + Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Only unadjusted estimates are reported Appendix 1 – tolerance values Table 3 (p-values and marginal effects)
		(*b*) Report category boundaries when continuous variables were categorized	Appendix 1
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	*See point 16*
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11-12 See figure below: power analysis
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Screenshot: Power analysis performed with G Power



BMJ Open

Disentangling the determinants of interest and willingness to pay for breast cancer susceptibility testing in the general population: A cross-sectional Web-based survey among women of Québec (Canada)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016662.R1
Article Type:	Research
Date Submitted by the Author:	24-Aug-2017
Complete List of Authors:	Blouin-Bougie, Jolyane; Université Laval, Management Amara, Nabil; Université Laval, Management Bouchard, Karine; Université Laval- Centre de recherche du CHU de Québec, Centre des maladies du sein Deschênes -Fabia Simard, Jacques; Université Laval- Centre de recherche du CHU de Québec, Medicine Dorval, Michel; Université Laval- Centre de recherche du CHU de Québec, Pharmacie
Primary Subject Heading:	Public health
Secondary Subject Heading:	Oncology, Health services research, Genetics and genomics
Keywords:	Interest, Willingness-to-pay, Breast cancer susceptibility testing, Women of the general population

Title

Disentangling the determinants of interest and willingness to pay for breast cancer susceptibility testing in the general population: A cross-sectional Web-based survey among women of Québec (Canada)

Authors & Affiliation

1. Jolyane Blouin-Bougie, PhD Candidate
(Corresponding author)
Department of management, Université Laval
2325, rue de la Terrasse, Pavillon Palasis-Prince, 1516
Québec, QC (Canada) G1V 0A6
(418) 656-2131 # 1379
Jolyane.blouin-bougie@fsa.ulaval.ca

2. Nabil Amara, PhD
Department of management, Université Laval
2325, rue de la Terrasse, Pavillon Palasis-Prince, 1519
Québec, QC (Canada) G1V 0A6
(418) 656-2131 # 4382
Nabil.amara@fsa.ulaval.ca

3. Karine Bouchard, MSc
Centre des maladies du sein Deschênes-Fabia
Centre de recherche du CHU de Québec-Université Laval
Hôpital du Saint-Sacrement, 1050, chemin Sainte-Foy
Québec, QC (Canada) G1S 4L8
(418) 525-4444 # 82721
Karine.Bouchard@crchudequebec.ulaval.ca

4. Jacques Simard, PhD
Faculty of Medecine, Université Laval
Centre de recherche du CHU de Québec-Université Laval
2705, boulevard Laurier, R4-4787
Québec, QC (Canada) G1K 7P4
(418) 654-2264
Jacques.Simard@crchul.ulaval.ca

5. Michel Dorval, PhD
Faculty of Pharmacy, Université Laval
Centre de recherche du CHU de Québec-Université Laval
Hôpital du Saint-Sacrement, 1050, chemin Sainte-Foy
Québec (Canada) G1S 4L8
(418) 682-8047
michel.dorval@pha.ulaval.ca

Key Words
Interest; Willingness-to-pay; Breast cancer susceptibility testing; Women of the general population

Abbreviations
BC = Breast cancer; BCST = Breast cancer susceptibility testing; PM = Personalized medicine; WTP = Willingness-to-pay

Words count
4602 (excluding title page, abstract, references, figures and tables)

Abstract

Objectives: To identify common and specific individual factors that favour or impede women's interest in and willingness-to-pay (WTP) for breast cancer susceptibility testing (BCST) and to identify the most impactful factors on both outcomes measures. The underlying assumption is that interest is a prerequisite to WTP.

Design and Methods: This study used a self-administered cross-sectional web-based questionnaire that included hypothetical scenarios about the availability of a new genetic test for breast cancer.

Participants: French-speaking women of the general population of Québec (Canada), aged between 35 and 69, were identified from a Web-based panel (2410 met the selection criteria, 1160 were reached, and 1031 completed the survey).

Measures: The outcomes are the level of interest in and the WTP for BCST. Three categories of individual factors identified in the literature were used as potential explanatory factors, i.e., demographic, clinical, and psychosocial.

Results: Descriptive statistics indicated that the vast majority of sampled women are interested in BCST (90%). Among those interested, more than half of them are willing-to-pay for such a test (57%). The regression model also pointed out several factors associated with both outcomes (e.g., age, household income, family history, locus of control (powerful others), or numeracy). Marginal effects estimates were also used to highlight the most impactful factors for each outcome (*interest*: anxiety (.409), loci of control-powerful others (0.441) and chance (-.244), family history (.357); *WTP*: locus of control-powerful others (.283), family history (.208), household income (-.154)).

Conclusion: The results of this study provide a proxy of the readiness of women of the general population to use and to collectively pay for BCST. They also offer insights for developing inclusive and specific strategies to foster informed decision-making, and guide the services offered by health organizations corresponding to women's preferences and needs.

Strengths and limitations of this study

- ∝ In accordance with economic theory, this study proposes a conceptually-driven two-step regression model allowing testing of several explanatory factors of interest in and WTP for breast cancer susceptibility testing.
- ∝ This study also presents insights for developing inclusive and specific strategies that could support women's informed decision-making toward BCST and the range of service offerings by health organizations with regards to this test
- ∝ Respondents' interest and WPT are measured using a hypothetical scenario; this may have led to an overestimation of the level of interest and the sum paid out-of-pocket in a realistic situation.
- ∝ Results presented in this study should be cautiously extrapolated to other neighbouring populations as interest in and WTP for genetic testing could greatly vary form populations, tests and methods used.

Introduction

Personalized medicine (PM) is an important growing area of research.[1] In Canada, as in other developed countries, it is viewed as a significant driving economic sector,[2-4] and an encouraging avenue to improve the delivery of health care services[5-7] through patient stratification approaches.[7-9] The goal of PM might be notably achieved by the use of genetic tests. They sustain two main finalities of PM: one is preventive, the other is curative. Indeed, genetic tests could be indicated for healthy patients (i.e., to assess ones' susceptibility to develop a disease and to provide risk management recommendations) or be used for the benefits of ill patients (i.e., to specify diagnosis and prognosis, and to support treatment decisions).[10] This distinction is essential as the decision to be genetically tested is an individual one and may depend on whether the finality of the genetic tests used is preventive or curative, that is to say that the person is healthy or ill.[11] Although the development of PM and genetic knowledge base is seen as promising for the management of multiple diseases, breast cancer prevention remains of premier interest. [8 12-14] The focus of this paper is stated as follows: to assess the interest in and the value attributed by women of the general population of Quebec (Canada) to breast cancer susceptibility testing (BCST). The aim is to gain insight into the readiness of this target population to integrate and use genetic information for BC prevention. In this paper, we refer to BCST as genetic tests (i.e., carrier or predictive testing) that lead to the identification of genetic variants that substantially increase BC risk.

Five main reasons explain the importance of BCST in Québec (Canada). Firstly, BC is one of the leading causes of death among Canadian women. Indeed, the reduction of the burden of this disease is among health care priorities in Canada, as demonstrated by ongoing national BC screening programs.[15 16] Secondly, besides the identification of at-risk women, BCST aims to provide suitable risk-management recommendations adapted to women's BC risk level and preferences (e.g., type and interval of screening - mammograms or MRI - or consideration of prophylactic interventions - mastectomy or chemoprevention).[10 17 18] Thirdly, these genetic tests are currently used in highly-specialized genetic clinics[8 19] since the commercialization of the BRCA1/2 mutation carrier test in the mid-90's.[20] This confers a well-established experience in managing the genetic risk of BC on which to build for the expansion of genetic services to the general population.[21] In point of fact, in Canada - as in other countries - BCST is

only offered to some newly diagnosed BC patients and their relatives, and to those with a strong BC family history. Fourthly, several mutations (i.e., rare genetic variations) on different genes and polymorphisms (i.e., SNPs: common genetic variations present within particular sub-populations) are now known as BC susceptibility risk factors and can be detected simultaneously with recent technologies (e.g., next-generation sequencing, panel-gene testing).[21-24] Some genetic variants are moreover associated with greater risks than others. For instance, a mutation on *BRAC1, BRCA2, TP53 or PTEN* confers a high risk, as a mutation on *CHECK2, PALB2* or *ATM* confers a moderate risk of developing BC.[22-24] Stratifying healthy women's BC risk is thus viewed, in Canada and overseas, as an opportunity to adapt BC screening programs to maximize benefits and minimize drawbacks for the general population and the health care systems in a foreseeable future.[7 9 12 21 25] Lastly, private companies (although few in Canada) provide some BC genetic tests directly to consumers[26 27] thus overriding the necessity for assessment and support by health care professionals.[18 28 29] This raises many concerns, markedly regarding the consumer's understanding of the test results and their implications(e.g., worries, risk of discrimination, repercussions on family members),[10 26 28] The tests' validity, the appropriateness of genetic markers assessed, and the reliability of risk estimates for which no evidence-based recommendations may have been yet established are also among concerns for some experts.[24]

Previous studies have shown that women might demonstrate interest in and willingness to pay for genetic testing even it is not associated with treatment options, as genetic test results may reduce uncertainty, offer some reassurance, guide life or family planning decisions, and may be useful to other family members.[11 30-32] However, how and why Canadian women value BCST remains unclear, even though these are imperative questions for decision-makers and managers involved in the development of PM, the improvement of BC preventive services, or the regulation of DTC genetic testing.

Background

The literature on interest in and willingness-to-pay (WTP) for genetic testing has gradually increased during the last decade and underlined some directions for futures studies.[11 30] Firstly, a great variability exists regarding populations (patients, general population, family members, etc.) and health conditions studied when measuring levels of interest[11] and estimating WTP values.[30] This point supports the

relevance of conducting a research for BCST in the particular context of Québec. Secondly, insufficient theoretical foundation is provided in previous studies when assessing interest and WTP.[11 30] To deal with this issue, we identified in the literature a list of recurrent individual variables empirically tested in the context of cancer susceptibility testing (Appendix 1). Inspired by the classifications of Sweeny et al.[11] and Lin et al.[30], these variables were thereafter classified into three categories: demographic, medical, and psychosocial. Thirdly, previous study results did not allow an understanding of how preferences and WTP values vary according to individual factors, nor tried to present the magnitude of their impact.[30] For that reason, we assessed the marginal effects of individual factors associated with interest in and WPT for BCST. Finally, interest and WTP are often assessed independently with similar variables.[11 30] Further, while the literature shows the existence of an association between interest in and cost of genetic tests for cancer susceptibility,[26 33-35] there is no consensus on which influences the other. Consistent with economic theory,[33 36 37] which supposes that a person's decision is a sequential process «where the decision of whether or not to consume a particular commodity is followed by the choice of how much to consume»,[37] we propose a two-step model where WTP is conditional on interest.

In line with the above observations, the following section provides detailed information on the method used to disentangle individual factors that influence interest in and WTP for BCST and to identify the most impactful factors on both outcomes measures from a sample of women living in Québec (Canada).

Methods

Sample

The target population was made up of French-speaking women of the general population aged between 35 to 69 living in the province of Québec in Canada. The sample was selected from an internet panel maintained by a survey firm and weighted for age, regions, and education level according to Statistics Canada census profiles.[38] The sample size was calculated prior to data collection with a margin of error of 3% at a 95% confidence interval and validated with a *post-hoc* power analysis.

Data collection

A cross-sectional web-based survey developed from a literature review on genetic risk communication was used for this study. Respondents were asked to focus on their: general health state, BC clinical history and risk factors, level of literacy and numeracy regarding various ways of presenting BC risk, interest in and opinions regarding the use of BCST, reactions toward various life events, general psychological health state, and demographic characteristics. Most of the items were measured on a 5 or 6-points Likert scale. The questionnaire was pre-tested with eligible women in February 2012. The questionnaire was adapted for a Web platform and a survey link was sent by the firm to a sample of 2410 eligible women in March 2012. Three prize draws were offered to the participants: one of $3,000 and two of $1,000.

Measures

A hypothetical scenario was presented to women indicating that a new genetic test now available on the market could be used to assess their BC risk, and to adapt their screening modalities should their risk level be higher than that of the general population. The respondents were also advised of the hypothetical nature of the test, and that fees would not necessarily be charged as genetic tests requiring blood testing are generally covered by the public health insurance system in Canada, once approved by authorities. No specifications on the modalities under which this test could be offered or on the genes being assessed by this test was provided to the participants as more research is needed, regarding variants that should be included in a BCST targeting women of the general population.[8 24] Following that, respondents were firstly asked to rank their level of interest in receiving this test on a 5-point Likert scale. They were thereafter asked how much they would be willing to pay out of their pocket for this test on an ordinal scale. Detailed information regarding operational measures of outcomes and explanatory factors, including coding and main references, is presented in Appendix 2.

All clinical information needed to estimate the BC life-time risk of the respondents according to the Gail Model parameters was collected for descriptive purposes.[39] Some potential explanatory variables underlined in the literature were not included in the analysis for methodological concerns such as distribution of respondents or theoretical redundancy. However, no variables were removed from the

models on the basis of low statistical significance because they were assumed to be of theoretical interest and expected to have some effect on women's interest in and WTP for BCST.

Chosen measures were assessed with validated scales or in accordance with the scientific literature. The constructs with multiple-item scales (i.e., loci of control, monitoring, and anxiety) were evaluated with a principal components factor analysis; the unidimensionality criterion was satisfied. Cronbach's alpha (α) showed that items forming each of them were reliable. Finally, reported tolerance statistic values were all higher than 0.2 (Appendix 2); there were no multicollinearity concerns.[40]

Statistical analysis

According to the assumption adopted in this study, a two-step approach was used to investigate: 1) women's interest in a BC screening test that may lead to more frequent screening should their risk level be higher than that of the general population and then, for those interested, 2) women's level of WTP for this genetic test. This approach corresponds to sample-selected outcomes that refer to the situation where responses to a variable (Y) are conditional on a variable (Z). In this case, WTP is conditional on interest (INTER). So, women who responded, in the first step, '*Not at all interested*' in BCST were discarded from the second analysis, i.e., the model on WTP.[41 42]

The dependent variable in each step was modeled as an ordered logit model.[43 44] This type of model uses an intermediate continuous variable Y^* (qualifications made by women regarding the dependent variable: INTER or WTP) in a latent regression with a set of independent variables X_i. The range of the unobserved Y related to INTER and WTP was subdivided, respectively, in five (1= *Not interested at all* to 5= *Extremely interested*) and three (1= $*0*, 2= *1 to $100,* 3= *$101 and over*) adjacent intervals representing the classes of an observed variable, Z. For each dependent variable (INTER and WTP), the outcome of respondent *i* is represented by the latent index:

$$Y_i^* = \beta_1 X_{1i} + \ldots\ldots\ldots\ldots + \beta_k X_{ki} + \varepsilon_i = \beta X + \varepsilon$$

Where:

Y_i^* = the value of the index to the observation *i*

X = a vector of independent variables

β = the vector of parameters to be estimated

ε = the error term

The β coefficients inform on the signs and significance of the explanatory variables, but do not take into account the scope of these coefficients.[44] In order to assess the magnitude of their impact on interest in and WTP for BCST, the marginal effects of the significant independent variables were ascertained with LIMDEP version 8.0 Econometrics Software Package.[45] Marginal effects can be an informative means for summarizing how change in a response is related to change in a covariate.[46 47] This could be useful in targeting the most influential factors when designing interventions.

Moreover, a *post-hoc* power analysis with the statistical program G*power 3.1 was conducted to assess the appropriate sample size for statistical analysis to be performed, and the possibility of committing a Type I or II errors.[48 49] When using an alpha of 0.05, a power level of 0.90, and an odd ratio of 1.42, the minimal sample size was determined to be 479 respondents. Given this result, our sample was sufficiently large to meet these data considerations, i.e. the number of valid cases included in sample-selected regression model (n = 635 [INTER model]; n = 544 [WPT model]) was higher than what is required to detect a "true" effect when it exists.

Results

Descriptive statistics

Overall, 1160 women were reached with the data collection procedure used. Among them, 40 clicked the questionnaire's link after the data collection period, 81 did not complete the questionnaire, and 8 cancelled their panel subscription. The survey generated 1031 usable questionnaires for a net response rate of 43% (i.e., when we consider all women that were not reached among eligible participants).

As shown in Table 1, the sample was mostly composed of white educated women, in a civil union, and living in a large urban area (> 100,000 inhabitants). Descriptive statistics also revealed that 89% of the respondents were interested in BCST that may lead to more frequent screening, and 57% were willing to

pay a certain amount of money to get the test. Moreover, most of the respondents overestimated both their personal BC lifetime risk (mean = 33.05%; SD = 22.25%) and that of women in the general population (Figure 1). However, according to the Gail Model parameters,[39] approximately 85% of the respondents had less than a 15% life-time risk of BC.

[Table 1 and Figure 1]

Ordered logit regressions

The results of the estimation of the two ordered logit models are presented in Table 2. The computation of the measures of goodness of fit of the two models leads to the conclusion that they were well behaved. This is indicated by the thresholds in increasing order ($\alpha_1<\alpha_2<\alpha_3$) and the Chi-squared statistics that were much larger than the critical value (step 1- INTER: χ^2 (21) = 65.861; p < .000; step 2- WTP: χ^2 (21) = 60.961; p < .000). In addition, the «predictive power» of the model appeared to be acceptable (50.23%, and 53.31%, respectively, for INTER and WTP regressions). The Nagelkerke R^2 (Pseudo- R^2), which is not directly comparable to the R^2 derived in conventional OLS regression,[44] varied between .104 and .120. This is acceptable for models with qualitative dependent variables.

[Table 2]

Common explanatory of interest and WTP

For both models, the results suggest that having a BC family history rather than none, having a locus of control highly attributed to powerful others, being widowed, separated or divorced rather than being married or in a union, and having a perception of health status as good instead of excellent or very good, are all significantly associated with a higher interest in and higher WTP for BCST.

Conversely, having a high numeracy score compared to a low numeracy score, a household income less than $55,000 comparatively to a household income of $75,000 and over, and being aged under 50 rather than being aged 50 and over, are all significantly associated with a lower interest in and lower WTP for BCST. The variables biopsy, parity, and education appeared to have no impact on either interest in nor WTP for BCST.

Regarding marginal effects, the coefficients show that BC family history, household income, and locus of control- powerful others are the common explanatory variables that have the highest impact on women's interest in and WTP for BCST.

Specific factors associated with interest in BCST

Furthermore, there were several explanatory variables that were significantly associated only with interest in BCST. Indeed, being a high monitor compared to a low monitor, and having a higher perceived risk of BC are significantly associated with a higher interest, whilst being highly optimistic rather than being poorly optimistic, and having a locus of control highly attributed to chance are significantly associated with a lower interest for BCST.

More specifically, locus of control -powerful others, level of anxiety, and BC family history stand with the highest marginal impact values, respectively of .441, .409, and .357. For the two former continuous variables, this implies that a positive relative change of 10% on these factors increases the level of women's interest in BCST by 4.41% and 4.09%. For the categorical variable, it means that interest in BCST is 35.7% greater among women with a family history of BC comparatively to those without.

Most impactful factors on WTP for BCST

For the WTP model, variables with the highest marginal effects are locus of control- powerful others (marginal effect = .283), BC family history (marginal effect = .208), and household income (marginal effect = -.154, -.103 and -.079). These coefficients indicate that for a positive relative change of 10% on the locus of control- powerful others score, women's WTP for BCST would increase by 2.83%. This also means that WTP for BCST is 20.8% greater among women with a family history compared to those without, and is as much as 15.4% lower among women with a household income of less than $75,000$ compared to those with an income of $75,000$ and over.

Discussion

This study investigated the common and specific individual factors associated with interest in and WTP for BCST that may allow for more frequent screening if one's BC risk level is higher than that of the general

population. Overall, women's age, household income, marital status, and family history were significantly associated with both interest in and WTP for BCST. Optimism, monitoring, external loci of control (powerful others and chance), anxiety, numeracy, perceived risk, and health status had a significant impact on women's interest in BCST, but one:s locus of control (powerful others), numeracy, and perceived health status remained significant for explaining WTP for such a test. Moreover, estimation of the marginal effects indicated that factors which impacted the most interest in BCST were anxiety, loci of control- powerful others and chance, and family history. Locus of control- powerful others, BC family history, and household income had a greater impact regarding WTP for BCST.

