EXPLORATION OF THE OPTIMAL MODEL OF FAMILY MEMBER OUTREACH IN PATIENTS WITH CANCER PREDISPOSITION SYNDROME

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Abstract

Background Individuals with a family history of cancer predisposition syndrome are at an elevated risk of multiple cancers. However, approximately 50% of at-risk individuals do not attend genetic counselling and, therefore, cannot benefit from risk-reducing strategies that could decrease the occurrence of cancers associated with the condition. Consequently, it is imperative to explore options to increase hereditary cancer risk communication within affected families for more optimal uptake of genetic counselling.

Methods A national cross-sectional study was conducted using an online survey to investigate how probands (the first member in a family to have genetic testing) would like to inform their relatives of the risk of hereditary cancer. Relatives also had the opportunity to respond to questions on how they would like to be informed.

Results Generally, there was a high level of acceptance for the health care professionals' involvement in risk communication among the study's participants. Preferences for family member outreach in hereditary cancer syndrome were related to demographic characteristics such as education level, annual income, marital status and geographic location. In addition, having a previous cancer diagnosis and other factors such as confidence in speaking with relatives, support from family members and concerns about causing distress were also related. Similarities were noted between the probands and relatives on outreach preferences related to demographic characteristics.

Conclusion Even though the family-mediated approach is currently standard care, this method might not be sufficient in cancer risk communication and alternative options that allow for the probands' involvement with the healthcare provider's assistance should be explored.

GENERAL SUMMARY

Cancer predisposition syndrome or hereditary cancer accounts for a small proportion of all cancers. However, there is strong evidence of reduced cancer morbidity and mortality when individuals at high cancer risk due to cancer predisposition syndromes can be identified before a cancer is diagnosed and access prevention and screening.

The index case or the first person tested in a family (referred to as the proband) is usually given a letter at the time of disclosure of genetic testing results. The proband is expected to share these letters with at-risk relatives, yet the literature reveals that genetic testing and counselling rates among affected relatives are suboptimal.

This study explored and described preferences for various methods of family member outreach among affected individuals. Results should assist with creating patient-centred communication support policies in the care of patients affected by cancer predisposition syndromes and suggest valuable areas for future research.

Co-Authorship Statement

While I am the sole author of this thesis, publications arising from this investigation will include my committee members.

Primary Investigator and author of thesis – Kimberly Burke (KB), Memorial University of Newfoundland.

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The study was conceived of by HE and LD. The study's design, measures and method were conceived in collaboration with the committee members. Additional input on the survey was sought from HE and representatives from Ovarian Cancer Canada (OCC). As the primary investigator (PI), KB completed all data collection and analysis. In addition, HE provided guidance and statistical expertise for data analysis.

All committee members provided scientific advice for this thesis. HE was, however, the primary editor of this work. LD, KH and BW were secondary editors. All authors approved the final thesis.

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I am grateful for the support that was given to me by my supervisor and co-supervisor during this project. Dr. Etchegary, I appreciated your traditional approach in guiding me through the different phases of this investigation. You gave me enough information to develop my thought processes and analytical skills applicable to research. You were also gentle in your approach. I often felt like giving up, and you reminded me that I was almost at the end. I later learned that this was not always the case. I was faced with many challenges, some of which you were aware of, and I believe your background in psychology enabled you to propel me through my first research. Thank you for the expertise that you brought to this research committee. Dr. Dawson, Thank you for your contribution to this project. You emphasized the importance of networking in research. Through the connections that you made and the relationships that you formed with your patients over the years, I was able to advertise my work across numerous platforms. You often gave your input from a clinician's perspective, clearly stating what the primary objectives of this study should be based on the type of information that healthcare providers might be interested in for them to better assist their patients. Thank you for your input and expertise from the lens of a healthcare provider.

In continuance of my expression of gratitude, I would like to acknowledge Drs. Hodgkinson and Wilson, for sharing their knowledge and expertise throughout this project. Thank you also for the time that was invested in bringing this project to an end.

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COVID-19 Impact Statement

I commenced my graduate studies in September 2020. In all my years of previous studies, I had no experience with learning in a virtual context. I had to adapt to this setting since the COVID-19 pandemic dictated that students pursuing higher education conform to this mode of delivery since May 2020. Transitioning from an in-person to an online classroom was challenging as the primary mode of communication with my professors and committee was via email. Regarding my committee, the only exception was when we had our general meetings. Often, emailed instructions were misunderstood or overlooked, and as a result, it was difficult to comprehend what was expected of me for the literature review. I completed this section of my work later than I initially anticipated. A direct implication of email communication is not receiving an immediate response. I also lost the opportunity of being able to approach other colleagues or faculty members on matters that were not entirely clear to me. The delayed completion of a satisfactory draft of my literature review meant that other research areas would have also been behind schedule. Later in my studies, I was able to adapt to emailing as the principal mode of communication.

Fortunately, an online survey was used for my data collection, so this phase of my research project was not negatively affected by the lockdown that resulted from the pandemic. However, I believe completing my data analysis would have been quicker if I had met with my supervisor in person rather than via Webex, given the many variables I worked with. I had to revisit this section because I did not clearly understand the initial instructions. Nevertheless, I was able to finish it without an overly long delay. Further, the pandemic likely contributed to the survey's low response rate. Data collection occurred during a time when providers were overwhelmed with Covid and helping advertise research simply could not be a priority; eligible patients may also have been overwhelmed

with the pandemic, facing delays in their own cancer screening, or simply tired of online sessions. It is likely the pandemic affected the final response rate.

Despite losing out on the experience of pursuing my studies on campus and not being able to connect with my colleagues and faculty members, amidst the challenges that I faced with converting to online learning, I was able to navigate through the various phases of conducting my research. However, my learning and skills gained as a new researcher were not compromised. I am grateful for the support given to me, and my getting to this phase is also attributable to my perseverance.

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List of Abbreviations

AB - Alberta

ASMR – Age Standardized Mortality Rate

ATM - ATM Serine/Threonine Kinase

BC – British Columbia

BCW – Black Canadian Women

BCCA - British Columbia Cancer Agency

BRCA – Breast Cancer Gene

BRCAT – Breast Cancer Risk Assessment Tool

BOADICEA - Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm

CAGC – Canadian Association of Genetic Counsellors

CDC – Center for Disease Control and Prevention

CHD – Chromodomain Helicase DNA Binding Protein

CGA - Collaborative Group of the Americas

CHEK2 - Checkpoint Kinase 2

COVID-19 - Coronavirus Disease of 2019

CRC – Colorecta Cancer

DNA – Deoxyribonucleic acid

EOC – Epithelial Ovarian Cancer

EPCAM – Epithelial Cell Adhesion Molecule

FCGR – Family Communication of Genetic Risk

FMA – Family Mediated Approach

GCSS – Genetic Counselling Satisfaction Scale

GTT – Genetic Targeted Testing

HBOC – Hereditary breast and ovarian cancer

HIPAA - Health Insurance Portability and Accountability Act

HNPCC – Hereditary non-polyposis colorectal cancer

HREB – Health Research Ethics Board

IBIS - Tyrer-Cuzick Risk Calculator for Breast Cancer Risk Assessment

LS – Lynch Syndrome

LSI - Lynch Syndrome International

mAGIC - Mobile Application for Genetic Information on Cancer

MB – Manitoba

MICRA – Multidimensional Impact of Cancer Risk Assessment

MLH – MutL homolog (mut=mutation)

MMR – Mis-match Repair

MOH – Ministry of Health

MSH - MutS Homolog

MSI-H - Microsatellite Instability High

MSI – Microsatellite Instability

NB - New Brunswick

NBN - Nibrin

NB – New Brunswick

NL - Newfoundland

NS – Nova Scotia

OCC – Ovarian Cancer Canada

OFCCR - Ontario Familial Colon Cancer Registry

ON - Ontario

PALB2 – Partner and Localizer of BRCA2

PEI – Prince Edward Island

PI – Primary Investigator

PMS1 – PMS1 Homolog 2, Mismatch Repair System Component (Postmeiotic Segregation Increased)

PREMM5 - PREdiction Model for gene Mutations 5

PTEN - Phosphatase and Tensin Homolog

PV – Pathogenic Variant

QC - Quebec

RAD - RAD1 Checkpoint DNA Exonuclease

RCT – Randomized Control Trial

RRSO – Risk-reducing Salpingo-oophorectomy

SD – Standard Deviation

SK - Saskatchewan

STK11 - Serine/Threonine Kinase 11

TP53 – Tumor Protein 53

TPB – Theory of Planned Behaviour

UK – United Kingdom

UN – United Nations

UNESCO - United Nations Educational, Scientific and Cultural Organization

YBCS – Young Breast Cancer Survivor

CHAPTER 1: INTRODUCTION

In Canada, lung cancer, colon cancer and breast cancer account for almost half of all new cancer diagnoses (Canadian Cancer Statistics, 2021). Lung cancer causes more deaths than colon cancer, breast cancer and prostate cancer combined. In relation to age standardized incidence rates, the most commonly diagnosed cancers in Canadians aged 30 to 49 are breast cancer (23%), thyroid cancer (12%), colon cancer (9%) and melanoma (7%). In Canadians ages 50 to 84 years, lung cancer, breast cancer, colorectal and prostate cancers were prevalent. Among those age 85 years and older, colorectal, lung and breast cancers were common diagnoses, followed by vesical and prostate cancer.

Inherited cancers account for about 10% of all cancers, affecting multiple organ systems and often occurring at younger ages (Wang et al., 2015; Walsh et al., 2010). Lifetime cancer surveillance and prevention are recommended for families with an inherited cancer predisposition. For instance, a woman with a proven pathogenic variant (PV) in BRCA1 has an approximately 30% and 40% risk of breast and ovarian cancer, respectively (Hu et al., 2021; Petrucelli et al., 2010; Risch et al., 2006). This is in contrast to a lifetime risk of 12.4% (Momenimovahed & Salehiniya, 2019) and 1.4% (Parker et al., 2019) for breast and ovarian cancer respectively among women in the general population. Recommendations according to international screening guidelines for annual breast examination starting at age 25 years, annual breast MRI with contrast between 25 - 29 years and annual mammogram with consideration for breast MRI with contrast between 30 - 75 years will increase the overall life expectancy to 72.52 years, with the maximum achieved when screening is started at age 25 (Bevers et al., 2022; Daly et al., 2022; Lowry et al., 2011) and the approximate risk reduction may be as high as 37% (Domcheket al., 2010). In Canada, however, screening guidelines for high-risk individuals vary across provinces. For example, in Ontario annual breast MRI with contrast is recommended plus or minus an annual mammogram between 30-69 years. In Alberta, it is

recommended that high-risk individuals commence screening with an annual mammogram with or without contrast at five to ten years earlier than the age of the index case, and that this is done no later than age 40 years. Similarly, in Prince Edward Island, screening with annual mammography with or without contrast should begin ten years prior to the family member's age at which the cancer occurred (Canadian Cancer Society, 2023). For the remaining provinces, screening schedules are determined after consultation with a genetic specialist and are based on the family history (Canadian Cancer Society, 2023).

Risk-reducing salpingo-oophorectomy (RRSO) by age 40 provides an 80% risk reduction of ovarian cancer (due to the high potential for recurrence in occult carcinomas found during RRSO despite postoperative chemotherapy) and a 15% absolute survival gain compared to no RRSO (Cancer Australia, 2011; Kurian et al., 2010; Marchetti et al., 2014; Piedimonte et al., 2020). RRSO provides a 70% improvement in all-cause mortality (Marchetti et al., 2014). For patients with Lynch Syndrome, the risk of colorectal cancer is 10-20% for *MSH6* and *PMS2* mutations and 40-80% for *MLH1* and *MSH2* mutations (with an overall risk of 52-82%) (Parfrey et al., 2017; Provenzale et al., 2016). Surveillance colonoscopy in individuals with a positive family history of colorectal cancer (CRC) is associated with an 80% reduction in CRC, and colonoscopy every 1-2 years in mutation carriers is associated with a 10-year mean survival improvement for cancer diagnosis made before age 65 (Provenzale et al., 2016). The 10-year crude survival may be as high as 93% for stage I disease, 94% for stage II and 82% for stage III, with no significant differences related to the causal MMR mutations (Seppälä, et al., 2020; Parfrey et al., 2017).

The clinical significance of gene identification in cancer predisposition syndrome is the opportunity to offer preventative strategies to unaffected relatives and decrease morbidity and mortality (Buchanan et al., 2021). Other advantages include targeted treatment options and a decrease in the economic

burden associated with the diagnosis and treatment of the conditions (Guzauskas et al., 2022; Guzauskas et al., 2020; Lopez-Acevedo et al., 2015; Hampel et al., 2011). Thus, there are clinical and health system benefits to identifying individuals at risk for cancer predisposition syndrome. The three Tier 1 genetic disorders identified by the Center for Disease Control and Prevention (CDC) are Lynch syndrome (*LS*) or Hereditary Non-Polyposis Colorectal Cancer (*HNPCC*), Hereditary Breast and Ovarian Cancer (*HBOC*) and Familial Hypercholesterolemia. Tier 1 genomic applications "are those having significant potential for positive impact on public health based on available evidence-based guidelines and recommendations." (Centers for Disease Control and Prevention [CDC], 2014).

These genetic conditions have an autosomal dominant inheritance pattern (Figure 1), implying a 50% chance of the mutated gene being passed on to carriers' offspring. Although autosomal dominant inheritance pattern is observed in many different diseases, this study is focused on Lynch Syndrome and *HBOC*.

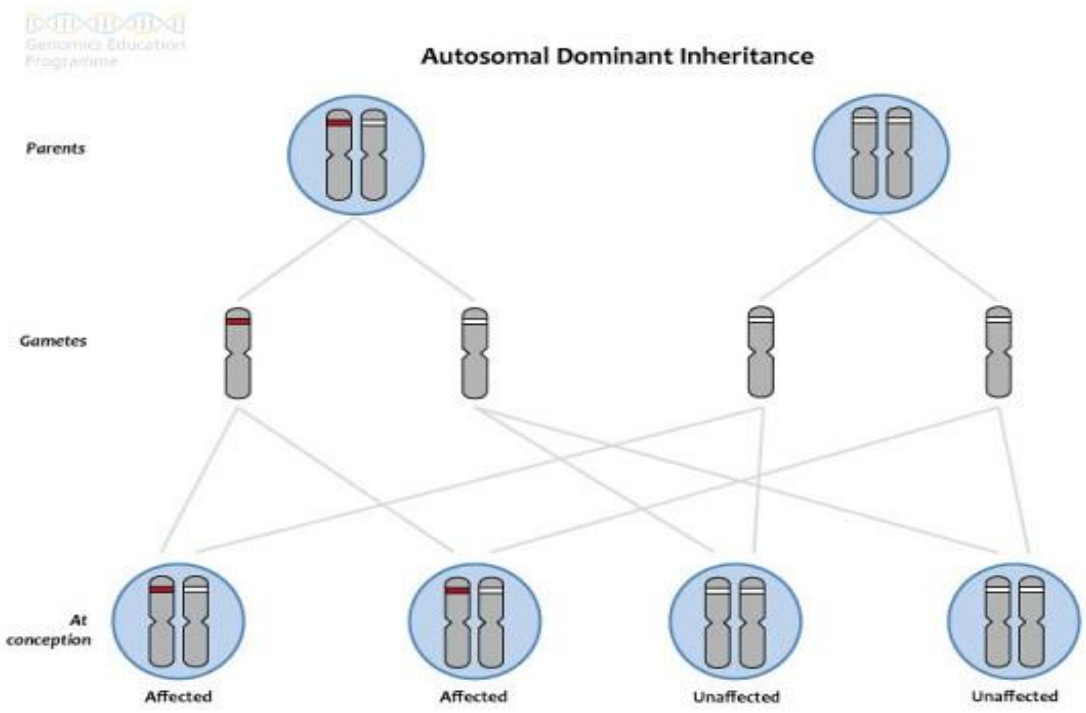


Figure 1.1: Schematization of an autosomal dominant pattern of inheritance

"Autosomal Dominant Inheritance" by Health Education England's Genomics Education Programme, 2022. Used under Creative Commons license (CC-BY-NC- 4.0)/ Cropped from original. https://www.genomicseducation.hee.nhs.uk/image-library/

1.1 The general mechanism behind genetic cancers

According to Knudson's two-hit theory (Wang et al., 2018), the loss of function model explains the mechanism behind hereditary cancers. Affected individuals possess one allele with the mutation. The influence of environmental factors leads to the inactivation of the second gene. The result of this process is a somatic alteration. For the same condition to occur in an individual without a genetic

predisposition, both alleles of a gene must be inactivated. Phenotypic manifestations of disease occur when a target gene or protein expresses both alleles' alteration. This mechanism explains why hereditary cancers generally present at an earlier age than somatic cancers.

1.2 The discovery of Lynch syndrome

Dr. Alfred Warthin is credited with being the first to describe hereditary cancers in the 1890s (Wang et al., 2015). Advancements were made to his work, and in the 1960s, Dr. H. Lynch reported on large extended families with extremely high rates of a digestive genetic cancer, leading to the term "Lynch Syndrome" (Wang et al., 2015). The genes involved in Lynch Syndrome are *MLH1*, *MSH2*, *MSH6* and *PMS2*. The *EPCAM* gene was discovered later (Gille et al., 2002) and is related to the *MSH2* gene. Corrective cellular mechanisms, such as the mismatch repair system, exist for genetic repair.

1.3 The discovery of the *BRCA* gene mutations in HBOC

The successful discovery of the *BRCA* 1 gene was made through collaborative efforts and announced in 1994. Events leading to this finding involved the analysis of blood DNA from large families with a history of early onset of breast and ovarian cancer (Wooster et al., 1994). The *BRCA* 2 gene was later found in 1995 (Wooster et al., 1995; King et al., 2014).

It is estimated that 25% of epithelial ovarian cancers (EOC) are heritable and are caused by *BRCA* gene mutations (Weissman et al, 2012; Walsh et al., 2010).

1.4 Risk stratification

An individual can be stratified as average risk or high risk for developing cancer using predictive risk models (APPENDICES 1-3). Some of these models are reliant on family history; for example, the PREMM 5 Model classifies persons as being at high risk of Lynch syndrome-associated endometrial cancer if the calculated lifetime risk is approximately 20-25% (Barneton et al., 2006; Kartrinos et al., 2017; Chen et al., 2006; (Colon Cancer Genetics Group University of Edinburgh and MRC Human genetics Unit, 2019); PREMM 5 Model, 2017). In other Lynch syndrome-related cancers such as colon cancer, ureteral and reno-pelvic (including endometrial), 50% of families meeting the Amsterdam II criteria have an MMR mutation (APPENDIX 2) (Gupta et al., 2017). Another study suggested the Bethesda criteria might be more accurate since up to 65% of *MLH1* and *MSH2 MSI* tumors were detected (Raedle et al., 2001). Similarly, the revised Bethesda criteria has a high odds ratio of 33.3 (95% CI, 4.3 – 250) for detecting carriers an *MLH1* or *MSH* germline mutation (APPENDIX 3). Using the Gail model for breast cancer risk prediction, patients with a calculated 5-year risk of >1.7% are considered as being at high risk and should be recommended for preventative management (Costantino et al., 1999; Rockhill et al., 2001; Quante et al., 2012). There is, however, a newer predictor model that calculates the future risks of developing breast or ovarian cancer using information on family history, lifestyle and hormonal risk factors. This is the CanRisk Web Tool (CanRisk, 2022) and it incorporates version six (v6) of the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) (APPENDIX 3). The CanRisk Web Tool calculates cancer risk for rare pathogenic variants in moderate and high-risk breast cancer and ovarian cancer susceptibility genes and in common breast and ovarian cancer genetic susceptibility variants using Polygenic Risk Scores and mammographic density.

A multifactorial approach is used for the various existing models and factors that are taken into account include genetic variants and relational susceptivity, reproductive, hormonal, anthropomorphic, lifestyle and imaging elements (APPENDIX 1) (Rosner et al., 2005; Pfeiffer et al., 2013; Colditz, 2000; Claus et al., 1994; Barneton et al., 2006; Lee et al., 2019; Carver et al., 2020).

1.5 Very high cancer risks

The discovery of the genes involved in hereditary cancer syndromes revolutionized genetic medicine. These discoveries mean that individuals and families can now understand, calculate risk and implement prevention and risk management strategies.

A study conducted with pairs of twins from Sweden, Denmark and Finland to estimate the effect of heritability in cancer causation found statistically significant effects for 35% of *HNPCC* and 42 % for breast cancer. The estimates for shared environmental effects were up to 20% and were not statistically significant. The study revealed a predilection for heritability in organs such as the prostate, and breasts (Lichtenstein et al., 2000). Another study conducted among Nordic twins reported a significant cumulative cancer risk among monozygotic twins that was higher than dizygotic twins (Mucci et al., 2016). The study reported that 38% of monozygotic (who share 100% of their genetic material) and 26% of dizygotic pairs (who share 50% of their genetic material) were diagnosed with the same cancer. The results from this study were analysed based on an individual's risk given their twin's diagnosis and also according to interindividual genetic differences. The high estimates reported support the significance of familial risk in hereditary cancer.

Lynch syndrome causes approximately 3% of colorectal cancers (*CRC*), according to estimates from the Finnish population (Samowitz et al., 2001). Women with Lynch syndrome have a 10-15 % risk of developing ovarian cancer (Bewtra et al., 1992), a 16-71% lifetime risk of endometrial cancer (Parker

et al., 2019) and up to an 80% lifetime risk of colorectal cancer (Bhattacharya et al., 2022; Parker et al., 2019). The mean age of diagnosis is approximately 16-20 years younger than that of sporadic ovarian cancer. Lynch syndrome-associated ovarian cancer is usually diagnosed at stages I and II. In contrast, sporadic and *BRCA*-related ovarian cancer is diagnosed at the more advanced stages III and IV (Crispens., 2012). Thus, identifying at-risk individuals before cancer develops offers the potential for early intervention and improved outcomes. There has been a decrease in the incidence of and mortality of colorectal CRC as a result of prevention and early detection through cancer screening. The incidence of CRC per 100,000 people decreased from 54.5 to 38.6 between the year 2000 and 2014 (Ness & Llor, 2022).

The risk of developing hereditary ovarian cancer in women with a *BRCA1* gene mutation is approximately 40%, while for *BRCA2*, it is approximately 17% (Dorling et al., 2021). To put this risk in perspective, among mutation carriers, the risk of ovarian cancer is 20-30 times higher than the population risk of 1.4% (Brenner et al., 2020; Akbari et al., 2017). Previous studies have identified earlier onset ovarian cancer with *BRCA1* as opposed to *BRCA2*. (Risch et al., 2001; Petrucelli et al., 2010). The lifetime risk of breast cancer may be as high as 82% in females who carry *BRCA1/2* mutations (King et al., 2003). According to results from a meta-analysis of twenty-two studies involving 500 male and female germline mutation carriers (289 *BRCA1* and 221 *BRCA2* mutation carriers), the estimated cumulative incidence for *BRCA1*-related breast cancer is 65% and 45% for *BRCA2* (Antoniou et al., 2003). In a more recent comparative study, the mean cumulative risk of breast cancer from the aggregation of ten studies (1020 *BRCA1* and 621 *BCRA2* mutation carriers) reported a 57% (95% CI 47% to 66%) risk for *BRCA1* related breast cancer and a risk of 49% (95% CI, 40% to 57%) for *BRCA2* (Chen et al., 2007). The occurrence increases among individuals of Askenazi Jewish Ancestry, with a prevalence of 1/40 (Palomaki et al., 2015). Recently, Manchanda et al., 2019 reported the overall *BRCA* prevalence as 2.9% within the general population, with a prevalence of *BRCA1* of

1.55% and *BRCA2* of 1.35%. Considering general population numbers, this suggests a high number of individuals potentially at risk for cancer predisposition syndromes.

Among males, the absolute risk of *BRCA1* related breast and pancreatic cancer is approximately 0.4% and 2.5% respectively, up to 80 years. Also, among males, absolute risk of *BRCA2* related pancreatic cancer and prostate cancer is approximately 2.5% and 27% respectively. (Li et al., 2022).

1.6 The prevalence of hereditary cancer syndromes according to Canadian provincial-based studies

The exact population prevalence of Lynch syndrome (*LS*) across Canada is unknown; however, the literature has shown that LS accounts for approximately three to five percent of all colorectal cancers and varying associated risks for *LS* mutations in gynecological cancers such as endometrial cancer and ovarian cancer (Bonadona et al., 2011). *CRC* is the third most diagnosed cancer and the second leading cause of death. In 2019, 26,300 Canadians were diagnosed with *CRC* and 9500 died from the condition (Canadian Cancer Statistics, 2021). Newfoundland has the highest rate of *CRC* in the world. In a study conducted by Parfrey et al., 2017. Lynch syndrome screening was offered to individuals with a family history of *CRC*. Of the 1091 individuals identified, 51% provided a family history, and of this subset, 72% were at low or intermediate-low risk of *CRC* while 28% were at high and intermediate-high risk of being affected. The risk estimation was made by a geneticist and was determined by family history (number of first and second-degree relatives with *CRC* and family size), the Amsterdam criteria, the modified Amsterdam criteria and the Bethesda criteria.

Similarly, the Hereditary Cancer Program of the BC Cancer Agency (BCCA) has provided genetic testing for Lynch syndrome within the province since 2004. The province's population is approximately 4.380 million, and screening among individuals at high risk of or affected by *LS* has established an estimated prevalence of 1/531 and approximately 8000 people carrying the mutation

(Cremin et al., 2010). A recent study was conducted within the province among 245 index patients with LS mutations (Beard et al., 2020). Less than 50% of eligible first-degree relatives underwent genetic testing, 32.6% (268/821) and carrier testing was performed in only 382 eligible relatives with a mean age of testing of 41.5 years. Sixty-seven percent of cancer diagnoses were made before genetic testing.

Gynecological malignancies may be equivalent to or exceed the risk of colorectal malignancies in Lynch syndrome. These malignancies are usually the primary or "sentinel" cancer in women with *LS* (Clarke et al., 2012; Lu et al., 2005). A retrospective chart review of individuals diagnosed with endometrial cancer due to Lynch syndrome using the Tom Baker Cancer Centre *LS* screening protocol (Cameron et al., 2020) in Calgary, Alberta, was conducted between April 1, 2013, and April 1, 2015. Six patients (1.6%) among a cohort of 375 tested positive for an *LS* mutation, 294 (78.4 %) tested negative, and 75 (20%) were unknown because of protocol non-compliance. The prevalence of Lynch syndrome was approximately 2 %.

