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ORIGINAL RESEARCH

The Use of Family History Questionnaires: An Examination of Genetic Risk Estimates and Genetic Testing Eligibility in the Non-responder Population

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Abstract The use of mailed family history questionnaires (FHQs) has previously been established to be an effective method for obtaining family history information for the triage of patients for genetic counseling and genetic testing of hereditary breast and ovarian cancer syndrome; yet only 53% of patients complete their FHQ within 6 months from the date of mailing (Armel et al. Journal of Genetic Counseling, 18(4):366–378, 2009). Although literature exists evaluating why women may not attend genetic counseling, no data are currently available examining genetic risk or genetic testing eligibility in the population of patients not returning their FHQ (non-responders). Concern exists that if non-responders are not followed-up for the purpose of triage for genetic counseling, individuals at high-risk for a hereditary cancer syndrome may be missed. This article explores the demographics of the non-responder population to assess genetic risk estimates for mutations in the *BRCA1* and *BRCA2* genes and genetic testing eligibility as compared to a responder population of patients who completed a mailed FHQ. A total of 430 pedigrees were obtained, 215 from non-responders and 215 from responders. Results of this study indicate that 69% of non-responders were either unreachable by telephone (42%), declined an appointment (19%), or were previously seen in another center for a genetic counseling visit (8%). Additionally, results indicate that non-responders are less likely to be eligible for genetic testing (40%) as compared to responders (57%) (p=0.0004). Together these data shed light on a population of patients for which limited information exists and suggest that we question how and to what extent clinics should pursue non-responders, particularly in light of global reductions in health care funding.

Keywords Genetic counseling · Family history · Questionnaire · Attendance rate · Genetic testing eligibility · Genetic risk estimate · Hereditary breast and ovarian cancer syndrome

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Introduction

Current statistics within North America indicate that 1/71 women will develop ovarian cancer during their lifetime; translating to roughly 2,500 new diagnoses per year in Canada (Canadian Cancer Society 2009a). More striking, 1/9 women will develop breast cancer during their lifetime leading to roughly 22,900 new diagnoses per year in Canada (Canadian Cancer Society 2009b). While the combined incidence of these cancers is relatively common, only 5–10% of all breast and ovarian cancers are hereditary, with the majority linked to mutations in the *BRCA1* and *BRCA2* genes (Miki et al. 1994; Wooster et al. 1994). Associated with mutations in these two genes are cumulative breast cancer risks ranging from 54 to 84%, and cumulative ovarian cancer risks ranging from 11 to

42% (Antoniou et al. 2005; Easton et al. 1995, 1997; Ford et al. 1998). Given growing public knowledge of the increased risks for developing breast, ovarian, and other related cancers associated with mutations in these genes, awareness of the availability of genetic counseling and genetic testing for Hereditary Breast and Ovarian Cancer Syndrome (HBOCS) has increased. As a result of growing public awareness, the demand for genetic counseling and testing has risen over time.

In addition to the increasing demand for genetic counseling, budgetary constraints have led to increased pressure to maintain quality clinical services with less financial resources. Consequently, many genetic counselors now find themselves searching for ways to improve efficiency, enabling them to see a growing number of patients in the same or shorter period of time. As such, many hereditary cancer clinics have employed the use of Family History Questionnaires (FHQs), which provide opportunities for prospective patients to document their family history information prior to scheduling an appointment with a genetic counselor. Although no supporting data exist, it is anticipated that FHQs may improve counseling efficiency by reducing the time spent by a genetic counselor in direct patient contact in order to construct a pedigree. Furthermore, recent work examining the effectiveness of mailed FHQs revealed the majority of study subjects do not incur a change to their risk estimate for having a *BRCA1* or *BRCA2* mutation or to their genetic testing eligibility status, despite changes to their family history incurred during the genetic counseling session (Armel et al. 2009). Earlier results from a prostate clinic study also demonstrated that while 94% of family histories gathered by FHQ acquired a change following intervention by a study assistant, only 4% had a change to the family's risk category (Brener et al. 1996).