While we try to avoid as much as possible sources of bias, readers are advised to consider results in light of some limitations. First, our findings might be considered as representative of French-speaking women aged between 35 and 69 living in Québec (Canada), but should be cautiously extrapolated to other similar or neighbouring populations. Indeed, previous studies called attention to the great variability regarding interest level and WPT estimates across populations studied for genetic testing in general.[11 30] Second, our response rate may seem low (43%), but several prior studies on interest and WTP for genetic testing obtained comparable response rates [50-52] and our sample size is relatively large (*n* = 1031). Third, self-reported data like those used in this study are subject to a social desirability bias. Fourth, as done in previous studies,[26 32 33 53] a hypothetical scenario was used in this study. Nonetheless, given this hypothetical bias, reported results on the degree of interest and level of WTP should not be taken as an objective uptake measure of testing, but as a measure of intention.[11 26 51] Other studies have also demonstrated that revealed measures of WTP overestimate the sum paid out-of-pocket in a realistic situation.[26 32 54] Fifth, different measures of WTP or elicitation techniques to value BCST in the general population in Québec, and more broadly Canada, should be used to confirm our findings. Indeed, the literature revealed discrepancies between studies of WTP estimates according to measures and methods employed for similar tests.[30] Moreover, we used only one item to measure WTP. Even though many studies opted for double or multiple biding items, it has been demonstrated that each of the measurement methods has its strengths and limitations, but that, above all, the level of accuracy gained by the econometric model used afterward are negligible in the case of sample sizes like ours.[55] Finally, as this paper only focused on individual factors, future studies should investigate other potential factors

associated with interest and WTP, like those at the organizational, social or environmental level, and more explicitly ground the explanatory variables in theoretical frameworks. Other aspects could contribute to the choice of being genetically tested, and this may vary by type of genetic tests and the purpose of its use.[11 30]

Potential implications

The findings of this study provide a proxy for the readiness of women of the general population of Québec to get genetically tested for BC susceptibility and the amount they expect to be acceptable to pay for such services in private settings and DTC genetic testing. In Canada, health care services are managed at a provincial level, and health care systems are publicly-funded, while there are some private health care delivery channels (e.g., private clinics, complementary private insurance market).[56] In that context, these results provide insights on the willingness of the general population to collectively pay for BCST. They may also provide insights on their degree of openness toward a new co-payment method for such a test or may support the setting of insurance co-payments, if any, in some situations.[30 57] As the results show, a majority of the women were interested in BCST (~90%), and more than half were willing to pay a certain amount of money for such a test. Indeed, nearly 35% of the women of our sample would pay up to $100, 15% up to $250, and only 7% more than $250. It is however important to note that a great proportion of them were not willing to pay (24%) or did not provide information on the survey item assessing their WTP for BCST (18% of missing data). Overall, this suggests that the women of Québec have mitigated enthusiasm toward BCST if they have to pay for it. This is consistent with another study on genetic testing led in the Canadian context. [35] While it may reflect some important values of Canadian citizens that is embodies in the Medicare system,[56] previous studies led in private healthcare systems as in the USA reported similar findings regarding WTP.[33 52]

Furthermore, the results suggest that many psychosocial factors are associated with women's interest in and WTP for BCST. It is worth mentioning, firstly, that women's interest in and WTP for BCST should be analyzed in light of another important finding: women greatly overestimated both their personal lifetime risk of developing BC and that of women of the general population. Similar results were also found in other populations.[58-60] This overestimation may be due to a lack of knowledge, a low level of numeracy or

otherwise unrealistic worries about BC.[58-60] In addition, as reported by other studies,[26 52] more anxious, less optimistic women and those with poor numeracy skills are more interested in BCST and thus, will probably more extensively use such services. This may suggest that some moderating psychosocial variables enacted throughout the women's decision process to get tested or not. Moreover, it could result in a biased level of interest in and WTP for BCST. Indeed, as revealed in this study, the higher the women's BC risk perceptions are, the higher their level of interest in BCST is. This is in line with the findings of several previous studies that evaluated interest for cancer susceptibility testing.[33 61-64]

Furthermore, one of the most impactful factors on women's interest and WTP is the external health locus of control-powerful others. It implies that a woman who believes that others she considers as experts are largely responsible for her health is more interested in and willing to pay for BCST. This result suggests that health care providers' recommendations, public health or for-profit organizations' communication campaigns or marketing strategies might have an impact on some women's interest in and WTP for BCST. Prior studies have reported similar results in the context of BC screening.[65 66] Beyond that, private companies' DTC advertising efforts may take advantage of actual consumers' emotional concerns or knowledge deficit in genetics.[29 52] These companies should thus be fully encouraged to incorporate adapted modes of communication and provide personalized risk counselling to consumers, instead of their current approach of "one-size-fits-all".[29] On the other hand, interventions designed to improve women's empowerment toward their breast health and BC prevention also have the potential to reduce their interest in and WTP for BCST.

These facts lead, as others proposed,[11 26 33] to reiterate the necessity to put a stronger emphasis on popular education, and to develop educational material toward genetics and the notion of risk to ensure that the choice of getting tested for BC susceptibility is made following an informed decision-making process, and based on more objective and realistic risk perceptions of BC. As a starting point, we suggest that some lessons learned from public health and charity organization messages and decision aids (e.g., information from leaflet or web page, communication campaigns, and other health promotion strategies) about cancer screening[65 66] may serve as a building block for the dissemination of BCST information among the general population. Moreover, the literature on BC risk communication may provide important

cues on the most comprehensive ways risk and genetic information should be transmitted to women of the general population.[67 68] For instance, explaining to women how family history impacts on their risk among other risk factors, stating clearly the prevalence and risk of BC from a genetic point of view, or clarifying the benefits and consequences of being tested for BC susceptibility, might improve women's awareness and knowledge of BCST, may reduce anxiety or worries about BC risk or even motivate some of them to seek out more information about their BC risk. Interventions improving knowledge and awareness, as well as fostering objective BC risk evaluation, have the potential to improve ethical and informed decision-making,[65 66] but may also slightly decrease interest in and WTP for BCST.[11 33 34]

The findings of this study may also help health organizations, either private or public, to better define the range of service offerings. Indeed, taking the pulse of the end-users is an important element which could allow to adjust service delivery modalities to public or consumers' preferences and needs.[33 34] For instance, following results discussed previously on perceived risk, numeracy, anxiety or optimism, it seems that reassurance, support, and education as provided in highly specialized services of genetic counselling are important elements to be adapted for public health care settings - such in the case of the implementation of a BC risk stratification program - and to be provided by private companies selling BC genetic tests directly to consumer in order to minimize drawbacks for women (e.g., anxiety, miscomprehensions, etc.).[29 33 52]

Finally, study results related to some medical and demographic factors could provide insightful paths of action for developing strategies targeting specific sub-groups of women in the population. First, women with a BC family history are at greater risk of BC, and are more interested in and willing to pay for BCST. Thus, they may value and get more benefits from such testing than those without family history, but providers must ensure that their interest and willingness to take the test is based on an informed decision instead of the results of biased self-estimations of BC risk. This notably suggests that continuing to educate and raise awareness among primary care providers in BC family history-taking and BCST may be relevant as they are the professionals seen on a regular basis or who are the most accessible to women of the general population.[13] Second, paying more attention to young women (35 to 49 years old) in clinical encounters could be a winning strategy. It might contribute to the demystification of the notion of risk and

the genetic component of BC into the next generation of women who will be likely invited into BC screening or stratification programs. Furthermore, familial and genetic BC are often developed at a younger age than the sporadic form of BC.[69] So, this could lead to discussions and to recommendations of early risk management strategies for young women at greater risk of BC who are less interested in and attribute less value to BCST in taking into consideration their specificities and potentials needs (e.g., family-planning decisions).[70 71] Lastly, considering that the study's results indicated that interest in and WTP for BCST increased with income, which was also pointed out by previous studies on genetic testing,[33 57] interventions designed for women from lower-resourced neighbourhoods or targeting physicians with a large panel of women with low income could prevent some inequalities in the uptake of BCST (e.g., health or life insurances and employment discrimination, limited access to health services given the cost (if the test is pay out of pocket or partially reimbursed by private insurances) or the way the risk assess, i.e., the risk factors considered, notably age, ethnicity, and family history).[72 73] Moreover, the link between income and interest in BCST should be deeply assessed in future studies as inconsistent findings are underlined in the literature on cancer susceptibility testing with relating concepts. For instance, previous authors found mixt results regarding its association with the socio-economic status.[33 61 62] As this concept reflects more broadly family or household resources, including education, employment, goods and revenues, one hypothesis may be that some confounding or moderating variables are involved into the decision-making process of women opting or not for BCST.

Conclusion

This study disentangles common and specific individual determinants of interest in and WTP for BCST by women of the general population of Québec (Canada). Overall, the results provide a proxy for the readiness of the general population to pay for BCST. It also presents insights for developing inclusive and specific strategies that could support women's informed decision-making toward BCST and the range of service offerings by health organizations with regards to this test. For managers and decision-makers involved in BC prevention, thinking to adjust or to extend BC genetic services and desiring to adapt it to public preferences and needs, this study highlights two ways of proceeding that could be profitable from a social and economic point of view. The first is to develop interventions targeting the whole population,

such as health promotion campaigns, by focusing on the psychosocial factors, given the number of significant factors explaining interest in and WTP for BCST. The second is to tailor interventions to particular sub-populations by considering the most impactful factors associated to interest in and WTP for BCST, such as family history backgrounds or strata of household income.

References

1. Khoury MJ, Coates RJ, Fennell ML, et al. Multilevel research and the challenges of implementing genomic medicine. *JNCI Monographs* 2012;2012(44):112-20.
2. Health Leaders Media - a division of HCPro Inc. In collaboration with Price Water House Cooper. The Impact of Personalized Medicine Today Massachusetts, United-States2010 [Available from: www.healthleadersmedia.com/breakthroughs.
3. Schleidgen S, Klingler C, Bertram T, et al. What is personalized medicine: sharpening a vague term based on a systematic literature review. *BMC medical ethics* 2013;14(1):55.
4. Regroupement en soins de santé personnalisés au Québec (RSSPQ). Proposition pour l'élaboration de la Politique nationale sur la recherche et l'innovation. Les soins de santé personnalisés : une opportunité unique d'innovation pour le Québec, 3 avril 2013:12.
5. Welch BM, Kawamoto K. Clinical decision support for genetically guided personalized medicine: a systematic review. *Journal of the American Medical Informatics Association* 2013;20(2):388-400.
6. Diamandis M, White NMA, Yousef GM. Personalized Medicine: Marking a New Epoch in Cancer Patient Management. *Mol Cancer Res* 2010;8:1175-87. doi: doi: 10.1158/1541-7786.MCR-10-0264
7. Gouvernement du Canada - Canadian Institutes of Health Research. Personalized Medicine, 2015:Online.
8. Foulkes WD, Knoppers BM, Turnbull C. Population genetic testing for cancer susceptibility: founder mutations to genomes. *Nat Rev Clin Oncol* 2016;13(1):41-54. doi: 10.1038/nrclinonc.2015.173
9. Dent T, Jbilou J, Rafi I, et al. Stratified cancer screening: the practicalities of implementation. *Public Health Genomics* 2013;16(3):94-99.
10. Ginsburg GS, Willard HF. Genomic and personalized medicine: foundations and applications. *Translational research* 2009;154(6):277-87.
11. Sweeny K, Ghane A, Legg AM, et al. Predictors of Genetic Testing Decisions: A Systematic Review and Critique of the Literature. *Journal of Genetic Counseling* 2014;23(3):263-88. doi: 10.1007/s10897-014-9712-9
12. Burton H, Jackson C, Abubakar I. The impact of genomics on public health practice. *British medical bulletin* 2014;112(1):37-46.
13. Chowdhury S, Dent T, Pashayan N, et al. Incorporating genomics into breast and prostate cancer screening: assessing the implications. *Genetics in Medicine* 2013;15(6):423-32.
14. Evans DGR, Donnelly LS, Harkness EF, et al. Breast cancer risk feedback to women in the UK NHS breast screening population. *Br J Cancer* 2016;114(9):1045-52. doi: 10.1038/bjc.2016.56
15. Gouvenement du Canada - Statistiques Canada. Le cancer au Canada : cancers du poumon, du côlon et du rectum, du sein et de la prostate. 2011 [Available from: http://www.statcan.gc.ca/pub/82-624-x/2011001/article/11596-fra.htm.
16. International Agency for Reseach on Cancer - World Health Organanization. Cancer Incidence in Five Continents Vol. X. IARC Scientific Publication No 164. Lyon, France, 2014:1365 pp.
17. Amara N, Blouin-Bougie J, Jbilou J, et al. The knowledge value-chain of genetic counseling for breast cancer: an empirical assessment of prediction and communication processes. *Familial Cancer* 2016;15(1):1-17. doi: 10.1007/s10689-015-9835-7
18. O'Daniel J. The Prospect of Genome-guided Preventive Medicine: A Need and Opportunity for Genetic Counselors. *Journal of genetic counseling* 2010;19(4):315-27. doi: 10.1007/s10897-010-9302-4
19. Howell A, Astley S, Warwick J, et al. Prevention of breast cancer in the context of a national breast screening programme. *Journal of Internal Medicine* 2012;271(4):321-30. doi: 10.1111/j.1365-2796.2012.02525.x
20. Parthasarathy S. Architectures of Genetic Medicine: Comparing Genetic Testing for Breast Cancer in the USA and the UK. *Social Studies of Science* 2005;35(1):5-40. doi: 10.1177/0306312705047172
21. Howe R, Miron-Shatz T, Hanoch Y, et al. Personalized Medicine Through SNP Testing for Breast Cancer Risk: Clinical Implementation. *Journal of Genetic Counseling* 2015;24(5):744-51. doi: 10.1007/s10897-014-9803-7
22. Evans DG, Howell A. Can the breast screening appointment be used to provide risk assessment and prevention advice? *Breast Cancer Research* 2015;17(1):84-84 1p. doi: 10.1186/s13058-015-0595-y
23. Couch FJ, Nathanson KL, Offit K. Two decades after BRCA: setting paradigms in personalized cancer care and prevention. *Science* 2014;343(6178):1466-70. doi: 10.1126/science.1251827
24. Easton DF, Pharoah PDP, Antoniou AC, et al. Gene-Panel Sequencing and the Prediction of Breast-Cancer Risk. *New England Journal of Medicine* 2015;372(23):2243-57. doi: 10.1056/NEJMsr1501341
25. Eccles SA, Aboagye EO, Ali S, et al. Critical research gaps and translational priorities for the successful prevention and treatment of breast cancer. *Breast Cancer Research* 2013;15(5):1-37. doi: 10.1186/bcr3493
26. Graves K, Peshkin B, Luta G, et al. Interest in genetic testing for modest changes in breast cancer risk: implications for SNP testing. *Public Health Genomics* 2011;14(3):178.
27. Goldsmith L, Jackson L, O'Connor A, et al. Direct-to-consumer genomic testing: systematic review of the literature on user perspectives. *European Journal of Human Genetics* 2012;20(8):811-16.
28. Zimmern RL, Khoury MJ. The impact of genomics on public health practice: the case for change. *Public Health Genomics* 2012;15(3-4):118-24.
29. Bellcross CA, Page PZ, Meaney-Delman D. Direct-to-consumer personal genome testing and cancer risk prediction. *The Cancer Journal* 2012;18(4):293-302.
30. Lin P-J, Cangelosi MJ, Lee DW, et al. Willingness to pay for diagnostic technologies: a review of the contingent valuation literature. *Value In Health* 2013;16(5):797-805.
31. Kopits IM, Chen C, Roberts JS, et al. Willingness to pay for genetic testing for Alzheimer's disease: a measure of personal utility. *Genetic testing and molecular biomarkers* 2011;15(12):871-75.
32. Neumann PJ, Cohen JT, Hammitt JK, et al. Willingness - to - pay for predictive tests with no immediate treatment implications: a survey of US residents. *Health economics* 2012;21(3):238-51.
33. Bosompra K, Ashikaga T, Flynn BS, et al. Psychosocial factors associated with the public's willingness to pay for genetic testing for cancer risk: a structural equations model. *Health Education Research* 2001;16(2):157-72.
34. Matro JM, Ruth KJ, Wong Y-N, et al. Cost sharing and hereditary cancer risk: Predictors of willingness-to-pay for genetic testing. *Journal of genetic counseling* 2014;23(6):1002-11.

35. Ries NM, Hyde-Lay R, Caulfield T. Willingness to pay for genetic testing: a study of attitudes in a Canadian population. *Public Health Genomics* 2010;13(5):292-300. doi: 10.1159/000253120
36. Lazaridis P. Demand elasticities derived from consistent estimation of Heckman-type models. *Applied Economics Letters* 2004;11(8):523-27. doi: 10.1080/1350485042000207234
37. Saha A, Capps O, Byrne PJ. Calculating marginal effects in dichotomous - continuous models. *Applied Economics Letters* 1997;4(3):181-85. doi: 10.1080/135048597355474
38. Statistics Canada. Enquête sur la santé dans les collectivités canadiennes (ESSC), 2010:417pp.
39. Gail MH, Brinton LA, Byar DP, et al. Projecting Individualized Probabilities of Developing Breast Cancer for White Females Who Are Being Examined Annually. *Journal of the National Cancer Institute* 1989;81(24):1879-86. doi: 10.1093/jnci/81.24.1879
40. Field A. Discovering statistics using IBM SPSS statistics: Sage 2013.
41. Breen R. Regression models: Censored, sample selected, or truncated data: Sage 1996.
42. Lennox CS, Francis JR, Wang Z. Selection models in accounting research. *The Accounting Review* 2011;87(2):589-616.
43. Aldrich JH, Nelson FD. Linear probability, logit, and probit models: Sage 1984.
44. Greene WH, Hensher DA. Modeling Ordered Choices: A Primer 1ed: Cambridge University Press; 2010.
45. Greene WH. LIMDEP: Version 8.0: Econometric Modeling Guide: Econometric Software 2002.
46. Hanmer MJ, Ozan Kalkan K. Behind the Curve: Clarifying the Best Approach to Calculating Predicted Probabilities and Marginal Effects from Limited Dependent Variable Models. *American Journal of Political Science* 2013;57(1):263-77. doi: 10.1111/j.1540-5907.2012.00602.x
47. D'Este P, Amara N, Olmos-Peñuela J. Fostering novelty while reducing failure: Balancing the twin challenges of product innovation. *Technological Forecasting and Social Change* 2016;113:280-92.
48. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behavior research methods* 2009;41(4):1149-60.
49. Portney LG, Watkins MP. Foundations of clinical research: applications to practice. 3rd ed. Philadelphia, USA: FA Davis Co. 2015.
50. Neumann PJ, Hammitt JK, Mueller C, et al. Public attitudes about genetic testing for Alzheimer's disease. *Health Affairs* 2001;20(5):252-64.
51. Lacour RA, Daniels MS, Westin SN, et al. What women with ovarian cancer think and know about genetic testing. *Gynecologic oncology*;111(1):132-36. doi: 10.1016/j.ygyno.2008.06.016
52. Miron-Shatz T, Hanoch Y, Doniger GM, et al. Subjective but not objective numeracy influences willingness to pay for BRCA1/2 genetic testing. *Judgment and Decision Making* 2014;9(2):152-58.
53. Michael F. Drummond MJS, Karl Claxton, Greg L. Stoddart, George W. Torrance. Methods for the Economic Evaluation of Health Care Programmes. 4 ed2015.
54. Cookson R. Willingness to pay methods in health care: a sceptical view. *Health economics* 2003;12(11):891-94.
55. Calia P, Strazzera E. Bias and efficiency of single versus double bound models for contingent valuation studies: a Monte Carlo analysis. *Applied Economics* 2000;32(10):1329-36. doi: 10.1080/000368400404489
56. Loeppky R. Canada, Health and Historical Political Economy. *Journal of Australian Political Economy* 2014(73):172.
57. Kilambi V, Johnson FR, González JM, et al. Valuations of Genetic Test Information for Treatable Conditions: The Case of Colorectal Cancer Screening. *Value in Health* 2014;17(8):838-45.
58. Rutherford EJ, Kelly J, Lehane EA, et al. Health literacy and the perception of risk in a breast cancer family history clinic. *The Surgeon* 2016 doi: http://dx.doi.org/10.1016/j.surge.2016.06.003
59. MacTiernan A, Fritschi L, Slevin T, et al. Public perceptions of cancer risk factors: a Western Australian study. *Health Promotion Journal of Australia* 2014;25(2):90-96. doi: https://doi.org/10.1071/HE13081
60. Fehniger J, Livaudais-Toman J, Karliner L, et al. Perceived Versus Objective Breast Cancer, Breast Cancer Risk in Diverse Women. *Journal of Women's Health (15409996)* 2014;23(5):420-27. doi: 10.1089/jwh.2013.4516
61. Bosompra K, Flynn BS, Ashikaga T, et al. Likelihood of undergoing genetic testing for cancer risk: a population-based study. *Preventive Medicine* 2000;30(2):155-66.
62. Bunn JY, Bosompra K, Ashikaga T, et al. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. *Preventive medicine* 2002;34(6):567-77.
63. Kinney AY, Croyle RT, Dudley WN, et al. Knowledge, attitudes, and interest in breast-ovarian cancer gene testing: a survey of a large African-American kindred with a BRCA1 mutation. *Preventive medicine* 2001;33(6):543-51.
64. Reitz F, Barth J, Bengel J. Predictive value of breast cancer cognitions and attitudes toward genetic testing on women's interest in genetic testing for breast cancer risk. *GMS Psycho-Social Medicine* 2004;1:Doc03.
65. Hersch J, Nickel B, Ghanouni A, et al. Improving communication about cancer screening: moving towards informed decision making. *Public health research & practice* 2017;27(2)
66. Vrinten C, McGregor LM, Heinrich M, et al. What do people fear about cancer? A systematic review and meta-synthesis of cancer fears in the general population. *Psycho-Oncology* 2017;26(8):1070-79. doi: 10.1002/pon.4287
67. Dorval M, Bouchard K, Chiquette J, et al. A focus group study on breast cancer risk presentation: one format does not fit all. *European Journal of Human Genetics* 2013;21(7):719.
68. Julian-Reynier C, Welkenhuysen M, Hagoel L, et al. Risk communication strategies: state of the art and effectiveness in the context of cancer genetic services. *European journal of human genetics: EJHG* 2003;11(10):725.
69. Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *American journal of human genetics* 1995;56(1):265.
70. Evans C, Hamilton JR, Tercyak PK, et al. Understanding the Needs of Young Women Regarding Breast Cancer Risk Assessment and Genetic Testing: Convergence and Divergence among Patient-Counselor Perceptions and the Promise of Peer Support. *Healthcare* 2016;4(3):19. doi: 10.3390/healthcare4030035
71. Ahmad S, Fergus K, McCarthy M. Psychosocial issues experienced by young women with breast cancer: the minority group with the majority of need. *Current opinion in supportive and palliative care* 2015;9(3):271-78.
72. Gouvernement du Québec - Commission de l'éthique en science et en technologie. Soins de santé personnalisés: Document de consultation Québec, 2012:44.