Another provincial-based study showed more positive test results among individuals at high risk of Lynch syndrome who were identified based on their tumor immunohistochemistry staining or family history. These individuals were identified and offered genetic testing through the Ministry of Health and Long-Term Care (MOH) in Ontario. A total of 1425 individuals were tested. Five hundred and ninety-seven were tested for a known family mutation of which 298 (49.9%) were positive. Six-hundred and sixty-two subjects were tested because their tumors were deficient in one or more MMR genes and from this group, 251 of them had a germline mutation (37.9%) Additionally, 193 individuals were referred because of their positive family history, of which 34 (17.6%) carried an *LS* mutation (Wang et al., 2016).

A chart review of 3251 patients from the Mount Sinai Hospital in Toronto with a personal or family history of *HBOC* was included in an incidence study (Lerner-Ellis et al., 2020). Overall, 9.1% (295) had a positive (pathogenic or likely pathogenic) result, and 27.1% (882) had an inconclusive result (a variant of uncertain significance). Pathogenic variant suggests that the variant is the cause of the disease, likely pathogenic variant suggests that the variant is considered the probable, while a variant of uncertain significance has characteristics that are independent of the disease-causing mutation on the background of conflicting evidence. The genes with the highest prevalence of positive results were *BRCA2* (2.2%, 71/3235), *BRCA1* (1.9%, 62/3235), and *CHEK2* (1.4%, 40/2916). Of the positive cases, 9.8% (29) had a pathogenic or likely pathogenic variant in a gene associated with Lynch syndrome (*MSH6, MSH2, MLH1,* or *PMS2*).

While we do not have precise prevalence estimates, these studies reveal relatively high prevalence rates suggesting there are reasonably high numbers of individuals across Canada at risk for these inherited cancers, further underscoring the importance for exploring approaches that could increase the sharing of hereditary cancer risk information within affected families.

1.7 A guiding theory for determining the optimal outreach method based on factors known to influence risk communication.

The ecological model details the factors that influence interfamilial communication in *HBOC* at the individual level, the familial level and the community level (Nycum et al., 2009). The model outlines that probands may face difficulty communicating complex information at the individual level and are opposed to being the bearer of "bad news." Similarly, an individual's risk perception, personal feelings, conflicting sense of responsibility, and the content of the communication may encourage or impede hereditary risk communication. The proximity of relationships influences communication at

the family level, where close relatives are more inclined to share risk information among themselves than with relatives who are estranged emotionally or separated by physical distance. Reconstituted families and the family's experience with cancer may facilitate or create barriers for risk communication at the corresponding level, according to the model. Cultural contexts related to the prevalence of values of privacy and autonomy, and the community's undertaking of the responsibility for risk information are integrated at the community level. The ecological model was chosen as the conceptual framework for this thesis in place of other models, for example, the family communication of genetic test result (FCGR) communication framework (Shah et al., 2018), and the theory of planned behaviour (TPB) (Wiens et al., 2013) since it is holistic, and integrates several factors that influence hereditary risk communication.

The FCGR communication framework includes the following four elements of communication: influential factors, communication strategies, communication occurrences and reaction to communication (Shah et al., 2018). Influential factors are those that pertain to family dynamics, the understanding of the disease and experience with the same, emotions toward risk communication, and sociocultural factors. Communication strategies speak to the delivery and content of the communication. Communication occurrences look at the extent to which risk information is shared, while outcomes of communication are related to the relatives' reaction to risk information as well as uptake to genetic screening and testing. This model does not account for societal norms related to privacy and autonomy and one's perceived responsibility for communicating risk information. Neither does it consider the perception of personal risk or the nature of the genetic test result. Given these limitations, it was not chosen as the conceptual framework for determining communication preferences.

The six constructs of the theory of planned behaviour (TPB) are attitude, behavioural intention, subjective norms, social norms, perceived power, and behavioural control (Wiens et al., 2013). Attitude points to an individual's positive or negative consideration toward performing a behaviour. Behavioural intention cites the influence of motivational factors. Subjective norms allude to one's belief of whether they will be accepted by peers or persons deemed important to them if they engage in a behaviour. Social norms define the customs of a group of people or a larger cultural context. Perceived power refers to factors that drive or deter one's comportment and perceived behavioural control speaks to one's understanding of their capability to perform a desired behaviour. Though the theory of planned behaviour has been proposed as a guiding tool to assist genetic health professionals match appropriate interventions based on patients' personality, past experiences, gender, disease severity and perceived cultural norms (Wiens et al., 2013), it also has limitations. It doesn't account for emotions that might influence behaviour such as fear, anxiety or previous experiences (Boston University of Public Health, 2016). Another limitation is that the TPB assumes that individuals are equipped with resources needed to execute the desired behaviour successfully.

In light of these alternative models' limitations, the ecological model was thought to be a better guiding conceptual framework for the current study.

CHAPTER 2: LITERATURE REVIEW

Electronic databases were searched for studies that were relevant for the literature review. These included the following: Cochrane Central Register of Controlled Trials, CINAHL, PubMed, and EMBASE.

Study titles, abstracts and full texts were reviewed.

Key Search Terms: Hereditary cancer, cancer predisposition, outreach, family letters.

Operators Used: AND, OR

Population: Cancer predisposition AND hereditary cancer

Limits Used: A search was conducted for studies published from inception to the present. Only studies found in English were reviewed.

Additional Strategies Used:

Population:

(“Cancer predisposition” [MeSH Terms] OR “Hereditary cancer” [MeSH Terms] OR “Genetics cancer” [MeSH Terms])

AND

("Lynch syndrome" [Mesh Terms])

AND

(“Breast cancer” [MeSH Terms])

AND

(“Ovarian cancer” [MeSH Terms])

AND

(“BRCA1” [MeSH Terms])

AND

("BRCA2" [MeSH Terms])

Intervention: ("Outreach letters" [MeSH Terms] OR "Family letters" [MeSH

Terms] OR "Outreach" [Mesh Terms]

AND

("Letters" [MeSH Terms])

AND

("Survey" [MeSH])

AND

("Questionnaire" [MeSH Terms])

Outcome: ("Genetic counseling" [MeSH Terms] OR "Genetic screening

[MeSH Terms]" OR "screening" [MeSH Terms])

AND

("Surveillance" [MeSH Terms])

This section will explore the barriers and facilitators to cascade screening for hereditary cancer syndromes and the factors influencing risk communication among affected individuals along with the other elements of the ecological model. Accordingly, laws related to the privacy and confidentiality of genetic information will be examined. There will be an appraisal of the literature on methods of hereditary cancer risk communication that have been investigated in previous studies. This section will end with a review of studies related to other hereditary conditions that might also be prevented through cascade screening.

2.1 Cascade Screening

Cascade screening is the sequential process by which family members of a person with an identified genetic mutation are contacted and informed about the family's inherited risk and their eligibility for genetic counselling and testing. As noted, the standard of care in genetic counselling is by means of a family letter provided to the proband to share with relatives. Since healthcare providers are generally restricted from directly informing relatives of their increased risk because of concerns about individual privacy, the proband is encouraged to share the letter with all at-risk relatives. The ultimate goal is to identify any other variant carriers in the family who can avail of genetic counselling and testing. Identifying high-risk family members enables evidence-based risk management and care as early as possible, ultimately preventing cancer.

While the benefits of identifying families at risk of hereditary cancer have been established (Ness & Llor, 2022; Bevers et al., 2022) the number of relatives per index case who avail themselves for risk-reducing management in accordance with evidence-based guidelines relative to the total number of family members at risk has maintained a steady rate of approximately 50% across numerous geographical regions (Loader et al., 2002; Lowery et al., 2010; Hinchcliff et al., 2019; Menko et al., 2013; Marleen et al., 2019). Thus, despite carriers of a cancer mutation being encouraged to share risk information with relatives, a significant number do not avail of genetic counselling and testing. The literature identifies several barriers and facilitators to genetic testing uptake and family communication about inherited risk that may contribute to this suboptimal uptake rate.

2.2 Barriers and facilitators to genetic testing in people identified as being at-risk through cascade screening

As identified in many studies, the primary motivators for patients to attend *HBOC* genetic counselling is 1) to gain information on personal breast cancer risk, 2) concerns about having a strong family history of *HBOC,* 3) to ascertain risk for family members, and 4) to help in decision making. In some jurisdictions, cost is the primary barrier to accessing counselling, testing or risk reduction interventions. (Wakefiled et al., 2011; Morgan et al., 2009). The non-coverage of genetic counselling in the United States poses a significant barrier to cascade screening, even with laboratory payment assistance programs for genetic testing (Lin et al., 2021). Similarly, in developing countries like Kenya and Brazil the high cost of genetic services is a significant barrier to cascade screening (Zhong et al., 2021; Lourenção et al., 2022).

Breast cancer survivors have reported that the main reason for seeking genetic counselling was to understand their cancer risk and concern about a strong family history of *HBOC.* They recounted a lack of awareness of the *BRCA* pathogenic/likely pathogenic variants (Chin et al., 2005). Other studies have reported the involvement of process barriers and desired outcomes (Hendricks-Sturrup et al., 2021).

Process barriers include consultation wait time, location, duration of counselling sessions and the service provided. Across Canada, 111 clinical geneticists work closely with the genetic counsellors. These specialists are involved in the research of genetic disorders and collaborate with genetic counsellors in offering science-based management directives for the care of individuals with or predisposed to genetic conditions. Recent reports reveal an uneven distribution of 484 genetic counsellors or 1.28 per 100 000 population. Approximately 89% of genetic counsellors reside in Ontario (235), British Colombia (90), Quebec (60) and Alberta (45). On the other hand, there are no genetic counsellors in New Brunswick, the Northwest Territories and Nunavut (Lambert et al., 2021).

The approach to genetic counselling varies from province to province. In provinces with an increased number of genetic counsellors, an initial in-person consultation might be scheduled, with virtual follow-up visits except for a positive genetic test result. In provinces or territories with no genetic counsellors, patients are seen by a genetic counsellor from a neighboring province via telehealth (Sillon et al, 2015). Consultation wait times are quite lengthy in these provinces in comparison to Ontario that has more genetic counsellor and the average time is 1 month to 2 years (Cancer Care Ontario, 2018). In provinces with fewer genetic counsellors like Newfoundland, the wait time for genetic services might be as long as 3 years (Hynes et al., 2020).

Desired outcomes for patients are reduced anxiety, improved genetic knowledge and risk perception (Shiloh et al., 1990; Brian et al., 2000). The manner in which genetic counselling sessions are delivered may reduce adverse psychosocial outcomes (Kent et al., 2000), and individuals who do not attend these sessions may not benefit from counselling services and could suffer unwarranted anxiety and stress over the implications of a positive test result or worry about making seemingly unnecessary treatment decisions. At-risk individuals who do not attend genetic counselling might also be unaware of genetic testing (Gammon et al., 2011).

Barriers and facilitators to genetic testing and management in Lynch syndrome have been classified as person-centered barriers/facilitators, provider barriers/facilitators and healthcare system barriers/facilitators. Person-centered barriers/facilitators are related to risk perception, decision making and motivation towards management. Provider facilitators/barriers are based on perceptions of physician awareness. During a study that was conducted with primary care providers from Alberta and Saskatchewan, evidence showed that family physicians were more likely to misinterpret genetic information and this could negatively impact patients with a personal or family history of a genetic disorder (Skinner et al., 2021). This therefore means that despite an insufficient number of genetic specialists across Canada, delegating genetic consultations to uncertified specialists could lead to lack

of trust and potential adverse health outcomes. Healthcare system barriers/facilitators pertain to continuity of care and service coordination (Watkins et al., 2011). Other reasons for not attending genetic counselling are not finding the time to attend and refusing genetic testing (Wakefield et al., 2011)

It is clear that despite the etiology of cancer, known barriers and facilitators to genetic testing are consistent (Geer et al., 2001; Delikurt et al., 2014; Wakefield et al., 2011; Anderson et al., 2012; Watkins et al., 2011). The decision to undergo genetic testing is also influenced by one's perceived risk, lived experience of seeing cancer in the family and sociodemographic characteristics such as age, marital status and having children. Uptake of genetic counselling is directly related to increasing age, being married and having children (Srinivasan et al., 2020). Concerns about the implications for other family members are a positive motivator for genetic counselling and testing, more so for parents with young children. The impact of family dynamics and communication patterns are strongly related to the uptake of counselling and testing (Forrest et al., 2003; Armstrong et al., 2005; Miller et al., 2005; Peters et al., 2005; Wang., 2005; Silva et al., 2022), underscoring the importance of better understanding attitudes and preferences towards various outreach strategies.

2.3 Whose responsibility is it for sharing risk information?

Under the current practice, it is the responsibility of probands to communicate risk information to relatives. While providers have expressed willingness to assist in the process, it is ultimately the proband who has to inform their relatives, according to the current practice (Young et al., 2020). International guidelines state that confidentiality is not absolute and that healthcare providers may intervene under exceptional circumstances, such as when the proband refuses to share risk information or doubts that risk conversations with family members occurred (Godard et al., 2006). However, healthcare providers should act cautiously under these circumstances since the patient-provider

relationship can be disrupted (Kohut et al., 2007; Falk et al., 2003). Patients have agreed that the healthcare provider should communicate risk information to relatives in cases of complex family dynamics with limitations to specific information that could reveal another relative's identity (Weaver et al., 2015; Pentz et al., 2005).

Many studies have investigated the dissemination of genetic risk information within the family, but there is a paucity of studies that have gathered information on the views of family members on how they would like this information to be communicated (Marleen van den Heuvel et al., 2019; Green et al., 1997). Most patients have reported wanting to be involved in sharing risk information with relatives actively (Pentz et al., 2012; Montgomery et al., 2013; Alegre et al., 2019). However, for family members with a cancer diagnosis, the responsibility of informing other relatives can be emotionally demanding (McGarragle et al., 2019).

2.4 Laws that Determine the Current Practice of Outreach Methods and Duty of Care

In many countries, the family-mediated approach is considered the standard of care in informing individuals of their hereditary cancer risk. In Canada, the implementation of more direct outreach methods has been impeded by provincial and federal privacy laws concerned with disclosing genetic information. The Genetic Non-discrimination Act under Bill S-201 was declared on May 04, 2017. This law prohibits the solicitation of genetic testing or the disclosure of one's genetic information for purposes other than the individual's health care unless the information is released after informed consent (Bill S-201 Clause 2). Exceptions are made for health care providers under limited specific circumstances, such as sharing genetic information with professionals involved in a patient's circle of care and research (Clause 6) (Laws-lois.justice.gc.ca. 2021; Legislative Summary of Bill S-201: An Act to prohibit and prevent genetic discrimination, 2022).

The Supreme Court of Canada rendered judgment on the Genetic Non-Discriminatory Act on July 10, 2020. The court considers it a criminal act for insurance companies and employers to force people to pursue genetic testing before entering into a contract. In addition, the sharing of genetic test results against an individual's consent is also a contravention of this law (Reference re Genetic Non-Discrimination Act, 2020). The court made this decision under the privileges given to the federal government by the Canadian constitution to make criminal laws.

In the United Kingdom, revised regulations permit the disclosure of genetic information once identifying details are maintained privately (Consent and confidentiality in genomic medicine 3rd edition., 2021). Similarly, the amended Privacy Act in Australia dictates that genetic information may be disclosed without consent to prevent serious harm to life, health, and safety once identifying information is concealed. However, genetic health practitioners employed within the public system are not bound by the federal law that governs genetic non-disclosure (Privacy Act 1988; Meggiolaro et al., 2020).

During a recent court ruling over a case related to a genetic condition in the UK, the verdict was given that the healthcare providers were legally obligated to communicate the risk of a hereditary condition to their patient's offspring, which could, in turn, influence reproductive decisions, despite there being no consent. This declaration was based on the CAPARO test, a three-stage test based on foreseeability, proximity and fairness (Foster and Gilbar 2021). Feasibility is concerned with whether carelessness could have resulted in harm; proximity describes the relationship between the parties involved, while fairness establishes whether it is reasonable to determine that duty of care was owed to the claimant (Duty of Care Lecture, 2018). However, the presiding judge acknowledged that the decision made in this instance was case-specific and may not apply to all litigations related to the communication of genetic information.

This recent court ruling in the UK may represent a change in the responsibility of the health care providers towards their patients' relatives who are at risk of a hereditary condition with special consideration in cases of serious threat to a pregnant woman or an unborn child. Within Canada, however, the supreme court's ruling places restrictions on the health care provider's role in the absence of informed consent. In addition, a breach of confidentiality within the Canadian jurisdiction is considered a public health offence. Thus, in Canada, the onus is left to the proband's moral obligation to communicate the risk of heritability to their family members.

In the United States, the Health Insurance Portability and Accountability Act of 1996 (HIPAA) under the Privacy Rule protects against the disclosure of a patient's health record contrary to the flow of health information concerned with that individual's well-being (CDC, 2021). Health Insurance Portability and Accountability Act of 1996; Supreme Court of Florida, 1995) Under HIPAA, approaches to patient-provider risk notification may include supporting the proband in informing their relatives, direct contact of relatives with the proband's consent and provider-to-provider communication that balances the interest of patient confidentiality and the relatives' right and consent to being informed of their inherent cancer risk (Henrikson et al., 2020). Similar laws exist in Switzerland regarding the protection of genetic information unless consent is provided (Regulatory Developments in Genetic Testing in Switzerland - OECD, 2022); however, a physician may request an opinion from the Expert Commission on Human Genetic Testing or request release from medical secrecy if consent is denied and genetic information is requested by family members, a spouse or partner (The Federal Assembly of the Swiss Confederation, 2014, Chapter 3.0, Art 19).

The legislation related to patient confidentiality in other Nordic countries with founder populations is no different despite them having established genetic cancer registries. The Finnish National Cancer Registry became operational in 1953, and the Danish National Cancer Registry which initiated

obligatory notification in 1943 can directly obtain the medical information of persons diagnosed with cancer. Despite this, that physician is prohibited from informing the proband's relatives of their diagnosis if a genetic mutation is diagnosed (Coleman et al., 1992). Also, Iceland has one of the world's most comprehensive genealogical population databases owned by deCode Genetics Inc. (Hakonarson et al., 2003). Genetic information is retained and patients have the right to object to the processing of their personal information (EEA Agreement: Annex XI to Regulation 2016/679, 2018; The Government of Iceland. The Health Ministry, 2014). However, the complexity of this genetic database does not permit that it surpasses the legal boundaries of The Patient's Right Act, which states that a practitioner may be released from confidentiality by the consent of his/her patient (Patients' Rights Act, No. 77/2014). Moreover, deCode, a biopharmaceutical company, is concerned with population-based research on disease outcomes and treatment responses.

International organizations such as The United Nations Educational, Scientific and Cultural Organization (UNESCO), an affiliate of the United Nations (UN) that seeks to build peace through international cooperation in education, science and culture, address the need for confidentiality; however, they maintain a neutral position on the right to inform relatives and how this should be done. The discretion is left to the national legislative bodies (Slokenberga et al., 2019). It is clear that unless under extreme circumstances for some jurisdictions and with no special provision for others, risk communication within the affected family is the proband's responsibility.

2.5 Communication of genetic risk information

The proband who tests positive for a genetic cancer mutation gene is expected to share this information with other family members since it is hoped that risk-reducing strategies will decrease morbidity and mortality among their susceptible relatives. The proband has a critical role in cascade screening because they ultimately initiate the outreach process, genetic counselling and testing of at-risk relatives. Gaining insight into the proband's experience of sharing information on cancer predisposition with relatives is worthwhile, primarily in relation to their concerns about communicating with relatives, level of satisfaction with using a family letter (i.e., standard care), and level of confidence in sharing inherited risk information. The relatives' perspective is also valuable, in particular those who declined genetic counselling.

A review of the literature highlighted several ways in which at-risk family members are informed of their risk of hereditary cancer syndromes. As noted, approaches may be family mediated or by direct contact with a healthcare provider. In the family-mediated approach (FMA), the proband is given a summary letter or family letter to share with their relatives and assist with verbal communication. Direct contact by a healthcare provider is typically limited by legal obligations to maintain confidentiality and protect the proband's privacy (section 2.1). In such cases, a healthcare provider may not share genetic test results with the proband's relatives without consent. Even in Nordic countries (Cancer Society of Finland, 2016) with established cancer registries, the practice is the same and governed by law as was carefully outlined. There are, however, dissimilarities when sharing a deceased patient's genetic test results with their relatives (International Agency for Research on Cancer, 2011). In Australia (Privacy Act 1988; Meggiolaro et al., 2020) and the UK (Royal College of Physicians, 2019), genetic information can be shared with relatives under exceptional circumstances once identifying information such as the proband's name and diagnosis are concealed.

The family-mediated approach is used almost exclusively in Canada and worldwide and remains the standard of care in hereditary cancer risk communication. However, several authors have reported that uptake of genetic counselling is suboptimal using this approach, with only approximately half of at-risk individuals utilizing the services (Hinchcliff et al., 2019; Loader et al., 2002; Lowery et al., 2010). Considering the interfamilial communication barriers associated with this outreach method, the low uptake of genetic counselling by at-risk relatives and the tremendous responsibility placed on probands to communicate risk information, there is justification for exploring outreach and communication preferences and experiences among probands and their at-risk relatives. An improved perspective on preferences for risk communication among affected individuals could contribute to implementing strategies to increase the uptake of genetic counselling and testing.

Communication preferences may be influenced by patient perceptions (Watkins et al., 2011) and characteristics, their informational needs (Wakefiled et al., 2011; Morgan et al., 2009; Chin et al., 2005; Peacock et al., 2006), geographical distance, family dynamics, and spatial and temporal barriers to accessing genetic counselling services (Shiloh et al., 1990; Brian et al., 2000). After carefully reviewing the literature, the remainder of this chapter will focus on the different outreach methods in HBOC and Lynch syndrome and much clearer insight will be gained regarding the most practical combination of methods that could potentially improve cascade screening and testing.

2.6 The Family Mediated Approach

There are barriers associated with risk communication using the family-mediated approach and the shared experience of both probands and relatives with this outreach method has been explored by other investigators. Affected individuals have shared their opinions on who should take on the informant's

role under given circumstances, the premises for communication with the family mediated approach and informational resources besides the family letter that might be helpful.

2.6.1 The proximity of relationships in risk communication and perception

In a study conducted by Katapodi et al. (2017), young breast cancer survivors (YBCS) were stratified according to race as black and white/other. Participants were recruited from the Michigan Cancer Surveillance Program. They were given a baseline survey to identify and recruit relatives to the study who were not previously diagnosed with cancer or had genetic testing. Preference was given to first or second-degree relatives and female relatives. Predictors of willingness to contact relatives included YBCS's characteristics, relatives' characteristics and other predictors based on the theory of planned behaviour such as knowledge and attitudes towards breast cancer, subjective norms, self-efficacy and family support. Black YBCS were more likely to invite younger relatives. Also, black YBCS were significantly more likely to be unwilling to invite relatives that lived within a 50-mile radius to genetic counselling when compared to white/other YBCS. Other reported findings were that those with a previous diagnosis of depression were 16% less likely to contact relatives. YBCS, with an increased number of relatives diagnosed with breast cancer and less motivation to comply with a health care provider's recommendation, were 8% less likely to initiate contact. Black YBCS with larger families were 26% more likely to contact at-risk family members and whose compliance was motivated by other family members were also 6% more likely to invite their relatives.

The study highlights the importance of social support, especially from relatives, in sharing risk information. The response rate among YBCS was 33%. Among the relatives who were invited to participate in the study, the response rate was 51.5% and is similar to the findings from other studies, even though YBCS were restricted to inviting first-degree or second-degree relatives and female

relatives (Hinchcliff et al., 2019; Loader et al., 2002; Lowery et al., 2010). Other investigations have reported probands being more inclined to share their genetic test results with first-degree relatives and female relatives (Fukuzaki et al., 2021; Garcia et al., 2020; Chopra et al., 2017; Fehniger et al., 2013; Nycum et al., 2009; MacDonald et al., 2007). Indeed, the degree of relatedness is a significant predictor of sharing risk information. Stoffel et al., 2008 found that 171 of 174 probands disclosed their genetic result to first-degree relatives, with fewer probands informing distant relatives.

Emotional separation and geographical distance were identified in earlier studies as barriers to cancer risk communication within affected families (Green et al., 1997). Communication with males is challenging because of their lack of interest and because they sometimes do not understand the implications for themselves. Especially in hereditary breast and ovarian cancer families, perceptions that men are not at risk are common, and many families will not be aware of the elevated risks of pancreatic cancer, prostate cancer or melanoma, for example, associated with BRCA2 gene mutation (Suttman et al., 2018; Rauscher., 2018). Family dynamics, the gender of recipients, and cultural concerns are all barriers that make it less likely for distant relatives and male counterparts to be informed of their hereditary cancer risk. Interventions to improve outreach to male relatives may need to be designed using communication explicitly directed to men (Dean et al., 2020). These might include social media educational outreach since men prefer information in bulleted lists or numbers (Dean et al., 2017; Rauscher et al., 2018).

In a randomized study, first-degree relatives of probands who were stratified as being affected or unaffected by breast and ovarian cancer were asked to interpret the proband's test result, share their risk perception, emotional response to being informed and their intention to attend genetic counselling and testing (Daly et al., 2016). Eighty-two percent of those informed by the proband interpreted the results correctly. Their interpretation did not differ by age, gender, or relationship to the proband or

study arm. Males were more likely to remember test results incorrectly. Seventy-four percent reported their risk perception as being average before the test result. Risk perception decreased after the genetic test results were revealed, regardless of whether the result was informative. Relatives of probands with an informative test result experienced more distress when compared to those whose probands had non-informative results. Those whose proband's test results were uninformative were more likely to report not being informed. Fourteen percent of the relatives found the test information very or somewhat difficult to understand. Another thirteen percent found the information very or somewhat upsetting. The intention to attend genetic counselling and testing was highest among relatives whose proband had an informative result. The high degree of relatedness resulted in a significant number of relatives receiving the correct information even though risk perception among relatives was overestimated. These authors reported that an informative test result is more likely to be shared than a non-informative test result. This is a cause for concern as family members may still be at elevated empiric risk due to family history despite uninformative testing and may miss the opportunity for preventative management due to lack of the probands' understanding of who needs to be told and who should not be based on their interpretation of their test result. Relatives of probands with an uninformative test result may be eligible for enhanced screening or preventative interventions based on pedigree risk assessment alone (Huszno et al., 2021; Eccles et al., 2015). Also, as reported in the study conducted by Katapodi et al. (2017), probands were more likely to inform female relatives than male relatives of their test results, and female relatives were more likely to report being informed of test results. The investigator reported no difference between the percentage of probands who shared their genetic information or distress with communication between the two study arms.