While these studies demonstrate the effectiveness of FHQs for obtaining family history information, it is important to note that in addition to the perceived benefits from the counselor's perspective, the use of FHQs is also desirable to patients. It has been demonstrated that patients prefer to know prior to genetic counseling what family history information is required of them, and those without complete family history information at the time of counseling deemed their risk assessments to be inaccurate (Hallowell et al. 1997). Likewise, another study reported that patients not only like using a FHQ, but 50% preferred a mailed out FHQ as it enabled them to research their family history in advance of counseling (Chalmers et al. 2001).

While FHQs have been shown to be effective in obtaining family history information and for the purpose of triaging referrals for genetic counseling, response rates from referred patients in a single published study are low, with only 53% returning a completed FHQ within 6 months from the date of mailing (Armel et al. 2009). Although no mandate exists requiring clinics in Canada to contact patients that do not return their FHQ (non-responders), it is anticipated that given this low response rate, hereditary cancer clinics may attempt to contact non-responders to facilitate the referral process and increase the numbers of non-responders triaged for genetic counseling. While it is anticipated that the use of FHQs enhances genetic counselor efficiency, the need to follow-up on non-responders may negate this benefit.

Presently, the majority of literature regarding non-responders has focused on understanding why prospective patients may not desire or attend a genetic counseling appointment for HBOCS. When making a decision regarding genetic counseling and testing for HBOCS, prospective patients must weigh the potential benefits of obtaining information against the possible risks, including the potential for increased psychosocial distress (Lerman et al. 1996). Previous studies have revealed that individuals who decline genetic testing and/or counseling for HBOCS may not believe the cancer in their family is hereditary and therefore have less interest in the counseling process (Cappelli et al. 1999; Geer et al. 2001; Rimer et al. 1996; Schlich-Bakker et al. 2007). Practical issues such as travel distance, work, familial or social obligations, and the time commitment necessary for the genetic counseling process have also been shown as potential barriers to participation in genetic testing (Cappelli et al. 1999; Foster et al. 2004; Geer et al. 2001; Lerman et al. 1996; Rimer et al. 1996; Schlich-Bakker et al. 2007). Furthermore, individuals who decline genetic counseling have expressed concern regarding the consequences of genetic testing including decreased insurability, increased anxiety regarding the health and emotional well being of themselves and other family members, as well as the concern that the frequency and diligence of breast cancer screening will be reduced should they receive negative genetic test results (Cappelli et al. 1999; Foster et al. 2004; Geer et al. 2001; Schlich-Bakker et al. 2007).

Purpose of the Study

While a body of literature exists exploring the practical and psychosocial factors that may influence an individual in their decision to undergo genetic counseling, no data are available examining the probability of *BRCA1* or *BRCA2* mutations or genetic testing eligibility in the non-responder population. Therefore, concern exists that if prospective patients who do not complete their FHQ are not followed-up, high-risk individuals may be missed. The purpose of this study was to investigate the non-responder population from the perspective of level of genetic risk and genetic testing eligibility.

Methods

Genetic Counseling

All new referrals to the Familial Breast and Ovarian Cancer Clinic (FBOCC) at Princess Margaret Hospital are mailed a package containing an introductory letter, the FHQ, a personal medical history questionnaire (PHQ), and two release-of-information forms to obtain pathology records for relatives affected by cancer. Once the completed FHQ and PHQ are returned, an appointment for genetic counseling is scheduled. From the information included on the FHQ and PHQ, a three-generation pedigree is created by either a genetic counseling student or a trained undergraduate co-operative education student. During the first appointment, the family history is reviewed and based on the pedigree, a probability estimate for having a mutation in *BRCA1* or *BRCA2* is assigned. For those patients who are eligible for genetic testing according to the Ontario Ministry of Health and Long Term Care (Appendix 1), a full pre-test counseling session is completed and a blood sample is drawn for those choosing to pursue testing. For patients who choose to pursue genetic testing, a follow-up appointment is scheduled when results are complete.