73. McClellan KA, Avard D, Simard J, et al. Personalized medicine and access to health care: potential for inequitable access? *European Journal of Human Genetics* 2013;21(2):143.
74. Gail MH. Twenty-five years of breast cancer risk models and their applications. *JNCI: Journal of the National Cancer Institute* 2015;107(5)
75. Fisher RA. Statistical methods and scientific inference. 1956
76. Lipsey MW. Design sensitivity: Statistical power for experimental research: Sage 1990.
77. Noymer A. Alpha, significance level of test. *Encyclopedia of survey research methods* 2008;18
78. Bottorff JL, Ratner PA, Balneaves LG, et al. Women's interest in genetic testing for breast cancer risk the influence of sociodemographics and knowledge. *Cancer Epidemiology Biomarkers & Prevention* 2002;11(1):89-95.
79. Biesecker BB, Ishibe N, Hadley DW, et al. Psychosocial factors predicting BRCA1/BRCA2 testing decisions in members of hereditary breast and ovarian cancer families. *American Journal of Medical Genetics* 2000;93(4):257-63.
80. Sanderson SC, O'Neill SC, Bastian L, et al. What can interest tell us about uptake of genetic testing? Intention and behavior amongst smokers related to patients with lung cancer. *Public Health Genomics* 2009;13(2):116-24.
81. Petersen GM, Larkin E, Codori A-M, et al. Attitudes toward Colon Cancer Gene Testing: Survey of Relatives of Colon Cancer Patients. *Cancer Epidemiology Biomarkers & Prevention* 1999;8(4):337-44.
82. Aizer AA, Chen M-H, McCarthy EP, et al. Marital Status and Survival in Patients With Cancer. *Journal of Clinical Oncology* 2013;31(31):3869-76. doi: 10.1200/jco.2013.49.6489
83. Dawood SS, Lei X, Dent R, et al. Impact of marital status on prognostic outcome of women with breast cancer. *J Clin Oncol (Meeting Abstracts)* 2014;32(15_suppl):594-.
84. Braithwaite D, Sutton S, Steggles N. Intention to participate in predictive genetic testing for hereditary cancer: the role of attitude toward uncertainty. *Psychology and Health* 2002;17(6):761-72.
85. Welkenhuysen M, Evers-Kiebooms G, Decruyenaere M, et al. A community based study on intentions regarding predictive testing for hereditary breast cancer. *Journal of medical genetics* 2001;38(8):540-47.
86. National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP). The Breast Cancer Risk Assessment Tool 3.0. In: U.S. Department of Health and Human Services, ed., 2011.
87. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. *Journal of personality and social psychology* 1994;67(6):1063.
88. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. *Journal of personality and social psychology* 1987;52(2):345.
89. Nordin K, Björk J, Berglund G. Factors influencing intention to obtain a genetic test for a hereditary disease in an affected group and in the general public. *Preventive medicine* 2004;39(6):1107-14.
90. Malcarne VL, Fernandez S, Flores L. Factorial validity of the multidimensional health locus of control scales for three American ethnic groups. *Journal of Health Psychology* 2005;10(5):657-67.
91. Cameron LD, Reeve J. Risk perceptions, worry, and attitudes about genetic testing for breast cancer susceptibility. *Psychology & Health* 2006;21(2):211-30.
92. KESSLER R, nbsp, C., et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine* 2002;32(06):959-76. doi: doi:10.1017/S0033291702006074
93. Schwartz LM, Woloshin S, Black WC, et al. The Role of Numeracy in Understanding the Benefit of Screening Mammography. *Annals of Internal Medicine* 1997;127(11):966-72. doi: 10.7326/0003-4819-127-11-199712010-00003
94. Trottier C, Mageau G, Trudel P, et al. Validation de la version canadienne-française du Life Orientation Test-Revised. *Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement* 2008;40(4):238.
95. Levy AG, Shea J, Williams SV, et al. Measuring perceptions of breast cancer risk. *Cancer Epidemiology Biomarkers & Prevention* 2006;15(10):1893-98.
96. French translation and validation of the Miller Behavioral Style Scale. INTERNATIONAL JOURNAL OF PSYCHOLOGY; 1996. PSYCHOLOGY PRESS 27 CHURCH RD, HOVE, EAST SUSSEX, ENGLAND BN3 2FA.
97. Talbot F, Nouwen A, Gauthier J. Is Health Locus of Control a 3 - factor or a 2 - factor construct? *Journal of clinical psychology* 1996;52(5):559-68.
98. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological medicine* 2002;32(06):959-76.

Acknowledgement/Funding sources

This research was supported by the Canadian Institutes of Health Research as a part of the CIHR Team in Familial Risks of Breast Cancer Grant (CRN-8752-1). The Government of Canada through Genome Canada and the Canadian Institutes of Health Research (GPH-129344), the *Ministère de l'Économie, de la Science et de l'Innovation* du Québec through Genome Québec, the Québec Breast Cancer Foundation for the PERSPECTIVE project also funded this study.

Conflict of interest: All authors declare no conflicts of interest in this paper.

Contributors: All authors were responsible for the project design. MD and KB were in charge of the survey development and the data collection, while JBB and NA made all the data analysis and drafted the preliminary version of the manuscript. All authors contributed to results interpretation and agreed on the final version of this article before submission.

Ethics approval: This study was approved by the *Comité d'éthique et de la recherche du CHU de Québec-Université Laval* (#2012-1584/2012-HSS-300-05).

Data sharing statement: No additional data are available.

Figure legends:

Figure 1
Respondents' distribution of reported BC life-time risk for a woman of the general population

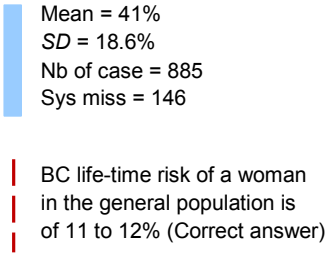


Table 1. Demographic characteristics of the sample*

Respondents' characteristics	*n* = 1031 (%)
Age	
35 to 49 years old	503 (48.8)
50 to 69 years old	528 (51.2)
Sys miss	0
Ethnicity	
White	977 (94.8)
Other	54 (5.2)
Sys miss	0
Marital status	
Widowed, divorced or separated	186 (18.1)
Single	152 (14.7)
Married or common-law	689 (66.9)
Sys miss	4 (0.4)
Education	
No diploma or secondary school	399 (38.7)
College or CEGEP diploma	265 (35.6)
University degree	367 (35.6)
Sys miss	0
Employment	
Full time	573 (55.6)
Part time	138 (13.4)
Retired	180 (17.5)
Student	15 (1.5)
Unemployed/not working	111 (10.8)
Sys miss	14 (1.4)
Household size	
1	135 (13.1)
2	403 (39.1)
3	192 (18.6)
4	181 (17.6)
5+	102 (9.9)
Sys miss	18 (1.7)
Location area	
Rural	146 (142.0)
Small urban	138 (13.4)
Medium urban	95 (9.2)
Large urban	636 (61.7)
Sys miss	16 (1.6)
Objective risk of BC[†]	
< 15%	878 (85.2)
= ou > 15%	122 (11.8)
Sys miss	31 (3.0)
Perceived personal risk	
< or =15%	229 (22.2)
15% >	555 (53.8)
Sys miss	247 (24.0)
Family History	
1 or more first degree relative	146 (14.2)
No family history	869 (84.4)
Sys miss	16 (1.6)
Interest	
Not interested	93 (9.0)
Somewhat interested	113 (11.0)
Moderately interested	221 (21.4)
Very interested	389 (37.7)
Extremely interested	200 (19.4)
Sys miss	15 (1.5)
Willingness-to-pay	
Do not want to pay	250 (24.2)
Between $1-$100	362 (35.1)
Between $101-$250	153 (14.8)
Between $251-$500	59 (5.7)
Between $501-$1,000	13 (1.3)
Over 1,000$	3 (0.3)
Sys miss	191 (18.5)

* Sys miss category is the sum of the system missing data, and the option of answers «do not know» and «do not want to answer»

† Calculated with the Gail model parameters (available online: http://www.cancer.gov/bcrisktool/). Absolute BC life-time risk of a woman of the general population is of 11 to 12%.However, risk prediction models used pure cumulative risk (i.e., when no competing mortality risk exist), which is often higher than the absolute risk.[74]

Table 2. Estimated ordered logit models of factors affecting women's interest and willingness-to-pay (WTP) for breast cancer susceptibility testing (BCST) allowing more frequent screening

	STEP 1		**STEP 2**	
	Outcome INTEREST [INTER] [1= Not interested at all to 5= Extremely interested]		**Outcome WILLINGNESS-TO-PAY** [WTP] [1= 0$; 2= 1 to 100$; 3=101$ and more]	
Explanatory factors	Coefficients (β)	Marginal effect†	Coefficients (β)	Marginal effect†
Sociodemographic factors				
Age [AGE]	-.215*	-.054	-.555***	-.058
Household income				
∝ Less than $25,000 [INC1]	-.667***	-.101	-2.081***	-.154
∝ $25,000 to $54,999 [INC2]	-.510***	-.098	-1.083***	-.103
∝ $55,000 to $74,999 [INC3]	-.074	---	-.762***	-.079
∝ $75,000 and over [INC4]	*Benchmark*		*Benchmark*	
Marital status				
∝ Widowed-Separated-Divorced [WSD]	.284*	.027	.381*	.038
∝ Single [SING]	.184	---	.201	---
∝ Married or in union [MARUN]	*Benchmark*		*Benchmark*	
Education				
∝ No diploma or secondary school diploma [EDUC1]	-.074	---	-.168	---
∝ College or CEGEP diploma [EDUC2]	-.218	---	-.004	---
∝ University diploma or degree [EDUC3]	*Benchmark*		*Benchmark*	
Medical factors				
Biopsy [BIOPSY]	-.213	---	-.358	---
Parity [PARITY]	.060	---	.131	---
Familial history [FAMHIS]	.319**	.357	.396**	.208
Psychological factors				
Optimism [OPTIMS]	-.299*	-.045	.122	---
Monitoring [MO_MBSS]	.464***	.054	.115	---
Health locus of control				
∝ Powerful others [PHLC]	.266***	.441	.211***	.283
∝ Internal [IHLC]	-.040	---	-.103	---
∝ Chance [CHLC]	-.190***	-.244	-.050	---
Anxiety [ANX_K6]	.332***	.409	.213	---
Numeracy [NUM]	-.421***	-.055	-.304*	-.094
Perceived risk of BC [RISK]	.070***	.092	-.002	---
Perceived health status				
∝ Good [GOOD]	.285**	.047	.513***	.035
∝ Fair-Bad [FAIRBAD]	.428	---	.378	---
∝ Excellent -Very good [EXVER]	*Benchmark*		*Benchmark*	
Ancillary parameters				
Threshold 1	-1.434		-2.346	
Threshold 2	-.248		-.153	
Threshold 3	.962			
Threshold 4	2.728			
Number of cases	635		544	
Likelihood Ratio (*df* = 21)	65.861		60.961	
Nagelkerke R^2 (Pseudo R^2)	.104		.120	
Percentage of correct predictions	50.23%		53.31%	

*; ** and *** indicate that variable is significant at 10%, 5% and 1%, respectively. Given the nature of the variables assessed and the mixed findings reported for almost all of them in the literature on cancer susceptibility testing, and the number of valid cases included in the analysis, we used three commonly used alpha thresholds to provide to readers more precisions on the significance of our results. [75-77]

† For continuous variables, values of marginal effect represent the variation in percentage on the outcome for 1% positive relative change in the corresponding explanatory factor, whilst for categorical variables, marginal effect values indicate the variation in percentage on the outcome if the sub-sample of respondents would share the same characteristic of those of the reference category.

Appendix 1. Literature overview on interest in and willingness to pay for cancer susceptibility testing (CST)

Explanatory factors		Outcome measures †		Definitions of factors, description of previous study results, and precisions
		Interest for CST	WTP for CST	
Socio-demographic factors	Age*	Age: NEG[33] POS [62 78 79] NS[26 80 57 81 61] Younger age: POS [63]	Age: NS [26 33] NEG[34 32]	Definition: Age of either patients or individuals of the general population ∝ Link between age and interest or WTP for CST are still equivocal. ∝ Systematic reviews conclusions: studies having assessed association between age and interest toward genetic tests proposed globally mixed findings and mostly inconsistent effects[11]; WTP values for dx tests can be positively influenced by older age.[30] ∝ Age is an important element of women's BC risk assessment: aging is associated with BC, but familial and genetic BC are often developed at a younger age than sporadic forms of BC.[69]
	Ethnicity	Race: NS [26 51 57 81]	Race: NS[26 51] Race: NS[34] Ashkenazi decent: NS[52]	Definition: Person's race or cultural traits relevant to particular group ∝ According to the literature on CST, race seems to not have any effect on interest and WTP. ∝ Systematic reviews conclusions: These variables have not been discussed for interest; WTP values for dx tests are positively influenced by a majority race or ethnicity, especially white Americans.[30] ∝ Some populations or groups of a particular biological background are at greater risk of BC (e.g., French-Canadian, Ashkenazi, Islanders). *N.B. The sample does not present sufficient variation in terms of ethnicity backgrounds (95% of White women) to be included in the statistical exercise.*
	Marital Status*	Marital status: NS[26 57 63] NEG[79]	Marital status: NS[26 34]	Definition: Person's legal marital status (e.g., common law, single, divorced…) ∝ According to the literature on CST, marital status seems to not have an effect on interest and WTP. ∝ Systematic reviews conclusions: Relationship between interest and marital status is supported by equivocal findings.[11] ∝ As genetic tests results might have important implications for family-planning decisions, it seems logical that marital status could influence genetic testing decisions.[11] This variable was also proved to be of great importance in cancer care. It has recently been demonstrated that unmarried persons were at a higher risk for cancer, undertreatment and death from cancer. [82 83]
	Education level*	Education: NS[26 51 63 81 84] Year of education: NEG[78]	Education: NEG.[32] POS.[34 51] NS.[26]	Definition: Person's highest completed degree or diploma. ∝ Link between education level and interest or WTP for CST is still equivocal. ∝ Systematic reviews conclusions: Interest toward genetic tests is inconsistent across studies.[11] WTP values are generally positively associated with education for dx tests.[30]
	Employment status/ primary activities	Employment: POS [57] NS [26 84]	Employment: NS [26 34]	Definition: Person's primary activities of a diary day; it can correspond to employment status for paid work (part- or full-time), but also to unpaid work such as study, housework, social support, volunteering, etc. ∝ Link between employment and interest or WTP for CST seems not significant. ∝ Systematic reviews conclusions: Few studies have assessed the link between employment and interest for genetic testing. Mixed findings are reported. [11]
	Income*	Household income: NS[26 63 81] POS.[57]	Household income: NS.[26 32 34]	Definition: Combined gross income of all members of a household. ∝ Link between income and interest or WTP for CST seems to not be significant. ∝ Systematic reviews conclusions: Associations of interest for genetic testing and income are inconsistent,[11] but WTP values for dx tests are generally positively associated with incomes. [30]
	Household size	Household size: POS.[57]	NA	Definition: Number of persons residing in a private household. ∝ There is insufficient information regarding household size and interest or WTP for CST. *N.B. This concept is partly assessed by marital status and parity for many respondents. It was eliminated.*
	SES	Socio-economic status: NEG[33 62] NS[61]	Socio-economic status: POS.[33]	Definition: SES is a concept that reflects more broadly familial resources, including education, employment, goods and revenues. ∝ There is insufficient information regarding SES and interest or WTP for CST. *N.B. As this concept is a mix of other retrieved sociodemographic characteristics in the literature, it has been discarded from the statistical models to avoid theoretical redundancy.*

Medical factors	Past medical exams/results*	Previous examination: MA[81] Timing of the most recent biopsy NS[26] Prior history of cancer: POS[63 78]	Personal breast cancer history: NS[26] Personal history of GI cancer: NS[34] Personal history of any cancer: NS[34]	Definition: Prior test results or health exams of an individual linked to the evaluated health condition. ∝ According to the literature on CST, past medical exams or results could have an impact on interest while they seem to not have an effect on WTP. ∝ Systematic reviews conclusions: It is not clear whether WTP values for dx tests were associated with past medical exams and results.[30] *N.B. Biopsy was used as a measure of past exam in the present study.*
	Children/ Parity*	Children: NS[57] POS[85]	NA	Definition: Woman having/giving birth to at least one child. ∝ Parity/parental status was insufficiently assessed for CST. ∝ Systematic reviews conclusions: Relationship between interest for genetic testing and parental status is still equivocal. [11] ∝ Nulliparty (never having given birth) is a risk factor as parity is a protective factor of BC. [86]
	Family history*	FDR had cancer: NEG[33] NS[26 81 84] POS[62 84 78] BC in family: POS[85 61] Number of first-degree relatives: POS [63]	FDR had cancer: NEG[33 34 81] NS[26 52] Family member tested positive: NS[52]	Definition: People who have one or more relatives (1st to 3rd degree) who have had a cancer dx. ∝ Family history seems to be associated with interest for CST while more evidence is needed for WTP for such a test. ∝ Systematic reviews conclusions: Generally, positive family history is associated with interest in genetic testing[11] and WTP for dx tests technologies.[30] ∝ Family history is an important risk factor of BC.[86]
Psychosocial factors	Optimism*/ Pessimism	Optimism NEG [33] POS[62 79] Pessimism: POS[62 61 33] (Depressive sx: POS[63])	Optimism: NEG[33] Pessimism : NS[33]	Definition: Person's tendency to have positive (optimists) or negative (pessimists) expectancies about their future (e.g., events, acts).[87] ∝ Mixed findings were reported regarding association between optimism/pessimism and interest for genetic testing and more research is needed for WTP in the context of CST. ∝ Systematic reviews conclusions: Person having a more positive outlook, highly optimistic or low in depression sx was more interested in genetic testing even if some mixed findings were reported for BC. [11] ∝ This construct is often measured with the Life Orientation Scale. [87]
	Monitoring*	Seek information: NS [62] Information seeking: NS[33] Preference for medical information: NS[61]	Information seeking: NEG[33]	Definition: Coping style based on personal information preferences about an event: information seekers are considered as high monitors and information avoiders are considered as low monitors. [11 88] ∝ In the context of CST, retrieved studies indicate that being an information seeker is not associated with interest for genetic testing. ∝ Systematic reviews conclusions: High monitors have more interest in genetic testing even if mixed findings are reported for some cancers. [11] ∝ This construct is often measured with the Miller Behavioral Style Scale. [88]
	Perceived control*	Perceived control: NS[89 84] POS[89] God Locus of Health control: NS[63]	Risk tolerance: NEG [32] Perceived control: POS [34]	Definition: Person's perception of his own ability to manage his health/disease risk. ∝ More research is needed toward perceived health control and interest as well as WTP for CST, but retrieved studies seem to indicate that it could have an impact on both outcome measures. ∝ Systematic reviews conclusions: Greater perceived control over the management and prevention of a disease is associated with interest for genetic testing. [11] For some disease without controllable risk factors, WTP values are higher.[30] ∝ This construct could be measured with the Multidimensional Health Locus of Control Scales.[90]
	Worries/ (Anxiety*)	Concerns about developing cancer: POS[81] Cancer worries: POS[26] NS[91] Intrusions-Worries: POS[64] Fears: NEG[64] Uncertainty: POS[84]	Worry about positive results: POS[34] NS[52] Cancer worries: POS[26]	Definition: Personal emotional aspects of risk for a specific health condition. [11] ∝ Worries toward cancer are generally associated with interest and WTP for CST. However, measures used by authors varied considerably. ∝ Systematic reviews conclusions: Mixed findings were reported regarding interest for genetic testing and disease-specific worries even if studies tend to support a positive association between those concepts. [11] *N.B. As this concept is related to disease-specific perceived risk [11] a scale of general psychological distress was used to measure respondents' level of anxiety. The K-6 was used.* [92]

Numeracy*	Understanding risk information: NS[26]	Understanding risk information: NEG[26] Objective numeracy: NS[52] Subjective numeracy: POS[52]	Definition: Person's ability to understand quantitative information and manipulate basic probability and numerical concepts.[93] ∝ There is insufficient information regarding numeracy and interest in CST. Mixed findings for WTP for CST are reported. It is important to note however the variation of the operationalization used to measure the concept of numeracy. ∝ Systematic reviews conclusions: this concept was not reported.
Knowledge	Genetic knowledge: NS[26 63 64] Knowledge of genetic test: POS [78] Awareness: NS[61]	Genetic knowledge: NS[26] Knowledge & awareness: NS[34]	Definition: Generally concerned about what a person knows about genetic risk or genetic test for a particular disease. ∝ Systematic reviews conclusions: Mixed findings were reported regarding its association with interest toward genetic testing. *N.B. This concept was not included in the statistical model as it was too correlated with perceived risk.*
General health*	Current health: NS [81] Health Behaviors:	NA	Definition: Perception of own actual health state. ∝ There is insufficient evidence regarding perceived health status and interest or WTP for CST. ∝ Systematic reviews conclusions: Few studies have assessed the relationship between general health and interest in genetic testing; equivocal results are reported.[11] More health conscious people are likely to accept higher WTP values.[30]
Perceived risk of BC*	Perceived susceptibility POS[33 62 61] Perception of risk: MA[81] Absolute perceived risk: NS[26] Comparative perceived risk: NS[26] Numeric perceived risk: NS[26] Perceived risk: NS[91 84] POS [63] Perceived vulnerability: POS[64]	Prior risk: NS[32] Perceived susceptibility: POS[33] Perceived susceptibility: NS[52] Perceived risk of having the mutation: POS[52] Absolute perceived risk: NS[26] Comparative perceived risk: NS [26 34] Numeric perceived risk: NS[26]	Definition: Generally, the person's estimation of his own likelihood of developing the disease in a specific time frame. ∝ Link between risk perception and interest or WTP for CST is still equivocal. ∝ Systematic reviews conclusions: In general, perceived risk is associated with an increased interest for genetic testing, but inconsistent findings were reported for some hereditary conditions. [11] Increased WTP values for dx tests were associated with higher risk perception.[30]

† NS.: association not significant; MA.: Marginally significant association; NEG.: negative association; POS.: positive association.
* Variables conserved in the regression models.