2.6.2 The proband's perceived responsibility in risk communication

Patients with a history of cancer maintain a sense of responsibility in ensuring that their relatives are notified. Kohut et al. (2007) surveyed participants from the Ontario Familial Colon Cancer Registry (OFCCR). Ninety-three percent of the participants thought it was their duty to inform their relatives, and 96.2% stated that they would reveal their cancer diagnosis to their family members. Only 18% of the participants indicated that a problematic relationship would prevent them from sharing risk information, and most (84%) indicated that sharing information about the family's risk would be difficult. One reason for not initiating dialogue was simply not having contact information for relatives. The proportion of individuals who would consent to the genetic counsellor releasing risk information to their relatives was high at 73.5%. Another 55.8% of the participants thought the genetic counsellor should contact family members they were not comfortable informing. During content analysis of open responses, twenty-seven of forty participants acknowledged that sharing genetic risk information was necessary. Some respondents believed that their relatives should receive this information from them or the healthcare professional without their consent. This study reveals that individuals with a previous diagnosis of CRC have a strong sense of a duty to warn and an obligation to prevent harm.

The desire for involvement in cancer risk reduction and the inclination toward informing relatives among this population may be accounted for by their affiliation with the cancer registry. However, a qualitative study conducted by Peterson et al. (2003) that included 39 participants with a family history of Lynch syndrome reported that essentially all subjects informed their at-risk relatives of cancer risk. The perceived responsibility of probands for informing relatives is similar in actionable cancer-predisposing syndromes. A prospective cohort study by Alegre and colleagues (Alegre et al., 2019) found no difference in interfamilial disclosure and genetic targeted testing (GTT) for individuals affected by *BRCA1/2* and mismatch repair gene (*MMR*) syndromes: *MLH1, MSH2, MSH6* and *PMS2*.

Interfamilial disclosure for *BRCA1/2* and *MMR* was 66% and 74%, respectively and GGT uptake, 36% and 40%, respectively. Of the 103 probands who participated in this study, 78.6% had a *BRCA1/2* mutation and 21.4% an *MMR* mutation. The mean interfamilial disclosure rate for the population was 68%, and *GGT* uptake among the informed relatives was 37%. Poor perception of the disclosure responsibility and hereditary transmission were barriers to effective communication. However, a new cancer diagnosis within the family would re-open discussions about genetic testing.

2.6.3 Shared experiences with risk communication

As a continuation of a randomized control trial where counselees were randomized to an intervention or control group, a total of 147 cancer genetic counselees and 81 of their at-risk relatives with a personal family history of *HBOC* and Lynch syndrome were interviewed during a descriptive exploratory study about the exchange of genetic information (Hayat Roshanai et al., 2010). The intervention group was equipped with additional information to improve knowledge about genetics, and their personal and family risk of cancer. These participants were assisted in improving the communication of risk information. Sixty percent of the counselees (N=44) from the intervention group and 51% (N=38) from the control group invited at least one at-risk relative to participate in the study. The study explored how counselees shared this information and their relative's reaction. Risk information was delivered to the counselees by a clinical geneticist. The intervention group was provided additional information, while the control group received standard information about their disorder. Ninety percent of the counselees and seventy percent of the relatives were women. A majority of the counselees had a family history of breast cancer. Seventy-three percent of counselees in both groups informed their relatives of the risk of hereditary cancer at the eight-month follow-up, even though 95% and above reported that they intended to at pre-counselling. Ninety-six percent of relatives in the intervention group and 89% from

the control group reported being informed. Furthermore, 90% of relatives from the intervention group and 92 % from the control group reported being informed of the severity of cancer risk.

In this same study, sixty-eight percent of counselees felt neutral or positive about informing their at-risk relatives, 9% expressed negative emotions, and 14% had positive and negative sentiments. Post communication, most counselees felt like their relatives responded positively (61%), 26% reacted neutrally, and 14% reacted negatively with sadness, anxiety, unease and fear. Direct communication (in-person or telephone) was had with 61/70 relatives, whereas six (8%) received this information through a healthcare channel. A significant number of the relatives were satisfied with the information (75% intervention and 67% controls). More than half the relatives in the intervention group felt that they should be informed by a family member and a third by a geneticist. Thirty-three percent of relatives in the control group thought that their family members should inform them, and 47% felt like the geneticist should.

This study's sample size was adequate. However, there were limitations regarding the diversity of the population since more women were included than men, and the high percentage of individuals who reported sharing or receiving risk communication in this study may be overestimated and may not be reflective of the entire population of affected individuals. In addition, higher risk communication among females reported in this study is in keeping with women being more actively involved in the risk communication process (Smith et al., 2015; Koehly et al., 2009; Patenaude et al., 2006; Wilson et al., 2004).

The participants in the intervention group were adequately prepared to communicate with relatives, yet several of them declined. Equal numbers of controls and subjects from the intervention group informed their relatives. There was also no difference between the relatives from the intervention and the control group who reported being informed. This finding suggests that other factors independent

of the proband's confidence or preparedness for sharing risk information impede interfamilial communication with the family-mediated approach. The study also highlighted that ensuring that probands are properly informed improves satisfaction since more relatives from the intervention group were content with the approach.

2.6.4 Expressed opinions on how family members should be informed of their inherent risk

Participants in a longitudinal qualitative study (Song et al., 2010) expressed their opinions on the context in which cancer risk information should be imparted to them. Sharing such information via phone calls or a family letter was not considered appropriate, especially if relatives had no previous knowledge of the condition and since these forms of communication have the potential for causing distress. Face-to-face communication was deemed more acceptable, especially in the setting of a family gathering, which also poses an opportunity to address negative emotional responses. Openness to communication within the family unit was reported to increase with social support. Some respondents felt responsible for informing relatives, mainly the next generation—the desire not to cause adverse psychological responses and social and geographical distance were barriers to information transmission. Similar to an early study conducted by Green et al. (1997), probands were unlikely to contact first or second-degree relatives with whom they had had an altercation or if there was emotional separation due to adoption, divorce, or disputes over the illness or death of a loved one.

Ratnayake et al. explored the preferences among probands who carry *BRCA1/2* pathogenic/likely pathogenic variants for informing their relatives about their risk of carrying the mutations and whether they needed information support while executing this task (Ratnayake et al., 2010). Of the 39 participants whose responses were included in the final analysis, 25 reported a preference for the family letter; ten wished to inform their relatives in person, while three opted for doing this over the phone.

Twenty-six participants preferred to inform their relatives without the involvement of a health professional. In contrast, nine participants reported that they preferred that a health professional assists in the process. Seven participants favoured verbal disclosure before sending and receiving a letter.

Thirty-three participants from the same study preferred that the letter be directly addressed to their relatives, and 12 of the 15 carriers thought their names should be included in the summary letter. Ten participants thought that the letter should be mailed by the proband, while seven thought it should be delivered in person. Several participants thought that the letter should be mailed directly from a health care professional. Others thought that a family member besides the proband could inform distant relatives. Information booklets and pamphlets were the most popular supportive aids among carriers and non-carriers, while DC ROM and an internet website were the least. Participants thought that the letters should have information on carrier status, availability of genetic testing, and risk management options. Fourteen participants required basic information, 11 preferred detailed information, and 13 thought the information should be simplified. First-degree relatives and female relatives were more likely to be informed, consistent with studies noted thus far. Reasons for non-disclosure were geographical distance, emotional distance, concerns for causing anxiety and lack of an appropriate opportunity.

2.6.5 Psychosocial responses to risk communication

Other investigators have reported adverse psychosocial outcomes with the family-mediated approach. These anticipated poor relative responses pose a potential barrier to initiating risk communication and may impede the sharing of the correct information. A qualitative content analysis was utilized to understand the experience of risk communication among 30 women affected by *HBOC* (Seven, et al., 2020). Twenty-nine women first disclosed their results to a first-degree relative. These women felt an

ethical and moral obligation to inform their relatives; however, this sense of responsibility was presaged by worry over family members' emotional responses, especially for children. A few participants maintained a neutral position. One carrier felt that her responsibility was limited to transmitting the information and that it was not extended to aiding her family members with decision-making. Most women were empowered after sharing the information. Women whose relatives expressed guilt, anxiety, lack of interest or denial regretted sharing the information.

Worry is a commonly reported negative psychological response associated with risk communication and genetic test results. Catania et al., 2015 reported that eighty-nine percent of individuals were worried about their risk of disease among the two-hundred and four individuals who sought genetic testing after their relative was diagnosed with breast cancer. Fifty-two percent stated that they felt different due to their personal or family history. Thirty-nine percent reported that their life choices were based on fear of cancer. Eighty-two percent of these subjects felt relieved after attending genetic counselling, and 50% felt positively influenced. These positive outcomes were attributed to the participants being seen in a clinic by a genetic expert. Despite their test result, participants felt less worried or uncertain and maintained favourable attitudes toward the condition. Higher cancer worry was also seen among individuals who contemplated attending counselling sessions and delayed attendance for up to 6 months (Kasting et al., 2019). Follow-up with a genetic counsellor has the advantage of decreasing adverse psychosocial responses, and in-person genetic counselling has been reported as being advantageous in overcoming psychosocial barriers to genetic testing, risk prevention and informational needs related to genetic risk factors (Brédart et al., 2021). These studies underscore the importance of not just risk communication with the approach taken, whether family mediated or direct, but also the importance of attendance to genetic counselling for correct information on risk stratification and preventative management options to be shared, that could help to decrease excessive worry about the possibility of carrying a genetic mutation. The method of informing relatives of their

risk, however, should be one that effectively motivates them to seek counselling given the advantages of doing so.

2.6.6 Desired outcomes of counselling services and the appropriateness of the different informational resources in risk communication

Peacock and colleagues conducted a discrete choice experiment to determine the strength of preference for different aspects of genetic counselling outcomes among women of Ashkenazi Jewish descent with the *BRCA1/2* pathogenic /likely pathogenic variants or a positive family history of these genetic mutations (Peacock et al., 2006). Sixty-seven percent of carriers and sixty-one percent of non-carriers were interested in risk information. Another twenty percent of the respondents ranked surveillance as the most important component of genetic counselling services, 15% opted for preparation for genetic testing, and 5% chose the direction in the decision for genetic testing. When asked about the least significant attributes, 50% chose direction, 20% surveillance, 25% preparation and 5% information. These differences were not significant between carriers and non-carriers. The study highlights the significance of risk information for persons affected by hereditary cancer syndromes since it was given the highest rank. This diversity in expected outcomes for genetic counselling services might be comparable to the disproportionate expectations during risk communication within the affected family.

Similarly, Holloway et al. (2004) conducted a cluster-randomized trial of a novel model of service delivery and standard delivery. Women at risk of *HBOC* randomized to standard care were sent a family history questionnaire, and the information was used to stratify them into low vs. moderate/high risk. Those randomized to novel service were invited to a community-based clinic, and their family history was obtained by a genetic nurse specialist. Whether in the novel service or standard care, women who were at low risk were sent an explanatory letter stating there was no need for further

follow-up. Conversely, those at moderate or high risk met with a genetic consultant and breast surgeon for risk management options.

When patients' expectations of cancer genetic services and satisfaction were compared, 96% of women were satisfied with the duration of the community-based clinic and 89-93% of women with the standard of care. Satisfaction did not differ by education level. Women at low risk were least satisfied with the service given, and sixty-eight percent of them found the information in the letter useful, while 32% thought the opposite. Thirty-six percent of low-risk women wanted additional information, and 38% thought they should have had a clinic appointment. The need for information was significant since 70% of the study's participants rated this very important.

The use of summary letters or family letters may not always be ideal in every situation of communicating risk information, even though this practice remains the standard of care. Cragun et al. (2020) reported the family letter as the most frequently used resource, though other printed materials were more suitable for risk communication. The study was conducted among women with inherited breast cancer susceptibility genes *BRCA1/2*, *PALB2*, *ATM* and *CHEK2* to investigate the usefulness of resources in communicating risk information to family members. Participants either spoke with a genetic counsellor or a health care provider such as an oncologist or a gynecologist. Ninety-three percent of participants who spoke with a genetic counsellor found helpful at least one family communication resource. Commonly used resources were a family letter (38%), printed materials (30%) and web-based information (23%). Participants reported that printed materials were the most helpful in risk communication (68%), followed by family sharing letters (62%) and web-based information (51%). The study reported a higher family communication rate among *BRCA* carriers than carriers of the other breast cancer susceptibility genes. A higher rate of family communication was also associated with high self-efficacy scores and younger participants. At the same time, no significant

associations were found between family communication and perceived hereditary cancer susceptibility, perceived severity or response efficacy. Rates of family communication were higher with untested first-degree and female relatives in this study.

There may be a lack of consistency in the information in the family letter and insufficient or no information on how or if affected relatives may pursue genetic counselling. This was highlighted during a structured content analysis of summary notes of patients with a pathogenic variant seen at the University of Texas MD Anderson Cancer Center (Makhnoon et al., 2021). Patients who underwent testing for two or more of the following breast cancer susceptibility genes and received a result were included in the search: *ATM, BRCA1, CDH1, CHEK2, NBN, NF1, PALB2, PTEN, STK11*and *TP53*. Thirty-three percent of the reviewed notes showed that specific relatives were named by their relationship to the patient, e.g., mother. The benefits of genetic counselling were outlined in 59% of the notes. One hundred summary notes discussed a family letter of which 46.7% specified the intended recipient and the letter's purpose, 9.3% only specified the intended recipient, and 12.1% only specified the purpose of the letter. The implications of the family letter were more likely to be discussed in the summary notes for high-risk patients than for moderate-risk patients (OR=3.24, 95% CI: 1.56- 6.85). The familial implications were also more likely to be discussed in the notes for high-risk patients (OR = 15.05, 95% CI: 5.42–62.58). Eighty-five percent (563/656) of the summary notes stated that a copy of the genetic test result would be given to the patient, with only 12.1% (68/563) of these notes specifying the implications for the relative. Seventeen of these notes gave instructions for scheduling a meeting with a genetic counsellor and 22 for out-of-state relatives to schedule an appointment with a genetic counsellor. It is clear from the published literature that there can be great variability in the information provided in family letters.

2.7 Direct Contact Approach

Given the demonstrated barriers and limited success of the family-mediated approach, the value of other strategies that might improve patient/relative satisfaction or access to testing and prevention should be investigated. Some of the barriers unique to the family-mediated approach may be mitigated with the direct contact approach. These barriers are 1) inconsistent risk communication, 2) emotional and physical separation, 3) concerns about disclosure and confidentiality and 4) concerns about causing worry among relatives. Even though a direct contact approach may overcome these barriers, concerns for privacy and confidentiality limit the universal adaptation of this method. Despite these limitations, studies have explored how the healthcare provider might assume a role in risk communication of genetic cancer risk without breaches of privacy.

Probands, relatives, and spouses of persons at risk of hereditary colorectal cancer were asked about the healthcare provider's role in informing implicated individuals of their inherited risk (Pentz et al., 2005). Respondents suggested that the influence of barriers to communication within the affected family could be minimized if health care providers intervened. Most of the participants believed that their relatives had the right to be privy to genetic risk and management information. Confidentiality concerns were centred around protecting the identity of the proband from some relatives while not preventing risk knowledge from being shared within the family. The support of the healthcare provider was emphasized, especially in informing children of how they may be affected. According to Patenaude and colleagues, mothers raising older children with a more positive attitude towards genetic testing within the pediatric population and who are capable of leading risk communication with their children might want to seek the advice of a healthcare provider before doing so (Patenaude et al., 2016). Some are even willing to share this information with young children but may seek counsel due to fear of inciting anger, resentment or worry. Healthcare providers who are not be fully equipped with the

resources to facilitate hereditary risk discussion with children may provide parents with a guide that may be helpful, and the literature shows that these healthcare providers are more likely to intervene where there is a strong family history of hereditary cancer (Werner-Lin et al., 2018; Hamilton et al., 2018).

A qualitative study was conducted with 12 probands and 46 relatives with HBOC and LS family histories (Henrikson et al., 2021). All participants had a first- or second-degree relative with HBOC, LS or a family history of other affected organs such as the uterus, pancreas or genitourinary involvement. Twenty-eight percent of the study population had a personal history of cancer. The relatives had a mean age of 50, with sixty-two percent female and fifty percent people of colour. The proband population was less diverse than the population of relatives, with participants over 50 years.

The investigators intended to gain feedback on the participants' experience with genetic counselling and testing and their opinion on a direct approach for informing relatives of their risk of a genetic cancer mutation. The feedback was predominantly positive for genetic counselling, and diverse experiences were shared for genetic testing. Some participants felt positive and well supported. Others felt worried, anxious and uncertain about the significance of their test result.

Participants believed that a health system-led direct contact approach would ensure the accuracy of genetic risk information and relatives being contacted promptly. They disclosed that a direct method of outreach should be an organizational collaboration and not the sole responsibility of the attending physician. Despite an acceptance of direct contact programs, the participants thought this should not replace patient-led contact. They cited some characteristics that a direct operation program should possess. These are as follows: consent given to a provider to contact relatives, a three-step contact (initial contact, conversation and finally disclosure) process so as not to violate the relatives' right of not wanting to be informed, establishing communication points, the recommendation for genetic

testing, follow-up steps and supporting patients with resources to assist them with the patient-led contact aspect of communication. Similarly, other investigators have conducted studies pertaining to the direct approach and reported this outreach method as being acceptable with a higher likelihood of the transmission of the correct information on risk association and prevention when compared to the family-mediated approach (Hadfield et al., 2009). The psychological response of relatives when using a direct approach may not be significantly different from that which is associated with the family-mediated approach, or even relatives receiving a phone call from the health care provider (Beri et al., 2018; Bradbury et al., 2018); however, the direct mediated approach (in person disclosure) has a higher potential for increasing the uptake to genetic counselling and testing among relatives (Aktan-Collan et al., 2007; Sermijn et al., 2016).

2.8 Technology Applied to Communication in Genetics

Beyond the expansion of clinical care through virtual platforms, other virtual care models of patient engagement have been explored to increase access and quality of medical care. Patient-facing applications have been used successfully for education and outreach. The popularity of these applications in managing diseases has led to an exploration of their utility in genetics. Disruptive technology revolutionized the healthcare system during the COVID-19 pandemic, and several online platforms have since been developed to accommodate patients' needs. Studies have shown an increased acceptance of telegenetics during this period when compared to before (Mitchell et al., 2005; Brown et al., 2021; Hilgart et al., 2012; Mahon et al., 2020; Mills et al., 202; Ravi et al., 2021; Baudier et al., 2023). These studies also reveal that both patients and genetic counsellors are satisfied with this method of delivery of genetic services, with a higher level of satisfaction among patients. Such findings evidence the advantage of video conferencing in overcoming barriers to accessibility and the need for

more studies to be done to investigate the use of other web-based platforms in outreach to relatives of probands who do not utilize genetic counselling services.

2.8.1 Web-based Platforms for increasing accessibility and uptake of genetic testing

Web-based platforms for outreach to individuals with difficulty accessing in-person genetic counselling due to a remote geographical location is convenient as outlined above. Notably, during these sessions, video conferencing with a genetic specialist provides a high degree of social presence; however, individuals in need of additional social or psychological support and who wish to discuss matters related to complex decision-making may benefit from additional face-to-face consultation (Zilliacus et al., 2010). For this reason, the use of web-based platforms for encouraging uptake of genetic counselling and risk information transmission has been explored in more recent studies for determinations to be made about its utility and potential efficacy in bridging some of the barriers that have already been identified with the family mediated approach (Pollard et al., 2020; Lee et al., 2020; Nycum et al., 2009; Pentz et al., 2005).

In a study conducted by Vogel et al. (2018), women diagnosed with ovarian or fallopian tube cancer were asked to give their opinion on using a mobile health app (mHealth) to encourage genetic counselling (Vogel et al., 2018). The participants noted that using the mobile app would require training, that it should allow for content review at any time, it should be easily shared with others, and the language should not be complex. A platform of this type may serve as an alternative for probands who experience difficulty sharing cancer risk information with relatives. The security features for mHealth were not shared with the participants, nor was information on how the target population would access the publication. A study citing the views from a more diverse population and addressing the outlined shortcomings would be needed to improve one's understanding of not just the proposed

benefit of improving uptake to genetic counselling but also, how the users would be able to securely access the app in a manner that safeguards them from breaches of privacy by outsiders for which its use is not intended.

2.8.2 The use of mobile health apps for increasing self-efficacy in decision making and the varying degree of acceptance of these apps across different studies

Vogel et al. (2019) later conducted a randomized controlled trial to test whether the Mobile Application for Genetic Information on Cancer (mAGIC) would increase self-efficacy in deciding to attend genetic counselling, family communication, knowledge of hereditary cancer and genetic counselling uptake. The information provided in the application was concerned with barriers, motivators and support for triggers to action based on the Fogg Behavior Model (Lawley et al., 2013) . This model puts forward that for someone to perform a targeted behaviour, they must be sufficiently motivated, perform the behaviour and be propelled to perform such behaviour. The Fogg Behavior Model is the foundation for persuasive technology for several conditions (Lawley et al., 2013; Said et al., 2018; Hui et al., 2018; Hashim et al., 2019). The mAGIC purposed to provide details on personal health, genetic counselling preparation and genetic testing. Videos, graphics and motivational messages moderately engaged patients over seven days with a total duration of 70-90 hours. The control group was given written information such as pamphlets. The uptake of genetic counselling for the intervention and the control groups was 54.5% and 38.6%, respectively ($p=0.14$) after three months of the study. When the study was expanded beyond the three months, 75.5% of participants from the intervention group and 68% of the controls self-reported genetic counselling attendance within one year of entering the study. Knowledge was statistically significant for the intervention group and confidence in making genetic counselling appointments and communicating cancer risk with other family members. Over 80% of

the participants were delighted with this deliverable and reported sharing the information with family and friends. Participants found the mobile phone application easy to use and helpful in providing information about ovarian cancer and its treatments. Unfortunately, the link to this app is not shared in this thesis since this was not provided or found during an internet search. Mahmood et al. (2019) found that individuals who used mHealth apps had a higher odds of using this platform in decision making and associated significant factors among users are age, gender, education level, occupational status and having a health care provider who could assist them. The acceptance of a mobile health app among younger and older adults is similar. Richards et al. (2019) found that acceptance should further increase with the progressive development of these apps tailored to the user's needs.

Haas et al. (2021) investigated the conceptual use of a mobile app during prototype testing and in-person interviews. Users created an account and then uploaded genetic test results. They later added the recipients through emails or text messaging by stating their relationship to them. The recipients were then prompted by an email message requesting that they download the ShareDNA app. Interviews were conducted to examine the benefit of the app and for quality assurance purposes. Fourteen participants were interviewed, including two individuals diagnosed with cancer and five with non-cancerous colonic polyps. Thirteen of the fourteen participants felt that they would use the app to share their results with relatives. Email, text messaging and in-person communication were preferred by individuals who lived close to their relatives. Communication using emails was preferred to the other methods since this was a habitual means of efficiently sharing a copy of the test results with many relatives. In addition, participants felt a sense of urgency and responsibility for sharing their test results with younger relatives, especially those with children or at the family planning stage. Twelve of the fourteen participants expressed that an app would be more acceptable among younger individuals than printed materials for risk communication.

The use of an app may facilitate the sharing of genetic risk information among families. Nonetheless, some participants thought that pre-discussion with relatives, whether in-person, via phone calls or by emails, would be necessary to avoid alarm (Haas et al., 2021). A mobile-based app could be a valuable tool to improve cascade screening for pathogenic/likely pathogenic test results. Resources could help encourage relatives to autonomously decide on genetic testing. The burden on the health system would be minimized if a mobile-based app was offered as a tool after genetic counselling that could assist patients in sharing genetic cancer information. This outreach method carries the advantage of overcoming communication barriers and barriers related to time and accessibility since users may gain access at their convenience. It also provides a medium for the sharing of accurate information. For more meaningful assumptions to be made, the applicability of the ShareDNA app should be investigated using a larger sample size.

Jujjavarapu and colleagues conducted another ShareDNA app investigation (Jujjavarapu et al., 2021). Its usability was tested among a population of 13 participants with a positive or negative DNA test result. There were nine male participants and four females and an average age of 67.5. The users were comfortable using the app but expressed concerns about difficulty selecting multiple contacts to share their results with at the same time, the meaning of specific icons and why they were asked to enter their password multiple times during a session. This feature was implemented to increase the security of patient data through encrypted transmission. Patients required minimum information for signing up for an account. The investigators compared ShareDNA to another app, FamGenix (Phillips et al., 2021) since both allowed patients to share their genetic test results through text messaging or email. In both apps, the information was stored on a secure Health Insurance Portability and Accountability Act server with encryption. ShareDNA (figure 2.1) is complimentary, while FamGenix (figure 2.2) is paid and uses genetic risk algorithms to generate pedigrees and to calculate hereditary cancer risk. The links to these apps are found below:

Figure 2.1: ShareDNA app icon.

Note: ShareDNA allows users to store their genetic test results and later share them with contacts from their phone's address book. This app was developed by the University of Washington (2020).

ShareDNA: https://apps.apple.com/us/app/sharedna/id1498271204

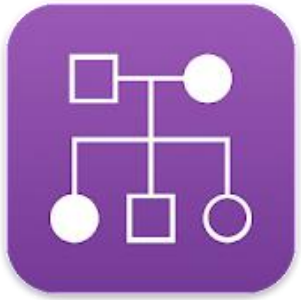


Figure 2.2: FamGenix app icon.

Note: FamGenix helps users track their family health history and determine their risk for inherited disease. Users can invite family members and share health information with them. They can also use the app to find a genetic counsellor to learn more about their risk. FamGenix was developed by FamHis Inc. (2020).

FamGenix: https://apps.apple.com/us/app/famgenix-family-health-history/id1483520084

Similarly, members of Lynch Syndrome International (LSI) and the Collaborative Group of the Americas (CGA) on Inherited Gastrointestinal Cancer were surveyed on the usability of a web-based platform that facilitated an online family mediated approach (Pande et al., 2021). The inclusion of both these groups decreased the effect of selection bias, primarily since LSI provided diversification and represented the actual target population that was not limited to a hospital setting. The survey aimed to introduce this platform to potential users and establish barriers that could be later addressed. Information technology security personnel developed a working prototype for FamilyCONNECT with features that allowed for secure access and the collection of family history by a family history questionnaire after informed consent. Another important feature was the possibility of extensive outreach via the inclusion of the family pedigree by the patient, and if necessary, by a healthcare provider.

The prototype was shared with 170 patients, including 84% mutation carriers, 9% untested, 2% true negatives and 2% unaware of their status. They were primarily women (89%) with a median age of 50 years and of diverse income and educational backgrounds. These participants were engaged for 60-90 minutes. The overall results showed that 87.3% of the participants indicated a willingness to use FamilyCONNECT, 92.6% had faith in the authentication steps, and 98.3 % were willing to share the platform with others. When asked about the timing for discussing genetic test results with family members, 69.6% felt that their relatives should immediately be informed, 30.4% thought it would be appropriate to wait 1-3 months to initiate verbal communication first. In comparison, 6.3% wanted to wait for three months. In a follow-up question, a third of the participants preferred to share genetic cancer risk information with their relatives before FamilyCONNECT, since some individuals thought that an invitation email could be mistaken as phishing or as a scam. On the other hand, 21.4% of index patients wanted their relatives to be connected directly with FamilyCONNECT. Another 44.6% stated they would only share this information with some family members; however, there was no specific

information on which relatives would be selected. The study reported that approximately 30-40% of the participants felt they should be actively involved in communicating genetic cancer information with their relatives.