Family History Questionnaire

The FHQ includes a series of questions and tables to elicit a three-generation pedigree for the patient's family (Armel et al. 2009). Information regarding cancer history is obtained on first and second degree relatives in addition to some third degree relatives, such as first cousins, but not for great aunts/uncles or great grandparents. Likewise, the PHQ obtains information including gender, age and level of education, current medication use, previous cancer diagnoses, past surgeries, chemoprevention, and abnormal breast and ovarian cancer screening results.

Follow-up of Non-responders

Patients who did not return a completed FHQ within 6 months from the date of mailing were defined as non-responders. They were contacted by telephone and offered the opportunity to provide their family history by telephone or to be sent another questionnaire by mail, fax, or e-mail. Six months was selected in order to provide ample time for patients to complete the FHQ and return it to the clinic. Non-responders were called three times prior to being deemed unreachable. For patients with voice mail, messages were left requesting the patient contact the clinic regarding their referral. All telephone calls were made by either a genetic counseling student or an undergraduate co-operative education student trained to obtain a three-generation pedigree. For non-responders who were unreachable, did not contact the clinic following a voice mail message, or declined an appointment, a letter was sent to the referring physician indicating either the inability to reach the patient or the patient's decision to decline an appointment. All letters indicated that the patient could be re-referred in the future.

Non-responders who provided a pedigree by telephone were informed that an appointment would be provided to eligible patients following triage by a genetic counselor. Low risk families with no eligible relatives for genetic testing were not offered appointments for genetic counseling due to limited resources. Such study participants were informed by telephone that they were ineligible and their referring physicians were mailed a letter informing them that their patient was not offered an appointment. However, if either the ineligible study participant or their referring physician still wished an appointment due to factors such as increased anxiety, an appointment was scheduled.

Participant Recruitment

A total of 215 pedigrees were obtained by telephone from non-responders between February 2006 and June 2009. Additionally, 215 pedigrees were retrospectively obtained from the files of patients who provided their family history by mailed FHQ and were therefore defined as responders. A sequential block of 215 responders were selected from files seen between October 2006 and October 2008. Approval for the study was obtained from the Princess Margaret Hospital research ethics board.

Non-responder Contact Outcomes

Given the significant volume of referrals and non-responders in a single year, it was decided that sufficient numbers to describe the contact outcomes of this population could be obtained by monitoring these data for a 12-month period during the study. In 2007, a total of 214 referrals were received for which no FHQ was returned. The outcome of these 214 referrals was recorded to determine the percentage of non-responders who were unreachable, the percentage who were reachable and declined an appointment, and the percentage who were reachable and deemed interested in having genetic counseling by providing a pedigree by telephone.

Reasons for Not Completing the FHQ

All 215 non-responders who provided their family history by telephone were asked to share their reasons for not completing the FHQ. Participants were asked to share their reasons for not completing the FHQ after providing their family history to the genetic counseling or co-operative

education student through an open-ended question. Of the 215 non-responders who provided a family history, 114 provided a total of 132 explanations for not having completed the FHQ. The authors grouped similar responses together and a total of six themes were identified. Each of the six themes was used as a category in to which each response was sorted. No formal qualitative analysis was performed on these data.

Appointment Outcomes

To determine how likely non-responders are to attend their genetic counseling appointments, the appointment outcomes of the 215 non-responders were obtained by retrospective review of the clinic's electronic database. Only non-responders who provided a pedigree by phone and were offered an appointment for genetic counseling were considered (n=178). The remaining 37 non-responders were not offered appointments for genetic counseling due to their family's ineligibility for genetic testing as determined by the Ontario Ministry of Health and Long Term Care. All non-responders who provided a pedigree by phone and were subsequently not offered an appointment for genetic counseling were informed by telephone and their physicians notified by letter.

As described under participant recruitment, a sequential block of 215 responders were selected from files seen between October 2006 and October 2008. Given that responders were retrospectively ascertained, all were previously seen for a genetic counseling appointment, and as such appointment outcomes for this population are unavailable.