Appendix 2. Operational definitions* of variables and descriptive statistics †

Variables	Main reference	Measure, items and coding (final model)		Mean (SD)	*n* (%)	Tolerance
Outcomes						
Interest [INTER]	Adapted from the study of Graves et al.[26]	Scenario Imagine that a new genetic test for breast cancer (BC) risk evaluation is available on the market. This test could inform on your personal risk level to develop BC. It could be possibly used to adapt BC screening tests frequency to your risk (more frequent screening if your risk is higher than that of the general population).	To what extent would you be interested in this test if it could allow you to get more frequent BC screening tests? 5 point-Likert scale coded as 1 if not interested at all 2 if somewhat interested- 5 if extremely interested (for step 2) Sys miss	3.48 (1,19)	1016 93 (9.0) 923 (89.5) 15 (1.5)	-
Willingness to pay [WTP]			How much would you be willing to pay for this test? Ordinal scale recoded as 1 if do not want to pay; 2 if between 1$ and 100$ 3 if 101$ and more Sys miss	1.97 (0.74)	840 250 (24.2) 362 (35.1) 228 (22.1) 191 (18.5)	-
Factors						
Age [AGE]	Statistics Canada, ESCC-2010[38]	Data available from firms' panel. Continuous variable recoded as dichotomous 1 if 50 to 69 years old[§] 0 if 35 to 49 years old Sys miss		50.32 (9.24)	 528 (51.2) 503 (48.8) 0	 .844
Household income [INC1] [INC2] [INC3] [INC4]		Check the answer that best described the gross income measure (before tax) of your household. Ordinal scale recoded as 1 if income less than $25, 000; 0 if else 1 if income between $25, 000$ and $54, 999$; 0 if else 1 if income between $55, 000$ and$ 74, 999$; 0 if else 1 if income between $75, 000$ and more; 0 if else Sys miss		-	 98 (9.5) 267 (25.9) 187 (18.1) 299 (29.0) 180 (17.15)	 .656 .620 .713 Ref.
Marital status [WDS] [SING] [MARUN]		What is your current marital status? Nominal variable recoded as 1 if widowed, divorced or separated; 0 if else 1 if single; 0 if else 1 if married or common-law; 0 if else Sys miss		-	 186 (18.0) 152 (25.7) 689 (66.8) 4 (0.4)	 .831 .764 Ref.
Education [EDUC1] [EDUC2] [EDUC3]		Data available from firms' panel. Ordinal variable recoded as dichotomous 1 if no diploma or secondary school diploma; 0 if else 1 if college or CEGEP diploma; 0 if else 1 if university degree; 0 if else Sys miss		-	 399 (38.7) 265 (35.6) 367 (35.6) 0	 .666 .742 Ref.
Biopsy [BIOPSY]	Adapted from the Breast Cancer Risk Assessment Tool of the NICE[86]	Have you ever had a breast biopsy or puncture? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	 117 (11.3) 943 (91.5) 31 (3.0)	 .916
Parity [PARITY]		Have you ever given birth to a child? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	 820 (79.5) 211 (20.5) 0	 .849

Familial history [FAMHIS]		How many women of your family's first degree relatives (FDR) ever had breast cancer? Ordinal variable coded as dichotomous	-		
		1 if 1 or more FDR		146 (14.2)	.873
		0 if no family history		869 (84.4)	
		Sys miss		16 (1.6)	
Optimism [OPTIMS]	Validated French Canadian version of the Life Orientation Test –Revised [94]	I'm always optimistic about my future. 5-point agreement Likert scale recoded as dichotomous			
		1 if agree or strongly agree;		172 (16.7)	.861
		0 if else		845 (82.0)	
		Sys miss		14 (1.4)	
Perceived health status	Statistics Canada, ESCC-2010[38]	In general, would you say that your health is … 5-point Likert scale recoded as			
[FAIRBAD]		1 if bad or fair; 0 if else		83 (8.1)	.773
[GOOD]		1 if good; 0 if else		387 (37.5)	.823
[EXVER]		1 if very good or excellent; 0 if else		561 (54.4)	Ref.
Numeracy [NUM]	Adapted from the numeracy test of Schawartz et al.[93]	Score of 3 items: total number of correct answers [range 0-3] a- Familiarity with probability: "Imagine that we flip a fair coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips? ____times out of 1,000." b- Conversion of percentage to proportion: "In a lottery, the chance of winning a $10 prize is 1%. What is your best guess about how many people would win a $10 prize if 1,000 people each buy a single ticket? person(s) out of 1,000." c- Conversion of proportion to percentage: "In a prize draw, the chance of winning a car is 1 in 1,000. What is the percentage of winning tickets?____%."	1.6 (1.0)	1031	
		Sys miss		0	
Perceived risk [RISK]	Adapted from Levy et al.[95]	What do you think your chance is of developing breast cancer in your lifetime? Continuous variables were 0% means "not at all likely" and 100% means "definitely likely"			
		Nb of cases	33.05 (22.2)	784 (76.0)	.836
		Sys miss		247 (24.0)	
Monitoring [MO_MBSS]	Validated French Canadian version of the MBSS[96]	8 items of monitoring for 2 scenarios (dentist: α = .696; sales: α = .720). Score coded as			
		0 if < or = 23 (low monitoring)		558 (54.1)	.921
		1 if > or = 23 (high monitoring)		467 (45.3)	
		Sys miss		6 (0.6)	
Health locus of control		3 scales (total of 9 items) for 3 types of locus of control (powerful others: α = .615; internal: α = .686; chance: α = .736). Weighted mean of a 6-point agreement Likert scale			
[PHLC]	Validated French Canadian version of the MHLC[97 90]	Powerful others	4.15 (1.08)	1027	.869
		Sys miss		4	
[IHLC]		Internal	5.00 (0.87)	1026	.911
		Sys miss		5	
[CHLC]		Chance	2.66 (1.32)	1021	.908
		Sys miss		10	
Anxiety [ANX_K6]	Validated psychological distress scale used by ESCC-2010 [38 98]	6 items of non-specific psychological distress (α = .831). Weighted mean of a 5-point frequency Likert scale	4.09 (0.63)		.795
		Nb of cases		1031	
		Sys miss		0	

* Items were initially in French as the survey was administered to a French speaking population. They are freely translated for comprehension purposes in this article.
† All missing data, including options "do not want to answer" or "don't know" were coded as missing system data ("sys miss"). Descriptive statistics are presented for the initial model, i.e., the Interest outcome measure.
§ This age group corresponds to eligible women to the PQDCS, the national breast cancer screening program in Québec (Canada).

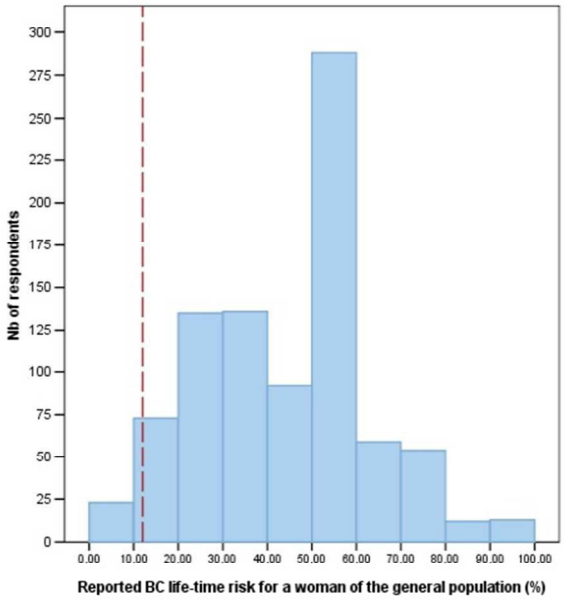


Figure 1
Respondents' distribution of reported BC life-time risk for a woman of the general population

67x50mm (300 x 300 DPI)

Appendix 1. Literature overview on interest and willingness to pay for cancer susceptibility testing (CST)

Explanatory factors		Outcome measures †		Definitions of factors, description of previous study results, and precisions
		Interest for CST	WTP for CST	
Socio-demographic factors	Age*	Age: NEG[33] POS [62 78 79] NS[26 80 57 81 61] Younger age: POS [63]	Age: NS [26 33] NEG[34 32]	Definition: Age of either patients or individuals of the general population ∝ Link between age and interest or WTP for CST are still equivocal. ∝ Systematic reviews conclusions: studies having assessed association between age and interest toward genetic tests proposed globally mixed findings and mostly inconsistent effects[11]; WTP values for dx tests can be positively influenced by older age.[30] ∝ Age is an important element of women's BC risk assessment: aging is associated with BC, but familial and genetic BC are often developed at a younger age than sporadic forms of BC.[69]
	Ethnicity	Race: NS [26 51 57 81]	Race: NS[26 51] Race: NS[34] Ashkenazi decent: NS[52]	Definition: Person's race or cultural traits relevant to particular group ∝ According to the literature on CST, race seems to not have any effect on interest and WTP. ∝ Systematic reviews conclusions: These variables have not been discussed for interest; WTP values for dx tests are positively influenced by a majority race or ethnicity, especially white Americans.[30] ∝ Some populations or groups of a particular biological background are at greater risk of BC (e.g., French-Canadian, Ashkenazi, Islanders). *N.B. The sample does not present sufficient variation in terms of ethnicity backgrounds (95% of White women) to be included in the statistical exercise.*
	Marital Status*	Marital status: NS[26 57 63] NEG[79]	Marital status: NS[26 34]	Definition: Person's legal marital status (e.g., common law, single, divorced…) ∝ According to the literature on CST, marital status seems to not have an effect on interest and WTP. ∝ Systematic reviews conclusions: Relationship between interest and marital status is supported by equivocal findings.[11] ∝ As genetic tests results might have important implications for family-planning decisions, it seems logical that marital status could influence genetic testing decisions.[11] This variable was also proved to be of great importance in cancer care. It has recently been demonstrated that unmarried persons were at a higher risk for cancer, undertreatment and death from cancer. [82 83]
	Education level*	Education: NS[26 51 63 81 84] Year of education: NEG[78]	Education: NEG.[32] POS.[34 51] NS.[26]	Definition: Person's highest completed degree or diploma. ∝ Link between education level and interest or WTP for CST is still equivocal. ∝ Systematic reviews conclusions: Interest toward genetic tests is inconsistent across studies.[11] WTP values are generally positively associated with education for dx tests.[30]
	Employment status/ primary activities	Employment: POS [57] NS [26 84]	Employment: NS [26 34]	Definition: Person's primary activities of a diary day; it can correspond to employment status for paid work (part- or full-time), but also to unpaid work such as study, housework, social support, volunteering, etc. ∝ Link between employment and interest or WTP for CST seems not significant. ∝ Systematic reviews conclusions: Few studies have assessed the link between employment and interest for genetic testing. Mixed findings are reported. [11]
	Income*	Household income: NS[26 63 81] POS.[57]	Household income: NS.[26 32 34]	Definition: Combined gross income of all members of a household. ∝ Link between income and interest or WTP for CST seems to not be significant. ∝ Systematic reviews conclusions: Associations of interest for genetic testing and income are inconsistent,[11] but WTP values for dx tests are generally positively associated with incomes. [30]
	Household size	Household size: POS.[57]	NA	Definition: Number of persons residing in a private household. ∝ There is insufficient information regarding household size and interest or WTP for CST. *N.B. This concept is partly assessed by marital status and parity for many respondents. It was eliminated.*
	SES	Socio-economic status: NEG[33 62] NS[61]	Socio-economic status: POS.[33]	Definition: SES is a concept that reflects more broadly familial resources, including education, employment, goods and revenues. ∝ There is insufficient information regarding SES and interest or WTP for CST. *N.B. As this concept is a mix of other retrieved sociodemographic characteristics in the literature, it has been discarded from the statistical models to avoid theoretical redundancy.*

Medical factors	Past medical exams/results*	Previous examination: MA[81] Timing of the most recent biopsy NS[26] Prior history of cancer: POS[63 78]	Personal breast cancer history: NS[26] Personal history of GI cancer: NS[34] Personal history of any cancer: NS[34]	Definition: Prior test results or health exams of an individual linked to the evaluated health condition. ∝ According to the literature on CST, past medical exams or results could have an impact on interest while they seem to not have an effect on WTP. ∝ Systematic reviews conclusions: It is not clear whether WTP values for dx tests were associated with past medical exams and results.[30] *N.B. Biopsy was used as a measure of past exam in the present study.*
	Children/ Parity*	Children: NS[57] POS[85]	NA	Definition: Woman having/giving birth to at least one child. ∝ Parity/parental status was insufficiently assessed for CST. ∝ Systematic reviews conclusions: Relationship between interest for genetic testing and parental status is still equivocal. [11] ∝ Nulliparty (never having given birth) is a risk factor as parity is a protective factor of BC. [86]
	Family history*	FDR had cancer: NEG[33] NS[26 81 84] POS[62 84 78] BC in family: POS[85 61] Number of first-degree relatives: POS [63]	FDR had cancer: NEG[33 34 81] NS[26 52] Family member tested positive: NS[52]	Definition: People who have one or more relatives (1st to 3rd degree) who have had a cancer dx. ∝ Family history seems to be associated with interest for CST while more evidence is needed for WTP for such a test. ∝ Systematic reviews conclusions: Generally, positive family history is associated with interest in genetic testing[11] and WTP for dx tests technologies.[30] ∝ Family history is an important risk factor of BC.[86]
Psychosocial factors	Optimism*/ Pessimism	Optimism NEG [33] POS[62 79] Pessimism: POS[62 61 33] (Depressive sx: POS[63])	Optimism: NEG[33] Pessimism : NS[33]	Definition: Person's tendency to have positive (optimists) or negative (pessimists) expectancies about their future (e.g., events, acts).[87] ∝ Mixed findings were reported regarding association between optimism/pessimism and interest for genetic testing and more research is needed for WTP in the context of CST. ∝ Systematic reviews conclusions: Person having a more positive outlook, highly optimistic or low in depression sx was more interested in genetic testing even if some mixed findings were reported for BC. [11] ∝ This construct is often measured with the Life Orientation Scale. [87]
	Monitoring*	Seek information: NS[62] Information seeking: NS[33] Preference for medical information: NS[61]	Information seeking: NEG[33]	Definition: Coping style based on personal information preferences about an event: information seekers are considered as high monitors and information avoiders are considered as low monitors. [11 88] ∝ In the context of CST, retrieved studies indicate that being an information seeker is not associated with interest for genetic testing. ∝ Systematic reviews conclusions: High monitors have more interest in genetic testing even if mixed findings are reported for some cancers. [11] ∝ This construct is often measured with the Miller Behavioral Style Scale. [88]
	Perceived control*	Perceived control: NS[89 84] POS[89] God Locus of Health control: NS[63]	Risk tolerance: NEG[32] Perceived control: POS [34]	Definition: Person's perception of his own ability to manage his health/disease risk. ∝ More research is needed toward perceived health control and interest as well as WTP for CST, but retrieved studies seem to indicate that it could have an impact on both outcome measures. ∝ Systematic reviews conclusions: Greater perceived control over the management and prevention of a disease is associated with interest for genetic testing. [11] For some disease without controllable risk factors, WTP values are higher.[30] ∝ This construct could be measured with the Multidimensional Health Locus of Control Scales.[90]
	Worries/ (Anxiety*)	Concerns about developing cancer: POS[81] Cancer worries: POS[26] NS[91] Intrusions-Worries: POS[64] Fears: NEG[64] Uncertainty: POS[84]	Worry about positive results: POS[34] NS[52] Cancer worries: POS[26]	Definition: Personal emotional aspects of risk for a specific health condition. [11] ∝ Worries toward cancer are generally associated with interest and WTP for CST. However, measures used by authors varied considerably. ∝ Systematic reviews conclusions: Mixed findings were reported regarding interest for genetic testing and disease-specific worries even if studies tend to support a positive association between those concepts. [11] *N.B. As this concept is related to disease-specific perceived risk [11] a scale of general psychological distress was used to measure respondents' level of anxiety. The K-6 was used.* [92]

Numeracy*	Understanding risk information: NS[26]	Understanding risk information: NEG[26] Objective numeracy: NS[52] Subjective numeracy: POS[52]	Definition: Person's ability to understand quantitative information and manipulate basic probability and numerical concepts.[93] ∝ There is insufficient information regarding numeracy and interest in CST. Mixed findings for WTP for CST are reported. It is important to note however the variation of the operationalization used to measure the concept of numeracy. ∝ Systematic reviews conclusions: this concept was not reported.
Knowledge	Genetic knowledge: NS[26 63 64] Knowledge of genetic test: POS [78] Awareness: NS[61]	Genetic knowledge: NS[26] Knowledge & awareness: NS[34]	Definition: Generally concerned about what a person knows about genetic risk or genetic test for a particular disease. ∝ Systematic reviews conclusions: Mixed findings were reported regarding its association with interest toward genetic testing. *N.B. This concept was not included in the statistical model as it was too correlated with perceived risk.*
General health*	Current health: NS [81] Health Behaviors:	NA	Definition: Perception of own actual health state. ∝ There is insufficient evidence regarding perceived health status and interest or WTP for CST. ∝ Systematic reviews conclusions: Few studies have assessed the relationship between general health and interest in genetic testing; equivocal results are reported.[11] More health conscious people are likely to accept higher WTP values.[30]
Perceived risk of BC*	Perceived susceptibility POS[33 62 61] Perception of risk: MA[81] Absolute perceived risk: NS[26] Comparative perceived risk: NS[26] Numeric perceived risk: NS[26] Perceived risk: NS[91 84] POS [63] Perceived vulnerability: POS[64]	Prior risk: NS[32] Perceived susceptibility: POS[33] Perceived susceptibility: NS[52] Perceived risk of having the mutation: POS[52] Absolute perceived risk: NS[26] Comparative perceived risk: NS [26 34] Numeric perceived risk: NS[26]	Definition: Generally, the person's estimation of his own likelihood of developing the disease in a specific time frame. ∝ Link between risk perception and interest or WTP for CST is still equivocal. ∝ Systematic reviews conclusions: In general, perceived risk is associated with an increased interest for genetic testing, but inconsistent findings were reported for some hereditary conditions. [11] Increased WTP values for dx tests were associated with higher risk perception.[30]

† NS.: association not significant; MA.: Marginally significant association; NEG.: negative association; POS.: positive association.
* Variables conserved in the regression models.

Appendix 2. Operational definitions* of variables and descriptive statistics †

Variables	Main reference	Measure, items and coding (final model)		Mean (SD)	*n* (%)	Tolerance
Outcomes						
Interest [INTER]	Adapted from the study of Graves et al.[26]	Scenario Imagine that a new genetic test for breast cancer (BC) risk evaluation is available on the market. This test could inform on your personal risk level to develop BC. It could be possibly used to adapt BC screening tests frequency to your risk (more frequent screening if your risk is higher than that of the general population).	To what extent would you be interested in this test if it could allow you to get more frequent BC screening tests? 5 point-Likert scale coded as 1 if not interested at all 2 if somewhat interested- 5 if extremely interested (for step 2) Sys miss	3.48 (1,19)	1016 93 (9.0) 923 (89.5) 15 (1.5)	-
Willingness to pay [WTP]			How much would you be willing to pay for this test? Ordinal scale recoded as 1 if do not want to pay; 2 if between 1$ and 100$ 3 if 101$ and more Sys miss	1.97 (0.74)	840 250 (24.2) 362 (35.1) 228 (22.1) 191 (18.5)	-
Factors						
Age [AGE]	Statistics Canada, ESCC-2010[38]	Data available from firms' panel. Continuous variable recoded as dichotomous 1 if 50 to 69 years old[§] 0 if 35 to 49 years old Sys miss		50.32 (9.24)	 528 (51.2) 503 (48.8) 0	 .844
Household income [INC1] [INC2] [INC3] [INC4]		Check the answer that best described the gross income measure (before tax) of your household. Ordinal scale recoded as 1 if income less than $25, 000; 0 if else 1 if income between $25, 000$ and $54, 999$; 0 if else 1 if income between $55, 000$ and$ 74, 999$; 0 if else 1 if income between $75, 000$ and more; 0 if else Sys miss		-	 98 (9.5) 267 (25.9) 187 (18.1) 299 (29.0) 180 (17.15)	 .656 .620 .713 Ref.
Marital status [WDS] [SING] [MARUN]		What is your current marital status? Nominal variable recoded as 1 if widowed, divorced or separated; 0 if else 1 if single; 0 if else 1 if married or common-law; 0 if else Sys miss		-	 186 (18.0) 152 (25.7) 689 (66.8) 4 (0.4)	 .831 .764 Ref.
Education [EDUC1] [EDUC2] [EDUC3]		Data available from firms' panel. Ordinal variable recoded as dichotomous 1 if no diploma or secondary school diploma; 0 if else 1 if college or CEGEP diploma; 0 if else 1 if university degree; 0 if else Sys miss		-	 399 (38.7) 265 (35.6) 367 (35.6) 0	 .666 .742 Ref.
Biopsy [BIOPSY]	Adapted from the Breast Cancer Risk Assessment Tool of the NICE[86]	Have you ever had a breast biopsy or puncture? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	 117 (11.3) 943 (91.5) 31 (3.0)	 .916
Parity [PARITY]		Have you ever given birth to a child? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	 820 (79.5) 211 (20.5) 0	 .849

Familial history [FAMHIS]		How many women of your family's first degree relatives (FDR) ever had breast cancer? Ordinal variable coded as dichotomous 1 if 1 or more FDR 0 if no family history Sys miss	-	 146 (14.2) 869 (84.4) 16 (1.6)	 .873
Optimism [OPTIMS]	Validated French Canadian version of the Life Orientation Test –Revised [94]	I'm always optimistic about my future. 5-point agreement Likert scale recoded as dichotomous 1 if agree or strongly agree; 0 if else Sys miss		 172 (16.7) 845 (82.0) 14 (1.4)	 .861
Perceived health status [FAIRBAD] [GOOD] [EXVER]	Statistics Canada, ESCC-2010[38]	In general, would you say that your health is … 5-point Likert scale recoded as 1 if bad or fair; 0 if else 1 if good; 0 if else 1 if very good or excellent; 0 if else		 83 (8.1) 387 (37.5) 561 (54.4)	 .773 .823 Ref.
Numeracy [NUM]	Adapted from the numeracy test of Schawartz et al.[93]	Score of 3 items: total number of correct answers [range 0-3] a- Familiarity with probability: "Imagine that we flip a fair coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips? ____times out of 1,000." b- Conversion of percentage to proportion: "In a lottery, the chance of winning a $10 prize is 1%. What is your best guess about how many people would win a $10 prize if 1,000 people each buy a single ticket? person(s) out of 1,000." c- Conversion of proportion to percentage: "In a prize draw, the chance of winning a car is 1 in 1,000. What is the percentage of winning tickets?____%." Sys miss	1.6 (1.0)	1031 0	
Perceived risk [RISK]	Adapted from Levy et al.[95]	What do you think your chance is of developing breast cancer in your lifetime? Continuous variables were 0% means "not at all likely" and 100% means "definitely likely" Nb of cases Sys miss	33.05 (22.2)	784 (76.0) 247 (24.0)	.836
Monitoring [MO_MBSS]	Validated French Canadian version of the MBSS[96]	8 items of monitoring for 2 scenarios (dentist: α = .696; sales: α = .720). Score coded as 0 if < or = 23 (low monitoring) 1 if > or = 23 (high monitoring) Sys miss		 558 (54.1) 467 (45.3) 6 (0.6)	 .921
Health locus of control [PHLC] [IHLC] [CHLC]	Validated French Canadian version of the MHLC[97 90]	3 scales (total of 9 items) for 3 types of locus of control (powerful others: α = .615; internal: α = .686; chance: α = .736). Weighted mean of a 6-point agreement Likert scale Powerful others Sys miss Internal Sys miss Chance Sys miss	 4.15 (1.08) 5.00 (0.87) 2.66 (1.32) 	 1027 4 1026 5 1021 10	 .869 .911 .908
Anxiety [ANX_K6]	Validated psychological distress scale used by ESCC-2010 [38 98]	6 items of non-specific psychological distress (α = .831). Weighted mean of a 5-point frequency Likert scale Nb of cases Sys miss	4.09 (0.63)	 1031 0	.795

* Items were initially in French as the survey was administered to a French speaking population. They are freely translated for comprehension purposes in this article.
† All missing data, including options "do not want to answer" or "don't know" were coded as missing system data ("sys miss"). Descriptive statistics are presented for the initial model, i.e., the Interest outcome measure.
§ This age group corresponds to eligible women to the PQDCS, the national breast cancer screening program in Québec (Canada).