The genetic services providers who participated in the study revealed that the preoccupation with confidentiality was a principal barrier followed by a lack of institutional resources and structure for outreach and timing (Pande et al., 2021). Fifty percent of them reported that confidentiality would still be an obstacle even with institutionally approved consent to contact relatives. Contacting relatives via email was the most preferred method among these providers (55%). However, 38% preferred conventional mail and 7% opted for a telephone call. They unanimously agreed that FamilyCONNECT would increase the percentage of relatives for genetic counselling and testing. Barriers such as accuracy of the information, difficulty finding time, lack of accessibility and other process barriers may potentially be minimized with FamilyCONNECT, with the same implied advantage for the mobile apps that were previously discussed. However, the efficacy of FamilyCONNECT in increasing cascade screening needs to be further investigated. Evidence needs to be presented for its validity in meeting the informational needs of the intended population while maintaining its users' privacy. Pande et al. (2021) reported on the prototype testing for this app, therefore, it is presumed that future studies with the finished product will focus on the limitations that were recognized.

2.8.3 Continued investigation into the usefulness of telegenetics in genetic risk communication and outreach

An ongoing study explores the roles of a web-based platform in sharing cancer-risk information (Lynch, 2022). This is an observational investigation with an estimated enrollment of 10000 participants expected to culminate in 2048. This study involves a web-based family outreach program

to facilitate self-directed detailed family history and enable interfamilial risk-sharing. In addition, it aims to increase predictive testing and the decision for risk-reducing surgical management options. Given the large study population and the extended time frame, meaningful inferences will be made regarding the practicality and impact of a web-based outreach method for persons affected by hereditary cancer especially with regards to the acceptance for this method with the progression of time. With the universality of telemedicine and other web-based health management modalities, some level of conditioning to the digitalization of healthcare has already been achieved, and there is no doubt that there is an associated convenience. The results from this ongoing observational study may prove greater acceptability of a web-based platform compared to standard care once privacy and confidentiality issues are adequately addressed. The other studies that were discussed previously were limited by factors such as lack of diversification and a small study population (Haas et al., 2021; Jujjavarapu et al., 2021; Pande et al., 2021). Not only should this study overcome said limitations, but it should heighten the awareness of the use of web-based platforms for risk communication among the population of individuals affected by hereditary cancer (given the large study population of 10000 participants). This sort of awareness and perhaps acclimatization is needed since other studies revealed that individuals felt more comfortable with the conventional methods of informing their relatives such as sending emails or post (Haas et al., 2021), despite suboptimal responses from relatives, revealed in their low uptake of genetic counselling (Loader et al., 2002; Lowery et al., 2010; Hinchcliff et al., 2019; Menko et al., 2013; Marleen et al., 2019; O'Neil et al, 2006; Suthers et al., 2006; Hodgson et al., 2014).

2.9 Findings from studies of other hereditary conditions

The dilemmas of family member outreach in hereditary illness extend beyond hereditary cancer. Many other disease states have hereditary causes with preventative intervention, meaning that family communication has value and that research in these diseases can be relevant to hereditary cancer families. A literature search undertaken by Roberts et al. (2018) and colleagues to explore barriers and facilitators to cascade testing for conditions beyond inherited cancers, included several disorders with varying forms of inheritance such as autosomal dominant, X-linked, autosomal recessive and chromosomal translocations. The review focused on barriers, facilitators, cost-effectiveness, implementation issues, registries and policy interventions related to cascade screening. The search was conducted for studies from 1990 to 2017 relevant to the topic of interest. One hundred and twenty-two studies were included with 25 different genetic disorders. The most common genetic disorders that were discussed were Lynch syndrome (N=14, 11.5%), hereditary breast and ovarian cancer (N=16, 13.1%) and familial hypercholesterolemia (N=35, 28.7%). Other disorders were: hereditary hemorrhagic telangiectasia, familial long QT syndrome, genetic mutations in pancreatic cancer, hereditary pancreatitis, hypertrophic cardiomyopathy, hereditary hemochromatosis, familial adenomatous polyposis, Huntington's disease, cystic fibrosis, *MUTHY* associated polyposis, retinoblastoma, paraganglioma syndrome type 1, fragile X syndrome, familial non-syndromal thoracic aortic aneurysms, alpha-thalassemia, beta-thalassemia, primary open-angle glaucoma, hereditary atypical hemolytic uremic syndrome, alpha(1)-antitrypsin deficiency, hemophilia A, and Duchenne muscular dystrophy.

Two studies in the review reported the acceptability of a genetic-registry-based approach, facilitating outreach to at-risk relatives; acceptability was higher among probands with X-linked and chromosomal translocation disorders (Bhatnagar et al., 2000; Blase et al., 2007) compared to disorders with other

patterns of inheritance. The family-mediated approach was reported to have a low or suboptimal uptake in two studies (Bradbury et al., 2008; Breheny et al., 2006). These findings are similar to hereditary cancer studies mentioned previously (Loader et al., 2002; Lowery et al., 2010) (Hinchcliff, et al., 2019; Menko et al., 2013; Marleen et al., 2019; O'Neill et al., 2006) (Suthers et al., 2006; Hodgson et al., 2014). It was also found that supporting the proband in communicating with their relatives did not increase family member attendance at counselling sessions (Montgomery et al., 2016; Hodgson et al., 2015). Though in-person counselling was preferred to online counselling, this did not improve testing uptake (Suthers et al., 2006), similar to findings in the inherited cancer literature (Hadfield et al., 2009; Sermijn et al., 2016). Robertson et al. (2018) also reviewed a UK study that found that cascade screening led by a primary care provider using a direct approach was cost-effective when compared to that done by a specialist (Pears et al., 2014). Cost-effectiveness depended on the condition and treatment; overall, this was declared as acceptable.

Identified barriers from the same scoping review that was conducted by Robertson et al. (2018) were: having little knowledge about cascade screening, limited communication skills, decreased knowledge or interest among primary care providers, negative psychological responses such as anxiety and depression, geographical distance, little communication to male relatives and distant relatives and concerns related to cost. Many of these barriers to family communication were also noted earlier in the hereditary cancer literature (Wakefiled et al., 2011; Morgan et al., 2009; Chin et al., 2005; Peacock et al., 2006; Seven et al., 2020; Catania et al., 2015; Daley et al., 2016; Hinchcliff et al., 2019; Loader et al., 2002; Lowery et al., 2010). The reviewers (Robertson and colleagues) identified areas for further research, such as the need for diversity to attain the generalizability of study findings. For studies that reported on composition by sex (N=33), 30 (25%) of these studies had a predominantly female population. It was also identified that several studies reported similar outcomes, such as genetic test results (N=51, 41.8%). The author reported that investigations into outcomes related to the

sustainability of different outreach methods were lacking. Only two randomized controlled trials (RCT) were included in this review of 122 studies, reflecting the deficiency of investigations of good experimental designs.

A recent randomized controlled trial investigated the effects of a tailored approach on the uptake of genetic counselling compared to the standard family-mediated approach, (van den Heuvel et al., 2021). This study was conducted among individuals with inherited cardiac conditions such as cardiomyopathies and primary arrhythmia syndromes. The intervention engaged the proband in selecting which relatives they wanted to inform and which relatives they thought the genetic counsellor should inform. These probands were also asked to consent to their relatives being sent a family letter irrespective of whether they had already informed them. The letters had a link to a website and did not reveal the probands' identity. For the intervention group, the website provided tailored information about the condition and the procedure for predictive DNA testing. The controls received a link that referred them to a website with general information.

Probands with a pathogenic or likely pathogenic variant, who were the first in their family to visit the cardiogenic outpatient clinic for counselling about genetic testing and who had at least one living adult relative, were invited to participate in the study. In addition, adult first and second-degree relatives were also invited to participate in the study. Ninety-six probands met the inclusion criteria.

Four hundred and eighty-three relatives were eligible for genetic counselling and predictive DNA testing (control: N=252, 52%; intervention: N=231, 48%). Genetic counselling uptake among the controls was 38% and 37% for the intervention group, with no significant difference between the two groups (p=0.973). Twenty-four relatives did not receive a family letter from the genetic counsellor because the proband did not consent to contact them or provide their contact information. More probands from the intervention group were satisfied with the tailored approach (control: 66%,

intervention: 97%; p =0.001) and felt more supported in informing their relatives (control: 66%, intervention: 94%; p=0.003). Despite their high level of satisfaction, a significant number of probands thought that the approach needed improvement (control: 25%; intervention: 86%; $p < 0.001$) and reported feeling pressure to inform their relatives (control: 22%; intervention: 81%; $p < 0.001$). Nine months after the study (T2), only a few relatives visited the websites (control: N=7; intervention: N=2). There was no significant difference between the genetic counselling uptake for both groups. This could be attributed to the fact that few relatives accessed the websites. The authors did not report on the reasons for relatives not visiting these websites and providing this information would be useful in making determinations such as the link being missed or whether patients were satisfied with the information in the family letter and did not see the need to seek more information. The probands' high level of satisfaction with the tailored approach could reflect the interaction had with the genetic counsellor and is similar to the level of satisfaction with a direct contact approach reported in other studies (Henrikson et al., 2021; Aktan-Collan et al., 2007).

Despite the focus of this study being on hereditary cancer syndromes, it was instructive to look at some of the challenges in risk communication that characterize other hereditary disorders. The barriers to communication that were identified for hereditary cancer syndromes were also found in other hereditary conditions. This finding is crucial to making a convincing argument for other methods of communication to be explored, especially as it relates to broaching a direct method of communication with the family-mediated approach. Considering only about 10% of cancers are hereditary, policymakers might not be encouraged to make even minor changes to protocols on patient confidentiality for such a small percentage of the population. However, highlighting the barriers to risk communication with a single approach that affects more than just a tenth of the population, might be sufficient for a complementary method of risk communication to be considered in order for the maximum potential of cascade screening to be achieved.

2.10 Summary of the literature review

The different methods of family member outreach were explored in this literature review. A direct approach to inviting relatives to genetic counselling seems ideal for reaching a greater percentage of the target population, above the approximate 50% that has been reported across the literature with the use of the family-mediated approach. Unfortunately, healthcare providers are unable to contact relatives directly regarding their cancer predisposition due to privacy and confidentiality laws that are in favour of the protection of the probands' medical information.

Some of the shortcomings of the FMA were revealed as personal concerns, specifically, worry over relatives' response to being informed and fear of evoking negative emotional responses among relatives. There is also a tendency for probands to inform relatives with a high degree of relatedness and emotional closeness even though the evidence suggests that distant relatives can also benefit from engaging in cancer screening and opt for preventative management. On the contrary, a positive attribute of the FMA is that there is an opportunity for social support from family members, even though web-based platforms can also offer support through engagement with family members or a community of individuals with a similar condition.

Due to the laws that prohibit the use of a direct outreach method across numerous jurisdictions, its use cannot be adopted or is restricted in a few counties (used only in extreme cases). In search of an alternative to the problem of suboptimal outreach and the unrealized maximum potential for preventative management, implementing an organizational initiative that hybrids the family-mediated approach with a direct contact approach would be instrumental. Notwithstanding, this method should allow for the probands' consent while respecting their privacy. This hybrid approach would especially be effective in outreach to relatives with whom the proband is no longer in contact due to emotional or

physical separation. With a collaborative approach, individuals who experience distress could then benefit from the appropriate follow-up.

Investigations on web-based platforms have revealed an advantage of convenience and this method can complement a direct approach or a family-mediated approach depending on the circumstances. Telegenetics needs to be further explored, especially with diverse levels of satisfaction with the family letter and studies showing a decrease in the generational gap with technological devices such as smartphones. With web-based platforms, individuals are able to choose how much information they require to make an informed decision for genetic counselling and testing.

There is enough evidence to suggest that no single outreach method will solve the suboptimal attendance of at-risk relatives to genetic counselling. The research question and study in this master's thesis add to the literature by establishing which methods might be most acceptable to both probands and at-risk relatives. Outreach preferences will be explored based on clinical and socio-demographic characteristics, allowing a better understanding of variability that could help inform outreach strategies in practice. This investigation is valuable since it includes measuring preferences for conventional outreach methods and incorporates items measuring newer methods that are relatively understudied in the literature. Findings from this study should inform future experimental designs that can measure preferred outreach strategies' impact and feasibility in practice.

CHAPTER 3: METHODS

3.1 Study Design

The current research was a cross-sectional online survey study. The research was approved by the Newfoundland and Labrador Health Research Ethics Board (HREB) on September 10, 2021 (Ref # 2021.154)

3.2 The Target Population

The study targeted participants within Canada above the age of 18 years. The inclusion criteria were: carriers of *BRCA 1* and *2* pathogenic variants, carriers of Lynch syndrome pathogenic variants, previous history or no previous history of cancer, having at least one relative at increased risk of genetic cancer who is eligible for genetic counselling, being a member of a family with an identified *BRCA1/2* or LS mutation who was informed of the family's risk by a proband, having the ability and or willingness to provide informed consent and having the ability to understand English Language.

3.3 Survey Design

An online survey was chosen for this study, given the national focus and pandemic restrictions on face-to-face research interactions during data collection. The questionnaire for this study was informed by the literature (Read et al., 2005; DeMarco et al., 2004; McAllister et al., 2011; Cella et al., 2002) (Nycum et al., 2008), as well as team members' clinical and research design experiences with further input from patient partners. The survey went through many iterations by the committee members and the primary investigator; however, the final consensus on questions was made by the committee

members. Further input was later obtained from patient partners who validated and co-designed the questionnaire by providing feedback on its readability, relevance based on their personal experiences and made suggestions about questions that they thought should be further clarified or included.

Items from the Psychological Adaptation to Genetic Information Scale (PAGIS) (Read et al., 2005) influenced survey items on support, certainty, and self-efficacy. Other items were influenced by the The Multidimensional Impact of Cancer Risk Assessment (MICRA) Questionnaire (Cella et al., 2002), the Genetic Counselling Satisfaction Scale (GCSS) (DeMarco et al., 2004), The Perceived Personal Control (PPC) Questionnaire (McAllister et al., 2011) and elements from the ecological model (Nycum et al., 2008).

The survey included several content areas, including attitudes and beliefs about risk information sharing, preference for different outreach methods, and sociodemographic items (See Appendix H for the survey instrument). Most survey items were measured on a 5-point Likert scale from Strongly Disagree to Strongly Agree, where higher scores indicated greater agreement with attitude and opinion items.

The survey used skip logic to provide items relevant to probands (the 'informers') and their relatives (the 'informed'). This feature changed the question participants could see next based on how that answered the current question. Questions directed to the informers ascertained how confident they felt in sharing risk information, how much they felt supported by their family members, their perceived responsibility to share risk information, whether or not they were worried about sharing the information, distress in relatives upon being informed, and how useful they felt the family letter was in facilitating communication. The relatives who were informed, but did not themselves share hereditary cancer risk information, were asked to share their level of satisfaction with being informed using the family-mediated approach. They were also asked about how much they felt in control based

on their comprehension of the implications of the information (cognitive control), the management of their elevated risk (behavioural control) and about their level of distress. The primary outcome variables measured for all respondents was their preference for three different outreach methods:

i. Preference for the family-mediated approach (e.g., the use of the family letter provided by a genetics service),

ii. Preference for active contact taken by a healthcare provider with or without a follow-up email or phone call, and

iii. Preference for communicating inherited cancer risk using a website or a mobile health application.

Potential variables related to outreach preferences were also measured and included demographic and clinical items. These included: age, parity, time since cancer diagnosis, number of first-degree relatives informed, number of second-degree relatives informed, level of perceived hereditary cancer risk, genetic test result, type of cancer diagnosis, marital status, education, gender, rural/urban location of residence, and income.

3.4 Survey piloting

Piloting was carried out to check for readability, to shape the content and structure of the survey, and to assess for the ease of completion related to the length of the survey. Piloting was done with three patients known to the clinicians on the research team and in their circle of care, representatives from Ovarian Cancer Canada known to the team, and multiple iterative reviews by study team members. Minor changes were made to the survey following reviews. For example, one patient suggested an additional option for question 10.

"For Question number 10, could a response of Unsure / Can't recall be added. For example, I was informed regarding Lynch Syndrome in 1992/1993. Certainly, some persons may not recall after so many years".

Upon reflection and team member feedback, 'prefer not to answer/don't know' was added as a response option to several other survey items as well.

Other patients suggested the survey content areas were comprehensive, reflected the issues they faced in communicating with family members about inherited risk and had no additional suggestions. The review from Ovarian Cancer Canada and study team members also resulted in some minor changes. For example, the former reviewer asked:

Q36 – Are you purposely being vague about the definition of low-middle-high? If not, should define what you mean by that.

36. In what income bracket would you put yourself?

- ○ *Low*
- ○ *Middle*
- ○ *High*

The income item was modified to use a range of income amounts instead, as used by Statistics Canada (Canadian Community Health Survey - Annual component (CCHS) - 2021).

From a research team member:

Section 2 heading – suggest you remove "The family mediated approach" – this is what we, as researchers, call this approach. However, if someone thinks this is some kind of official labelling that they didn't get, then they may feel the section does not apply to them. I assume there is some kind of skip pattern happening so that participants move on directly to the next relevant question if they did not get a family letter. (Somehow, I prefer "a family letter" to "the family letter" – a bit softer?)

Upon review, some survey headings were removed and skip logic was used in Qualtrics XM (Qualtrics, Provo, UT) to ensure the right items were being asked of either the informers or the informed. The skip logic feature created a custom path through the survey so that the survey items varied based on whether the participant answered the survey items from the perspective of an informer (proband) or the informed (relative). The background and consent opening information of the survey and the final demographic items were available to all respondents.

3.5 Survey Administration and Recruitment

The cross-sectional survey was designed and distributed online across Canada on the Qualtrics XM Platform (Qualtrics, Provo, UT); the online survey tool approved at Memorial University. The survey was shared with individuals affected by mutations causing LS and HBOC. Relatives who were informed, but did not themselves share hereditary cancer risk information with other family members, were also asked to share their experiences.

3.5.1 Informed consent

Information regarding the study's objectives, purpose and all elements of informed consent were provided at the beginning of the survey. Participants were asked to indicate their eligibility for the

survey through the online platform and a click button to consent to participate before proceeding. Participants were invited to complete the online survey, lasting about 15-20 minutes at a time convenient to them. No identifying information was collected from respondents.

3.5.2 Recruitment

The survey advert and link were shared widely across Canada through multiple networks starting in October 2021 and into early January 2022.

Patients attending the NL Hereditary Cancer Prevention clinic and the BC Gynecologic Cancer Survivorship Clinic were invited to join the study by their physician (team member Dr. Lesa Dawson), and interested participants were encouraged to share study information with relatives. Team members are also members of the Canadian Cancer Genomics Community of Practice. This group was established in 2020 and comprises Canadian hereditary cancer providers (geneticists, genetic counsellors, oncologists), patients and researchers. A short presentation about the study was made to group members during a regular meeting in September 2021 by team member Dr. Etchegary. The online communication platform used by that group is called Basecamp, with 164 members subscribed to receive email alerts. The study ad was posted to Basecamp's message board on October 18, 2021, with follow-up messages sent one and two weeks later.

In Newfoundland, the survey link was shared with three other oncologists who care for patients affected by hereditary cancers and the cancer genetic counsellor at the Provincial Medical Genetics Program. It was also shared with a prominent LS researcher and the SPOR NL Support Unit. They posted the ad to their social media site for sharing with over 200 subscribers in NL (patients, providers, healthcare system decision-makers and students).

The survey ad was shared with the Canadian Association of Genetic Counsellors (CAGC) who sent emails to genetic specialist across Canada. The ad was also sent to social media group administrators, providers, researchers and patient partners within team members' networks outside of NL. For example, a geneticist in BC, a genomics researcher in ON, and several patient partners. These partners are themselves affected by hereditary cancers and are current or former research patient partners of study team members. After approval was obtained from group administrators, the ad and link to the survey were posted by the following Facebook and Instagram groups: the Jacqueline Rush Foundation, lynch syndrome spouses, breastcancersoc, coloncanada, *BRCA* Sisterhood Canada, *BRCA1* And *BRCA2* GENETIC BREAST CANCER AND OVARIAN GENE, *MSH2* Lynch Syndrome Support Group, Lynch syndrome, Lynch Syndrome Support Group/LSI, BCW in action. Several surgeons and gastroenterologists in the Peel region of Ontario were approached by the primary investigator and asked to share the survey with their patients who matched the criteria.

3.6 Power and Sample size

Very little literature has described preferences for various methods of communicating hereditary cancer risk and it was not possible to use prior work to calculate an effect size. For this reason, a medium effect size was chosen for power calculations (as suggested by Cohen 1992).

Power analysis for a two-tailed Mann-Whitney U test indicated that the minimum sample size to yield a statistical power of at least 0.8 with an alpha of 0.05 at the 95% confidence limit, equal group sizes, and a medium effect size ($d = 0.5$) is 134 (Faul et al., 2009). For a chi-square goodness-of-fit test with 2 degrees of freedom, the minimum sample size to achieve a statistical power of 0.8 with an alpha of 0.05 and a medium effect size ($w = 0.3$) is 88. Computational methods for analyzing power for a Kruskal-Wallis test are mostly unavailable, anda medium effect size ($p = 0.3$) for a two-tailed

Spearman correlation test indicated that the minimum sample size to yield a statistical power of at least 0.8 with an alpha of 0.05 is 82. The letters *d*, *w* and *p* denominate the effect size index for the Mann-Whitney U test, the Kruskal-Wallis test and the two-tailed Spearman correlation, respectively.

Accounting for missing data that may result from incomplete questionnaires, the adjusted sample size calculations are as follows (Ap et al., 2016):

For the Mann-Whitney U test: $N^1 = \frac{N}{1-q} = \frac{135}{1-0.1} = 150$

For the chi-square goodness-of-fit test: $N^1 = \frac{N}{1-q} = \frac{88}{1-0.1} = 98$

For the Spearman correlation test: $N^1 = \frac{N}{1-q} = \frac{82}{1-0.1} = 92$ (rounded up to the nearest even number)

Where q is conventionally taken as 10%.

3.7 Data management

Survey data from Qualtrics XM (Qualtrics, Provo, UT) was imported into IBM Statistical Package for Social Science (SPSS) Statistics 27 (IBM Corp., 2020) and stored electronically in a password-protected data file on a password-protected computer of the primary investigator (Kimberly Burke). No personal identifying information was collected from survey respondents.

3.8 Data Cleaning and Coding

Multiple steps were taken to ensure that data were accurately entered into SPSS. Frequency checks for each survey item were first run to ensure no data point was outside of the response scale options. No data was found outside of range. In addition to frequency checks, data cleaning also included a 10% random data entry sample check. This resulted in a 0% data entry error.

Some of the categories for the nominal demographic variables, marital status, level of education and annual income, were aggregated in Table 1 to account for very small cell sizes in some of the categories (e.g., n=1 or 2). For example, for marital status, married and living common-law were combined. Similarly for annual income, the $ 50, 000 to less than $ 90, 000 income range incorporated an income of $ 50, 000 to less than $ 60, 000, $ 60, 000 to less than $70, 000, $ 70, 000 to less than $ 80, 000 and $ 80, 000 to less than $ 90, 000. Provinces were grouped according to regions in the following manner: Prairie Provinces (Manitoba, Saskatchewan, Alberta), Western Provinces (British Colombia), Atlantic Provinces (Newfoundland, New Brunswick, Prince Edward Island and Nova Scotia) and Central Provinces (Ontario and Quebec).

The "I prefer not to say" responses were included in descriptive results in Table 1, but those with a frequency less than two were not included in the statistical analyses. The non-binary/third gender category (Table 1) was also removed from further analysis as only one participant fell in this category and comparing their responses would not have been statistically or clinically meaningful with an n of 1. These responses were coded as -99 (labelled as missing data). Finally, one informer (proband) was not seen by a genetic specialist and reported having a negative test result. This informer was removed from the table of clinical characteristics (table 2) and from the final analysis since they completed less than 20% of the survey.

The responses "A mutation other than *BRCA 1* and *BRCA 2* that causes hereditary breast and ovarian cancer (HBOC)" and "Other genetic test results" from Table 2 were later removed from the statistical analysis since they did not meet eligibility criteria.

3.9 Data Analysis

Survey data were analyzed using SPSS Software 27.0 (IBM Corp., 2020). Descriptive statistics were reported for all survey items, including demographic and self-reported clinical, psychosocial and outcome items. Open-ended questions were categorized as "other" during the descriptive analysis. They were subdivided based on similarity, and their frequencies were tabulated while additional explanations was provided in the results section.

The Mann-Whitney U test (Non-Parametric Independent Samples t-Test) was used to assess for differences between the informers who received a family letter and those who did not receive a family letter. No differences were found, so these items were combined in Table 4. The items on preferences (the primary outcome) were not combined (Table 6).

Univariate analyses examining the factors that influence preference for family member outreach were conducted. Analyses between the association of clinical, social, and demographic factors and outreach preference among the informers (probands) were determined using the Mann-Whitney U test for binomial variables and the Kruskal Wallis test for variables with more than two categories. An alpha value of 0.05 or less was considered statistically significant.

The Kruskal-Wallis test compared the number of times a category from one variable ranked higher than another category of the same variable. Rank 1 is used for the lowest score, rank 2 for the next lowest score, and so on. If more than one category had the same score, they were assigned the same

ranking (Conover et al., 1981). SPSS Software 27.0 (IBM Corp., 2020) executed the analysis by adding the ranks and dividing them by the number of scores. Once the data were ranked, calculations were carried out on the ranks to calculate the chi-squared (χ^2) test statistic, which was then used compute a *p*-value.

If the result from the Kruskal–Wallis tests were significant, post-hoc analyses were conducted using the Dunn test to determine if there were significant differences between the subgroups and the mean ranks and medians were reported. The determination of the rank levels for the Mann-Whitney U test was similar to that of the Kruskal-Wallis test, however, calculations were conducted using the ranks and the scores to ascertain the *U* statistic. The *U* statistic was used to obtain the *p*-value by computing the *z*-score (Conover et al., 1981).