Probability Estimates and Genetic Testing Eligibility

Based on the family history obtained from either the FHQ or as reported by the patient over the telephone, each family was given a probability estimate for the likelihood of having a mutation in *BRCA1* or *BRCA2*. In the FBOCC, probability estimates are divided into three categories; low, moderate and high. These categories were created to provide patients with a quantifiable estimate for the chance of finding a mutation in their family rather than their personal chance of having a *BRCA1* or *BRCA2* mutation. Low risk denotes a probability of having a *BRCA1* or *BRCA2* mutation of 15% or lower, moderate risk implies a probability of 16–30%, and high risk is classified as greater than 30%. The cut-off of 15% was originally chosen for the low risk category as the early literature suggested an individual with a diagnosis of ovarian cancer (depending on the histology) had a 12–16% chance of carrying a *BRCA1* or *BRCA2* mutation (Risch et al. 2001). As the FBOCC was originally designed as a familial ovarian cancer clinic, there are a high proportion of patients attending the clinic with a personal or family history of ovarian cancer. A family with one isolated case of ovarian cancer is considered to be at low risk to have a *BRCA1* or *BRCA2* mutation: thus a cut-off of 15% for low risk was selected. In order to separate those families at high risk from those at medium risk, the cut-off for moderate risk was set at 30%. This cut-off was selected as two-first degree relatives, one with breast cancer and one with ovarian cancer, have a 23–28% chance of having a *BRCA1* or *BRCA2* mutation and would therefore be considered to be at moderate risk (Risch et al. 2006). However, two first-degree relatives with ovarian cancer have a 35–49% chance of having a mutation, and thus such a family would be considered high risk (Risch et al. 2006).

In order to determine familial risk estimates, the BRCAPRO model (Berry et al. 2002) was used for the highest risk member of the family. From clinical experience, this model is not accurate in the absence of a history of breast cancer; therefore the ovarian cancer literature was used when necessary, to more accurately assess risk (Risch et al. 2001, 2006).

The province of Ontario establishes eligibility for genetic testing using criteria set out by the Ministry of Health and Long Term Care. As a general guideline, genetic testing is available to an unaffected individual with at least a 10% chance of having a *BRCA1* or *BRCA2* mutation. For an individual with a diagnosis of breast or ovarian cancer, a defined set of criteria for assessing genetic testing eligibility exists (Appendix 1).

Data Analysis

For both the responder and non-responder populations, the number of 215 participants was selected to achieve a statistical power of 0.80. Descriptive statistics were used to summarize demographic variables and survey responses. The Pearson Chi-square Test was used to compare the variables of interest between the responders and non-responders. All statistical analyses were performed using SAS version 9.1 (Cary, NC). All statistical tests were two-sided, and p-values less than 0.05 were considered statistically significant.

Results

Participant Demographics

In total, 430 individuals participated in the study, including 215 non-responders and 215 responders (Table 1). Overall, 99% (n=427) of study participants were female with a mean age of 46.8 (Range: 19–86). Ninety percent of

Table 1 Participant demographics

Characteristic	Non-Responders	Responders	Total	%
Individuals	215	215	430	100
Women	214	213	427	99
Mean age (range)	45.3 (19–85)	48.2 (21–86)	46.8 (19–86)	
Cancer				
Any	76	124	200	47
Breast	53	87	140	33
Ovarian	15	31	46	11
Other	13	19	32	7
Ethnicity				
Caucasian	136	171	307	71
African	2	1	3	1
East Indian/Asian	18	26	44	10
Hispanic	1	5	6	1
Native Indian	2	1	3	1
West Indian	3	2	5	1
Mixed	10	9	19	5
Unavailable	43	0	43	10
Education				
Grade School	17	13	30	7
College	31	37	68	16
University	42	63	105	24
Post Graduate	18	33	51	12
Unavailable	107	69	176	41

participants self-identified ethnicity, with 79% (307/387) identifying as Caucasian. In addition, 47% (n=200) of participants reported a personal history of cancer.

Non-responder Contact Outcomes

In 2007, there were 214 referrals for which no FHQs were received. Using the 12 month time period, it was determined that 69% (n=147) were unreachable (42%), declined an appointment (19%), or had been seen in another genetics clinic (8%) (Fig. 1). Only 28% (n=60) provided a pedigree, which was assumed to be an interest in genetic counseling.