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

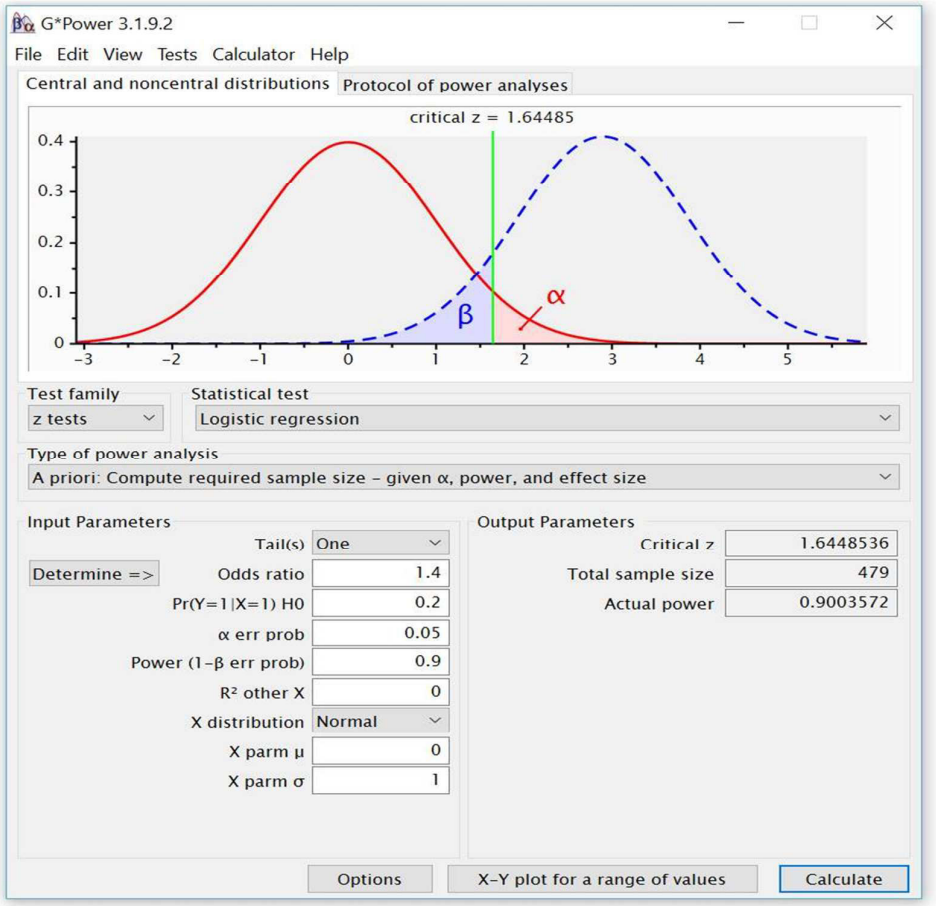
Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6 (4-6)
Methods			
Study design	4	Present key elements of study design early in the paper	
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7-8 + Appendix 1 and 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Appendix 2
Bias	9	Describe any efforts to address potential sources of bias	6; 7; 8; 12 (See figure below this table for power analysis)
Study size	10	Explain how the study size was arrived at	7; 9 + Appendix 2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8 + Appendix 2
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	Appendix 2
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-9
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for	7;9 + Table 2 + Appendix 2

		eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	8
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9-10 + Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Appendix 2
Outcome data	15*	Report numbers of outcome events or summary measures	Appendix 2 + Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Only unadjusted estimates are reported Appendix 2 – tolerance values Table 2 (p-values and marginal effects)
		(*b*) Report category boundaries when continuous variables were categorized	Appendix 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	*See point 16*
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13 + See figure below this table
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-16
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Screenshot: Power analysis performed with G Power



BMJ Open

Disentangling the determinants of interest and willingness to pay for breast cancer susceptibility testing in the general population: A cross-sectional Web-based survey among women of Québec (Canada)

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016662.R2
Article Type:	Research
Date Submitted by the Author:	27-Nov-2017
Complete List of Authors:	Blouin-Bougie, Jolyane; Université Laval, Management Amara, Nabil; Université Laval, Management Bouchard, Karine; Université Laval- Centre de recherche du CHU de Québec, Centre des maladies du sein Deschênes -Fabia Simard, Jacques; Université Laval- Centre de recherche du CHU de Québec, Medicine Dorval, Michel; Université Laval- Centre de recherche du CHU de Québec, Pharmacie
Primary Subject Heading:	Public health
Secondary Subject Heading:	Oncology, Health services research, Genetics and genomics
Keywords:	Interest, Willingness-to-pay, Breast cancer susceptibility testing, Women of the general population

Title

Disentangling the determinants of interest and willingness-to-pay for breast cancer susceptibility testing in the general population: A cross-sectional Web-based survey among women of Québec (Canada)

Authors & Affiliation

1. Jolyane Blouin-Bougie, PhD Candidate
(Corresponding author)
Department of management, Université Laval
2325, rue de la Terrasse, Pavillon Palasis-Prince, 1516
Québec, QC (Canada) G1V 0A6
(418) 656-2131 # 1379
Jolyane.blouin-bougie@fsa.ulaval.ca

2. Nabil Amara, PhD
Department of management, Université Laval
2325, rue de la Terrasse, Pavillon Palasis-Prince, 1519
Québec, QC (Canada) G1V 0A6
(418) 656-2131 # 4382
Nabil.amara@fsa.ulaval.ca

3. Karine Bouchard, MSc
Centre des maladies du sein Deschênes-Fabia
Centre de recherche du CHU de Québec-Université Laval
Hôpital du Saint-Sacrement, 1050, chemin Sainte-Foy
Québec, QC (Canada) G1S 4L8
(418) 525-4444 # 82721
Karine.Bouchard@crchudequebec.ulaval.ca

4. Jacques Simard, PhD
Faculty of Medecine, Université Laval
Centre de recherche du CHU de Québec-Université Laval
2705, boulevard Laurier, R4-4787
Québec, QC (Canada) G1K 7P4
(418) 654-2264
Jacques.Simard@crchul.ulaval.ca

5. Michel Dorval, PhD
Faculty of Pharmacy, Université Laval
Centre de recherche du CHU de Québec-Université Laval
Hôpital du Saint-Sacrement, 1050, chemin Sainte-Foy
Québec (Canada) G1S 4L8
(418) 682-8047
michel.dorval@pha.ulaval.ca

Key Words
Interest; Willingness-to-pay; Breast cancer susceptibility testing; Women of the general population

Abbreviations
BC = Breast cancer; BCST = Breast cancer susceptibility testing; PM = Personalized medicine; WTP = Willingness-to-pay

Words count
5 547 (excluding title page, abstract, references, figures and tables)

Abstract

Objectives: To identify common and specific individual factors that favour or impede women's interest in and willingness-to-pay (WTP) for breast cancer susceptibility testing (BCST), and to identify the most impactful factors on both outcome measures.

Design and Methods: This study used a self-administered cross-sectional web-based questionnaire that included hypothetical scenarios about the availability of a new genetic test for breast cancer.

Participants: French-speaking women of the general population of Québec (Canada), aged between 35 and 69, were identified from a Web-based panel (2410 met the selection criteria, 1160 were reached, and 1031 completed the survey).

Measures: The outcomes are the level of interest in and the range of WTP for BCST. Three categories of individual factors identified in the literature were used as potential explanatory factors, i.e., demographic, clinical, and psychosocial.

Results: Descriptive statistics indicated that the vast majority of sampled women are interested in BCST (90%). Among those, more than half of them are willing-to-pay for such a test (57%). The regression models pointed out several factors associated with both outcomes (e.g., age, income, family history, locus of control-powerful others), and marginal effects were used to highlight the most impactful factors for each outcome.

Conclusion: The results of this study provide a proxy of the readiness of women of the general population to use and to pay for BCST. They also offer insights for developing inclusive and specific strategies to foster informed decision-making, and guide the services offered by health organizations corresponding to women's preferences and needs.

Strengths and limitations of this study

- ∝ In accordance with the economic theory, this study proposes two ordered logit regression models allowing the testing of several explanatory factors of interest in and WTP for breast cancer susceptibility testing.
- ∝ This study also presents insights for developing inclusive and specific strategies that could support women's informed decision-making toward BCST and the range of service offerings by health organizations with regard to this test.
- ∝ Respondents' interest and WPT are measured using a hypothetical scenario; this may have led to an overestimation of the level of interest and the sum paid out-of-pocket in a realistic situation.
- ∝ Results presented in this study should be cautiously extrapolated to other neighbouring populations as interest in and WTP for genetic testing could greatly vary between populations, tests and methods used.

Introduction

Personalized medicine (PM) is an important growing area of research:[1] It is viewed as a significant driving economic sector[2] and an encouraging avenue to improve the delivery of healthcare services,[3-5] notably through patient stratification approaches.[5-7] The goal of PM might be notably achieved by the use of genetic tests. They sustain two main finalities of PM: one is preventive, the other is curative. Indeed, genetic tests could be indicated for healthy patients (i.e., to assess ones' susceptibility to develop a disease and to provide risk management recommendations) or be used for the benefit of ill patients (i.e., to specify diagnosis and prognosis, and to support treatment decisions).[8] This distinction is essential as the decision to be genetically tested is an individual one and may depend on whether the finality of the genetic tests used is preventive or curative,[9] that is to say that the person is healthy or ill.

Although the development of PM is seen as promising for the management of multiple diseases, breast cancer (BC) prevention remains of premier interest.[6 10-12] It is worth noting that since the commercialization of the BRCA1/2 mutation carrier test, many others genetic markers have been discovered. Indeed, several mutations (i.e., rare genetic variations) on different genes and polymorphisms (i.e., SNPs: common genetic variations present within particular sub-populations) are now known as BC susceptibility risk factors and can be detected simultaneously with recent technologies (e.g., next-generation sequencing, panel-gene testing).[13-17] Some genetic variants are moreover associated with greater risks than others. For instance, a mutation on *BRAC1, BRCA2, TP53 or PTEN* confers a high risk, as a mutation on *CHECK2, PALB2* or *ATM* confers a moderate risk of developing BC.[13 14 16] In this paper, we refer to carrier or predictive genetic tests, that lead to the identification of genetic variants that substantially increase BC risk, as breast cancer susceptibility tests (BCST). Besides the identification of at-risk women, BCST aim to provide suitable risk-management recommendations adapted to women's BC risk level and preferences (e.g., type and interval of screening - mammograms or MRI - or consideration of prophylactic interventions - mastectomy or chemoprevention).[8 18 19]

Given the increasing BC genetic knowledge base, stratifying healthy women's BC risk is viewed as an opportunity to adapt screening programs to maximize benefits and minimize drawbacks for the general population and the healthcare systems in a foreseeable future.[6 7 10 11 15 20 21] More research is however

needed regarding variants that should be included in BSCT targeting women of the general population.[6 16] In addition, scepticism exists for "whether publicly funded screening poses an acceptable burden on healthcare budgets".[22]

Up to now, however, these tests are generally offered to women by healthcare providers working in specialized clinical settings (e.g., genetic clinics or hereditary cancer programs), but are restricted to some particular group of patients.[6 20 23] Otherwise, women may access some BCST via private companies and laboratories.[24 25] Direct-to-consumer (DTC) genetic testing is however subject to arguments and contentions by researchers, professional societies, and government agencies. Their preoccupations notably concerned the overriding healthcare professionals' support (i.e., counselling services),[19 25 26] the consumer's understanding of the test results and their implications (e.g., worries, risk of discrimination, repercussions on family members),[8 26 27] the tests' validity, the appropriateness of genetic markers assessed, and the reliability of risk estimates, for which no evidence-based recommendations may have been yet established.[16 25]

In that context, it might be important to get the pulse of the end-users, and this is the focus of this paper: it aims to gain insight into the readiness of women of the general population of Québec (Canada) to integrate and use genetic information for BC prevention. Before going further, we present an overview of BC prevention services and the use of BCST in Canada.

BC Prevention in the Canadian context

Canada faces similar genetic services delivery challenges as other developed countries. One important particularity is the healthcare services' organization scheme: services are provided and managed at a provincial level, but protection and well-being are overseen by the federation.[28] The extent of the funding of health services, including genetic testing or BC prevention risk-management strategies, covered by the provincial healthcare systems, thus falls under some federal regulations.[28] This may result in some discrepancies in the scope of services provided across provinces. For instance, *The Québec Breast Screening Program* invites all women aged between 50 and 69 to have a mammogram every 2 years.[29] While other Canadian provinces offer similar free services, the age-range of the targeted women by screening programs may slightly vary from province to province. In addition, while there is no risk

stratification approach implemented in Canada, two Canadian provinces (Ontario and British Colombia) recently added some public healthcare facilities for high-risk women (i.e., have a known mutation on BRAC 1 or 2, a strong family history or had prior chest radiation).

BC genetic services were available in genetic clinics shortly after the discovery of BRAC1 and BRAC2 in the mid-90's in Canada.[23] It confers a well-established experience in managing the genetic risk of BC.[15] However, only a small proportion of women currently have access to BCST, given the requirements to meet for service qualification, the complexity of the service trajectory,[6] and the limited number of healthcare providers authorized to order a genetic test.[18] BCST are only offered to some newly diagnosed BC patients and their relatives, and to those with a strong BC family history.[23] The cost of these tests is covered for those who meet the criteria, and have been referred by their provider to a genetic clinic for counselling. Women may thus have to go through a long and complex process, which often implies meeting various providers before testing and choosing a risk-management strategy that best fits their preferences and needs.[6 18]

Furthermore, Canadian healthcare systems are known to be publicly-funded, but there are private healthcare delivery channels (e.g., private clinics, laboratories and companies, complementary private insurance market), and the health sector is facing continuous pressures for service privatization.[30] Some BCST are also directly available from private companies, given the greater number of firms offering these tests to consumers. Even though the majority of those societies are located in the United States, their geographic situation is of minor importance: genetic tests can be bought via the Web.[31]

Literature background

Notwithstanding the issues discussed above, previous studies have shown that women might demonstrate interest in and willingness-to-pay (WTP) for genetic testing as results may reduce uncertainty, offer some reassurance, guide life or family planning decisions, and may be useful to other family members.[9 24 27 32-34] The literature also underlined a great variability regarding populations (patients, general population, family members, etc.) and health conditions when measuring levels of interest[9] and estimating WTP values.[32] This point supports the relevance of conducting a study for BCST in the particular context of Québec. Moreover, while the literature shows the existence of an association

between interest in and cost of genetic tests for cancer susceptibility,[27 35-38] there is no consensus on which one influences the other. Consistent with the economic theory,[35 39] which supposes that a person's decision is a sequential process «where the decision of whether or not to consume a particular commodity is followed by the choice of how much to consume»,[39] we propose two regression models assessing 1) interest in BCST, and 2) WTP for this type of tests among those interested. In addition, many studies attempting to assess interest in genetic testing identify predictors in an *ad hoc* manner without grounding them in theory, which leads to inconsistent findings.[9] While the literature on WPT constitutes another stream of research, previous studies appeared to use numerous similar predictors.[9 32] To deal with these issues, we identified a list of recurrent individual variables empirically tested in the context of cancer susceptibility testing. Inspired by the classifications of Sweeny et al.[9] and Lin et al.,[32] these variables were thereafter classified into three categories: demographic, medical, and psychosocial. (see Appendix 1 for the literature overview). Finally, previous study findings did not allow a detailed understanding of how preferences and WTP values vary according to individual factors.[32] We then computed the marginal effects of individual factors associated with interest in and WPT for BCST. They are an informative means for summarizing how change in a response is related to change in a covariate.[40 41] This could be useful in targeting the most influential factors when designing interventions.

In light of the foregoing, the following section provides information on the method used to disentangle individual factors that influence interest in and WTP for BCST and to identify the most impactful factors on both outcome from a sample of women living in Québec (Canada).

Methods

Sample

The target population was made up of French-speaking women of the general population aged between 35 to 69, living in the province of Québec in Canada. The sample was selected from an internet panel maintained by a survey firm and weighted for age, regions, and education level according to Statistics Canada census profiles.[42] The sample size was calculated prior to data collection with a margin of error of 3% at a 95% confidence interval.

Data collection

A cross-sectional web-based survey developed from a literature review on genetic risk communication was used for this study. Respondents were asked to focus on their: general health state, BC clinical history and risk factors, level of literacy and numeracy, interest in and opinions regarding the use of BCST, reactions toward various life events, general psychological health state, and demographic characteristics. The questionnaire was validated by experts in familial BC and pre-tested by the survey firm with 20 eligible women in February 2012. Their comments were collected in-person or by telephone; minor changes were made to the questionnaire to improve understanding. The questionnaire was afterward adapted for a Web platform and a survey link was sent by the firm to a sample of 2410 eligible women in March 2012. Three prize draws were offered to the participants: one of $3,000 and two of $1,000.

Measures

In order to avoid respondents' confusion, women were firstly advised as follows (freely translated from French) before presenting to them the items on interest and WTP: "*The next questions aim to better understand your interest in genetic tests used to assess the risk of developing a disease. The following scenarios are fictive. We will ask you how much you will be willing to pay for a genetic test. This question is only useful for the purpose of this research and does not mean that fees would be necessarily charged to get access to this test. Indeed, genetic tests requiring a simple blood testing are generally freely provided in Canada*". A hypothetical scenario was then presented to women indicating that a new genetic test, now available on the market, could be used to assess their BC risk, and to adapt their screening modalities should their risk level be higher than that of the general population. No specifications on the modalities under which this test could be offered or on the genes being assessed by this test were provided to the participants. Following that, respondents were asked to rank their level of interest in receiving this test on a 5-point Likert scale ("*Not at all*" to "*Extremely interested*"). Those having indicated to be at least "*Somewhat interested"* in BCST were thereafter asked how much they would be willing to pay for this test on an 6-point ordinal scale ("*Do not want to pay*" to "*Would pay more than $1,000*"). All respondents who had indicated to be "*Not interested at all"* were not asked to answer the WTP item.

Detailed information regarding the scenario, operational measures of outcomes, and explanatory factors, including coding and main references, is presented in Appendix 2.

All clinical information needed to estimate the BC life-time risk of the respondents, according to the Gail Model parameters,[43] was collected for descriptive purposes. Some potential explanatory variables underlined in the literature were not included in the analysis for methodological concerns such as distribution of respondents or theoretical redundancy. However, no variables were removed from the models on the basis of low statistical significance because they were assumed to be of theoretical interest and expected to have some effect on women's interest in and WTP for BCST. Chosen measures were assessed with validated scales or in accordance with the scientific literature. The constructs with multiple-item scales (i.e., loci of control, monitoring, and anxiety) were evaluated with a principal components factor analysis; the unidimensionality criterion was satisfied. Cronbach's alpha (α) showed that items forming each of them were reliable. Finally, reported tolerance statistic values were all higher than 0.2 (Appendix 2); there were no multicollinearity concerns.[44]

Statistical analysis

A *post-hoc* power analysis was firstly conducted with G*Power 3.1.9 to ensure that we had an appropriate number of valid cases for statistical analyses to be performed, and to detect a true effect when it exists.[45] [46] Secondly, descriptive and bivariate analyses was carried out to detail the characteristics of the sample, and to assess statistical associations between outcome measures and individual factors believed to have an impact on interest and WTP for BSCT (data not shown). Thirdly, two ordered logit regression models [47-49] were estimated accordingly to the assumption adopted in this study.[A:50 51] They were used to investigate 1) women's interest in a BCST that may lead to more frequent screening should their risk level be higher than that of the general population with the original scale; and then, for those at least "*Somewhat interested*", 2) women's level of WTP for this genetic test with a measure capturing three levels of WTP

[A] The two models were estimated separately even though our approach might remind the Heckman' two-step sample selection procedure. This is mainly because the types of the dependent variables of our two models do not allow an appropriate use of Heckman's procedure. Indeed, ''the Heckman two-step estimator is specifically a probit model followed by a linear regression, and there is no simple analog for the Heckman method for discrete choice models despite the logical appeal of the process." Moreover, the use of models other that OLS in the second stage of Heckman's two-stage method as a frequent error in studies using this method.

(1= $0, 2= *1 to $100,* 3= *$101 and over*). Therefore, women who responded, in the first model, '*Not at all interested*' in BCST were not included in the second analysis, i.e., the model on WTP.

The ordered logit model uses an intermediate continuous variable Y^* (qualifications made by women regarding the dependent variable: INTER or WTP) in a latent regression with a set of independent variables x_i. The range of the unobserved Y related to INTER and WTP was subdivided, respectively, in five and three adjacent intervals representing the classes of an observed variable, Z. Thus, it assumes a continuous process relating an unknown variable Y to independent variables x_i. For each dependent variable (INTER and WTP), the outcome of respondent *i* is represented by the latent index:

$$Y_i^* = \beta_1 x_{1i} + \ldots\ldots\ldots\ldots + \beta_k x_{ki} + \varepsilon_i = \beta X + \varepsilon \qquad \text{[Equation 1]}$$

Where:

Y_i^* = the value of the index to the observation *i*

x = a vector of independent variables

β = the vector of parameters to be estimated

ε = the error term

Equation (1) cannot be estimated because Y^* is unobserved (latent index). However, we do observe the decision made by the respondents (the five and the three outcomes discussed above) as well as the *x*-vector. Thus, in order to estimate the models, the following assumptions are made:

$Z_i = 1$ (Outcome 1) if $Y^* < \alpha_1$

$Z_i = 2$ (Outcome 2) if $\alpha_1 \leq Y^* < \alpha_2$

...