Ordinal variables that were dependent on each other were further analyzed using the Spearman rank correlation. In Spearman rank correlation, correlation coefficients, $r_{s,}$ vary from 0 (no relationship) to 1 (perfect linear relationship) or -1 (perfect negative linear relationship). Positive coefficients indicate a direct relationship, indicating that as one variable increases, the other variable also increases. Negative correlation coefficients indicate an indirect relationship, indicating that as one variable increases, the other variable decreases (Cohen et al., 1988; Conover et al., 1981). Cohen's standard was used to evaluate the correlation coefficient, where 0.10 to .29 indicated a weak association between the two ordinal variables, 0.30 to 0.49 indicated a moderate association, and 0.50 or greater indicated a strong association (Cohen et al., 1988).

Further analysis was not conducted at the multivariate level due to low sample size and power and an insufficient number of observations per parameter.

CHAPTER 4: RESULTS

4.1 Section I – Descriptive Statistics

4.1.1 Survey response rate

One hundred and nineteen survey responses were initiated, and of these, 108 eligible participants indicated the perspective from which they would respond to the survey questions (informer, N=58; informed, N=50). Ultimately, 96 total respondents completed the surveys with variable response rates to different survey items. While multiple methods were used for advertising the survey, it is unknown how many people ultimately saw the survey advertisement and chose to participate. Organizations and individual contacts of the study team who agreed to help advertise the study did not retain logs of patient contact, nor was there any way to know if survey respondents shared the survey link with eligible family members. Ultimately, the survey response rate cannot be calculated.

4.1.2 Respondent demographics

The demographic characteristics of those who participated in the survey are summarized in Table 1. There was a predominance of female participants (informers=96%, informed=94%). Most study participants were above the age of 45 (mean age of the informers =56.89 ± 16.033; mean age of the informed=48.21 ± 11.362) and married with children. In this study, the informers were also called the proband and the informed, the relatives.

Table 4.1: Demographic characteristics of the study's participants.

DEMOGRAPHIC CHARACTERISTICS	Proband n (%)	Relatives n (%)
Total	46	48
Age		
34 and younger	3 (6.5)	4 (8.3)
35-44	5 (10.9)	18 (37.5)
45-54	10 (21.7)	14 (29.2)
55 and older	28 (60.9)	12(25)
Mean (SD)	56.89 (16.033)	48.21 (11.362)
Marital status		
Single- never married	1 (2.2)	4 (8.3)
Married/Living common-law	39 (84.8)	39 (81.3)
Divorced/Separated/Widowed	6 (13.0)	4 (8.3)
I prefer not to say	0	1 (2.1)
Number of children		
0	6 (13.0)	11 (22.9)
1-2	30 (65.2)	29 (60.4)
3 and more	10 (21.7)	8 (16.7)
Mean (SD)	2.09 (0.590)	1.93 (0.633)
Gender		
Male	2 (4.3)	2 (4)
female	44 (95.7)	45 (94)
Non-binary / third gender	0	1 (2)
Highest educational level		
High school diploma or less	7 (15.2)	6 (12.8)
Trade or college diploma	15 (32.6)	19 (40.4)
University, undergraduate degree	12 (26.1)	11 (23.4)
University graduate degree	12 (26.1)	11 (23.4)
Missing	0	1
Annual household income		
$ 49, 000 or less	4 (8.9)	3 (6.3)
$ 50, 000 to less than $ 90, 000	9 (20.0)	11 (22.9)
$ 90, 000 to less than $ 150, 000	11 (24.4)	17 (35.4)
$ 150, 000 and over	12 (26.7)	10 (20.8)
I prefer not to say	9 (20.0)	7 (14.6)
Province or territory do you live?		
Prairie Provinces (MB, SK, AB)	6 (13.0)	8 (16.7)
Western Region (BC)	12 (26.1)	10 (20.8)
Atlantic Provinces (NL, NB, PE, NS)	8 (17.4)	17 (35.4)
Central Provinces (QC, ON)	20 (43.5)	13 (28.1)
Urban or rural dwelling		
Small population centre	6 (13.3)	10 (21)
Medium population centre	5 (11.1)	13 (27)
Large urban population centre	27 (60.0)	23 (48)
Rural area	7 (15.6)	2 (4)
I prefer not to say	0	0

The self-reported clinical characteristics of respondents are summarized in Table 2. Individuals were asked about their perceived cancer risk before seeing a genetic specialist, their genetic test result, and whether they were diagnosed with cancer. Ten informers (probands) reported being carriers of the *BRCA1* mutation, including one who tested positive for both the *BRCA1* mutation and the *MUTYH* mutation. Nineteen informers carried the *BRCA2* gene mutation, including one participant with both the *BRCA2* and *ATM* mutation. One informer reported carrying both the *BRCA1* and *BRCA2* mutation and another, the *RAD51C* genetic mutation. Two other informers reported having a gene besides *BRCA1/2* that caused hereditary breast and ovarian cancer and 19 informers were carriers of mutations that cause Lynch syndrome (Table 2). Most respondents reported perceiving their cancer risk as moderate or high before being seen by genetics specialists, 68% of the informers and over 56% of the informed (Table 2).

Thirty-one informers reported being diagnosed with cancer. There were two informers with a diagnosis of both endometrial and colon cancer. One informer was diagnosed with endometrial, colon and thyroid cancer (Table 2). Cancers that were categorized as 'other' were thyroid cancer (n=1), adrenal cancer (n=1) and thyroid cancer (n=1). The frequency of cancer diagnoses among the informers was 37. Twenty-three informers indicated they were never diagnosed with cancer.

Table 4.2: Clinical characteristics of survey respondents

CLINICAL CHARACTERISTICS	INFORMER/PROBAND n (%)	RELATIVES/INFORMED n (%)
Perceived cancer risk		
High	26 (49.1)	12 (24)
Moderate	10 (18.9)	16 (32)
Low	11 (20.8)	10 (20)
Unknown/insufficient information	6 (11.3)	9 (18)
I was not seen by a genetic specialist	-	3 (6)
TOTAL	53 (51.46)	50 (48.54)
Genetic test result		
BRCA1	10 (19.2)	12 (24)
BRCA2	19 (36.5)	26 (52)
A mutation that causes Lynch syndrome	19 (36.5)	7 (14)
I did not have genetic testing	-	3 (6)
My BRCA1/2 or other mutation causing *HBOC* was negative	-	0
Other genetic test results	2 (3.9)	2 (4)
A mutation other than *BRCA1* or *BRCA2* that causes hereditary breast and ovarian cancer (HBOC)	2 (3.9)	0
TOTAL	52 (50.98)	50(49.02)
Cancer diagnosis		
Yes	31 (59.6)	9 (18)
No	21 (40.4)	41 (82)
TOTAL	52 (50.98)	50(49.02)
Number of years since the first diagnosis	Mean=2.65; SD=0.915	Mean=1.63; SD=0.518
Cancer that was diagnosed		
Breast cancer	13 (35.1)	5 (55.6)
Ovarian cancer	5 (13.5)	0
Endometrial cancer	7 (18.9)	2 (22.2)
Colon cancer	9 (24.3)	2 (22.2)
Other	3 (8.1)	0
TOTAL	37	9

Twenty-four percent of the informed (relatives) reported carrying a *BRCA1* mutation, 52 % a *BRCA2* mutation and 14 % reported carrying a mutation that causes Lynch syndrome. Other reported genetic mutations among the informed were the *PMS* gene and the *RAD 51C* genes. Nine of the informed reported a previous or current cancer diagnosis. Breast cancer was the most frequently diagnosed among this group (55.6%). Among the informed, other reported cancer diagnoses were colon cancer and endometrial cancer (Table 2).

4.1.3 Experiences with the family letter from the probands' perspective

The informers were asked if they received a family letter to share with their relatives to facilitate risk communication. Twenty-eight informers (53.8%) reported receiving a family letter, eighteen (34.6%) reported that they did not, while six (11.5%) were unable to recall. Some informers who selected "no" or "I do not recall" to this question explained that they were given an ancestry form, informational material, testing protocol information, their own genetic test result, or that of a relative. In open comments, one informer noted being given printed materials and stated that their aunt, who lived in another province and tested positive for a genetic mutation, was given a family letter.

Twenty-six informers who received a family letter noted with which side of their family they shared the letter or information. Nineteen (73.1%) shared the letter or information with relatives on their mother's side, and seven (26.9%) shared it with relatives on their father's side. They shared the letter with a total of twenty-eight first-degree relatives (mean=4.50 ±3.687) and twenty-eight-second-degree relatives (mean=3.71 ±4.438).

On the other hand, of 19 of the informers who did not receive a family letter, eight of them (44.4%) shared the information with relatives on their mother's side, and ten (55.6%) shared the information with relatives on their father's side. One did not respond to this question.

The informers given a family letter were asked about their perceived responsibility to communicate hereditary cancer information with their relatives and their experience with this process (risk communication using the family letter). The results are summarized in Table 3.

Table 4.3: Probands' perceived responsibility and experience in risk communication while using the family letter (standard care)

THE INFORMERS' RESPONSIBILITY IN HEREDITARY CANCER RISK COMMUNICATION AND SHARED EXPERIENCES	THE RESPONSE FREQUENCY FOR INFORMERS GIVEN A FAMILY LETTER					
	[1]Disagree strongly (%)	[2]Disagree somewhat (%)	[3]Uncertain (%)	[4]Agree somewhat (%)	[5]Agree strongly (%)	Mean ± Standard deviation
I do not think that I should have been the one to inform my relatives or share the information with them (N=29)	13 (44.8)	5 (17.2)	7 (24.1)	3 (10.3)	1 (3.4)	2.10 ±1.205
I do not believe it was my responsibility but I had no problem doing it (N=29)	9 (31)	6 (20.7)	3 (10.3)	7 (24.1)	4 (13.8)	2.69 ±1.491
I felt responsible; however, I would have liked the assistance of someone else i.e., family or health care provider (N=29)	4 (13.8)	4 (13.8)	4 (13.8)	11 (37.9)	6 (20.7)	3.38 ±1.347
I felt responsible for informing my children, siblings, parents and spouse (N=30)	0	1 (3.3)	1 (3.3)	2 (6.7)	26 (86.7)	4.77 ±0.679
I felt responsible for informing my aunts, uncles, nieces, grandchildren and grandparents (N=30)	1 (3.3)	4 (13.3)	1 (3.3)	9 (30.0)	15 (50.0)	4.10 ±1.185
I found the letter very useful in helping me to communicate the risk of hereditary cancer to my relatives (N=28)	0	0	5 (17.9)	10 (35.7)	13 (46.4)	4.29 ±0.763
The letter helped me to communicate with my relatives about hereditary cancer risk: however, some of my relative's asked questions that the letter couldn't explain (N=28)	2 (7.1)	7 (25.0)	8 (28.6)	8 (28.6)	3 (10.7)	3.11 ±1.133
I was able to read and understand what was in the letter, but it was hard for me to explain to my relatives in my own words (N=28)	9 (32.1)	8 (28.6)	1 (3.6)	7 (25)	3 (10.7)	2.54 ±1.453
I thought that the letter's content should have been in a more simplified form or language(N=28)	8 (28.6)	8 (28.6)	8 (28.6)	3 (10.7)	1 (3.6)	2.32 ±1.124
I felt satisfied with communicating with my relatives using the family letter about the risk of genetic cancer (N=28)	1 (3.6)	3 (10.7)	5 (17.9)	9 (32.1)	10 (35.7)	3.86 ±1.145
I was satisfied with my relative's response to me communicating cancer risk and sharing the summary letter (N=28)	1 (3.6)	6 (21.4)	6 (21.4)	9 (32.1)	6 (21.4)	3.46 ±1.170
Communicating genetic information was complex for me (N=30)	7 (23.3)	13 (43.3)	1 (3.3)	7 (23.3)	2 (6.7)	2.47 ±1.279
I did not feel confident in passing on the information about cancer risk because I did not feel like I could correctly communicate the information (N=30)	13 (43.3)	11 (36.7)	1 (3.3)	5 (16.7)	0	1.93 ±1.081
I did not feel confident in passing on this information because of the fear of causing distress among my relatives (N=30)	9 (30)	10 (33.3)	1 (3.3)	7 (23.3)	3 (10)	2.50 ±1.408

1 felt confident that the letter explained to my relatives what having the mutation meant (N=29)	1 (3.4)	1 (3.4)	7 (24.1)	10 (34.5)	10 (34.5)	3.93 ±1.033
I felt confident that the letter helped my relatives to understand the importance of genetic testing (N=29)	0	3 (10.3)	10 (34.3)	8 (27.6)	8 (27.6)	3.72 ±0.996
I felt confident that my relatives understood the implications of the information in the family letter for their own health (N=29)	0	5 (17.2)	8 (27.6)	9 (31.0)	7 (24.1)	3.62 ±1.049

*The responses on the Likert scale are numbered 1-5, with 5 having the highest rank.

These informers felt responsible for informing their relatives, especially first-degree relatives (93.4%). While 66.6% of informers who were given a family letter (strongly) disagreed that communicating genetic information was complex for them, almost two-thirds (58.6%) also indicated they would have liked the assistance of someone (a healthcare provider or family member) through the process. However, most informers did agree that the family letter was helpful (82.1% agreeing or strongly agreeing, M=4.29). In addition, informers felt confident that the letter explained to their relatives what having the mutation meant (69% agreed, M=3.93) and were satisfied with communicating using this method (67.8% agreed, M=3.86).

All informers (whether given a family letter or not) were asked to share their perception of their relatives' response to them during risk communication. In addition, these informers were also asked to share their experience with communicating with their relatives and their opinion on sharing their personal information with their relatives. The results from both groups (given a family letter or not) were combined and are summarized in Table 4. Note that some informers who were unable to recall being given a family letter responded to some of these items from the perspective of one who was given a letter to share with their relatives (Table 4).

These informers reported feeling that their relatives were grateful to receive hereditary risk information (64.6%) (Table 4). However, they also worried that their relatives would become anxious or depressed after being informed of their risk of hereditary cancer (62.6%).

Table 4.4: The shared experience of the informers who communicated hereditary cancer risk with their relatives.

EXPERIENCE WITH COMMUNICATING WITH RELATIVES	RESPONSE FREQUENCIES AMONG THE PROBANDS						
	[1]Disagree strongly (%)	[2]Disagree somewhat (%)	[3]Uncertain (%)	[4]Agree somewhat (%)	[5]Agree strongly (%)	Mean	Standard deviation
It was hard for me to talk to my relatives about the risk of hereditary cancer (N=48)	15 (31.3)	11 (22.9)	2 (4.2)	14 (29.2)	6 (12.5)	2.69	1.490
Some of my relatives were angry/upset (N=48)	15 (31.3)	2 (4.2)	7 (14.6)	19 (39.6)	5 (10.4)	2.94	1.465
Some of my relatives were uninterested when I shared the information about our family's inherited risk (N=48)	7 (14.6)	8 (16.7)	4 (8.3)	17 (35.4)	12 (25.0)	3.40	1.410
In general, my relatives were grateful for the information about our family's inherited cancer risk (N=48)	4 (8.3)	6 (12.5)	7 (14.6)	19 (39.6)	12 (25.0)	3.60	1.233
My relatives encouraged me to share the information with other relatives (N=48)	10 (20.8)	4 (8.3)	7 (14.6)	18 (37.5)	9 (18.8)	3.25	1.422
I worried that communicating the risk of hereditary cancer would bring about conflict in the family (N=48)	21 (43.8)	6 (12.5)	7 (14.6)	12 (25.0)	2 (4.2)	2.33	1.374
I worried that my family would become anxious or depressed after receiving the information (N=48)	3 (6.3)	10 (20.8)	5 (10.4)	21 (43.8)	9 (18.8)	3.48	1.203
I was concerned about sharing personal medical information with other family members (confidentiality) (N=48)	29 (60.4)	9 (18.8)	3 (6.3)	5 (10.4)	2 (4.2)	1.79	1.209
I worried that my relatives would not want me to know about their increased risk of cancer (N=48)	22 (45.8)	5 (10.4)	12 (25.0)	9 (18.8)	0	2.17	1.209
It would be acceptable to me if my name was shared with my relatives irrespective of the method that is used to communicate hereditary cancer risk information to them (N=48)	2 (4.2)	2 (4.2)	5 (10.4)	11 (22.9)	28 (58.3)	4.27	1.086
It would be acceptable to me if my genetic result was shared with my relatives regardless of how they are informed of their cancer risk (N=48)	2 (4.2)	2 (4.2)	4 (8.3)	14 (29.2)	26 (54.2)	4.25	1.062
It would be acceptable to me if my cancer diagnosis (if applicable) was shared with my relatives when they are being informed of their hereditary cancer risk (N=48)	1 (2.1)	0	6 (12.5)	12 (25.0)	29 (60.4)	4.42	0.871

*The responses on the Likert scale are numbered 1-5, with 5 having the highest rank.

Table 4 displays combined responses for the entire group of informers, both those who indicated they received a family letter and those who did not. However, closer inspection of the data revealed some slight differences in opinion between these two groups of informers that was explored further statistically. Differences were noted in the question items between informers (probands) who were given a family letter and those who were not given a family letter for acceptance in sharing the probands' name, genetic test results and cancer diagnosis with their relatives. It was more acceptable for probands who received a family letter to share their name (n=24), genetic test results (n=28) and cancer diagnoses (n=25) with their relatives than for those who indicated they were not given a letter (n=15, n=14, n=16 respectively). These frequencies are displayed in figures 1-3. A two-tailed Mann-Whitney test was conducted to examine whether the differences were statistically significant. These results are summarized in Table 5. The results of the two-tailed Mann-Whitney *U* test were not significant, based on an alpha value of 0.05. This suggests that the distribution of informers who found it acceptable to share their personal information was not significantly different between the informers who received a family letter and those who did not receive a family letter, with notably high acceptance of all informers for sharing their personal information with relatives (Figures 4.1a, 4.1b and 4.1c).

Figure 4.1a: Acceptability for sharing the proband's name with their relatives.

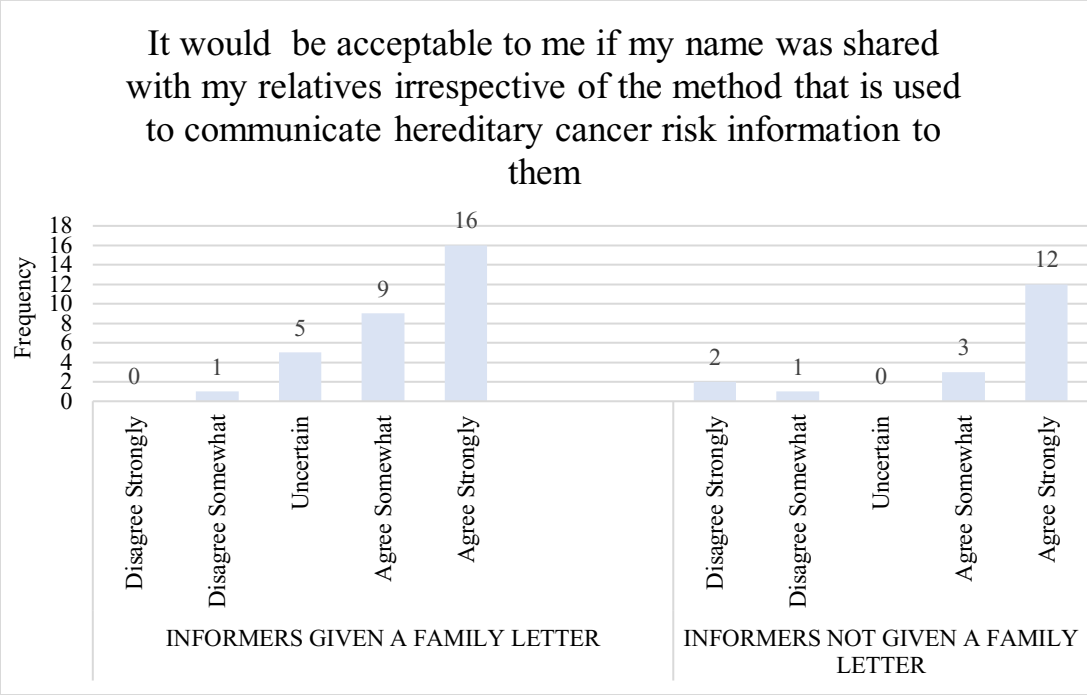
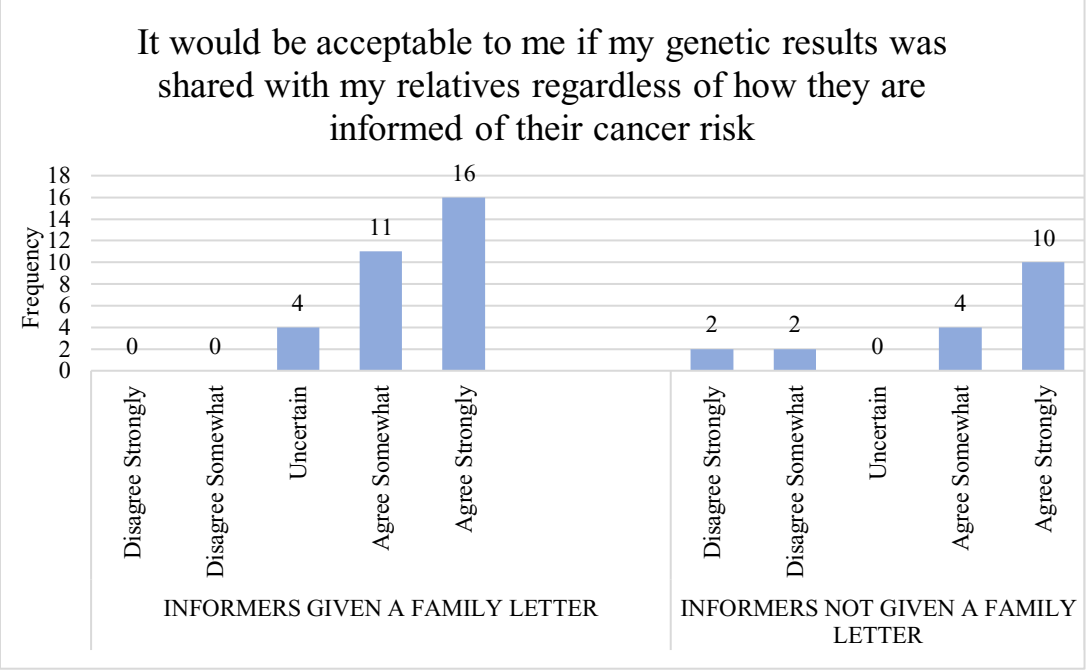


Figure 4.1b: Acceptability for sharing the probands' genetic test result with their relatives.



4.1c: Acceptability for sharing the probands' cancer diagnosis with their relatives.

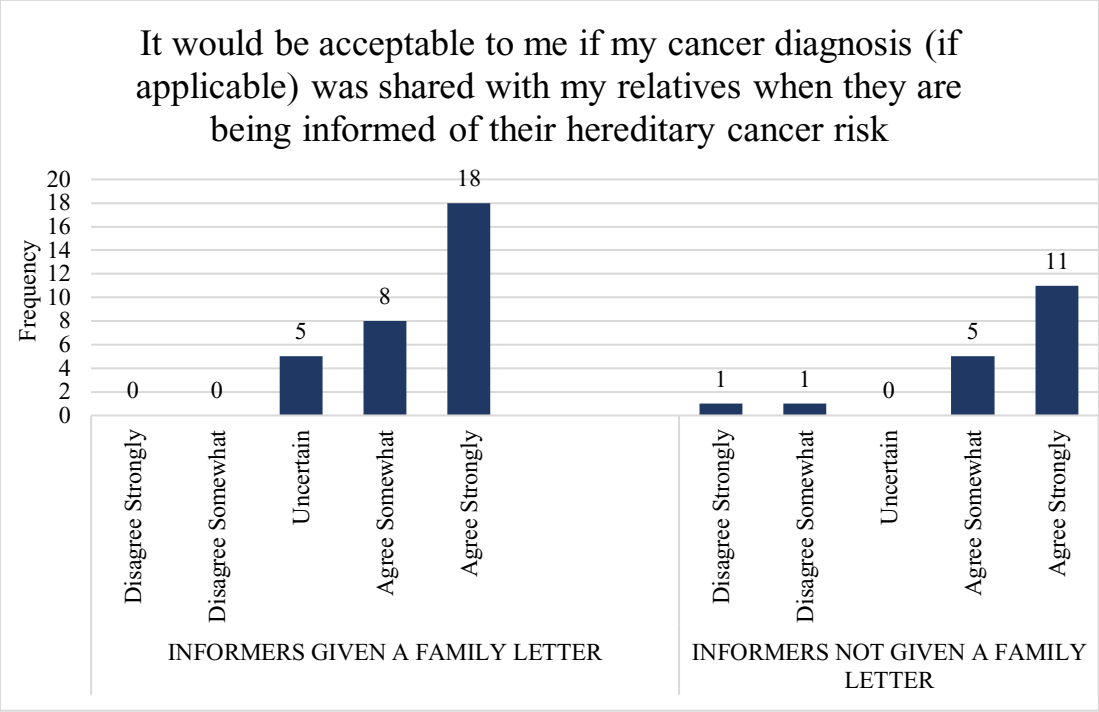


Table 4.5: The two-tailed Mann-Whitney two-sample rank-sum test examining whether there were significant differences between the two groups of informers.

	Mean Rank				
Did you receive a family letter?	Yes	No	*U*	*z*	*p*
It would be acceptable to share my name	23.68	25.86	294.50	-0.59	0.557
	Mean Rank				
Did you receive a family letter?	Yes	No	*U*	*z*	*p*
It would be acceptable to share my genetic test result	24.97	23.72	256.00	-0.33	0.741
	Mean Rank				
Did you receive a family letter?	Yes	No	*U*	*z*	*p*
It would be acceptable to share my cancer diagnosis	24.30	24.83	276.00	-0.15	0.884

4.1.4 Preference for hereditary risk communication from the probands' perspective

The informers were asked to share their preferences for hereditary cancer risk communication with their relatives (Table 6). More informers who were given a family letter thought that they should deliver the letter in person to their relatives (57%) than informers who were not given a family letter (33%). The informers who were not given a family letter felt more inclined to deliver the letter to close relatives and to mail the letter to more distant relatives (61%).

Table 4.6: Preference for family member outreach from the perspective of the informers.