Comparison of Non-responders to Responders

Comparison of non-responders to responders indicates that responders were more likely to have a personal diagnosis of

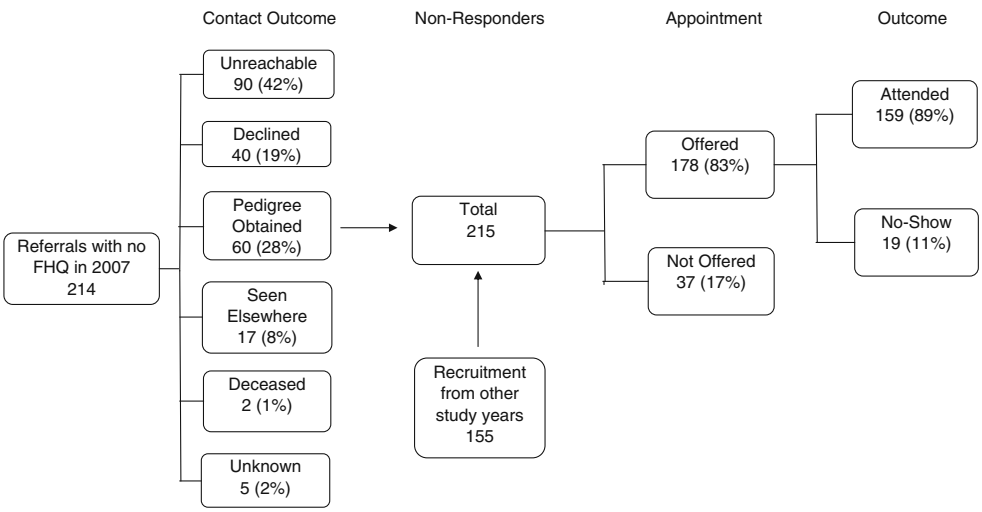

Fig. 1 Non-responder flowchart

cancer (58% versus 35%, X^2=21.537, p<0.0001) and were more likely to be eligible for genetic testing, either themselves (57% versus 40%, X^2=12.745, p=0.0004) or including a relative (82% versus 61%, X^2=22.155, p< 0.0001) (Table 2). In addition, there was no difference in level of education between the two groups (p=0.25) or in probability estimates using the three probability estimate categories of low, moderate and high risk for having a *BRCA1* or *BRCA2* mutation (p=0.21) (Table 2).

Non-responder Appointment Outcomes

Of the 215 non-responders who provided a family history by telephone, 83% (n=178) were offered an appointment for genetic counseling (Fig. 1). The remaining 17% (n=37) were not offered appointments as a result of not meeting eligibility requirements for genetic testing. Of those non-responders who were offered an appointment, 11% (n= 19/178) either cancelled or "no-showed" for their appointment, and 89% (n=159/178) attended (Fig. 1).

Reasons for Not Completing the FHQ

Of the 215 non-responders who provided a family history by telephone, 114 provided reasons for not completing the mailed FHQ (Fig. 2). A total of 132 reasons were obtained. Explanations for not completing the FHQ included: having limited family history information (25%), being busy, procrastinating, or having forgotten (26%), never having received the package (19%), and feeling overwhelmed or confused (19%).

Discussion

Family history questionnaires are widely used in cancer genetics services to obtain family history information prior to genetic counseling. However, despite their wide acceptance, minimal data exist evaluating their use in clinical practice. To date, evidence demonstrating the effectiveness of FHQs as a tool for triaging appointments for genetic counseling and genetic testing exists, yet many questions remain regarding the follow-up of non-responders who do not return completed FHQs. As previously described, a body of literature exists evaluating the practical and psychosocial reasons why individuals may not attend genetic counseling appointments (Cappelli et al. 1999; Foster et al. 2004; Geer et al. 2001; Lerman et al. 1996; Rimer et al. 1996; Schlich-Bakker et al. 2007), yet to date no published data exist examining genetic risk estimate or genetic testing eligibility in the non-responder population.