$Z_i = n$ (Outcome n) if $Y^* \geq \alpha_{n-1}$

The ordering requires the thresholds ($\alpha_1, \alpha_2 \ldots \alpha_{n-1}$) to satisfy $\alpha_1 < \alpha_2 \ldots < \alpha_{n-1}$. Parameters β and the thresholds ($\alpha_1, \alpha_2 \ldots \alpha_{n-1}$) are simultaneously estimated using the maximum likelihood method, which maximizes the probability of correct classifications. An application and a more detailed statistical description of the ordered logit models are presented by Amara et al.[52] All those analyses were performed with SPSS 13.0.[53] Finally, in order to assess the magnitude of the impact of explanatory variables on

interest in and WTP for BCST, the marginal effects of the significant independent variables were ascertained with LIMDEP 8.0 Econometrics Software Package.[54]

Results

Descriptive statistics

Overall, 1160 women were reached with the data collection procedure used. Among them, 40 clicked the questionnaire's link after the data collection period, 81 did not complete the questionnaire, and 8 cancelled their panel subscription. The survey generated 1031 usable questionnaires for a net response rate of 43% (i.e., when we consider all women who were not reached among eligible participants).

The sample was mostly composed of white educated women, in a civil union, and living in a large urban area (> 100,000 inhabitants) (Table 1). Moreover, most of the respondents overestimated both their personal BC lifetime risk (mean = 33.05%; SD = 22.25%) and that of women in the general population (Figure 1). However, according to the Gail Model parameters,[43] approximately 85% of the respondents had less than a 15% life-time risk of BC.

[Table 1 and Figure 1]

Descriptive statistics also revealed that 89% of the respondents were interested in BCST that may lead to more frequent screening, and 57% were willing to pay a certain amount of money to get the test. Furthermore, the One-way ANOVA performed on ranked data indicates that there is at least one mean rank difference between ranges of WPT ($F(2,837) = 83,992$; $p < .000$). The *Tamhanes' post-hoc* analysis, used when homogeneity of variances are not assumed (Levenes' test: $F(2,837) = 6,802$; $p. = .001$), shows that the mean rank of interest in BCST significantly varies across the three ranges of WTP values (Table 2): the more women are interest in BCST, the larger is the amount they are willing to pay for this tests.

[Table 2]

Common explanatory factors of interest and WTP

The results of the estimation of the two ordered logit models are presented in Table 3. For both models, the results suggest that having a BC family history rather than none, having a locus of control highly attributed to powerful others, being widowed, separated or divorced rather than being married or in a union, and having a perception of health status as good instead of excellent or very good, are all significantly associated with a higher interest in and higher WTP for BCST.

Conversely, having a high numeracy score compared to a low numeracy score, a household income of less than $55,000 comparatively to a household income of $75,000 and over, and being aged under 50 rather than being aged 50 and over, are all significantly associated with a lower interest in and lower WTP for BCST. The variables biopsy, parity, and education appeared to have no impact on either interest in nor WTP for BCST.

Regarding marginal effects, the coefficients show that BC family history, household income, and locus of control- powerful others are the common explanatory variables that have the highest impact on women's interest in and WTP for BCST.

[Table 3]

Specific factors associated with interest in BCST

Furthermore, there were several explanatory variables that were significantly associated only with interest in BCST. Indeed, being a high monitor compared to a low monitor, and having a higher perceived risk of BC are significantly associated with a higher interest, whilst being highly optimistic rather than being poorly optimistic, and having a locus of control highly attributed to chance are significantly associated with a lower interest for BCST.

More specifically, locus of control -powerful others, level of anxiety, and BC family history stand with the highest marginal impact values, respectively of .441, .409, and .357. For the two former continuous variables, this implies that a positive relative change of 10% on these factors increases the level of

women's interest in BCST by 4.41% and 4.09%. For the categorical variable, it means that interest in BCST is 35.7% greater among women with a family history of BC comparatively to those without.

Most impactful factors on WTP for BCST

For the WTP model, variables with the highest marginal effects are locus of control- powerful others (marginal effect = .283), BC family history (marginal effect = .208), and household income (marginal effect = -.154, -.103 and -.079). These coefficients indicate that for a positive relative change of 10% on the locus of control- powerful others score, women's WTP for BCST would increase by 2.83%. This also means that WTP for BCST is 20.8% greater among women with a family history compared to those without, and is as much as 15.4% lower among women with a household income of less than $75,000 compared to those with an income of $75,000 and over.

Discussion

This study provides evidence on the common and specific individual factors associated with interest in and WTP for BCST that may allow for more frequent screening if one's BC risk level is higher than that of the general population. The econometric exercise revealed that seven individual factors were found significantly associated with both interest in and WTP for BCST: age, household income, marital status, family history, locus of control (powerful others), perceived health status, and numeracy. Whilst, five factors were found significantly associated only with interest in BCST: optimism, monitoring, locus of control (chance), anxiety, and perceived risk. A quick comparison of our study results with the ones of the literature is available in Appendix 1.

The results of this study have limitations that inform the interpretation of its results and suggest further research. First, our findings might be considered as representative of French-speaking women aged between 35 and 69 living in Québec (Canada), but should be cautiously extrapolated to other similar or neighbouring populations. Previous studies called attention to the great variability regarding interest level and WPT estimates across populations studied for genetic testing in general.[9 32] Second, our response rate may seem low (43%), but several prior studies on interest in and WTP for genetic testing obtained comparable response rates.[55-57]. Third, self-reported data like those used in this study are subject to a social desirability bias. Fourth, as done in previous studies,[27 34 35 58] a hypothetical scenario was used in

this study. Then, reported results on the degree of interest in and WTP for BCST should not be taken as an objective uptake measure of testing, but as a measure of intention.[9 27 56] Other studies have also demonstrated that revealed measures of WTP overestimate the sum paid out-of-pocket in a realistic situation.[27 34 59] Fifth, different measures of WTP or elicitation techniques to value BCST in the general population in Québec should be used to confirm our findings. Indeed, the literature revealed discrepancies between studies of WTP estimates according to measures and methods employed for similar tests.[32] Moreover, we used only one item to measure WTP on an ordered scale. This is among the several ways used by authors to measure WTP,[33] even though many studies opted for double or multiple biding items.[60] Furthermore, it has been demonstrated that each of the measurement methods has its strengths and limitations, but above all, the level of accuracy gained by the econometric model used afterward is negligible in the case of sample sizes like ours (n = 1031).[60] Finally, as this paper only focused on individual factors, future studies should investigate other potential factors associated with interest in and WTP for BCST, like those at the organizational, social or environmental level, and should more explicitly ground the explanatory variables in theoretical frameworks. Other aspects could contribute to the choice of being genetically tested, and this may vary by type of genetic test and the purpose of its use.[9 32] This also has implications in terms of results' interpretation. Significance and effects of individual factors discussed above are subject to change if other contributing factors to the overall predictive power would be added in the respective equations of INTER and WTP modeling.[41]

Potential implications

The findings of this study firstly provide a proxy for the readiness of women of the general population of Québec to get genetically tested for BC susceptibility and the amount they expect to be acceptable to pay for such services in private settings, given the formulation of the scenario. While we did not assess various of payments vehicles, our results may provide insights 1) on the willingness of the general population to make accessible BCST to more women in the context of the current publicly funded system; 2) on their degree of openness toward a new co-payment method for such a test; or 3) on the setting of insurance co-payments, if any, in some situations.[22 32] As the results show, a majority of the women were at least somewhat interested in BCST (~90%), and more than half were willing to pay a certain amount of

money for such a test. Indeed, nearly 35% of the women of our sample would pay up to $100, 15% up to $250, and 7% more than $250. However, a great proportion of them was not willing to pay (24%) or did not provide information on the survey item assessing their WTP for BCST (18% of missing data, which includes 9% of respondents "*Not interested at all*" in BCST). Overall, this suggests that the women of Québec have mitigated enthusiasm toward BCST if they have to pay for it, which is consistent with another study led in the Canadian context.[37] While it may reflect some important values of Canadian citizens that are embodied in the Medicare system,[30] studies led in private healthcare systems reported similar findings.[35 57]

Secondly, the results suggest that many psychosocial factors are associated with women's interest in and WTP for BCST. Indeed, in line with the findings of several prior studies on cancer susceptibility testing,[35 61-64] our results reveal that the higher the women's BC risk perceptions are, the higher their level of interest in BCST is. It is worth mentioning, however, that women's interest in BCST should be analyzed in light of another important finding: women greatly overestimated both their personal lifetime risk of developing BC and that of women of the general population. Similar results were also found in other populations.[65-67] This overestimation may be due to a lack of knowledge, a low level of numeracy or otherwise unrealistic worries about BC.[65-67] In addition, as reported by other studies,[27 57] more anxious, less optimistic women and those with poor numeracy skills are more interested in BCST and thus, will probably more extensively use such services. This may suggest that some moderating psychosocial variables might influence the women's decision process to get tested or not. Moreover, it could result in a biased level of interest in and WTP for BCST.

Previous studies have also reported an association between perceived control or risk tolerance and interest in and WTP for cancer susceptibility testing.[34 35 68] Our results support this finding, but also indicate that one of the most impactful factors on women's interest and WTP is the external health locus of control-powerful others. It implies that a woman who believes that others she considers as experts are largely responsible for her health is more interested in and willing to pay for BCST. As underlined in studies on BC screening,[69 70] this result suggests that healthcare providers' recommendations, public health or for-profit organizations' communication campaigns or marketing strategies might have an impact

on some women's interest in and WTP for BCST. Beyond that, private companies' DTC advertising efforts may take advantage of actual consumers' emotional concerns or knowledge deficit in genetics.[25 57] These companies should thus be fully encouraged to incorporate adapted modes of communication and provide personalized risk counselling to consumers, instead of their current approach of "one-size-fits-all".[25]

These facts lead, as others proposed,[9 27 35] to reiterate the necessity of putting a stronger emphasis on popular education, and of developing educational material toward genetics and the notion of risk to ensure that the choice of getting tested for BC susceptibility is made following an informed decision-making process, and based on more objective and realistic risk perceptions of BC. As a starting point, we suggest that some lessons learned from public health and charity organization messages and decision aids (e.g., information from leaflet or web page, communication campaigns, and other health promotion strategies) about cancer screening[69 70] may serve as a building block for the dissemination of BCST information among the general population. The literature on BC risk communication may also provide important cues on the most comprehensive ways genetic risk should be transmitted to women of the general population.[71 72] Interventions improving knowledge and awareness, as well as fostering objective BC risk evaluation, have the potential to improve ethical and informed decision-making,[69 70] but may also slightly decrease interest in and WTP for BCST.[9 35 36]

Thirdly, the findings of this study may help health organizations, either private or public, to better define the range of service offerings or to adjust service delivery modalities to public or consumers' preferences and needs.[35 36] For instance, following results discussed previously on perceived risk, numeracy, anxiety or optimism, it seems that reassurance, support, and education as provided in highly specialized services of genetic counselling are important elements to be adapted for public health care settings - such as in the case of the implementation of a BC risk stratification program - and to be provided by private companies selling BCST directly to consumer in order to minimize drawbacks for women (e.g., anxiety, miscomprehensions, etc.).[25 35 57]

Finally, study results related to some medical and demographic factors could provide insightful paths of action for developing strategies targeting specific sub-groups of women in the population. For instance, women with a BC family history are more interested in and willing to pay for BCST. Several studies have

reported similar findings.[9 32 62 63 73 74] They are also at greater risk of BC.[75] Given their BC family history and their experience with this disease, some of them maybe more aware of their increased BC risk. In turn, they may attribute more value and get more benefits from such testing than those without family history. Improving BSCT access to those women, as other Canadian provinces did by adding public healthcare facilities, might be relevant. It could help to ensure that their interest and willingness to take the test is based on an informed decision instead of the results of biased self-(over)estimations of BC risk.

Moreover, paying more attention to young women (35 to 49 years old) in clinical encounters could be a winning strategy. It might contribute to the demystification of the notion of risk and the genetic component of BC into the next generation of women who will be likely invited into BC screening or stratification programs. Furthermore, familial and genetic BC are often developed at a younger age than the sporadic form of BC.[76] So, this could lead to recommendations of early risk-management strategies for young women at greater risk of BC, who are less interested in and attribute less value to BCST, in taking into consideration their specificities and potential needs (e.g., family-planning decisions).[77 78]

In addition, the study's results indicate that interest in and WTP for BCST increased with income. Even if this is in line with the budget constraint function of the economic theory,[35] and that previous studies pointed out similar findings,[22 32 35] inconsistent results are reported by a recent systematic review on interest in genetic testing.[9] Likewise, some authors found mixed results regarding its association with the socio-economic status.[35 61 62] As this concept reflects more broadly family or household resources, including education, employment, goods and revenues, one hypothesis may be that some confounding or moderating variables are involved in the decision-making process of women opting or not for BCST. Nevertheless, our results suggest that interventions designed for women from lower-resourced neighbourhoods or targeting physicians with a large panel of women with low income could prevent some inequalities in the uptake of BCST (e.g., health or life insurance and employment discrimination, limited access to health services given the cost (if the test is pay-out-of-pocket or partially reimbursed by private insurance) or in the way the risk is assessed, i.e., the risk factors considered, notably age, ethnicity, and family history).[79 80]

Conclusion

This study disentangles common and specific individual determinants of interest in and WTP for BCST among women of the general population of Québec (Canada). It also presents insights for developing inclusive and specific strategies that could support women's informed decision-making toward BCST and the range of service offerings by health organizations with regard to this test. For managers and decision-makers involved in BC prevention, thinking to adjust or to extend BC genetic services and desiring to adapt them to public preferences and needs, this study highlights two ways of proceeding that could be profitable from a social and economic point of view. The first is to develop interventions targeting the whole population, such as health promotion campaigns, by focusing on the psychosocial factors, given the number of significant factors explaining interest in and WTP for BCST. The second is to tailor interventions to particular sub-populations by considering the most impactful factors associated with interest in and WTP for BCST, such as family history backgrounds or strata of household income.

References

1. Khoury MJ, Coates RJ, Fennell ML, et al. Multilevel research and the challenges of implementing genomic medicine. *JNCI Monographs* 2012;2012(44):112-20.
2. Health Leaders Media - a division of HCPro Inc. In collaboration with Price Water House Cooper. The Impact of Personalized Medicine Today Massachusetts, United-States2010 [Available from: http://www.healthleadersmedia.com/breakthroughs.
3. Welch BM, Kawamoto K. Clinical decision support for genetically guided personalized medicine: a systematic review. *Journal of the American Medical Informatics Association* 2013;20(2):388-400.
4. Diamandis M, White NMA, Yousef GM. Personalized Medicine: Marking a New Epoch in Cancer Patient Management. *Mol Cancer Res* 2010;8:1175-87. doi: doi: 10.1158/1541-7786.MCR-10-0264
5. Gouvernement du Canada - Canadian Institutes of Health Research. Personalized Medicine 2015 [Online]. Available from: http://www.cihr-irsc.gc.ca/e/43627.html.
6. Foulkes WD, Knoppers BM, Turnbull C. Population genetic testing for cancer susceptibility: founder mutations to genomes. *Nat Rev Clin Oncol* 2016;13(1):41-54. doi: 10.1038/nrclinonc.2015.173
7. Dent T, Jbilou J, Rafi I, et al. Stratified cancer screening: the practicalities of implementation. *Public Health Genomics* 2013;16(3):94-99.
8. Ginsburg GS, Willard HF. Genomic and personalized medicine: foundations and applications. *Translational research* 2009;154(6):277-87.
9. Sweeny K, Ghane A, Legg AM, et al. Predictors of Genetic Testing Decisions: A Systematic Review and Critique of the Literature. *Journal of Genetic Counseling* 2014;23(3):263-88. doi: 10.1007/s10897-014-9712-9
10. Burton H, Jackson C, Abubakar I. The impact of genomics on public health practice. *British medical bulletin* 2014;112(1):37-46.
11. Chowdhury S, Dent T, Pashayan N, et al. Incorporating genomics into breast and prostate cancer screening: assessing the implications. *Genetics in Medicine* 2013;15(6):423-32.
12. Evans DGR, Donnelly LS, Harkness EF, et al. Breast cancer risk feedback to women in the UK NHS breast screening population. *Br J Cancer* 2016;114(9):1045-52. doi: 10.1038/bjc.2016.56
13. Evans DG, Howell A. Can the breast screening appointment be used to provide risk assessment and prevention advice? *Breast Cancer Research* 2015;17(1):84-84 1p. doi: 10.1186/s13058-015-0595-y
14. Couch FJ, Nathanson KL, Offit K. Two decades after BRCA: setting paradigms in personalized cancer care and prevention. *Science* 2014;343(6178):1466-70. doi: 10.1126/science.1251827
15. Howe R, Miron-Shatz T, Hanoch Y, et al. Personalized Medicine Through SNP Testing for Breast Cancer Risk: Clinical Implementation. *Journal of Genetic Counseling* 2015;24(5):744-51. doi: 10.1007/s10897-014-9803-7
16. Easton DF, Pharoah PDP, Antoniou AC, et al. Gene-Panel Sequencing and the Prediction of Breast-Cancer Risk. *New England Journal of Medicine* 2015;372(23):2243-57. doi: 10.1056/NEJMsr1501341
17. Michailidou K, Lindström S, Dennis J, et al. Association analysis identifies 65 new breast cancer risk loci. *Nature* 2017
18. Amara N, Blouin-Bougie J, Jbilou J, et al. The knowledge value-chain of genetic counseling for breast cancer: an empirical assessment of prediction and communication processes. *Familial Cancer* 2016;15(1):1-17. doi: 10.1007/s10689-015-9835-7
19. O'Daniel J. The Prospect of Genome-guided Preventive Medicine: A Need and Opportunity for Genetic Counselors. *Journal of genetic counseling* 2010;19(4):315-27. doi: 10.1007/s10897-010-9302-4
20. Howell A, Astley S, Warwick J, et al. Prevention of breast cancer in the context of a national breast screening programme. *Journal of Internal Medicine* 2012;271(4):321-30. doi: 10.1111/j.1365-2796.2012.02525.x
21. Onega T, Beaber EF, Sprague BL, et al. Breast cancer screening in an era of personalized regimens: A conceptual model and National Cancer Institute initiative for risk-based and preference-based approaches at a population level. *Cancer* 2014;120(19):2955-64.
22. Kilambi V, Johnson FR, González JM, et al. Valuations of Genetic Test Information for Treatable Conditions: The Case of Colorectal Cancer Screening. *Value in Health* 2014;17(8):838-45.
23. Narod SA. BRCA mutations in the management of breast cancer: the state of the art. *Nature Reviews Clinical Oncology* 2010;7(12):702-07.
24. Goldsmith L, Jackson L, O'Connor A, et al. Direct-to-consumer genomic testing: systematic review of the literature on user perspectives. *European Journal of Human Genetics* 2012;20(8):811-16.
25. Bellcross CA, Page PZ, Meaney-Delman D. Direct-to-consumer personal genome testing and cancer risk prediction. *The Cancer Journal* 2012;18(4):293-302.
26. Zimmern RL, Khoury MJ. The impact of genomics on public health practice: the case for change. *Public Health Genomics* 2012;15(3-4):118-24.
27. Graves K, Peshkin B, Luta G, et al. Interest in genetic testing for modest changes in breast cancer risk: implications for SNP testing. *Public Health Genomics* 2011;14(3):178.
28. Kristoffersson U, Schmidtke J, Cassiman J. Quality issues in clinical genetic services: Springer 2010.
29. Gouvernement du Québec. Québec Breast Cancer Screening Program 2017 [Available from: http://sante.gouv.qc.ca/en/programmes-et-mesures-daide/programme-quebecois-de-depistage-du-cancer-du-sein-pqdcs/ accessed November 12, 2017.
30. Loeppky R. Canada, Health and Historical Political Economy. *Journal of Australian Political Economy* 2014(73):172.
31. Ries N and Einsiedel E. Test génétiques offerts directement aux consommateurs via Internet – Enjeux et options stratégiques. In: Mémoires stratégiques, ed. Répercussions sociétales et politiques publiques: Génome Canada, 2010:9pp.
32. Lin P-J, Cangelosi MJ, Lee DW, et al. Willingness to pay for diagnostic technologies: a review of the contingent valuation literature. *Value In Health* 2013;16(5):797-805.
33. Kopits IM, Chen C, Roberts JS, et al. Willingness to pay for genetic testing for Alzheimer's disease: a measure of personal utility. *Genetic testing and molecular biomarkers* 2011;15(12):871-75.
34. Neumann PJ, Cohen JT, Hammitt JK, et al. Willingness-to-pay for predictive tests with no immediate treatment implications: a survey of US residents. *Health economics* 2012;21(3):238-51.