RESPONSE FREQUENCIES FOR THE PREFERENCES FOR COMMUNICATING HEREDITARY CANCER RISK												
	INFORMERS GIVEN A LETTER						INFORMERS NOT GIVEN A LETTER					
	[1]Disagree strongly (%)	[2]Disagree somewhat (%)	[3]Uncertain (%)	[4]Agree somewhat (%)	[5]Agree strongly (%)	Mean (N) ± Standard deviation	[1]Disagree strongly (%)	[2]Disagree somewhat (%)	[3]Uncertain (%)	[4]Agree somewhat (%)	[5]Agree strongly (%)	Mean (N) ± Standard deviation
I prefer to deliver the family letter in person to my relatives	0	6 (20)	7 (23)	11 (37)	6 (20)	3.57 (N=30) ±1.040	2 (11)	5 (28)	5 (28)	2 (11)	4 (22)	3.06 (N=18) ±1.349
I prefer to deliver the letter to close relatives and to mail the letter to my distant relatives	0	5 (17)	11 (37)	12 (40)	2 (7)	3.37 (N=30) ±0.850	1 (6)	1 (6)	5 (28)	5 (28)	6 (33)	3.78 (N=18) ±1.166
I would prefer to inform my relatives using the letter in the presence of a health care professional	8 (27)	7 (23)	9 (30)	3 (10)	3 (10)	2.53 (N=30) ±1.279	2 (11)	6 (33)	3 (17)	4 (22)	3 (17)	3.00 (N=18) ±1.328
I believe that I should share the family letter with my relatives; however, a health care provider should call them afterwards	1 (3)	3 (10)	6 (20)	12 (40)	8 (27)	3.77 (N=30) ±1.073	2 (11)	3 (17)	3 (17)	6 (33)	4 (22)	3.39 (N=18) ± 1.335
I feel it is my responsibility to inform my relatives with a family letter; however, a health care professional should send them a follow-up email	0	3 (10)	9 (30)	8 (27)	10 (33)	3.83 (N=30) ±1.020	2 (11)	3 (17)	3 (17)	7 (39)	3 (17)	3.33 (N=18) ± 1.283
I believe that my relative should be informed in person by a health care professional of the risk of hereditary cancer	1 (3)	6 (20)	7 (23)	10 (33)	6 (20)	3.47 (N=30) ±1.137	1 (6)	2 (13)	4 (25)	7 (44)	2 (13)	3.44 (N=16) ± 1.094
I would like to disclose the information without the involvement of a health care professional	2 (7)	7 (23)	13 (43)	6 (20)	2 (7)	2.97 (N=30) ±0.999	3 (19)	5 (31)	3 (19)	3 (19)	2 (13)	2.75 (N=16) ± 1.342
The health care professional should mail the family letter to my relatives	4 (13)	7 (23)	4 (13)	11 (37)	4 (13)	3.13 (N=30) ±1.306	3 (19)	3 (19)	3 (19)	4 (25)	3 (19)	3.06 (N=16) ± 1.436

The health care professional should send an email with information on hereditary cancer risk to my relatives	2 (7)	7 (23.)	3 (10)	13 (43)	5 (17)	3.40 (N=30) ±1.221	3 (19)	3 (19)	3 (19)	4 (25)	3 (19)	3.06 (N=16) ± 1.436
My relatives should receive a telephone call from a health care professional informing them about the risk of hereditary cancer	4 (13)	6 (20)	9 (30)	8 (27)	3 (10)	3.00 (N=30) ±1.203	3 (19)	6 (38)	4 (25)	2 (13)	1 (6)	2.50 (N=16) ± 1.155
I would prefer to share the link to a secure mobile health app or a website with my relative that has all the information they need about our family's cancer risk	1 (3)	4 (14)	8 (28)	11 (38)	5 (17)	3.52 (N=29) ±1.056	1 (6)	2 (13)	4 (25)	5 (31)	4 (25)	3.56 (N=16) ± 1.209
I would prefer if my health care provider shared a link to a secure mobile health app or a website with my relative that has all the relevant information they need about our family's inherited risk	1 (3)	3 (10)	10 (33)	12 (40)	4 (13)	3.50 (N=30) ±0.974	2 (13)	4 (25)	4 (25)	4 (25)	2 (13)	3.00 (N=16) ± 1.265

*The responses on the Likert scale are numbered 1-5, with 5 having the highest rank.

Note: This table demonstrates the percentage, means and standard deviations for items on preferences for family member outreach that were posed to the probands who participated in the study. The percentages may not equal 100% due to rounding.

While visual inspection reveals percentages of agreement with items appeared somewhat different, no significant differences were found on the items in Table 6 between the informers who received a family letter and the informers who did not receive a family letter after performing a series of Mann Whitney U tests (results not shown).

The results show that the informers agreed they should be involved in communicating hereditary cancer risk information to their relatives, but many would value the support of a health care provider. Sixty-

seven percent of the informers who received a family letter agreed that the health care provider should follow up with a phone call, while 55% of those who did not receive a family letter to communicate with their relatives also agreed. Similarly, 60% of the informers given a family letter thought that the health care provider should follow up with an email and 56% of those who were not given a family letter agreed. Fifty-three percent of the informers who were given a family letter thought that their relatives should be informed in person by a health care provider, and 57% of the informers not given a family letter agreed (Table 6). Thus, while informers agreed they had a role to play in communicating risk information to relatives, clearly, there were high levels of agreement with a role for healthcare providers in this process.

The idea of the health care provider sharing the link to a website or a mobile health app with relatives that had additional information was somewhat supported by the informers who received a family letter (53%) and less supported by the informers who were not given a family letter (38%), though not significantly. The results were similar for informers who thought they should share this link themselves (55% for informers who received a family letter and 38% for informers who did not receive a family letter). Very few informers thought their relatives should be informed without the assistance of a health care professional. Only 27% of the informers who received a family letter agreed with this statement, while 32% of those who did not receive a family letter agreed (Table 6).

The informers were asked to share their thoughts on any other suggestions for informing their relatives. One informer shared that they informed family members via text messaging and asked another family member to spread the word to distant relatives via Facebook. This informer expressed that a distant cousin benefited from risk-reducing oophorectomy after testing positive for a genetic mutation.

"I informed people by text. I also asked a sibling to help spread the word to extended and distant family contacts on facebook. I was devastated to learn that a cousin knew she had the same genetic mutation (3 years before I got ovarian cancer) but didn't inform anyone because she and her siblings assumed it started with her dad (my uncle) who also tested positive for the same genetic mutation. Some guilt was expressed by some members of her family that I could have been offered an opportunity at prevention, and other members of her family stuck to their position that there was no reason to believe it was a hereditary mutation beyond their nuclear family. After I informed other cousins, one proceeded with prevention (removal of ovaries) after she also tested positive and I was glad I gave her that opportunity that I wasn't given".

4.1.5 Experience with the family-mediated approach from the relatives' (informed) perspective

Those informed of their risk of hereditary cancer by their proband (the relatives) were asked to give their opinion on their level of satisfaction with the family-mediated approach and share their emotional responses (Table 7). Most of the informed (relatives) found the family letter helpful (79%) and understood the cause of their own risk (78%) and their eligibility for genetic counselling (89 %). On the other hand, most of them felt nervous (96%) or concerned (91%) upon receiving information about their personal risk. Nevertheless, they were happy that risk information was shared with them (88%) (Table 7).

Table 4.7: Feedback from relatives about being informed of their hereditary cancer risk.

RELATIVES' FEEDBACK ON BEING INFORMED	RESPONSE FREQUENCIES						
	[1]Disagree strongly (%)	[2]Disagree somewhat (%)	[3]Uncertain) (%)	[4]Agree somewhat (%)	[5]Agree strongly (%)	Mean	Standard deviation
The information in the letter was helpful (N=32)	0	1 (3)	6 (19)	5 (16)	20 (63)	4.38	0.907
The letter should have been more detailed (N=32)	3 (9)	1 (3)	14 (44)	6 (19)	7 (22)	3.42	1.177
Some of the terms used in the letter were not familiar to me; because of this, I did not find the letter useful (N=30)	11 (37)	6 (20)	8 (27)	5 (17)	0	2.23	1.135
I understood the meaning of the letter for my family's future and mine (N=33)	0	0	7 (21)	12 (36)	14 (42)	4.21	0.781
I understood what the cause of my own elevated risk was (N=33)	1 (3)	1 (3)	5 (15)	9 (27)	17 (51)	4.21	1.023
I understood I was eligible for genetic counselling (N=37)	1 (3)	1 (3)	2 (5)	6 (16)	27 (73)	4.54	0.931
I understood I could undergo genetic testing to determine if I had a cancer-causing mutation that would put me at an increased risk (N=37)	1 (3)	1 (3)	2 (5)	6 (16)	27 (27)	4.54	0.931
I understood that I could manage my personal inherited cancer risk and what my options were (N=38)	3 (8)	2 (5)	8 (21)	13 (34)	12 (32)	3.76	1.195
I felt angry/upset about receiving the information (N=43)	14 (33)	9 (21)	4 (21)	14 (33)	2 (5)	2.56	1.368
I felt sad (N=45)	2 (4)	2 (4)	4 (9)	15 (33)	22 (48)	4.18	1.072
I felt anxious/nervous (N=44)	1 (2)	0	1 (2)	18 (41)	24 (55)	4.45	0.761
I was concerned (N=44)	1 (2)	2 (5)	1 (5)	14 (32)	26 (59)	4.41	0.932
I felt a loss of control (N=44)	7 (16)	7 (16)	5 (11)	15 (34)	10 (23)	3.32	1.410
I was happy that my relatives shared the information with me(N=45)	0	3 (7)	2 (4)	2 (4)	38 (84)	4.67	0.853
I did not care much about receiving the information (N=44)	36 (82)	6 (14)	1 (2)	0	1 (2)	1.27	0.727

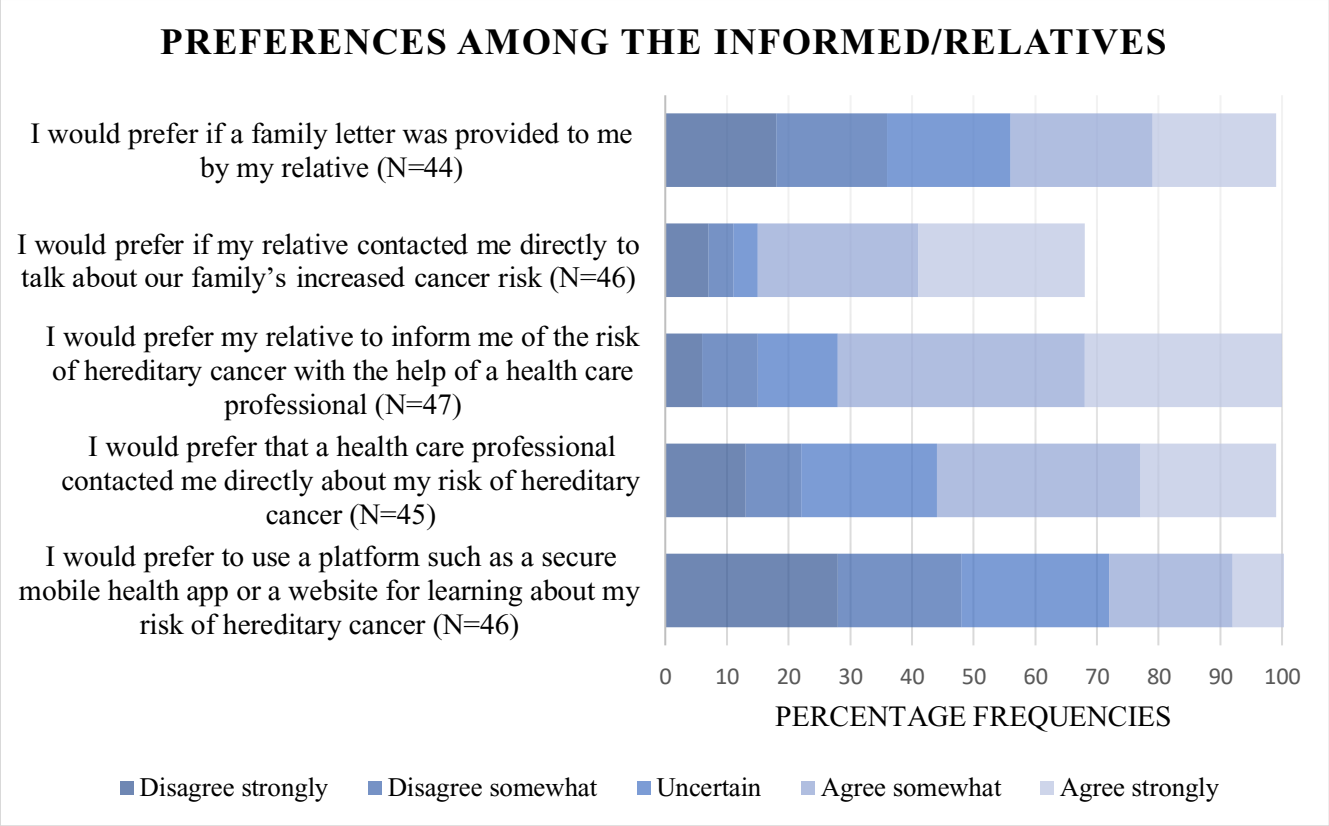
Note. Due to rounding errors, percentages may not equal 100%.

*The responses on the Likert scale are numbered 1-5, with 5 having the highest rank.

4.1.6 Preference for hereditary risk communication from the perspective of the informed (relative)

The informed (relatives) were also asked to share their opinions on how they would prefer to be informed of their hereditary cancer risk (Figure 5). Again, a majority of the informed preferred to be informed with the help of a health care professional (72%), and 53% thought that the informer (proband) should contact them directly. Fifty-five percent of them thought that a health care professional should contact them directly. On the other hand, only 29% agreed with using a mobile health app or website, which is less than what was observed for the informers (55% and 38% for informers who received a family letter and those who did not, respectively).

Figure 4.2: The preference for receiving hereditary cancer risk information among the informed.



4.2 Section II – Univariate Analysis

4.2.1 Relationship among clinical and demographic variables and outreach preferences

4.2.1.1 The informers (Probands)

There were significant associations between cancer diagnosis and two items measuring outreach preferences with a health care professional's involvement. In general, informers who had never been diagnosed with cancer indicated their agreement with the support of a health care professional. For example, informers with no cancer history were significantly more likely to agree that they should share the family letter with their relatives with a follow-up phone call from the healthcare professional, U = 376.5, z = 2.16, p = 0.031 (mean rank=29.92, *Mdn*=4) compared to those with a personal history of cancer (mean rank=21.25, *Mdn* =4).

Informers who were never diagnosed with cancer also thought it would be appropriate for the health care professional to send their relatives a follow-up email after the family letter was shared, U = 368.5, z = 2.172, p = 0.030 (mean rank = 29.97, *Mdn*=4) compared to those with a cancer diagnosis (mean rank=21.22, *Mdn*=3.5).

Furthermore, demographic variables were significantly related to endorsing the involvement of a healthcare professional in family communication. For example, annual income was related to agreement with having a healthcare professional make a follow-up phone call to relatives, $\chi 2(4) = 11.19$, p = .025. Informers who earned $49,000 or less were more likely to agree with this outreach (mean rank=33.75, *Mdn*=4.5) compared to those with an annual income of $50, 000 to less than $90, 000 (mean rank=13.72, *Mdn*=2).

Similarly, informers with an annual income of $49, 000 or less were more likely to agree that the healthcare professional should send their relatives a follow-up email, $\chi 2(4) = 9.81$, p = 0.044 (mean

rank=39.50, *Mdn*=5) compared to those whose annual income was $50, 000 to less than $90, 000 (mean rank=16.56, *Mdn* =3).

Marital status was also related to email outreach by a healthcare provider. Informers who were divorced/separated/widowed were more likely to agree with this outreach method $\chi 2(2) = 6.88$, $p = 0.032$ (mean rank=36.17, *Mdn*=5) than respondents who were married/living common-law (mean rank=21.78, *Mdn*=4).

Age and settlement among the informers were likewise related to agreement with items endorsing the help of healthcare providers in family outreach. Age was significantly related to preference for relatives to receive a phone call from a health care professional informing them of the risk of hereditary cancer $\chi 2(3) = 8.32$, $p = 0.040$. There was a trend for informers 34 and younger (mean rank=39.83, *Mdn*=3) to be more likely to prefer this method when compared to those who were 55 and older (mean rank=20.23, *Mdn*=2), though the pairwise comparison between the two groups was not significant. Preference for the health care professional informing relatives in-person of the risk of hereditary cancer was significant for the different levels of settlement ($\chi 2(3) = 8.80$, $p = 0.032$). Informers living in a small population centre (mean rank=32, *Mdn*=4) were more likely to agree with in-person communication from a healthcare provider than those from a large population centre (mean rank 13.10, *Mdn*=2).

Gender, education level, province of residence, number of children, mutation status (BRCA mutation, Lynch mutation or other mutation that causes HBOC) and perceived risk of hereditary cancer were not significantly associated with any outreach preferences among the informers.

There were no significant associations among the clinical and demographic variables with items measuring other outreach preferences. These included: the preference to deliver the letter in person to relatives; the preference to deliver the letter to close relatives and to mail the letter to distant

relatives; the preference for informing relatives using the letter in the preference of a healthcare professional; the preference for disclosing the information without the involvement of the health care professional; the preference for the health care professional mailing the family letter to relatives (without the informers' involvement); the preference for the health care professional sending an email with the information on hereditary cancer risk (again, without the informer being involved); the preference for sharing the link to a secure mobile app or a website with relatives that contains information the family's cancer risk; or, the preference for the health care provider to share such a link with relatives.

4.2.1.2 The informed (relatives)

Relatives with an advanced level of education and upper middle income were more likely to endorse family member communication without a health care professional's involvement. For example, relatives with a trade or college diploma (mean rank=25.66, *Mdn*=4.53) significantly preferred that their relatives contact them directly about the family's increased cancer risk when compared to respondents with a high school diploma or less (mean rank=5.70, *Mdn*=2.20), $\chi 2(3) = 13.06$, $p = 0.005$. Informed with a university graduate degree (mean rank=26.80, *Mdn*=4.70) also significantly preferred direct outreach by the proband when compared to those with a high school diploma or less (mean rank =5.70, *Mdn*=2.20). Annual income was also significantly associated with direct contact from probands without a healthcare provider's involvement, $\chi 2(4) = 11.12$, $p = 0.025$. Relatives with an income of $50, 000 to less than $90, 000 (mean rank=31.23, *Mdn*=4.91) appeared more likely to endorse this statement than those earning $49, 000 or less (mean rank =8.83, *Mdn*=3.33), although post-hoc tests were not significant.

Relatives residing in an Atlantic province (NL, NB, PE, NS) preferred the health care professional's involvement when being informed of their hereditary cancer risk. They were more likely to prefer that the health care professional contact them directly, $\chi^2(3) = 8.41$, $p = 0.038$ (mean rank=30.34, *Mdn*=4.19) compared to those from the Prairie provinces (AB, SK, MB) (mean rank=17.88, *Mdn*=2.88).

In like manner, relatives residing in an Atlantic province were significantly likely to prefer being informed of the risk of hereditary cancer with the help of the health care professional $\chi^2(3) = 8.63$, $p = 0.035$ (mean rank=29.79, *Mdn*=4.35) compared to those residing in a Prairie province (mean rank=14.00, *Mdn*=2.88). Outreach preferences did not differ among other provinces.

Relatives living in a rural area were also more likely to support being informed of their risk of hereditary cancer with the help of a health care professional (mean rank=40.0, Mdn=5.00), and this method of outreach was least supported by relatives who lived in a large urban population centre (mean rank=18.54, Mdn=3.30), $\chi^2(3) = 9.45$, $p = 0.024$.

Agreement with the item suggesting the proband share hereditary cancer risk information with the help of the health care professional was supported by relatives with a Lynch syndrome mutation (mean rank=35.14, Mdn=4.71), significantly more than relatives with a BRCA1 mutation (mean rank=20.50, Mdn=3.50), $\chi^2(3) = 8.58$, $p = 0.035$.

Among the informed/relatives, there were no significant associations among clinical and demographic characteristics for receiving the family letter from the proband (the informer) or the preference for the use of a platform such as a secure mobile health app or a website for learning about the risk of hereditary cancer.

4.2.2 Other factors that potentially influence the preferences for hereditary cancer risk communication

4.2.2.1 Informers' (Proband) Experience with informing relatives

Further analyses were conducted to explore the associations between the informers' previous experiences with risk communication and their preferred method of informing their relatives of hereditary cancer risk. The results showed significant correlations between outreach preferences and items related to the perceived usefulness of the family letter, self-efficacy and certainty (confidence) in risk communication, distress (concerns related to confidentiality or worry about causing conflict or distress among family members), support from relatives and perceived responsibility in risk communication.

No significant correlations were observed for the preferences for the proband or the health care professional sharing the link to a secure mobile health app or website with relatives. The following sections expand on the correlational analyses.

I. The usefulness of the family letter

Significant correlations were found between all the statements measuring the perceived usefulness of the family letter and the preference for the involvement of a health care professional. There was a significant negative correlation between informers who found the letter useful during risk communication and the preference for informing their relatives in the presence of a health care professional (r = - 0.568, p = 0.002). Informers who agreed that the letter was helpful in risk communication, but could not address some of the questions asked by their relatives, preferred that

their relatives be informed of the risk of hereditary cancer in person by a health care professional (r=0.449, p=0.017). They also preferred that the health care provider send an email with the information to their relatives (r=0.447, p=0.017) and that their relatives receive a phone call from the health care professional informing them of their risk (r=0.552, p=0.002).

Informers who could read and understand what was written in the letter but were unable to explain it in their own words preferred that the health care professional mail the family letter to their relatives (r = 0.384, p = 0.043) or send their relatives an email with the information on hereditary cancer risk (r = 0.474, p = 0.011).

Those who thought that the letter's content should have been in a more simplified form or language preferred to inform their relatives using the letter in the presence of a health care professional (r = 0.683, p = 0.000). They also thought that their relatives should be informed in person by a health care professional (r = 0.377, p = 0.048) or that they should receive a phone call from the health care professional informing them of their risk (r = 428, p = 0.023).

There was a negative correlation between feeling satisfied with communicating with relatives using the family letter and the preference for informing relatives of the risk of hereditary cancer in the presence of the health care professional (r = 0.436, p = 0.020).

II. *Self-efficacy and Certainty (confidence)*

Informers who received a family letter who agreed that risk communication was challenging were more likely to endorse outreach statements involving help from a healthcare provider. There was a significant positive correlation between informers who found it challenging to communicate genetic

information and the preference for informing their relatives with the family letter in the presence of the health care professional ($r = 0.397$, $p = 0.030$).

In addition, a strong positive correlation was observed between informers who did not feel confident in passing on the information because they did not feel they could correctly communicate risk information and the preference for using the family letter in the presence of the health care provider ($r = 0.382$, $p = 0.037$). There was also a positive correlation between the same statement and the preference for their relatives to receive an email from the health care professional informing them of their risk ($r = 0.371$, $p = 0.044$).

Conversely, informers who felt confident that their relatives understood the implications of the family letter for their own health preferred to communicate with their relatives without the health care professional's involvement (r=0.439, p=0.017). The informers who felt confident that the

family letter explained to their relatives what having the mutation meant still preferred to inform their relatives using the family letter in the presence of a health care professional ($r = 0.368$, $p = 0.050$).

There were no significant findings between outreach preference and informers' lack of confidence in passing on the information because of fear of causing distress among relatives or between preferences and the statements related to feeling confident that the family letter helped relatives understand the importance of genetic testing.

Table 4.8: Summary of the correlation between the preferred method of sharing risk information and the proband's experiences with risk communication related to the usefulness of the family letter, self-efficacy and certainty (confidence)

PREFERENCES FOR RISK COMMUNICATION	INFORMERS' EXPERIENCES WITH RISK COMMUNICATION (The usefulness of the family letter, self-efficacy and certainty)						
	1. I found the letter very useful…	2. The letter helped me to communicate with my relatives…	3. I was able to read and understand what was written…	4. I thought that the letter's…	5. I felt satisfied with communicating with my relatives…	6. I felt confident that the family letter …	7. I felt confident that my …
I prefer to deliver the family letter in person to my relatives							
I would prefer to inform my relatives using the letter in the presence of a health care professional	**r = - 0.568****			**r = 0.683****	**r = - 0.436***	**r = - 0.368***	
I believe that my relative should be informed in person by a health care professional of the risk of hereditary cancer		**r = 0.449***		**r = 0.377***			
I would like to disclose the information without the involvement of a health care professional							**r = 0.439***
The health care professional should mail the family letter to my relatives			**r = 0.384**				
The health care professional should send an email with information on hereditary cancer risk to my relatives		**r = 0.447***	**r = 0.474**				
My relatives should receive a telephone call from a health care professional informing them about the risk of hereditary cancer		**r = 0.552****		**r = 0.428***			

***P ≤ 0.05**

****P ≤0.01**

Please note that items on the informers' experiences with risk communication in the above table have been abbreviated. The complete expressions are found below:

[1] I found the letter very useful in helping me to communicate the risk of hereditary cancer to my relative

[2] The letter helped me to communicate with my relatives about hereditary cancer risk; however, some of my relatives asked questions that the letter did not address

[3] I was able to read and understand what was written in the letter, but it was hard for me to explain it to my relatives in my own words

[4] I thought that the letter's content should have been in a more simplified form or language

[5] I felt satisfied with communicating with my relatives using the family letter about the risk of genetic cancer

[6] I felt confident that the family letter explained to my relatives what having the mutation meant

[7] I felt confident that my relatives understood the implications of the information in the family letter for their own health

III. *Support from relatives and concerns about causing distress*

There was a significant negative correlation between informers who felt that their relatives were uninterested in risk communication and the preference for delivering the family letter in person to relatives (r = -0.460, p = 0.001). A significant negative correlation was also found between informers who found it hard to talk to their relatives and the preference for disclosure without the health care professional's involvement (r = -0.446, p = 0.002). Informers who found it difficult to talk to their relatives preferred to inform them using the family letter in the presence of the health care professional (r = 0.341, p = 0.018).

Informers who felt encouraged by their relatives believed they should share the family letter with them and that the health care provider should call them afterwards (r = 0.304, p = 0.036).

A significant negative correlation was found between informers who worried that communicating the risk of hereditary cancer would bring about conflict in the family and the preference for disclosing hereditary risk information without the health care professional's involvement (r = -0.394, p = 0.007). In addition, a significant negative correlation was also found between informers who worried that their relatives would suffer anxiety or depression and the preference for informing their relatives without the involvement of the health care professional (r = - 0.323, p = 0.028), as well as the preference for the health care provider sending their relatives an email with risk information (r = - 0.354, p = 0.016). This finding indicates that those who worried that risk communication would cause family conflict, depression, or anxiety would have liked the help of a healthcare professional.

The informers who were concerned about the sharing of their personal information preferred to inform their relatives using the family letter in the presence of the health care provider (r = 292, p = 0.044), or that the health care provider call their relatives to inform them of the risk of hereditary cancer (r = 0.296, p = 0.046).

A significant negative correlation was observed between informers who worried their relatives would not want them to know about their increased risk of cancer and the preference to deliver the letter to close relatives and to mail the letter to distant relatives (r = -0.287, p = 0.048). There were no significant correlations between outreach preference and upset or angry relatives.

IV. *Perceived responsibility*

Informers who did not think it was their responsibility to inform their relatives or to share the information with them preferred that their relatives be seen in person by a health care professional (r = 0.410, p = 0.027).