Results of this study demonstrate that as compared to responders, non-responders were significantly less likely to be themselves eligible for genetic testing for mutations in the *BRCA1* and *BRCA2* genes, as determined by the Ontario Ministry of Health and Long Term Care (40%

Table 2 Comparison of non-responders to responders

Characteristic	Non-Responders		Responders		p
	n	(%)	n	(%)	
Cancer Diagnosis	76	35	124	58	<0.0001
Education					0.25
Grade School	17	16	13	9	
College	31	29	37	25	
University	42	39	63	43	
Post Graduate	18	16	33	23	
Total	108	100	146	100	
Probability Estimate					0.21
Low	129	60	112	52	
Moderate	41	19	54	25	
High	45	21	49	23	
Total	215	100	215	100	
Genetic Testing Eligibility					<0.0001
Proband	86	40	123	57	
Relative	46	21	53	25	
Not eligible	83	39	39	18	
Total	215	100	215	100	

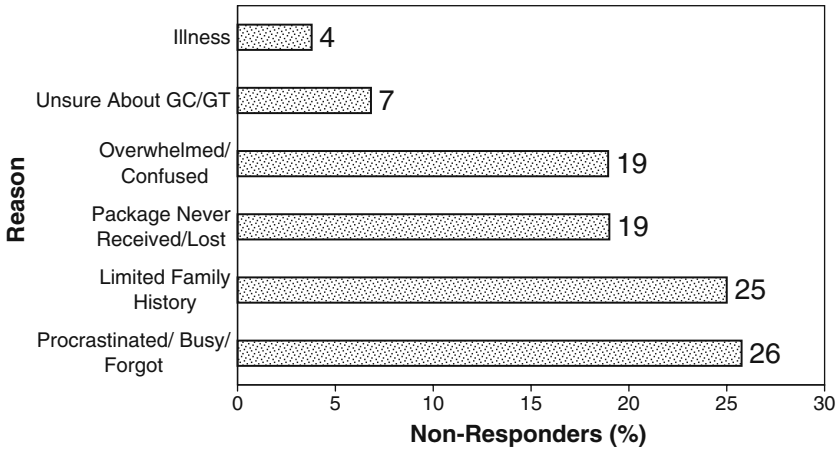

Fig. 2 Explanations for not completing the FHQ provided by non-responders (n=132)

versus 57%). In addition, responders were significantly more likely to have a personal diagnosis of cancer as compared to non-responders (58% versus 35%). The observation that responders are more likely to be eligible for genetic testing may be directly related to the fact that they are more likely to have a personal diagnosis of cancer. Certainly with a personal diagnosis of cancer, eligibility for genetic testing will be increased as the likelihood of finding a mutation will be higher as compared to an individual without a personal diagnosis.

Results of this study also demonstrate no difference between the responder and non-responder populations with respect to risk estimate for a *BRCA1* or *BRCA2* mutation. The lack of between-group differences may be attributable to the fact that risk estimates are assigned based on the family's overall chance of having a mutation rather than the consultand's individual chance of having a mutation. Therefore, while a family may be assigned a high chance of having a *BRCA1* or *BRCA2* mutation given the family history, it is possible the consultand referred for counseling may be more distantly related to the cancer history in the family, and themselves not eligible for genetic testing due to a low personal chance of having a mutation. Although one may be ineligible for genetic testing, it is important to note that genetic counseling may still be of benefit for accurate discussions of personal risk, cancer prevention measures and appropriate screening based on the family history.

Given the difference in genetic testing eligibility between the non-responder and responder groups, it is also important to consider that individuals may self-estimate their risk of having a mutation, with those at greater perceived risk demonstrating a greater motivation to pursue genetic counseling and in turn a greater likelihood for completing the mailed FHQ. Previous studies comparing perceived likelihood of carrying a genetic mutation and interest in genetic testing have demonstrated that individuals who felt they were at lower risk were significantly less likely to want genetic testing (Lerman et al. 1994; Struewing et al. 1995). Other research has demonstrated that women who are at an increased risk to carry a *BRCA1* or *BRCA2* mutation are the most likely to gain useful information from genetic testing and thus are most likely to pursue genetic counselling (Armstrong et al. 2000). These findings further strengthen the hypothesis that those with the greatest perceived risk are the most likely to follow through on the referral process (Armstrong et al. 2000). Additionally, studies looking at subject and family determinants in the uptake of genetic counseling demonstrated that being a patient with cancer or the first-degree relative of a patient with cancer resulted in a higher uptake of genetic counseling (Hagoel et al. 2000; Julian-Reynier et al. 2000). This finding, consistent with those from the responder population, may also be directly related to increased perceived risk.