35. Bosompra K, Ashikaga T, Flynn BS, et al. Psychosocial factors associated with the public's willingness to pay for genetic testing for cancer risk: a structural equations model. *Health Education Research* 2001;16(2):157-72.
36. Matro JM, Ruth KJ, Wong Y-N, et al. Cost sharing and hereditary cancer risk: Predictors of willingness-to-pay for genetic testing. *Journal of genetic counseling* 2014;23(6):1002-11.
37. Ries NM, Hyde-Lay R, Caulfield T. Willingness to pay for genetic testing: a study of attitudes in a Canadian population. *Public Health Genomics* 2010;13(5):292-300. doi: 10.1159/000253120
38. Lacour RA, Daniels MS, Westin SN, et al. What women with ovarian cancer think and know about genetic testing. *Gynecologic oncology* 2008;111(1):132-6. doi: 10.1016/j.ygyno.2008.06.016 [published Online First: 2008/08/08]
39. Saha A, Capps O, Byrne PJ. Calculating marginal effects in dichotomous - continuous models. *Applied Economics Letters* 1997;4(3):181-85. doi: 10.1080/135048597355474
40. Hanmer MJ, Ozan Kalkan K. Behind the Curve: Clarifying the Best Approach to Calculating Predicted Probabilities and Marginal Effects from Limited Dependent Variable Models. *American Journal of Political Science* 2013;57(1):263-77. doi: 10.1111/j.1540-5907.2012.00602.x
41. Mood C. Logistic regression: Why we cannot do what we think we can do, and what we can do about it. *European sociological review* 2010;26(1):67-82.
42. Statistics Canada. Enquête sur la santé dans les collectivités canadiennes (ESSC), 2010:417pp.
43. Gail MH, Brinton LA, Byar DP, et al. Projecting Individualized Probabilities of Developing Breast Cancer for White Females Who Are Being Examined Annually. *Journal of the National Cancer Institute* 1989;81(24):1879-86. doi: 10.1093/jnci/81.24.1879
44. Field A. Discovering statistics using IBM SPSS statistics: Sage 2013.
45. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G* Power 3.1: Tests for correlation and regression analyses. *Behavior research methods* 2009;41(4):1149-60.
46. Portney LG, Watkins MP. Foundations of clinical research: applications to practice. 3rd ed. Philadelphia, USA: FA Davis Co. 2015.
47. Aldrich JH, Nelson FD. Linear probability, logit, and probit models: Sage 1984.
48. Greene WH, Hensher DA. Modeling Ordered Choices: A Primer 1ed: Cambridge University Press; 2010.
49. Fullerton AS. A conceptual framework for ordered logistic regression models. *Sociological methods & research* 2009;38(2):306-47.
50. Bushway S, Johnson BD, Slocum LA. Is the magic still there? The use of the Heckman two-step correction for selection bias in criminology. *Journal of Quantitative Criminology* 2007;23(2):151-78.
51. Dubin JA, Rivers D. Selection bias in linear regression, logit and probit models. *Sociological Methods & Research* 1989;18(2-3):360-90.
52. Amara N, Ouimet M, Landry R. New evidence on instrumental, conceptual, and symbolic utilization of university research in government agencies. *Science Communication* 2004;26(1):75-106.
53. SPSS Inc. SPSS for Windows, Version 13.0. Chicago, USA: SPSS Inc., 2004.
54. Greene WH. LIMDEP: Version 8.0: Econometric Modeling Guide: Econometric Software 2002.
55. Neumann PJ, Hammitt JK, Mueller C, et al. Public attitudes about genetic testing for Alzheimer's disease. *Health Affairs* 2001;20(5):252-64.
56. Lacour RA, Daniels MS, Westin SN, et al. What women with ovarian cancer think and know about genetic testing. *Gynecologic oncology*;111(1):132-36. doi: 10.1016/j.ygyno.2008.06.016
57. Miron-Shatz T, Hanoch Y, Doniger GM, et al. Subjective but not objective numeracy influences willingness to pay for BRCA1/2 genetic testing. *Judgment and Decision Making* 2014;9(2):152-58.
58. Michael F. Drummond MJS, Karl Claxton, Greg L. Stoddart, George W. Torrance. Methods for the Economic Evaluation of Health Care Programmes. 4 ed2015.
59. Cookson R. Willingness to pay methods in health care: a sceptical view. *Health economics* 2003;12(11):891-94.
60. Calia P, Strazzera E. Bias and efficiency of single versus double bound models for contingent valuation studies: a Monte Carlo analysis. *Applied Economics* 2000;32(10):1329-36. doi: 10.1080/000368400404489
61. Bosompra K, Flynn BS, Ashikaga T, et al. Likelihood of undergoing genetic testing for cancer risk: a population-based study. *Preventive Medicine* 2000;30(2):155-66.
62. Bunn JY, Bosompra K, Ashikaga T, et al. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. *Preventive medicine* 2002;34(6):567-77.
63. Kinney AY, Croyle RT, Dudley WN, et al. Knowledge, attitudes, and interest in breast-ovarian cancer gene testing: a survey of a large African-American kindred with a BRCA1 mutation. *Preventive medicine* 2001;33(6):543-51.
64. Reitz F, Barth J, Bengel J. Predictive value of breast cancer cognitions and attitudes toward genetic testing on women's interest in genetic testing for breast cancer risk. *GMS Psycho-Social Medicine* 2004;1:Doc03.
65. Rutherford EJ, Kelly J, Lehane EA, et al. Health literacy and the perception of risk in a breast cancer family history clinic. *The Surgeon* 2016 doi: http://dx.doi.org/10.1016/j.surge.2016.06.003
66. MacTiernan A, Fritschi L, Slevin T, et al. Public perceptions of cancer risk factors: a Western Australian study. *Health Promotion Journal of Australia* 2014;25(2):90-96. doi: https://doi.org/10.1071/HE13081
67. Fehniger J, Livaudais-Toman J, Karliner L, et al. Perceived Versus Objective Breast Cancer, Breast Cancer Risk in Diverse Women. *Journal of Women's Health (15409996)* 2014;23(5):420-27. doi: 10.1089/jwh.2013.4516
68. Nordin K, Björk J, Berglund G. Factors influencing intention to obtain a genetic test for a hereditary disease in an affected group and in the general public. *Preventive medicine* 2004;39(6):1107-14.
69. Hersch J, Nickel B, Ghanouni A, et al. Improving communication about cancer screening: moving towards informed decision making. *Public health research & practice* 2017;27(2)
70. Vrinten C, McGregor LM, Heinrich M, et al. What do people fear about cancer? A systematic review and meta-synthesis of cancer fears in the general population. *Psycho-Oncology* 2017;26(8):1070-79. doi: 10.1002/pon.4287
71. Dorval M, Bouchard K, Chiquette J, et al. A focus group study on breast cancer risk presentation: one format does not fit all. *European Journal of Human Genetics* 2013;21(7):719.
72. Julian-Reynier C, Welkenhuysen M, Hagoel L, et al. Risk communication strategies: state of the art and effectiveness in the context of cancer genetic services. *European journal of human genetics: EJHG* 2003;11(10):725.

73. Bottorff JL, Ratner PA, Balneaves LG, et al. Women's interest in genetic testing for breast cancer risk the influence of sociodemographics and knowledge. *Cancer Epidemiology Biomarkers & Prevention* 2002;11(1):89-95.
74. Braithwaite D, Sutton S, Steggles N. Intention to participate in predictive genetic testing for hereditary cancer: the role of attitude toward uncertainty. *Psychology and Health* 2002;17(6):761-72.
75. National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP). The Breast Cancer Risk Assessment Tool 3.0. In: U.S. Department of Health and Human Services, ed., 2011.
76. Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *American journal of human genetics* 1995;56(1):265.
77. Evans C, Hamilton JR, Tercyak PK, et al. Understanding the Needs of Young Women Regarding Breast Cancer Risk Assessment and Genetic Testing: Convergence and Divergence among Patient-Counselor Perceptions and the Promise of Peer Support. *Healthcare* 2016;4(3):19. doi: 10.3390/healthcare4030035
78. Ahmad S, Fergus K, McCarthy M. Psychosocial issues experienced by young women with breast cancer: the minority group with the majority of need. *Current opinion in supportive and palliative care* 2015;9(3):271-78.
79. Gouvernement du Québec - Commission de l'éthique en science et en technologie. Soins de santé personnalisés: Document de consultation Québec, 2012:44.
80. McClellan KA, Avard D, Simard J, et al. Personalized medicine and access to health care: potential for inequitable access? *European Journal of Human Genetics* 2013;21(2):143.
81. Gail MH. Twenty-five years of breast cancer risk models and their applications. *JNCI: Journal of the National Cancer Institute* 2015;107(5)
82. Fisher RA. Statistical methods and scientific inference. 1956
83. Lipsey MW. Design sensitivity: Statistical power for experimental research: Sage 1990.
84. Noymer A. Alpha, significance level of test. *Encyclopedia of survey research methods* 2008;18

Acknowledgement/Funding sources

This research was supported by the Canadian Institutes of Health Research as a part of the CIHR Team in Familial Risks of Breast Cancer Grant (CRN-8752-1). The Government of Canada through Genome Canada and the Canadian Institutes of Health Research (GPH-129344), the *Ministère de l'Économie, de la Science et de l'Innovation* du Québec through Genome Québec, the Québec Breast Cancer Foundation for the PERSPECTIVE project also funded this study.

The authors also want to thank the reviewers for their insightful comments and suggestions on this manuscript.

Conflict of interest: All authors declare no conflicts of interest in this paper.

Contributors: All authors were responsible for the project design (led by JS and MD). MD and KB were in charge of the survey development and the data collection. JBB and NA made the data analysis and drafted the preliminary version of the manuscript. JBB, NA, KB, MD and JS contributed to results' interpretation, commented on drafts and agreed on the final version of this article.

Ethics approval: This study was approved by the *Comité d'éthique et de la recherche du CHU de Québec-Université Laval* (#2012-1584/2012-HSS-300-05).

Data sharing statement: No additional data are available.

Figure legends:

Figure 1
Respondents' distribution of reported BC life-time risk for a woman of the general population

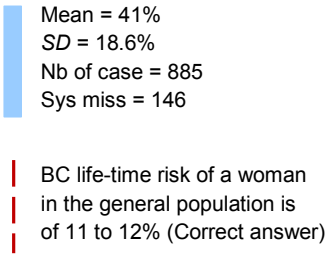


Table 1. Demographic characteristics of the sample*

Respondents' characteristics	*n* = 1031 (%)
Age	
35 to 49 years old	503 (48.8)
50 to 69 years old	528 (51.2)
Sys miss	0
Ethnicity	
White	977 (94.8)
Other	54 (5.2)
Sys miss	0
Marital status	
Widowed, divorced or separated	186 (18.1)
Single	152 (14.7)
Married or common-law	689 (66.9)
Sys miss	4 (0.4)
Education	
No diploma or secondary school	399 (38.7)
College or CEGEP diploma	265 (35.6)
University degree	367 (35.6)
Sys miss	0
Employment	
Full time	573 (55.6)
Part time	138 (13.4)
Retired	180 (17.5)
Student	15 (1.5)
Unemployed/not working	111 (10.8)
Sys miss	14 (1.4)
Household size	
1	135 (13.1)
2	403 (39.1)
3	192 (18.6)
4	181 (17.6)
5+	102 (9.9)
Sys miss	18 (1.7)
Location area	
Rural	146 (142.0)
Small urban	138 (13.4)
Medium urban	95 (9.2)
Large urban	636 (61.7)
Sys miss	16 (1.6)
Objective risk of BC[†]	
< 15%	878 (85.2)
= ou > 15%	122 (11.8)
Sys miss	31 (3.0)
Perceived personal risk	
< or =15%	229 (22.2)
15% >	555 (53.8)
Sys miss	247 (24.0)
Family History	
1 or more first degree relative	146 (14.2)
No family history	869 (84.4)
Sys miss	16 (1.6)
Interest	
Not interested	93 (9.0)
Somewhat interested	113 (11.0)
Moderately interested	221 (21.4)
Very interested	389 (37.7)
Extremely interested	200 (19.4)
Sys miss	15 (1.5)
Willingness-to-pay	
Do not want to pay	250 (24.2)
Between $1-$100	362 (35.1)
Between $101-$250	153 (14.8)
Between $251-$500	59 (5.7)
Between $501-$1,000	13 (1.3)
Over $1,000	3 (0.3)
Sys miss	191 (18.5)

* Sys miss category is the sum of the system missing data, and the option of answers "do not know" and "do not want to answer"

[†] Calculated with the Gail model parameters (available online: http://www.cancer.gov/bcrisktool/). Absolute BC lifetime risk of a woman of the general population is of 11 to 12%. However, risk prediction models used pure cumulative risk (i.e., when no competing mortality risk exists), which is often higher than the absolute risk.[81]

Table 2. Multiple mean group comparisons and post-hoc analysis: level of interest according to range of WTP

Level of interest in BCST by range of WTP values*	*Somewhat interested*	*Moderately interested*	*Very interested*	*Extremely interested*	Total	Subsets of level of WTP[†] according to interest in BCST (mean rank)		
Do not want to pay	68	84	72	26	250	421,76		
Between $0-$100	33	88	182	59	362		552,83	
More than $101	5	27	103	93	228			695,66
Total	106	199	357	178	840			

[*] All missing data, including options "*Do not want to answer*" or "*Do not know*", were coded as missing system data ("sys miss"). The 191 missing data on the WTP measure is distributed as follows: 15 missing system data on the Interest measures, 93 respondents "*Not at all interested*" in BCST, and 83 respondents having indicated to be at least "*Somewhat interested*" in BCST, but having indicated "*Do not want to answer*" or "*Do not know*" on the WTP measure.

[†] Multiple means comparisons based on Tamhane's test: the *post-hoc* analysis was performed following an One-way ANOVA on ranked data. The numbers in columns representig the subsets of level of WTP are mean rank of interest. All mean differences are significant at $p < .000$.

Table 3. Estimated ordered logit models of factors affecting women's interest and willingness-to-pay (WTP) for breast cancer susceptibility testing (BCST) allowing more frequent screenings

	STEP 1		STEP 2	
	Outcome INTEREST [INTER] [1= Not interested at all to 5= Extremely interested]		**Outcome WILLINGNESS-TO-PAY** [WTP] [1= $0; 2= $1 to $100; 3=1$01 and more]	
Explanatory factors	Coefficients (β)	Marginal effect†	Coefficients (β)	Marginal effect†
Sociodemographic factors				
Age [AGE]	-.215*	-.054	-.555***	-.058
Household income				
∝ Less than $25,000 [INC1]	-.667***	-.101	-2.081***	-.154
∝ $25,000 to $54,999 [INC2]	-.510***	-.098	-1.083***	-.103
∝ $55,000 to $74,999 [INC3]	-.074	---	-.762***	-.079
∝ $75,000 and over [INC4]	*Benchmark*		*Benchmark*	
Marital status				
∝ Widowed-Separated-Divorced [WSD]	.284*	.027	.381*	.038
∝ Single [SING]	.184	---	.201	---
∝ Married or in union [MARUN]	*Benchmark*		*Benchmark*	
Education				
∝ No diploma or secondary school diploma [EDUC1]	-.074	---	-.168	---
∝ College or CEGEP diploma [EDUC2]	-.218	---	-.004	---
∝ University diploma or degree [EDUC3]	*Benchmark*		*Benchmark*	
Medical factors				
Biopsy [BIOPSY]	-.213	---	-.358	---
Parity [PARITY]	.060	---	.131	---
Familial history [FAMHIS]	.319**	.357	.396**	.208
Psychological factors				
Optimism [OPTIMS]	-.299*	-.045	.122	---
Monitoring [MO_MBSS]	.464***	.054	.115	---
Health locus of control				
∝ Powerful others [PHLC]	.266***	.441	.211***	.283
∝ Internal [IHLC]	-.040	---	-.103	---
∝ Chance [CHLC]	-.190***	-.244	-.050	---
Anxiety [ANX_K6]	.332***	.409	.213	---
Numeracy [NUM]	-.421***	-.055	-.304*	-.094
Perceived risk of BC [RISK]	.070***	.092	-.002	---
Perceived health status				
∝ Good [GOOD]	.285**	.047	.513***	.035
∝ Fair-Bad [FAIRBAD]	.428	---	.378	---
∝ Excellent -Very good [EXVER]	*Benchmark*		*Benchmark*	
Ancillary parameters				
Threshold 1	-1.434		-2.346	
Threshold 2	-.248		-.153	
Threshold 3	.962			
Threshold 4	2.728			
Number of cases	635		544	
Likelihood Ratio (*df* = 21)	65.861		60.961	
Nagelkerke R^2 (Pseudo R^2)	.104		.120	
Percentage of correct predictions	50.23%		53.31%	

§ The computation of the measures of goodness of fit of the two models leads to the conclusion that they were well behaved. This is indicated by the thresholds in increasing order ($\alpha_1<\alpha_2<\alpha_3$) and the Chi-squared statistics that were much larger than the critical value ($p < .000$) in both models. The "predictive power" of the models and the Nagelkerke R^2 values also appeared to be acceptable for such qualitative models.

*; ** and *** indicate that variable is significant at 10%, 5% and 1%, respectively. Given the nature of the variables assessed and the mixed findings reported for almost all of them in the literature on cancer susceptibility testing, and the number of valid cases included in the analysis, we used three commonly used alpha thresholds to provide to readers more precisions on the significance of our results. [82-84]

† For continuous variables, values of marginal effect represent the variation in percentage on the outcome for 1% positive relative change in the corresponding explanatory factor, whilst for categorical variables, marginal effect values indicate the variation in percentage on the outcome if the sub-sample of respondents would share the same characteristic of those of the reference category.

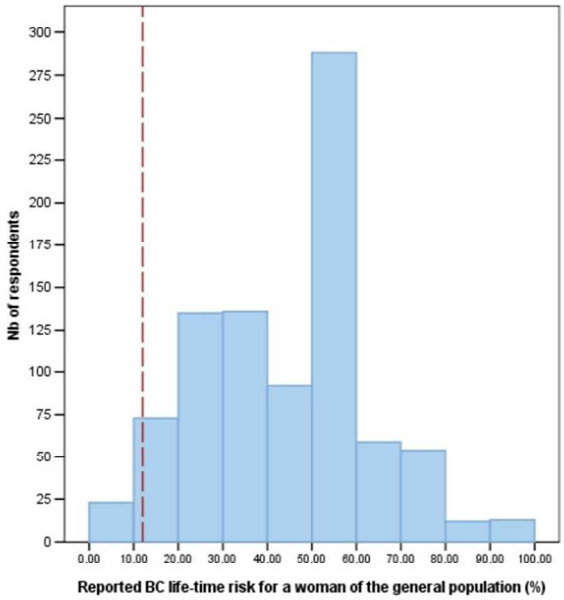


Figure 1
Respondents' distribution of reported BC life-time risk for a woman of the general population

67x50mm (300 x 300 DPI)

Appendix 1. Literature overview on interest in and willingness to pay for cancer susceptibility testing (CST) compared to our study results

	Explanatory factors	Outcome measures [†]		Definitions of factors, description of previous study results, and precisions	Our study results	
		Interest in CST	WTP for CST		Interest in BCST	WTP for BCST
Socio-demographic factors	Age*	Age: NEG[1] POS [2-4] NS[5 6 7 8 9] Younger age: POS [10]	Age: NS [5 1] NEG[11 12] POS[12]	Definition: Age of either patients or individuals of the general population • Link between age and interest or WTP for CST are still equivocal. • Systematic reviews conclusions: studies having assessed association between age and interest toward genetic tests proposed globally mixed findings and mostly inconsistent effects[13]; WTP values for dx tests can be positively influenced by older age.[14] • Age is an important element of women's BC risk assessment: aging is associated with BC, but familial and genetic BC are often developed at a younger age than sporadic forms of BC.[15]	MA	POS
	Ethnicity	Race: NS [5 7 8 16]	Race: NS[5 16] Race: NS[11] Ashkenazi decent: NS[17]	Definition: Person's race or cultural traits relevant to particular group • According to the literature on CST, race seems to not have any effect on interest and WTP. • Systematic reviews conclusions: These variables have not been discussed for interest; WTP values for dx tests are positively influenced by a majority race or ethnicity, especially white Americans.[14] • Some populations or groups of a particular biological background are at greater risk of BC (e.g., French-Canadian, Ashkenazi, Islanders).[18]	*N.B. The sample does not present sufficient variation in terms of ethnicity backgrounds (95% of White women) to be included in the statistical exercise.*	
	Marital Status*	Marital status: NS[5 8 10] NEG[4]	Marital status: NS[5 11]	Definition: Person's legal marital status (e.g., common law, single, divorced…) • According to the literature on CST, marital status seems to not have an effect on interest and WTP. • Systematic reviews conclusions: Relationship between interest and marital status is supported by equivocal findings.[13] • As genetic tests results might have important implications for family-planning decisions, it seems logical that marital status could influence genetic testing decisions.[13] This variable was also proved to be of great importance in cancer care. It has recently been demonstrated that unmarried persons were at a higher risk for cancer, undertreatment and death from cancer. [19 20]	MA (WSD)	MA (WSD)
	Education level*	Education: NS[5 7 10 16 21] Year of education: NEG[3]	Education: NEG.[12] POS.[11 16] NS.[5]	Definition: Person's highest completed degree or diploma. • Link between education level and interest or WTP for CST is still equivocal. • Systematic reviews conclusions: Interest toward genetic tests is inconsistent across studies.[13] WTP values are generally positively associated with education for dx tests.[14]	NS	NS
	Employment status/ primary activities	Employment: POS [8] NS [5 21]	Employment: NS [5 11]	Definition: Person's primary activities of a diary day; it can correspond to employment status for paid work (part- or full-time), but also to unpaid work such as study, housework, social support, volunteering, etc. • Link between employment and interest or WTP for CST seems not significant. • Systematic reviews conclusions: Few studies have assessed the link between employment and interest for genetic testing. Mixed findings are reported. [13]	*N.B. This concept is often correlated with income and education; it was removed from the statistical exercises for parsimonious reasons.*	