Similarly, a significant positive correlation was observed between informers who believed it was not their responsibility to inform their relatives but had no problem doing it and the preference for the health care professional informing their relatives in person ($r = 0.556$, $p = 0.002$). These informers also preferred that their relatives receive a phone call from the health care provider informing them of the hereditary cancer risk ($r = 0.399$, $p = 0.032$).

On the contrary, a significant negative correlation was found between informers who felt it was their responsibility to inform their relatives but would like the assistance of someone such as a family member or a health care provider and the preference for delivering the family letter in person to their relatives ($r = - 0.486$, $p = 0.008$). Therefore, informers who desired the help of a healthcare professional with family communication were less likely to agree with delivering the family letter themselves.

Statements on perceived responsibility that were not significantly correlated with outreach preferences were as follows: “I felt responsible for informing my children, siblings, parents and spouse,” and “I felt responsible for informing my aunts, uncles, nieces, grandchildren and grandparents.”

Table 4.9: Summary of the correlation between the preferred method of sharing risk information and the proband's experiences with risk communication related to support from their relatives, concerns for causing distress among their relatives and their perceived responsibility in informing their relatives.

PREFERENCES FOR RISK COMMUNICATION	EXPERIENCES WITH RISK COMMUNICATION (Support from relatives, concerns for causing distress and perceived responsibility)									
	1. It was hard for me…	2. Some of my relatives were…	3. My relatives encouraged …	4. I worried that communicating the…	5. I worried that my family …	6. I was concerned about sharing…	7. I worried that my relatives …	8. I do not think that …	9. I do not believe …	10. I felt responsible; however…
1. I prefer to deliver the family letter…		**r = -0.460****								**r = -0.486****
2. I prefer to deliver the letter to close relatives…							**r = -0.287***			
3. I would prefer to inform my relatives using the letter…	**r = 0.341 ***					**r = 0.292**				
4. I believe that my relative should be informed …								**r = 0.41 0***	**r = 0.556* ***	
5. I would like to disclose the information without …	**r = - 0.446 ****			**r = - 0.394****	**r = - 0.323***					
7. The health care professional should send an email…					**r = - 0.354***					
8. My relatives should receive a telephone…			**r = 0.304***			**r = 0.296***			**r = 0.399***	

P ≤ 0.05

****P ≤0.01**

Please note that the items on probands' experience with risk communication, as well as the items on the probands' preferences from the above table have been abbreviated. The full item wording is found in the foot notes below:

Items on experience with risk communication:

[1]It was hard for me to talk to my relatives about the risk of hereditary cancer

[2] Some of my relatives were uninterested when I shared the information about our family's inherited risk

[3] My relatives encouraged me to share the information with other relatives

[4] I worried that communicating the risk of hereditary cancer would bring about conflict in the family

[5] I worried that my family would become anxious or depressed after receiving the information

[6] I was concerned about sharing personal medical information with other family members (confidentiality)

[7] I worried that my relatives would not want me to know about their increased risk of cancer

[8] I do not think that I should have been the one to inform my relatives or share the information with them

[9] I do not believe it was my responsibility but I had no problem doing it

[10] I felt responsible; however, I would have liked the assistance of someone else

Items on preferences:

[1]I prefer to deliver the family letter in person to my relatives

[2] I prefer to deliver the letter to close relatives and to mail the letter to my distant relatives

[3] I would prefer to inform my relatives using the letter in the presence of a health care professional

[4] I believe that my relative should be informed in person by a health care professional of the risk of hereditary cancer

[5] I would like to disclose the information without the involvement of a health care professional

[6] The health care professional should send an email with information on hereditary cancer risk to my relatives

[7] My relatives should receive a telephone call from a health care professional informing them about the risk of hereditary cancer

4.2.2.2 The informeds' (relatives) experience of being told about their risk of hereditary cancer

Analyses were conducted to explore the associations between outreach preferences and the informeds' previous experiences with being informed of the risk of hereditary cancer by the proband. Significant correlations were found between outreach preferences and items related to the informeds' satisfaction with the family letter, their cognitive control with risk information and their emotional responses to being told about their risk. However, there were no significant correlations between items that explored the informeds' previous experience with being told about their risk and the preference for their relatives providing them with a family letter or the preference for them to learn about their hereditary cancer risk using a secure mobile health app or a website.

I. *The informeds' satisfaction with the family letter*

From the informeds' perspective, a significant correlation was observed between outreach preference and satisfaction with information (the family letter), since those who felt that the letter should have been more detailed preferred being informed by the informer (proband) with the health care professional's help ($r = 0.461$, $p = 0.021$). Similarly, the informed who felt like some of the items in the letter were not familiar to them and, as a result, did not find the letter useful preferred that the health care professional contact them directly about their risk of hereditary cancer ($r = 0.447$, $p = 0.019$).

There was no significant correlation between outreach preference and the informed finding the information in the family letter helpful.

II. The informeds' cognitive and behavioural control related to risk information and management

The health care professional directly contacting the informed was not preferred in instances where the informed understood the meaning of the family letter for their family's future (r = - 0.0417, p = 0.022) and where the informed understood the cause of their own elevated risk (r = - 0.396, p = 0.030).

There were no significant correlations between outreach preferences and items that explored themes related to behavioural control (understanding of the eligibility for genetic counselling, genetic testing and management of personal risk).

III. The informed's emotional response to being told about their hereditary cancer risk

The informed who were concerned after learning about their hereditary cancer risk preferred that the proband contact them directly to talk about the family's increased cancer risk (r = 0.353, p = 0.024).

The informed who felt a loss of control also preferred that the proband contact them directly to talk about the family's increased cancer risk (r = 0.337, p = 0.029).

There were no significant correlations between outreach preferences and items that explored other themes related to emotional response, i.e., feelings of anger, fear, anxiety, gratitude and indifference).

Table 4.10: Summary of the correlation between the informeds' (relatives') preferences for being informed about their risk of hereditary cancer and their previous experiences of being informed by the proband.

PREFERENCES FOR BEING INFORMED	THE INFORMEDS' EXPERIENCES WITH BEING INFORMED					
	The letter should have been more detailed	Some of the terms used in the letter were not familiar to me; because of this, I did not find the letter useful	I understood the meaning of the letter for my family's future and me	I understood what the cause of my own elevated risk was	I was concerned	I felt a loss of control
I would prefer if my relative contacted me directly to talk about our family's increased cancer risk					**r = 0.353***	**r = 0. 337***
I would prefer my relative to inform me of the risk of hereditary cancer with the help of a health care professional	**r = 0.461***					
I would prefer that a health care professional contact me directly about my risk of hereditary cancer		**r = 0.447***	**r = - 0.417***	**r = - 0.396***		

***P ≤ 0.05**

****P ≤0.01**

CHAPTER 5: DISCUSSION

This national cross-sectional study explored the preferences for hereditary cancer risk communication within families affected by HBOC and LS. Study results could be useful to health providers in supporting probands to effectively communicate risk information within their families. Having a better understanding of how affected families would like to be advised of their cancer risks could potentially lead to an increase in the percentage of relatives who attend genetic counselling from the sub-optimal 50% reported in the literature (Loader et al., 2002; Lowery et al., 2010; Hinchcliff et al., 2019; Menko et al., 2013; Marleen et al., 2019). By increasing attendance to genetic counselling, more at-risk individuals might benefit from preventative strategies before cancer development.

The study's results showed that most informers (i.e., probands) felt responsible for informing their relatives about their risk of hereditary cancer and indicated they had communicated with many of them, especially first-degree relatives. Notably, a third of the probands reported not receiving a family letter despite this being standard care in Canada. It is unknown whether no letter was actually provided or if this finding is the result of a simple recall issue. Most probands who received the family letter found it useful but still valued the help of a healthcare provider in informing their relatives. There were very few instances where informers felt that they could inform their relatives without the assistance of a healthcare professional. For example, informers who felt confident that their relatives understood the implications of the information in the family letter for their own health preferred to inform their relatives without a healthcare professional's involvement. On the other hand, informers who indicated it was hard to talk to their relatives and that communicating genetic

information could cause conflict, depression or anxiety within the family were less likely to prefer informing their relatives without the assistance of the health care professional.

From the perspective of the relatives (i.e., the informed), those with middle to upper income and a higher level of education preferred that their probands contact them directly about the family's hereditary risk. Similarly, relatives concerned about losing control after being informed about their risk also preferred that their relatives contact them directly. Relatives who understood the meaning of the letter for their future, their family's future and the cause of their own elevated risk were less likely to prefer the involvement of the health care professional. However, relatives who indicated they found it challenging to understand the meaning of the letter were more likely to prefer that a healthcare professional contact them directly, as well as relatives who resided in the Atlantic provinces.

In previous chapters, barriers related to the communication of hereditary cancer risk were reviewed, and it was noted that many of these barriers were similar across HBOC and Lynch syndrome. Nycum et al. (2009) reasonably outlined the barriers to risk communication using the ecological model as being at the individual, family, and community levels. This conceptual framework will provide the basis for the discussion of risk communication preferences related to the sociodemographic and clinical characteristics of the individuals from this study using especially the individual and familial components of the ecological model while making reference to findings from previous investigations. Outreach preferences and other factors influencing risk communication will also be discussed.

5.1 Elements which characterize the individual level of risk communication and their relation to preferences for family member outreach

The individual characteristics of probands from families with a high predisposition for hereditary cancer syndrome influence risk communication patterns and will influence how relatives receive the information. The results showed that there was generally a high acceptance among the probands for participating in risk communication; however, there remained high agreement with items measuring opinion on assistance from a health care professional (Andersson et al., 2020).

5.1.1 Vulnerability and receptivity of risk information related to maturity, phases of the family cycle, life stages and events

Age is related to risk communication. Seven et al. (2020) showed that increasing age of relatives, particularly first-degree relatives, was associated with an increased likelihood of being informed of hereditary cancer risk by the proband. Seven et al. (2020) also found that older probands were more likely to communicate risk information and to prefer to be involved in communicating hereditary cancer risk to their relatives than younger probands. Henrikson et al. (2021) reported that older participants expressed that a health system-led direct contact approach would ensure that the correct information is passed on to relatives in a timely manner; however, they did not believe that such a system should replace the family-mediated approach. The mean age of the relatives in the aforementioned study was 50.1(range 19 - 82), and that of the proband was 61.2 (range 34 - 77), similar to the current study. In the study by Pentz et al. (2005), the average age of both relatives and probands was 48 years. It was shown that individuals thought that the proband or another family member was responsible for sharing risk information. Only a quarter of the participants thought that

a health care professional should be involved. The health care professional's involvement was considered appropriate in cases with family-based barriers such as fragile or estranged relationships due to emotional or social distance. These results are similar to the current findings in that probands who believed communication would cause emotional upset or worry wanted support from a provider. This study's results also align with the findings from Henrikson et al. (2021) as it demonstrated that younger informers were more likely to indicate wanting a health care provider to contact their relatives directly; older informers were less likely to be in agreement with this method of outreach. A similar communication pattern was seen in a non-probability population-based study by Makhnoon et al. (2021). Participants with a mean age of 42.1 years, with or without a personal or family history of breast, ovarian or colon cancer, were likely to discuss genetic cancer testing with a health care provider than older participants. This could be because older individuals have more experience with communication. These different preferences for communication support could be because older individuals might have more experience and a better understanding of the disease. They might also be more capable of handling complex matters pertaining to the family. Henrikson et al. (2021) found that the preferences for risk communication among the relatives and probands were not statistically different. The results from our study, however, showed that probands had a higher level of agreement for the involvement of the health care provider than relatives.

The phases of an individual's family cycle and the occurrence of life events are important influences on the preferred method of risk communication. For example, study results show that individuals who are married/living common law may not prefer an approach that does not allow for face-to-face contact, such as having the health care professional send their relatives an email. On the other hand, probands who are divorced/separated/widowed may be in agreement with an indirect form of risk communication. Coupling or marriage provides for more encouragement and social support. These associations are in keeping with findings from studies which elaborated on the importance of family

dynamics in risk communication (Armstrong et al., 2005; Miller et al., 2005; Peters et al., 2005; Wang., 2005). Individuals who are not supported by relatives or whose relatives are seemingly disinterested in learning about their risk are less inclined to interpersonal forms of risk communication, such as informing their relatives in person using a family letter.

Income and education were also related to communication preferences among study respondents. Low-income earners preferred that the health care professional send their relatives an email or give them a phone call, while probands with an above-average income preferred to contact their relatives directly. Similarly, relatives with an advanced education also preferred that the proband contact them directly without the health care professional's involvement, a logical finding since they may be better able to understand risk information. Seven et al. (2020) found that having an advanced education was more likely to facilitate disclosure. Concerning low-income individuals who are at risk of hereditary cancer, Joseph et al. (2012) found no difference in communication preferences between individuals who were directly scheduled for genetic counselling when compared to individuals who were notified of their risk and left to schedule the appointments themselves despite there being a higher acceptance for a direct approach. Similar to the results from this study, there seems to be a higher acceptance of a direct contact approach for genetic counselling among low-income relatives and probands.

5.1.2 Content of communication and other cross-cutting factors

Studies have reported a high acceptance of risk communication without the health care professional's involvement (Ratnayake et al., 2010). Others have endorsed the involvement of the healthcare professional and the index case (the proband) in informing relatives (Henrikson et al., 2021), similar to the findings from this study. However, the sharing of the family letter is not always deemed

appropriate by implicated individuals (Song et al., 2010), especially in situations where relatives have no previous knowledge of their hereditary cancer risk and since there is a lack of consistency in the information provided in family letters (Makhnoon et al., 2021). In addition, other supplemental materials may better clarify hereditary risk (Cragun et al., 2020). In cases where the family letter might not be able to address the various questions that relatives might ask or where relatives are not satisfied because of the need for more information in making an informed decision, the health care professional could provide support whether through a follow-up phone call, email or by in-person consultations. Professionals might also offer advice to probands on reputable information resources for relatives.

Responses to survey items suggested instances where a health care provider's direct contact was preferred. For example, when probands had difficulty communicating complex information. There were significant correlations between items that tested the probands' satisfaction or confidence in communicating complex genetic information and some of the items on preferences for risk communication. Probands who were least satisfied with the family letter or did not find the information in the family letter helpful while informing their relatives were more likely to want health care professionals to assist them during risk communication. Howell et al., 2004 found that low-risk women who were given an explanation letter were unsatisfied and required additional information, while Hayat Roshanai et al. (2010) showed that the relatives of probands who were supported by the health care professional during communication had increased levels of satisfaction and that they were also more likely to attend genetic counselling. Of the 70 relatives, 61 were subject to direct communication from the proband (in-person or via telephone), and six relatives received risk information through a health care channel. This study reported a high acceptance of the family-mediated approach among those relatives whose probands were supported by a health care professional. Sixty-eight percent of the probands felt positive or neutral about informing their

relatives; however, there was low acceptance for the family-mediated approach among the relatives in the control group (33%), and 47% of them preferred that a geneticist inform them about their risk.

Contrary to the findings from Hayat Roshanai et al. (2010), our study revealed that the health care professional might not be needed if there is perceived certainty that the information was communicated correctly and that the relatives understood the implications of their risk. Probands who found the family letter useful and who we able to interpret and explain the content in the family letter were least likely to desire the assistance of the health care professional. However, even with a high level of certainty in communicating cancer risk and sharing genetic test results, there are certain aspects of risk information that might be challenging to convey or for which relatives may need further clarification (Petersen et al., 2018).

Results revealed that probands affected by Lynch syndrome were more likely to indicate they wished for the assistance of a health care professional than probands affected by hereditary breast and ovarian cancer. HBOC caused by the BRCA1/2 mutations causes tumours of the breast, ovaries, the fallopian tubes and, in rare cases, peritoneal tumours. No screening methods are currently acceptable for ovarian cancer, and patients are offered risk-reducing management options according to their age and reproductive desires. On the other hand, the management of LS may be more complex since several mutations are involved, the onset of cancer is earlier than with other hereditary cancer syndromes, and specific screening guidelines and recommendations are associated with each identified mutation. Furthermore, in addition to several mutations, several organs might be affected, including the colon and other organs of the digestive system, ovaries, prostate, breasts, brain and urinary system (Cohen et al., 2014). Therefore, probands may be more likely to need a health care professional's assistance in communicating risk information on Lynch syndrome, given its

complexity and the variations in its presentation. This finding could have direct implications for practice as it highlights a subset of patients who may require additional communication support.

Interestingly, Alegre et al. (2019) and Garcia et al. (2020) found no difference in interfamilial communication between individuals affected by *BRCA1/2* and the mismatch repair genes *(MLH1*, *MSH2*, MSH6 and *PMS2*). Future research that directly compares communication preferences and support needs among mutation subtypes would be valuable to help allocate scarce support resources. Emerging studies are investigating the clinical management and outcomes of moderate and low penetrance genes in HBOC. These genes are associated with a high level of distress and uncertainty among affected individuals, which translates to challenges in risk communication within affected families (Carlsson et al., 2022). The health care provider's assistance might be needed to guide family members who possess these moderate to low penetrance genes, particularly as risk management guidelines for these mutations are currently emerging.

5.1.3 Psychosocial considerations

Worry appears to be a significant barrier to risk communication (Seven et al., 2020; Catania et al., 2015; Kasting et al., 2019). While a high percentage of probands endorsed feeling the responsibility to inform their relatives, they also were concerned about the potential for their relatives to worry about the risk of hereditary cancer within the family. This study's results revealed that probands who worried that risk communication would cause conflict in their family were less likely to endorse informing their relatives without the help of a health care professional. Probands who worried that their relatives might become depressed or anxious were also not accepting of informing their relatives of the risk of hereditary cancer without the involvement of the health care professional, nor were they accepting of the health care professional sending them an email. While we did not ask

probands what they might instead suggest in these situations, it is evident that the health care provider's involvement might be necessary. Interaction with a health care professional carries the benefit of decreasing negative psychosocial responses (Catania et al., 2015; Kasting et al., 2019). Seven et al. (2020) reported that probands whose relatives expressed guilt, anxiety, disinterest or denial were unsatisfied with the family-mediated approach. The health care professional who is experienced in communicating with patients is better able to deescalate problematic situations through techniques such as motivational interviewing and should be able to reasonably assist a resistant, upset or angry relative in understanding the importance of sharing the information with them. While health care professionals cannot contact relatives directly without the proband's consent, having the proband inform their relatives in the presence of a health care professional would be an excellent opportunity to foster effective communication, especially in foreseeable and anticipated difficult situations. Health care professionals could also brainstorm strategies to support probands who believe their relatives might be worried.

5.2 Communication patterns based on the family dynamics and their relationship to outreach preferences

5.2.1 Disproportionate patterns of risk communication

The male component of heritability is often neglected, especially for HBOC, and there is a tendency for probands to share genetic risk information with first-degree relatives and female relatives (Nycum et al., 2009; Green et al., 1997; Smith et al., 2015; Koehly et al., 2009; Patenaude et al., 2006; Wilson et al., 2004; Dean et al., 2020). These findings are reflected in the current results where probands were more likely to share risk information with their first-degree relatives and with their mother's side of the family. However, there were only four male participants in this study. Other

studies have also reported a predominance of female participants (Henrikson et al., 2021, Pande et al., 2021). The imbalance in risk communication between males and females and the decreased awareness among males on how they can transmit the disease (Dean et al., 2020) could explain why other studies have found that they are more likely to report incorrect test results (Daly et al., 2016). These findings underscore the need for more work to be done in designing communication models that are explicitly directed toward males (Dean et al., 2020).

5.2.2 The relationship between risk communication preferences and physical and emotional closeness

Emotional and geographic closeness is positively related to risk communication, as is family members' support (Katapodi et al., 2017; Green et al., 1997; Ratnayake et al., 2010). Willingness to communicate with family members has been shown to increase with social support (Song et al., 2010). During our study, social support was explored by asking the informers (probands) to rate how much they felt encouraged by their relatives. Further analysis was carried out to see how probands being supported (encouraged) by their relatives influenced their preferences for hereditary cancer risk communication. The results showed that even though probands felt encouraged by their relatives, they were less inclined to communicate with them directly and would prefer the health care professional's involvement. This underscores probands' desire for assistance with risk communication, even those who feel encouraged by relatives.

5.2.3 Family Experiences with cancer and outreach preferences

Taber et al. (2014) found that females with a personal or family history of genetic cancer diagnosis were more inclined to share their cancer diagnosis with their relatives compared to those without a personal or family history of cancer. Chopra et al. (2017) found that individuals without a cancer diagnosis were motivated to seek genetic counselling. Despite few studies exploring the effects of a cancer diagnosis on risk communication within affected families, this factor appears to be a facilitator rather than a barrier. Having a cancer diagnosis within the family also has the advantage of initiating discussions on the topic and increasing the likelihood of interfamilial communication (Pollard et al., 2020). The results from this study add to the body of findings suggesting that individuals without a cancer diagnosis desire the health care professional's involvement after first contacting their relatives about their inherited risk. Probands not diagnosed with cancer are more likely to want the health care professional to give their relative a follow-up phone call or send them a follow-up email. The findings imply that the family-mediated approach limits risk communication among probands with little experience with cancer and that the health care professional's assistance is needed.

5.3 Cultural and community values' influence on preferences for risk communication

5.3.1 Values of privacy and autonomy

Across numerous jurisdictions, laws are in place to protect the proband's privacy and prohibit sharing their personal information without their consent. It is noteworthy that in light of these unwavering laws, probands in the current study were largely accepting of sharing their personal information such as their name, cancer diagnosis, and genetic test result with their relatives. One study explored the proband's consent for sharing their genetic test results with their relatives before

they were given their results (Henrikson et al., 2021). There was a high acceptance among the probands for this approach, in line with current results. However, despite favourable attitudes toward sharing personal information, some probands were concerned about sharing their personal information and would prefer to inform their relatives using the family letter in the presence of the health care professional or that their relatives receive a phone call from the health care professional informing them of their risk. Probands who worry that their relatives would not want them to know about their increased cancer risk prefer to deliver the family letter to close relatives and mail it to distant relatives. These findings are similar to those reported by Pentz et al. (2005) where confidentiality concerns among the probands were centred around protecting their personal information from some of their relatives. Hence, a discussion with genetics providers about these attitudes (about privacy) can help determine and better understand the kind of support they might want for talking with relatives.

5.3.2 Values related to responsibility

In standard care, the proband's responsibility is to communicate the risk of hereditary cancer to their relatives by sharing the family letter (Young et al., 2020). The probands have shouldered the informant's role (Peterson et al., 2003; Alegre et al., 2019) even under stressful circumstances such as having a cancer diagnosis and yet, have expressed a willingness to ensure that relatives are aware of their risk (Kohut et al., 2007). Even with a heightened sense of responsibility in informing their relatives of their risk of hereditary cancer, probands might still desire the support of the health care professional since the results showed that these probands were less likely to prefer to deliver the family letter in person to their relatives. Interestingly, probands who did not believe it was their responsibility to inform their relatives but had no problem doing it preferred that the health care

professional participate in risk communication by sending their relatives the family letter by post, by sending them an email or by calling them. This implies that even if the health care professional does assist with informing family members, the proband who is unwilling would still share risk information with their relatives. However, questions remain about how dedicated unwilling probands might be to ensure that all implicated relatives are correctly informed. Probands who simply expressed that it was not their responsibility to inform their relatives also preferred that the health care professional inform their relatives in person of their elevated cancer risk.

5.3.3 Communication patterns based on cultural settings and community infrastructure

Within different jurisdictions, there are variations in the family-mediated approach. For example, one proband who participated in this study explained that they were given informational material, while their relative from another province was given a family letter (section 4.1.3). Relatives from the Atlantic provinces preferred that the health care professional contact them directly or that the proband inform them with the help of the health care professional. On the other hand, relatives from the Prairie provinces disagreed. The literature shows that there are approximately nine genetic counsellors in NL, 21 in NS, 1 in PEI and 0 in NB, compared to 45 in AB, 8 in SK and 14 in MB (Lambert et al., 2021). The desire for the health care professional's involvement in hereditary risk communication by relatives from the Atlantic regions could be due to fewer regulated specialists in these provinces and the need for an improvement in this area. In addition, there is a shortage of genetic specialists with an increasing demand for their services in North America and generally worldwide (Etchegary et al., 2021; Haga et al., 2013).

The results also showed that probands living in a small population centre were more likely to prefer being informed of their hereditary cancer risk in-person by the health care professional when

compared to probands from a large population centre. Infrastructural differences between one setting and another appear to influence how probands might want to inform the relatives and how the relatives prefer being informed. Little information was found in the literature about how implicated individuals from a rural or urban setting would like to be informed about the risk of hereditary cancer. It has been shown, however, that decreased rates of genetic testing in rural areas result from not having a nearby clinic and decreased access to genetic counsellors. Video conferencing is a practical solution to the problem of not having sufficient genetic counsellors within rural settings (Fogleman et al., 2019). Information on risk communication related to population setting was explored by Zilliacus et al., 2010 and this was in relation to genetic counselling services. According to the investigators, telegentics can increase access to rural areas while decreasing patient travel time. The same investigators found no differences between face-to-face genetic counselling and telegentics in the information gained by patients and found that telegenetics may, however, be superior for patient satisfaction with genetic services while decreasing personal feeling of loss of control (Zilliacus et al., 2011). However, the results from the current study showed that participants had little threshold for using similar platforms such as a website or mobile health apps during risk communication, indicating these alternatives to in-person counselling will not be acceptable to all. Again, this highlights the shortage of genetic counsellors more broadly and the need to explore alternative models for facilitating risk communication in families beyond web-based approaches.

One such alternative is genetic group counselling (GGC). Investigators have found that individuals who attend these sessions are satisfied with hereditary cancer risk explanation and would recommend these sessions to others (Hynes et al., 2020; Schwartz et al., 2014; Ridge et al., 2009). These sessions have the advantage of involving the health care professional; they decrease the burden of genetic counsellors, given that there are only a few of them, and also help ensure that correct risk management information is given to implicated family members (Jonnagadla et al., 2022). Group

genetic counselling may also be used in conjunction with other methods of communication (Cohen et al., 2013; Trepanier and Allain, 2013). Evidence suggests that health care professionals might also support probands with hereditary cancer risk disclosure through follow-up telephone calls (Forrest et al., 2007; Hodgson et al., 2016), by assisting the probands to improve their communication skills, providing additional tailored information (Montegomery et al., 2013; Bodurtha et al., 2014) and by providing complementary videographic information (Montegomery et al., 2013; Roshanai et al., 2010).