To gain a better understanding of the reasons non-responders did not complete their mailed FHQs, all 215 non-responders were invited by open ended question to share their reasons for not completing the FHQ. While it is plausible that reasons for non-response could be related to barriers due to the design and use of the FHQ, only 19% cited being overwhelmed or confused as their reason for not completing it. The majority of participants cited reasons for non-response that were related to being busy or having forgotten (26%) or to having limited knowledge of their family history (25%). While none of the reasons for non-response were related to lack of perceived risk or lack of perceived benefit of genetic counseling, 7% of non-responders indicated their reasons for not completing the FHQ related to uncertainty about having genetic counseling or genetic testing. No patients described fear as the reason for not completing the FHQ, although this may be unconsciously reflected in those patients describing uncertainty about the genetic counseling and testing process. Clearly caution must be used in interpreting these results as the information was obtained over the telephone in a non-anonymous fashion, thereby increasing the likelihood that non-responders did not

feel comfortable disclosing their true feelings. Additionally, responses are not available for a large percentage of non-responders, creating potential bias in these results.

Given previous data suggesting individuals with decreased perceived risk are less likely to attend genetic counseling appointments, the attendance rate of non-responders versus the reported attendance rate in the literature was compared. Given that responders were retrospectively ascertained it was not possible to compare attendance rates between non-responders and responders within the study. Informal experience in this clinic indicates a no-show/cancellation rate for new patients of 9% (unpublished data). A study investigating the no-show/cancellation rate within 20 non-cancer specific Canadian genetics clinics estimated an overall 11% rate of failed appointments (Humphreys et al. 2000). Among non-responders, the rate of no-shows/cancellations was 11%, consistent with the published literature, although slightly higher than the average for new patients scheduled to be seen by this clinic.

Practice Implications

Given the significant time invested to contact non-responders, the outcomes of all non-responder referrals were tracked for a 12 month period in 2007. The results confirm that follow-up of the non-responder population remains a challenge, with the majority of non-responders (61%) either unreachable or not interested in genetic counseling. Furthermore, overall results indicate that of those non-responders providing a pedigree by telephone, only 40% were themselves eligible for genetic testing. These results suggest the importance of carefully considering if and how the practice of follow-up for the non-responder population will be carried out, particularly in light of the low success rate for contacting these patients. Rather than pursuing non-responders with multiple telephone calls, genetic counselors may wish to consider closing the circle of care by providing a follow up letter to both the non-responder and referring health care provider. Such a letter can include an invitation to re-contact the clinic, should they decide to pursue genetic counseling in the future. Furthermore, a letter of this type can also serve as a method to educate referring health care providers about genetic testing eligibility and help to bolster the numbers of appropriate referrals.

While clinics may choose not to follow-up on non-responders either with telephone calls or by simple means such as sending a closing letter as described above, it is important to consider that providing genetic counseling services to the non-responder population is beneficial. Although these patients may be less likely to be eligible for genetic testing, as demonstrated by the results of this study, genetic counseling can provide them with accurate information regarding their risk estimate and appropriate screening and prevention strategies given their family history. This information may be particularly valuable to those patients who have inaccurately estimated their risk status.

Study Limitations and Research Recommendations

The authors recognize that limitations to the current study exist. Firstly, the studied population is relatively homogeneous, with the majority of patients being Caucasian, female, and highly educated. Additionally, the demographics of the unreachable non-responder population may be different from those of the non-responder population that was reachable by telephone. Given the high number of non-responders that were unreachable, it is plausible that language barriers, lower socioeconomic status, or other factors may contribute to additional barriers to completing the FHQ. Moreover, selecting a 6 month time frame to contact non-responders was done in order to provide ample time for patients to complete their FHQs and return them to the clinic. This time frame was chosen to help separate responders from non-responders, but it may also be a limitation of the study. It is also acknowledged that limited published data exist regarding the non-responder rate, and the data published in this study are reflective of a single clinic's experience. Furthermore, caution should be used in interpreting the qualitative data regarding reasons non-responders did not return their FHQ, as these data were collected in a non-anonymous manner and did not capture 47% of non-responders.