	Income*	Household income: NS[5 7 10] POS.[8]	Household income: NS.[5 11 12]	Definition: Combined gross income of all members of a household. • Link between income and interest or WTP for CST seems to be not significant. • Systematic reviews conclusions: Associations of interest for genetic testing and income are inconsistent,[13] but WTP values for dx tests are generally positively associated with incomes.[14]	POS (INC1, INC2)	POS (ALL)
	Household size	Household size: POS.[8]	NA	Definition: Number of persons residing in a private household. • There is insufficient information regarding household size and interest or WTP for CST.	*N.B. This concept is partly assessed by marital status and parity for many respondents. It was eliminated from the statistical exercise.*	
	SES	Socio-economic status: NEG[1 2] NS[9]	Socio-economic status: POS.[1]	Definition: SES is a concept that reflects more broadly familial resources, including education, employment, goods and revenues. • There is insufficient information regarding SES and interest or WTP for CST.	*N.B. This concept is a mix of other retrieved sociodemographic characteristics in the literature; it has been discarded from the statistical exercise to avoid theoretical redundancy.*	
Medical factors	Past medical exams/ results*	Previous examination: MA[7] Timing of the most recent biopsy: NS[5] Prior history of cancer: POS[10 3]	Personal BC history: NS[5] Personal history of GI cancer: NS[11] Personal history of cancer: NS[11]	Definition: Prior test results or health exams of an individual linked to the evaluated health condition. • According to the literature on CST, past medical exams or results could have an impact on interest while they seem to not have an effect on WTP. • Systematic reviews conclusions: It is not clear whether WTP values for dx tests were associated with past medical exams and results.[14]	*N.B. Biopsy was used as a measure of past exam in the present study.* NS	NS
	Children/ Parity*	Children: NS[8] POS[22]	NA	Definition: Woman having/giving birth to at least one child. • Parity/parental status was insufficiently assessed for CST. • Systematic reviews conclusions: Relationship between interest for genetic testing and parental status is still equivocal. [13] • Nulliparty (never having given birth) is a risk factor as parity is a protective factor of BC.[23]	NS	NS
	Family history*	FDR had cancer: NEG[1] NS[5 7 21] POS [2 21 3] BC in family: POS[22 9] Number of FDR: POS [10]	FDR had cancer: NEG[1 11 7] NS[5 17] Family member tested positive: NS[17]	Definition: People who have one or more relatives (1st to 3rd degree) who have had a cancer dx. • Family history seems to be associated with interest for CST while more evidence is needed for WTP for such a test. • Systematic reviews conclusions: Generally, positive family history is associated with interest in genetic testing[13] and WTP for dx tests technologies.[14] • Family history is an important risk factor of BC.[23]	POS	POS

Psychosocial factors	Optimism*/ Pessimism	Optimism NEG [1] POS [2 4] Pessimism: POS[2 9 1] (Depressive sx: POS[10])	Optimism: NEG[1] Pessimism: NS[1]	Definition: Person's tendency to have positive (optimists) or negative (pessimists) expectancies about their future (e.g., events, acts).[24] • Mixed findings were reported regarding association between optimism/pessimism and interest for genetic testing and more research is needed for WTP in the context of CST. • Systematic reviews conclusions: Person having a more positive outlook, highly optimistic or low in depression sx was more interested in genetic testing even if some mixed findings were reported for BC.[13] • This construct is often measured with the Life Orientation Scale.[24]	NEG	NS
	Monitoring*	Seek information: NS [2 1] Preference for medical information: NS[9]	Information seeking: NEG[1]	Definition: Coping style based on personal information preferences about an event: information seekers are considered as high monitors and information avoiders are considered as low monitors.[13 25] • In the context of CST, retrieved studies indicate that being an information seeker is not associated with interest for genetic testing. • Systematic reviews conclusions: High monitors have more interest in genetic testing even if mixed findings are reported for some cancers.[13] • This construct is often measured with the Miller Behavioral Style Scale.[25]	POS	NS
	Perceived control*	Perceived control: NS[26 21] POS[26] God Locus of Health control: NS[10]	Risk tolerance: NEG [12] Perceived control: POS [11]	Definition: Person's perception of his own ability to manage his health/disease risk. • More research is needed toward perceived health control and interest as well as WTP for CST, but retrieved studies seem to indicate that it could have an impact on both outcome measures. • Systematic reviews conclusions: Greater perceived control over the management and prevention of a disease is associated with interest for genetic testing. [13] For some diseases without controllable risk factors, WTP values are higher.[14] • This construct could be measured with the Multidimensional Health Locus of Control Scales.[27]	POS (PHLC) NS (IHLC) NEG (CHLC)	POS (PHLC) NS (IHLC, (CHLC)
	Worries/ Anxiety*	Concerns about developing cancer: POS[7] Cancer worries: POS[5] NS[28] Intrusions-Worries: POS[29] Fears: NEG[29] Uncertainty: POS[21]	Worry about positive results: POS[11] NS[17] Cancer worries: POS[5]	Definition: Personal emotional aspects of risk for a specific health condition. [13] • Worries toward cancer are generally associated with interest and WTP for CST. However, measures used by authors varied considerably. • Systematic reviews conclusions: Mixed findings were reported regarding interest for genetic testing and disease-specific worries even if studies tend to support a positive association between those concepts. [13]	*N.B. As this concept is related to disease-specific perceived risk, [13] a scale of general psychological distress was used to measure respondents' level of anxiety. The K-6 was used.* [30]	
					POS	NEG
	Numeracy*	Understanding risk information: NS[5]	Understanding risk information: NEG[5] Objective numeracy: NS[17] Subjective numeracy: POS[17]	Definition: Person's ability to understand quantitative information and manipulate basic probability and numerical concepts.[31] • There is insufficient information regarding numeracy and interest in CST. Mixed findings for WTP for CST are reported. It is important to note however the variation of the operationalization used to measure the concept of numeracy. • Systematic reviews conclusions: this concept was not reported.	NEG	NS

Knowledge	Genetic knowledge: NS[5 10 29] Knowledge of genetic test: POS [3] Awareness: NS[9]	Genetic knowledge: NS[5] Knowledge & awareness: NS[11]	Definition: Generally concerned about what a person knows about genetic risk or genetic test for a particular disease. • Systematic reviews conclusions: Mixed findings were reported regarding its association with interest toward genetic testing.	*N.B. This concept was not included in the statistical model as it was too correlated with perceived risk.*	
General health*	Current health: NS [7] Health Behaviors:	NA	Definition: Perception of own actual health state. • There is insufficient evidence regarding perceived health status and interest or WTP for CST. • Systematic reviews conclusions: Few studies have assessed the relationship between general health and interest in genetic testing; equivocal results are reported.[13] More health conscious people are likely to accept higher WTP values.[14]	NEG (GOOD)	NEG (GOOD)
Perceived risk of BC*	Perceived susceptibility POS[1 2 9] Perception of risk: MA[7] Absolute perceived risk: NS[5] Comparative perceived risk: NS[5] Numeric perceived risk: NS[5] Perceived risk: NS[28 21] POS [10] Perceived vulnerability: POS[29]	Prior risk: NS[12] Perceived susceptibility: POS[1] Perceived susceptibility: NS[17] Perceived risk of having the mutation: POS[17] Absolute perceived risk: NS[5] Comparative perceived risk: NS [5 11] Numeric perceived risk: NS[5]	Definition: Generally, the person's estimation of his own likelihood of developing the disease in a specific time frame. • Link between risk perception and interest or WTP for CST is still equivocal. • Systematic reviews conclusions: In general, perceived risk is associated with an increased interest for genetic testing, but inconsistent findings were reported for some hereditary conditions.[13] Increased WTP values for dx tests were associated with higher risk perception.[14]	POS	NS

[†] NS: association not signifiant; MA: Marginally signifiant association; NEG: negative association; POS: positive association.
* Variables conserved in the regression models.

References

1. Bosompra K, Ashikaga T, Flynn BS, et al. Psychosocial factors associated with the public's willingness to pay for genetic testing for cancer risk: a structural equations model. *Health Education Research* 2001;16(2):157-72.
2. Bunn JY, Bosompra K, Ashikaga T, et al. Factors influencing intention to obtain a genetic test for colon cancer risk: a population-based study. *Preventive medicine* 2002;34(6):567-77.
3. Bottorff JL, Ratner PA, Balneaves LG, et al. Women's interest in genetic testing for breast cancer risk the influence of sociodemographics and knowledge. *Cancer Epidemiology Biomarkers & Prevention* 2002;11(1):89-95.
4. Biesecker BB, Ishibe N, Hadley DW, et al. Psychosocial factors predicting BRCA1/BRCA2 testing decisions in members of hereditary breast and ovarian cancer families. *American Journal of Medical Genetics* 2000;93(4):257-63.
5. Graves K, Peshkin B, Luta G, et al. Interest in genetic testing for modest changes in breast cancer risk: implications for SNP testing. *Public Health Genomics* 2011;14(3):178.
6. Sanderson SC, O'Neill SC, Bastian L, et al. What can interest tell us about uptake of genetic testing? Intention and behavior amongst smokers related to patients with lung cancer. *Public Health Genomics* 2009;13(2):116-24.
7. Petersen GM, Larkin E, Codori A-M, et al. Attitudes toward Colon Cancer Gene Testing: Survey of Relatives of Colon Cancer Patients. *Cancer Epidemiology Biomarkers & Prevention* 1999;8(4):337-44.
8. Kilambi V, Johnson FR, González JM, et al. Valuations of Genetic Test Information for Treatable Conditions: The Case of Colorectal Cancer Screening. *Value in Health* 2014;17(8):838-45.
9. Bosompra K, Flynn BS, Ashikaga T, et al. Likelihood of undergoing genetic testing for cancer risk: a population-based study. *Preventive Medicine* 2000;30(2):155-66.
10. Kinney AY, Croyle RT, Dudley WN, et al. Knowledge, attitudes, and interest in breast-ovarian cancer gene testing: a survey of a large African-American kindred with a BRCA1 mutation. *Preventive medicine* 2001;33(6):543-51.
11. Matro JM, Ruth KJ, Wong Y-N, et al. Cost sharing and hereditary cancer risk: Predictors of willingness-to-pay for genetic testing. *Journal of genetic counseling* 2014;23(6):1002-11.
12. Neumann PJ, Cohen JT, Hammitt JK, et al. Willingness ‐ to ‐ pay for predictive tests with no immediate treatment implications: a survey of US residents. *Health economics* 2012;21(3):238-51.
13. Sweeny K, Ghane A, Legg AM, et al. Predictors of Genetic Testing Decisions: A Systematic Review and Critique of the Literature. *Journal of Genetic Counseling* 2014;23(3):263-88. doi: 10.1007/s10897-014-9712-9
14. Lin P-J, Cangelosi MJ, Lee DW, et al. Willingness to pay for diagnostic technologies: a review of the contingent valuation literature. *Value In Health* 2013;16(5):797-805.
15. Easton DF, Ford D, Bishop DT. Breast and ovarian cancer incidence in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. *American journal of human genetics* 1995;56(1):265.
16. Lacour RA, Daniels MS, Westin SN, et al. What women with ovarian cancer think and know about genetic testing. *Gynecologic oncology*;111(1):132-36. doi: 10.1016/j.ygyno.2008.06.016
17. Miron-Shatz T, Hanoch Y, Doniger GM, et al. Subjective but not objective numeracy influences willingness to pay for BRCA1/2 genetic testing. *Judgment and Decision Making* 2014;9(2):152-58.
18. Narod SA. BRCA mutations in the management of breast cancer: the state of the art. *Nature Reviews Clinical Oncology* 2010;7(12):702-07.
19. Aizer AA, Chen M-H, McCarthy EP, et al. Marital Status and Survival in Patients With Cancer. *Journal of Clinical Oncology* 2013;31(31):3869-76. doi: 10.1200/jco.2013.49.6489
20. Dawood SS, Lei X, Dent R, et al. Impact of marital status on prognostic outcome of women with breast cancer. *J Clin Oncol (Meeting Abstracts)* 2014;32(15_suppl):594-.
21. Braithwaite D, Sutton S, Steggles N. Intention to participate in predictive genetic testing for hereditary cancer: the role of attitude toward uncertainty. *Psychology and Health* 2002;17(6):761-72.
22. Welkenhuysen M, Evers-Kiebooms G, Decruyenaere M, et al. A community based study on intentions regarding predictive testing for hereditary breast cancer. *Journal of medical genetics* 2001;38(8):540-47.
23. National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP). The Breast Cancer Risk Assessment Tool 3.0. In: U.S. Department of Health and Human Services, ed., 2011.
24. Scheier MF, Carver CS, Bridges MW. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. *Journal of personality and social psychology* 1994;67(6):1063.
25. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. *Journal of personality and social psychology* 1987;52(2):345.
26. Nordin K, Björk J, Berglund G. Factors influencing intention to obtain a genetic test for a hereditary disease in an affected group and in the general public. *Preventive medicine* 2004;39(6):1107-14.
27. Malcarne VL, Fernandez S, Flores L. Factorial validity of the multidimensional health locus of control scales for three American ethnic groups. *Journal of Health Psychology* 2005;10(5):657-67.
28. Cameron LD, Reeve J. Risk perceptions, worry, and attitudes about genetic testing for breast cancer susceptibility. *Psychology & Health* 2006;21(2):211-30.

29. Reitz F, Barth J, Bengel J. Predictive value of breast cancer cognitions and attitudes toward genetic testing on women's interest in genetic testing for breast cancer risk. *GMS Psycho-Social Medicine* 2004;1:Doc03.
30. KESSLER R, nbsp, C., et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological Medicine* 2002;32(06):959-76. doi: doi:10.1017/S0033291702006074
31. Schwartz LM, Woloshin S, Black WC, et al. The Role of Numeracy in Understanding the Benefit of Screening Mammography. *Annals of Internal Medicine* 1997;127(11):966-72. doi: 10.7326/0003-4819-127-11-199712010-00003

Appendix 2. Operational definitions* of variables and descriptive statistics †

Variables	Main reference	Measure, items and coding (final model)		Mean (SD)	*n* (%)	Tolerance
Outcomes						
Interest [INTER]	Adapted from the study of Graves et al.[1]	Scenario Imagine that a new genetic test for breast cancer (BC) risk evaluation will be available soon on the market. This test could inform if your personal risk level to develop BC is higher, lower or equal to the population risk. This test could be also possibly used to adapt BC screening tests frequency to your risk (for instance, recommendations of more frequent screening if your risk is higher than of the risk of the general population or less frequent if your risk is lower than that of the risk of the general population).	To what extent would you be interested in this test if it could allow you to get more frequent BC screening tests if your risk is higher than the one of the general population? 5 point-Likert scale coded as 1 if not interested at all 2 if somewhat interested- 5 if extremely interested (for step 2) Sys miss	3.48 (1,19)	1016 93 (9.0) 923 (89.5) 15 (1.5)	-
Willingness to pay [WTP]			How much would you be willing to pay for this test? 6-point ordinal scale recoded as 1 if do not want to pay; 2 if between $1 and $100 3 if $101 and more Sys miss	1.97 (0.74)	840 250 (24.2) 362 (35.1) 228 (22.1) 191 (18.5)	-
Factors						
Age [AGE]	Statistics Canada, ESCC-2010[2]	Data available from firms' panel. Continuous variable recoded as dichotomous 1 if 50 to 69 years old[§] 0 if 35 to 49 years old Sys miss		50.32 (9.24)	 528 (51.2) 503 (48.8) 0	 .844
Household income [INC1] [INC2] [INC3] [INC4]		Check the answer that best described the gross income measure (before tax) of your household. Ordinal scale recoded as 1 if income less than $25,000; 0 if else 1 if income between $25,000$ and $54,999$; 0 if else 1 if income between $55,000$ and$ 74,999$; 0 if else 1 if income between $75,000$ and more; 0 if else Sys miss		-	 98 (9.5) 267 (25.9) 187 (18.1) 299 (29.0) 180 (17.15)	 .656 .620 .713 Ref.
Marital status [WDS] [SING] [MARUN]		What is your current marital status? Nominal variable recoded as 1 if widowed, divorced or separated; 0 if else 1 if single; 0 if else 1 if married or common-law; 0 if else Sys miss		-	 186 (18.0) 152 (25.7) 689 (66.8) 4 (0.4)	 .831 .764 Ref.
Education [EDUC1] [EDUC2] [EDUC3]		Data available from firms' panel. Ordinal variable recoded as dichotomous 1 if no diploma or secondary school diploma; 0 if else 1 if college or CEGEP diploma; 0 if else 1 if university degree; 0 if else Sys miss		-	 399 (38.7) 265 (35.6) 367 (35.6) 0	 .666 .742 Ref.
Biopsy [BIOPSY]	Adapted from the Breast Cancer Risk Assessment Tool of the NICE[3]	Have you ever had a breast biopsy or puncture? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	 117 (11.3) 943 (91.5) 31 (3.0)	 .916
Parity [PARITY]		Have you ever given birth to a child? Dichotomous variable coded as 1 if yes 0 if no Sys miss		-	 820 (79.5) 211 (20.5) 0	 .849

Familial history [FAMHIS]		How many women of your family's first degree relatives (FDR) ever had breast cancer? Ordinal variable coded as dichotomous 1 if 1 or more FDR 0 if no family history Sys miss	-	146 (14.2) 869 (84.4) 16 (1.6)	.873
Optimism [OPTIMS]	Validated French Canadian version of the Life Orientation Test –Revised [4]	I'm always optimistic about my future. 5-point agreement Likert scale recoded as dichotomous 1 if agree or strongly agree; 0 if else Sys miss		172 (16.7) 845 (82.0) 14 (1.4)	.861
Perceived health status [FAIRBAD] [GOOD] [EXVER]	Statistics Canada, ESCC-2010[2]	In general, would you say that your health is … 5-point Likert scale recoded as 1 if bad or fair; 0 if else 1 if good; 0 if else 1 if very good or excellent; 0 if else		83 (8.1) 387 (37.5) 561 (54.4)	.773 .823 Ref.
Numeracy [NUM]	Adapted from the numeracy test of Schwartz et al.[5]	Score of 3 items: total number of correct answers [range 0-3] a- Familiarity with probability: "Imagine that we flip a fair coin 1,000 times. What is your best guess about how many times the coin would come up heads in 1,000 flips? ____times out of 1,000." b- Conversion of percentage to proportion: "In a lottery, the chance of winning a $10 prize is 1%. What is your best guess about how many people would win a $10 prize if 1,000 people each buy a single ticket? person(s) out of 1,000." c- Conversion of proportion to percentage: "In a prize draw, the chance of winning a car is 1 in 1,000. What is the percentage of winning tickets?____%." Sys miss	1.6 (1.0)	1031 0	
Perceived risk [RISK]	Adapted from Levy et al.[6]	What do you think your chance is of developing breast cancer in your lifetime? Continuous variables where 0% means "not at all likely" and 100% means "definitely likely" Nb of cases Sys miss	33.05 (22.2)	784 (76.0) 247 (24.0)	.836
Monitoring [MO_MBSS]	Validated French Canadian version of the MBSS[7]	8 items of monitoring for 2 scenarios (dentist: α = .696; sales: α = .720). Score coded as 0 if < or = 23 (low monitoring) 1 if > or = 23 (high monitoring) Sys miss		558 (54.1) 467 (45.3) 6 (0.6)	.921
Health locus of control [PHLC] [IHLC] [CHLC]	Validated French Canadian version of the MHLC[8 9]	3 scales (total of 9 items) for 3 types of locus of control (powerful others: α = .615; internal: α = .686; chance: α = .736). Weighted mean of a 6-point agreement Likert scale Powerful others Sys miss Internal Sys miss Chance Sys miss	 4.15 (1.08) 5.00 (0.87) 2.66 (1.32) 	 1027 4 1026 5 1021 10	 .869 .911 .908
Anxiety [ANX_K6]	Validated psychological distress scale used by ESCC-2010 [2 10]	6 items of non-specific psychological distress (α = .831). Weighted mean of a 5-point frequency Likert scale Nb of cases Sys miss	4.09 (0.63)	 1031 0	.795

* Items were initially in French as the survey was administered to a French speaking population. They are freely translated for comprehension purposes in this article.
† All missing data, including options "do not want to answer" or "don't know" were coded as missing system data ("sys miss"). Descriptive statistics are presented for the initial model, i.e., the Interest outcome measure.
§ This age group corresponds to eligible women to the PQDCS, the national breast cancer screening program in Québec (Canada).

References

1. Graves K, Peshkin B, Luta G, et al. Interest in genetic testing for modest changes in breast cancer risk: implications for SNP testing. *Public Health Genomics* 2011;14(3):178.
2. Statistics Canada. Enquête sur la santé dans les collectivités canadiennes (ESSC), 2010:417pp.
3. National Cancer Institute (NCI) and the National Surgical Adjuvant Breast and Bowel Project (NSABP). The Breast Cancer Risk Assessment Tool 3.0. In: U.S. Department of Health and Human Services, ed., 2011.
4. Trottier C, Mageau G, Trudel P, et al. Validation de la version canadienne-française du Life Orientation Test-Revised. *Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement* 2008;40(4):238.
5. Schwartz LM, Woloshin S, Black WC, et al. The Role of Numeracy in Understanding the Benefit of Screening Mammography. *Annals of Internal Medicine* 1997;127(11):966-72. doi: 10.7326/0003-4819-127-11-199712010-00003
6. Levy AG, Shea J, Williams SV, et al. Measuring perceptions of breast cancer risk. *Cancer Epidemiology Biomarkers & Prevention* 2006;15(10):1893-98.
7. French translation and validation of the Miller Behavioral Style Scale. INTERNATIONAL JOURNAL OF PSYCHOLOGY; 1996. PSYCHOLOGY PRESS 27 CHURCH RD, HOVE, EAST SUSSEX, ENGLAND BN3 2FA.
8. Talbot F, Nouwen A, Gauthier J. Is Health Locus of Control a 3 - factor or a 2 - factor construct? *Journal of clinical psychology* 1996;52(5):559-68.
9. Malcarne VL, Fernandez S, Flores L. Factorial validity of the multidimensional health locus of control scales for three American ethnic groups. *Journal of Health Psychology* 2005;10(5):657-67.
10. Kessler RC, Andrews G, Colpe LJ, et al. Short screening scales to monitor population prevalences and trends in non-specific psychological distress. *Psychological medicine* 2002;32(06):959-76.

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-7
Objectives	3	State specific objectives, including any prespecified hypotheses	7 (4-7)
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	7-8
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9 + Appendix 1 and 2
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	Appendix 2
Bias	9	Describe any efforts to address potential sources of bias	7-8 + 13-14 (See figure below this table for power analysis)
Study size	10	Explain how the study size was arrived at	7 + Appendix 2
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-10 + Appendix 2
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-10
		(*b*) Describe any methods used to examine subgroups and interactions	NA
		(*c*) Explain how missing data were addressed	Appendix 2
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8-10
		(*e*) Describe any sensitivity analyses	NA
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for	8-10 + Table 2 and 3 + Appendix 2

		eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11 + Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Appendix 2
Outcome data	15*	Report numbers of outcome events or summary measures	Appendix 2 + Table 2 and 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Only unadjusted estimates are reported Appendix 2 – tolerance values Table 3 (p-values and marginal effects)
		(*b*) Report category boundaries when continuous variables were categorized	Appendix 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	*See point 16*
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	22

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Screenshot: Power analysis performed with G Power