While the results of this study provide valuable information regarding risk estimates and genetic testing eligibility of the non-responder population, they also support current literature demonstrating that patients with cancer are more motivated to schedule genetic counseling compared to those without a personal diagnosis of cancer. Future directions for research include evaluating the origin of referrals in the non-responder versus responder populations. It is possible that differences in uptake may also be reflected in the origin of the referral, whether it be from an oncologist, another specialist, a family physician, or a self-referral. While none of the participants in the present study were referred due to a known familial *BRCA1* or *BRCA2* mutation, previous data indicate that in such families, a lower uptake of genetic counseling or testing was associated with being referred by one's doctor versus being self-referred (Hagoel et al. 2000). Additionally, minimal information exists regarding the reasons for non-completion of the FHQ in the non-responder population, particularly in the large proportion of patients who are unreachable. Certainly the feedback obtained from non-responders regarding non-completion of the FHQ may serve as the basis for a more controlled and comprehensive project addressing barriers to the design and use of FHQs.

Conclusions

Overall, this study has provided information regarding genetic risk estimates and genetic testing eligibility for a population of patients for which little information exists. While the benefits of providing genetic counseling services to all referred patients is recognized, it is important to consider the effort required to follow-up on all referrals who do not return their mailed FHQ. This study has demonstrated that follow-up by telephone call results in a low yield of patients interested in genetic counseling and eligible for genetic testing. Given today's economic climate when health care funding and resources are at a minimum, clinics that use FHQs must best decide if and how to follow-up on their non-responder population. Simple time saving methods such as sending a letter to the patient and referring physician may prove effective at closing the circle of care but may still not result in an increase of the numbers of non-responders seen for genetic counseling. As previously described, further studies exploring barriers to the design and use of FHQs may prove critical to reducing the size of the non-responder population.

Appendix 1

Eligibility criteria for genetic testing for mutations in *BRCA1* and *BRCA2* in the province of Ontario

Testing for Affected Individuals with Breast or Ovarian Cancer

At least one case of cancer:

1. Ashkenazi Jewish and breast cancer <50 years, or ovarian cancer at any age.
   Note: testing limited to ethnic specific mutations, unless other criteria given in this list are met.
2. Breast cancer <35 years of age.
3. Male breast cancer.
4. Invasive serous ovarian cancer at any age.

At least 2 cases of cancer on the same side of the family:

5. Breast cancer <60 years, and a first or second-degree relative with ovarian cancer or male breast cancer.
6. Breast and ovarian cancer in the same individual, or bilateral breast cancer with the first case <50 years.
7. Two cases of breast cancer, both <50 years, in first or second-degree relatives.
8. Two cases of ovarian cancer, any age, in first or second-degree relatives.
9. Ashkenazi Jewish and breast cancer at any age, and any family history of breast or ovarian cancer. *Note: testing limited to ethnic specific mutations, unless other criteria given in this list are met.*

At least three cases of cancer on the same side of the family:

10. Three or more cases of breast or ovarian cancer at any age.

Testing for Unaffected Individuals (this should be done only if affected individuals are unavailable e.g. deceased)

11. Relative of individual with known *BRCA1* or *BRCA2* mutation. *Note: specific family mutation only tested.*
12. Ashkenazi Jewish and first or second-degree relative of individual with: breast cancer <50 years, or-ovarian cancer at any age, or-male breast cancer, or-breast cancer, any age, with positive family history of breast or ovarian cancer
    Note: testing limited to ethnic specific mutations, unless meet other criteria
13. A pedigree strongly suggestive of hereditary breast/ovarian cancer, i.e. risk of carrying a mutation for the individual being tested is >10%.

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