5.4 Strengths

This study contributes to the body of literature that focuses on how individuals affected by cancer predisposition syndrome would like to inform their relatives of the risk of hereditary cancer and how relatives would like to be informed. Few investigations have explored specific communication preferences of probands, and even fewer still explored how relatives prefer to receive risk information. New knowledge about specific outreach preferences of both probands and relatives has been generated by this work. This study also investigated some factors that influence risk communication and how these are related to communication preferences among affected individuals. The results from this study will be of interest to health care providers who might then implement strategies in supporting probands when conveying risk information to their families. It is anticipated that implementing such strategies could increase the number of relatives who seek genetic counselling from the reported 50% (Loader et al., 2002; Lowery et al., 2010; Hinchcliff et al., 2019; Menko et al., 2013; Marleen et al., 2019), thereby allowing more relatives to receive information to make an informed decision about risk-reducing management options.

The study had a national focus and included both probands and relatives, providing a broad perspective on communication experiences and preferences. The study was advertised widely through various social media platforms, researchers, providers and patient partners from several provinces across Canada. The probands did not differ significantly from the relatives regarding clinical and demographic variables. Most studies on hereditary risk communication include one population or the other. By including both, this study highlighted important differences in communication preferences among probands and at-risk relatives that should be useful in designing supportive communication strategies in practice and in the design and evaluation of tailored communication interventions in research.

Our study allowed participants to choose how they would like to share or receive risk information from several different options, including conventional options such as sharing a family letter, receiving a phone call or sending an email, but also newer methods that are currently being explored in research, such as the use of web-based platforms. This study provides a better understanding of the factors associated with preferences for these specific methods.

5.5 Limitations

Most participants were female, and the number of study participants was small for a national survey. We suspect Covid burden contributed to the low response rate, both in terms of provider ability and time to help recruit eligible patients and respondent interest in research during pandemic concerns and lockdowns. Based on these limitations, the results might not be generalizable to all patients affected by HBOC and LS. In addition, the assumption can be made that there was clustering in survey responses; however, whether the participants were formally related was not measured.

Participation in the online survey was voluntary. Individuals who participated in the survey are those most likely to seek health information or be most interested in discussing hereditary risk. This, therefore, means that little feedback would have been obtained from individuals who are among the 50% of relatives who fail to attend genetic counselling. Such an assumption could also explain why only two male relatives participated in the survey since studies have shown that men are generally unaware of their contribution to genetic cancer or how they might be affected by hereditary cancer and have little interest in risk information (Suttman et al., 2018; Rauscher., 2018; Daly et al., 2016).

The survey used was not a validated questionnaire. It was constructed from a compilation of different survey questions found in similar studies of interest and questions that the research committee incorporated. Thus, its psychometric properties are unknown.

There were three different populations in the survey, one for informers who received a family letter, another for those who did not receive a family letter and a third for the relatives who were informed of the risk of hereditary cancer by the index case. While planning for this investigation, it was not intended to divide the informers into those who received a letter and others who did not. This adjustment was made after piloting. The survey was then divided into these three blocks before being published by Qualtrics XM (Qualtrics, Provo, UT). Some informers who received a family letter could have responded to the survey items from the perspective of one who did not receive a family letter because a standard family letter is not given in every province, which might have caused some confusion. Survey participants were also asked to respond to the items based on previous experiences, which may have introduced recall bias. Before being published, the survey was divided so that 32 questions pertained to the informers who received a family letter, 24 to those informers who did not receive a family letter and 18 to the informed (relatives). This meant that there was an overlapping of questions since some of them were relevant to all three groups. It is unknown how

much respondent burden was induced by the survey. However, patient partners' reviews did not raise survey length as a concern.

5.6 Future research

More research needs to be done regarding outreach preferences given the suboptimal uptake of genetic counselling among relatives of index cases (Loader et al., 2002; O'Neill et al., 2006; Suthers et al., 2006; Lowery et al., 2010; Menko et al., 2013; Hodgson et al., 2014; Hinchcliff et al., 2019; Marleen et al., 2019). Nevertheless, the results obtained from this study can help health care providers tailor supportive approaches for assisting probands with risk communication and can be used as a foundation for future investigations. From the literature review, a handful of studies of high-quality design have been done in this area, so future research initiatives will need to build on this and related studies. An observational qualitative research method might be used for comparing the different approaches to genetic counselling, for example in-person, virtual conference between the specialist and patient, and group sessions. Follow up interviews could then be done to obtain their feedback from participants on the level of satisfaction with the information that was communicated, approval of the setting, and how confident they felt that they could share this information with other family members. Qualitative data analysis could also be employed to examine the content of family letters or other resources that are given to family members at the end of genetic counselling sessions across the different provinces. Other areas for investigation include discourse analysis on the communication between health care providers and implicated individuals, as well as between the index case and their relatives.

Other studies could better design items to measure preferences without using survey skip logic that might have been confusing for the participants. A qualitative approach could also be taken to

understand precisely when and how a provider's help is wanted. For instance, when exactly would a proband want a provider to call or email relatives (before or after the proband has spoken with them)? Our study was unable to answer questions of this kind. Other studies could also ascertain information on the different informational materials that probands are given to share with their relatives across the different provinces since it was noted by some survey respondents that a family letter was not always provided. The effectiveness of these different informational resources could also be compared.

We found that most probands desired the involvement of the health care professional when communicating hereditary cancer risk with their relatives, except those who had advanced education, higher incomes and those who were satisfied with their relative's response to them. Risk communication can be complex, and the same level of satisfaction might not be experienced across the board when sharing risk information with relatives. Also, demographic characteristics that facilitate information transmission are not independent of factors that influence communication in hereditary cancer, such as concerns for relatives' psychological response and certainty that relatives understand the implications of their own risk. Direct communication between the health care professional and relatives is prohibited by law, and there is no outlined responsibility for the health care professional to assist index cases in risk communication. Once evidenced by future research, the efficacy of tailored approaches might assist policymakers in outlining the roles of health care professionals in supporting probands with risk communication while respecting the privacy of the proband.

Finally, awareness needs to be raised about hereditary cancers among providers and the general public (some of whom are at-risk relatives). This might help open communication channels more

broadly. Future research could design and evaluate awareness building initiatives for both providers and the general public.

5.7 Implications and recommendations for practice

The study results have direct implications for health care providers. Information is provided on groups of individuals who might need additional assistance when sharing risk information with their relatives. The results showed that probands who were never diagnosed with cancer need additional support and also probands with little social support, such as those who are single or divorced. Younger probands also preferred the health care professional's involvement instead of having to conduct risk communication on their own. Both probands and relatives who were low-income earners would like the health care professional to be involved in risk communication. The proband's satisfaction with risk communication and certainty that their relatives understood the meaning and implications of their inherent risk were in favour of leading risk communication without the assistance of a health care professional. On the other hand, worry about a relative's response to risk information, a previous negative experience with communicating with relatives, lack of confidence and difficulty sharing genetic information favoured the health care professional's involvement.

These findings help outline areas of exploration and discussion for genetic health care providers and probands that should assist in identifying the kind of support a proband may require (and desire) with risk communication. Given that we know that many probands need help when sharing risk information with their relatives, other resources, as well as communication modalities, could be further explored besides the family letter, such as video graphics and group counselling sessions.

CONCLUSION

The aim of this cross-sectional study was to explore the preferences for hereditary cancer risk communication among individuals affected by HBOC and Lynch syndrome. Even though the family-mediated approach is standard care, the results showed that this method might not be sufficient in cancer risk communication and that alternative methods should be explored. This study successfully highlighted circumstances during which the health care professional's assistance with risk communication might be predominantly preferred; however, there are well known restrictions to their involvement due to privacy laws. Tailored approaches should then be considered that outline the exact roles and limitations of the health care professional when assisting the proband. It is also noteworthy to mention that even though probands wanted their health care professional to be involved in risk communication, they still wanted to be part of this process. There were only a few instances where the proband wanted to communicate with relatives on their own.

This investigation identified groups of individuals who may find it difficult to communicate cancer risk and also those who were more comfortable doing so. Similar information was gathered from individuals who received risk information. Importantly, the results showed that individuals with no previous cancer diagnosis found it difficult to communicate with their relatives. Few studies done previously ascertained information on how cancer diagnosis affected risk communication.

Study results should assist providers in their efforts to support families communicate about inherited cancer risk. Ultimately, it is hoped that effective risk communication can help increase the number of at-risk relatives who undergo genetic testing and subsequent life-saving risk management.

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APPENDICES

APPENDIX A: Predictive models used to estimate age-specific absolute risks of breast and gynecologic cancers

Model	Family History (input)	Pathogenic Variants	Risk Factors	Risk Estimate Generated
Breast Cancer Risk Assessment Models				
Models for Average-Risk Women				
Gail/BCRAT	First-degree relatives (breast cancer)	No	Yes	Breast cancer
Pfeiffer (breast)	First-degree relatives (breast, ovarian cancers)	No	Yes	Breast cancer
Colditz and Rosner	None	No	Yes	Breast cancer
Models for High-Risk Women				
Claus	Multigenerational (breast cancer)	No	No	Breast cancer
BRCAPRO	Multigenerational (breast, ovarian cancers)	*BRCA1/BRCA2*	No	Breast cancer; % risk of carrying *BRCA1*/*BRCA2* pathogenic variant
IBIS	Multigenerational (ovarian cancer)	*BRCA1/BRCA2*	Yes	Breast cancer; % risk of carrying *BRCA1*/*BRCA2* pathogenic variant
BOADICEA	Multigenerational (pancreatic, breast, ovarian cancers)	*BRCA1/BRCA2*	No	Breast and ovarian cancer; % risk of carrying *BRCA1*/*BRCA2* pathogenic variant
Ovarian Cancer Risk Assessment Models				
Models for Average-Risk Women				
Rosner	None	No	Yes	Ovarian cancer
Pfeiffer (ovarian)	First-degree relatives (breast, ovarian cancers)	No	Yes	Breast cancer
Models for High-Risk Women				
BOADICEA	Multigenerational (pancreatic, breast, ovarian cancers)	*BRCA1/BRCA2*	No	Breast and ovarian cancer; % risk of carrying *BRCA1/BRCA2* pathogenic variant
Endometrial Cancer Risk Assessment Models				
Models for Average-Risk Women				
Pfeiffer (endometrial)	None	No	Yes	Endometrial cancer
Models for High-Risk Women				
PREMM5	Multigenerational (colon, endometrial and other Lynch syndrome–associated cancers and polyps)	No	No	% Risk of carrying *MLH1*, *MSH2*, *MSH6* pathogenic variant
MMRpro	Multigenerational (colon, endometrial cancers)	No	No	% Risk of carrying *MLH1*, *MSH2*, *MSH6* pathogenic variant
MMRpredict	Multigenerational (colon, endometrial cancers)	No	No	% Risk of carrying *MLH1*, *MSH2*, *MSH6* pathogenic variant

(Genetics of Breast and Gynecologic Cancers (PDQ®)–Health Professional Version, 2022).

APPENDIX B: Amsterdam II criteria (Gupta et al., 2017)

The criteria are as follows:

One relative should be a first-degree relative of the other two
At least two successive generations should be affected
At least one Lynch syndrome-associated cancer should have been diagnosed before age 50 years

*FAP should be excluded

*Tumor should be verified by pathological examination

APPENDIX C: The Revised Bethesda Guidelines for testing colorectal tumors for microsatellite instability (MSI) (Gupta et al., 2017)

Revised Bethesda Guidelines
Tumors from individuals should be tested for MSI in the following situations: 1. Colorectal cancer diagnosed in a patient younger than 50 years of age. 2. Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors, regardless of age. 3. Colorectal cancer with the MSI-H histology diagnosed in a patient who is less than 60 years of age. 4. Colorectal cancer diagnosed in one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years. 5. Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age.

APPENDIX D: Ecological model - factors influencing intrafamilial communication of HBOC genetic information (Nycum et al., 2009)

The individual level

Perception of personal risk

- *Difficulty in understanding complex information*
- Cancer-related stress and diagnosis

Vulnerability and receptivity of relatives

- Relatives' age, life stage, maturity
- Life events

Content of communication

- Difficulty in understanding/communicating complex information
- Include discussion of prevention and surveillance measures

Timing of communication

- Immediately once results are obtained
- Wait for the 'right time'
- Create an occasion specifically for the purpose of communication
- Involve family early in the process

Personal feelings

- Around being the bearer of 'bad news'
- Around having passed on a hereditary condition
- Around testing negative when other family members are positive

The familial level

Proximity of relationship

- Close relatives communicated with more than distant ones
- Spouses and sisters communicated with more than other relatives
- Female/younger relatives communicated with more than male/older relatives
- Reasons for not communicating: social, emotional or geographic distances
- Communication may be support-seeking
- Communication seen as a parental responsibility

Family forms

- Genetic and lay notions of family do not always correspond
- Reconstituted families can be a barrier to communication

Family relationships

- Family cohesion/openness may facilitate communication
- Communication may affect family relationships

Family experiences with cancer

- Experience with cancer may facilitate communication or create a barrier

The community level

Cultural context

- Prevalence of values of privacy and autonomy within a culture/community
- Taking on responsibility for hereditary risk information as a community

Gender

- Different patterns of communication along gender lines
- Women as the 'gatekeepers' of genetic information
- Women may experience conflicting obligations to themselves and to family members
- Increasing generation of information may unduly burden women

Cross-cutting factors

Complexity of HBOC genetic results

- Information is complex and difficult to understand
- Even where information is well understood, evidence shows that communication is defective
- Role of health professionals or counselor

Certainty of HBOC genetic results

- HBOC results may be more or less conclusive
- Lack of certainty around results may result in a perception that communication will do no good
- Role of health professionals

Responsibilities

- Influencing factors can interact in ways that give rise to conflicting senses of responsibility

APPENDIX E – Health Research Ethics Board Approval

Research Ethics Office
Suite 200, Eastern Trust Building 95 Bonaventure Avenue
St. John's, NL A1B 2X5

NEWFOUNDLAND AND LABRADOR
HREB
HEALTH RESEARCH ETHICS BOARD

September 10, 2021

6461 Valiant Heights, Mississauga
Ontario L5W1C9

Dear Dr Burke:

Researcher Portal File # 20220670
Reference # 2021.154

RE: Exploration of the optimal model for family member outreach in patients with cancer predisposition syndromes: A Canadian survey study.

Your application was reviewed by a subcommittee under the direction of the HREB and your response was reviewed by the Chair and the following decision was rendered:

X	Approval
	Approval subject to changes
	Rejection

Ethics approval is granted for one year effective September 8, 2021. This ethics approval will be reported to the board at the next scheduled HREB meeting.

This is to confirm that the HREB reviewed and approved or acknowledged the following documents (as indicated):

- Application, approved

- Research proposal, approved
- Email text, approved
- Study questionnaire with opening consent, approved
- Poster, approved
- Information Letter 09/02/2021, approved

Please note the following:

- This ethics approval will lapse on September 8, 2022. It is your responsibility to ensure that the Ethics Renewal form is submitted prior to the renewal date.
- This is your ethics approval only. Organizational approval may also be required. It is your responsibility to seek the necessary organizational approvals.
- Modifications of the study are not permitted without prior approval from the HREB. Request for modification to the study must be outlined on the relevant Event Form available on the Researcher Portal website.
- Though this research has received HREB approval, you are responsible for the ethical conduct of this research.
- If you have any questions please contact info@hrea.ca or 709 777 6974.

The HREB operates according to the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2), ICH Guidance E6: Good Clinical Practice Guidelines (GCP), the Health Research Ethics Authority Act (HREA Act) and applicable laws and regulations.

We wish you every success with your study.

Sincerely,

Dr Fern Brunger, Chair Non-Clinical Trials Committee
Health Research Ethics Board

APPENDIX F – study information sheet

STUDY INFORMATION

Individuals with a family history of cancer predisposition syndrome resulting from the BRCA1/2 and Lynch syndrome mutations may benefit from early prevention through risk-reducing screening and surgical management options. Cancer prevention in this population is imperative since some hereditary cancers occur at young ages, often with high morbidity and mortality.

Despite efforts to increase the number of at-risk relatives who attend genetic counselling, a significant number of these individuals are not utilizing such services. Previous research has identified barriers to effective family communication about hereditary cancer risk.

In this study, we are interested in whether methods of outreach beyond sharing a family letter might be preferred by these families, including direct contact by a healthcare provider or genetics service. Ultimately, we hope to collect information on preferences for receiving and sharing information on hereditary cancer predisposition and the factors that may influence these preferences.

To explore this issue, we are inviting: 1) members of families affected by BRCA or Lynch syndrome, including carriers of these mutations, those testing negative, and unaffected at risk relatives, 2) over the age of 18 years, 3) from anywhere across Canada to complete an online, anonymous survey. It should take 15-20 minutes to complete. Responses will be collected and stored in Canada on the Qualtrics survey platform, approved by Memorial University. Responses are anonymous and explore opinion on various methods of sharing hereditary cancer risk information in the family. We hope that a better understanding of outreach preferences can ultimately inform how best to support patients' talk with family members about hereditary cancer risk and ensure at-risk relatives receive this information.

If you have questions regarding your rights as a research participant please contact the Health Research Ethics Authority at (709) 777-6974 or info@hrea.ca.

Sincerely,

Kimberly Burke, Masters candidate (Principal Investigator)
Faculty of Medicine, Memorial University
Email: kburke20@mun.ca

Dr. Holly Etchegary (supervisor)
Faculty of Medicine, Memorial University
Email: holly.etchegary@med.mun.ca; Phone: 709-864-6605

APPENDIX G – email text to be sent to community organizations, clinical organizations, or research team contacts to assist with study advertising

The subject line of the email: Please share: hereditary cancer research study

Dear [xx],

Researchers at Memorial University are conducting an online survey study about how patients at risk for hereditary cancer share risk information with their families. Studies have shown that approximately 50% of the relatives of probands who carry BRCA1/2 or Lynch mutations attend genetic counselling and testing. This means a large percentage of those at risk for these hereditary cancers are not accessing genetic testing and risk-reducing management options.

We are interested in whether methods of outreach beyond sharing a family letter might be preferred by these families, including direct contact by a healthcare provider or genetics service. Ultimately, we hope to collect information on preferences for receiving and sharing information on hereditary cancer predisposition and the factors that may influence these preferences.

We would appreciate your help with advertising the survey. It takes 15-20 minutes to complete and is relevant to all families with an identified BRCA or Lynch syndrome mutation. A study advert is attached. Please share it and/or this survey link widely through your network(s):

If you have questions regarding your rights as a research participant please contact the Health Research Ethics Authority at (709) 777-6974 or info@hrea.ca.

Sincerely,

Kimberly Burke, Masters candidate (Principal Investigator)
Faculty of Medicine, Memorial University
Email: kburke20@mun.ca

Dr. Holly Etchegary (supervisor)
Faculty of Medicine, Memorial University
Email: holly.etchegary@med.mun.ca; Phone: 709-864-6605

APPENDIX H – Survey Poster

APPENDIX I – Survey Questionnaire

Sharing hereditary cancer information within the family

INFORMATION AND CONSENT

We are inviting residents of Canada aged 18 and older affected by hereditary breast and ovarian cancer syndrome (HBOC) and Lynch syndrome (LS) to participate in a survey about the preferred method of sharing information about hereditary cancer in the family.

Please read the following consent agreement to inform you about the survey, then proceed when ready.

No special background or knowledge is needed to complete the survey. Taking part in this study is voluntary. It is up to you to decide whether to be in the study or not. You can decide not to take part in the study. If you decide to take part and complete the survey, you are free to stop at any time. Taking part in this survey will not affect any healthcare you or your family receive.

DESCRIPTION OF STUDY
This study is being conducted by researchers at Memorial University in St. John's, NL. It aims to explore the opinions of individuals from families with identified BRCA 1/2 and Lynch mutations about methods of informing relatives about their risk of inherited cancer. We would like to hear about the experience of telling other family members about the family risk. We also hope to hear from people who were told about their risk by a relative but may not themselves have informed others in the family. In both cases, we are interested in your opinions on different ways of informing relatives about their genetic cancer risk.

The survey takes about 15-20 minutes to fill out. There are no right or wrong answers; we are only interested in your opinions. If you come to a question you do not want to answer or do not understand, you can skip it.

The data collected will be used for scientific research to better understand different methods for informing at-risk relatives about their inherited cancer risk. We hope that understanding the experience of being the person who had to inform other relatives about their risk, or the experience of being a family member who was informed, will allow us to identify all possible ways at-risk individuals could be identified so they might benefit from genetic counselling and life-saving interventions.

PRIVACY
Protecting your privacy is an important part of this study. Your answers to the following survey are anonymous, and no effort will be made to use the information to identify who you are. The answers you provide us are confidential and will only be reported in grouped responses (e.g., the percentage of people who agreed or disagreed with a survey item). Your name will not be recorded or used in any papers or reports prepared from the survey data.

You may have found this survey through social media, but no information you provide here is linked to outside profiles (e.g., a Facebook account). This survey is administered using Qualtrics, Memorial University's approved online survey tool. Survey data are stored in Canada and Memorial University's license agreement with Qualtrics meets the privacy, security and legislative requirements of the University.

LIABILITY STATEMENT
By completing this survey, you are implying that you are consenting to be in this study. Giving us your consent tells us you understand the information about the research study. By consenting to be a participant in this study, you are not giving up your legal rights. Researchers involved in this research study still have their legal and professional responsibilities.

ACCESS TO RECORDS
Since the survey will be completed anonymously, we are unable to provide you access to records of your survey responses once it has been collected.

USE OF YOUR STUDY INFORMATION
The research team will collect and use only the information they need for this research study. This information will include your:
- Understanding of your cancer risk, previous cancer diagnosis and mutation status
- Experience of talking with relatives about their hereditary cancer risk
- Experience of being informed about hereditary cancer risk
- Opinions on different ways of informing relatives about their risk of hereditary cancer
- Demographic information, such as age, sex, gender, marital status, parity and education level

Collected data will be kept secure by the research team, under the responsibility of Kimberly Burke, the study principal investigator.

QUESTIONS OR PROBLEMS?
If you have any questions about taking part in this study, you can contact the primary investigator in charge of the study at this institution. That person is:

Kimberly Burke		Dr. Holly Etchegary
Primary Investigator		Supervisor
Clinical Epidemiology		Faculty of Medicine, Memorial University
Email: kburke20@.mun.ca	or	Email: holly.etchegary@med.mun.ca; Phone 864-6605

FURTHER CONTACT DETAILS:
You can also talk to someone who is not involved with the study at all but who can advise you on your rights as a participant in any research study. This person can be reached through:

ETHICS OFFICE
Health Research Ethics Authority
709-777-6974 or by email at info@hrea.ca

*** 1. Do you consent to participate in this study?**

By selecting "Yes" and click "Next," you are consenting to be in this study. It tells us you understand the information about the research study. When you select "yes" and consent to be a participant in this study, you are not giving up your legal rights. Researchers or agencies involved in this research study still have their legal and professional liabilities

- ○ Yes
- ○ No

ELIGIBILITY

*** 2. Are you 18 years old or older?**

- ○ Yes
- ○ No

*** 3. Are you a resident of Canada?**

- ○ Yes
- ○ No

Please choose which perspective you will provide on the survey – that of the person who informed others in the family about cancer risk (the 'informer') or the person who received hereditary cancer risk information from a family member (the 'informed').

***4. I will answer survey questions from the perspective of (please choose one):**

- ○ Informer
- ○ Informed

SECTION 1 – BACKGROUND INFORMATION

5. What was your perception of your risk of getting cancer before you were seen by a genetic specialist?

○ High ○ Moderate ○ Low

○ Unknown/Insufficient information ○ I was not seen by a genetic specialist

6. What is your genetic test result?

○ BRCA1 ○ BRCA2 ○ Lynch syndrome

○ I did not have genetic testing ○ Not sure

○ My BRCA1/2 or Lynch mutation test result was negative

Other, please describe _____

7. Have you ever been diagnosed with cancer?

○ Yes ○ No

8. How long since you were diagnosed with cancer?
Please state the number of years since the first diagnosis
_____ (drop-down menu)

9. What was your diagnosis? Select all that apply

○ Breast cancer ○ Ovarian cancer ○ Endometrial cancer

○ Colon cancer
Other, please describe

SECTION 2 – THE FAMILY MEDIATED APPROACH – FOR INDIVIDUALS WHO <u>SHARED</u> THE FAMILY LETTER (i.e., the 'Informers')

10. Did you receive a family letter that explained your risk of hereditary cancer?

○ Yes ○ No

If you selected "No" and you were given other materials, please list them

_____

11. How many relatives were you asked to share the letter with?

_____

12. How many relatives did you share the letter with?

_____

13. How many first-degree relatives did you share the family letter with? First-degree relatives are children, brothers and sisters, and parents.

_____

14. How many second-degree relatives did you share the family letter with? Second-degree relatives are aunts, uncles, nephews, nieces, grandchildren and grandparents

_____

15. If you were asked to share the family letter with your relatives, we are interested in your opinion about the responsibility for informing at-risk relatives about family cancer risk and your experiences.

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I do not think that I should have been the one to inform my relatives or share the information with them**					
II.	**I do not believe it was my responsibility, but I had no problem doing it**					
III.	**I felt responsible; however, I would have liked the assistance of someone else, i.e., another family member or a healthcare provider**					
IV.	**I felt responsible for informing my children, siblings, parents and spouse**					
V.	**I felt responsible for informing my aunts, uncles, nieces, grandchildren and grandparents**					

SECTION 3 – YOUR EXPERIENCE IN COMMUNICATING CANCER RISK TO YOUR RELATIVES

If you shared the family letter with relatives, please indicate your level of agreement with the following items

16. We are interested in whether you found the family letter helpful in communicating cancer risk to your relatives.

Perceived usefulness of family letter

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I found the letter very useful in helping me to communicate the risk of hereditary cancer to my relatives**					
II.	**The letter helped me to communicate with my relatives about hereditary cancer risk; however, some of my relatives asked questions that the letter did not address**					
III.	**I was able to read and understand what was written in the letter, but it was hard for me to explain it to my relatives in my own words**					
IV.	**I thought that the letter's content should have been in a more simplified form or language.**					

17. How satisfied were you with using a family letter to inform your relatives about their inherited cancer risk?

Satisfaction with communication

		Disagree strongly	Disagree Somewhat	Uncertain	Agree Somewhat	Agree Strongly
I.	**I felt satisfied with communicating with my relatives using the family letter about the risk of genetic cancer**					

II.	**I was satisfied with my relative's response to me communicating cancer risk and sharing the summary letter**					

Self-efficacy

18. Now, we are interested in how prepared you felt to share the information with your relative. Please choose one response for each item that follows.

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**Communicating genetic information was complex for me**					
II.	**I did not feel confident in passing on the information about cancer risk because I did not feel like I could correctly communicate the information**					
III.	**I did not feel confident in passing on this information because of the fear of causing distress among my relatives**					

Certainty

19. Were you confident that the family letter's information helped your relatives understand their increased risk of hereditary cancer?

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I felt confident that the family letter explained to my relatives what having the mutation meant**					
II.	**I felt confident that the family letter helped my**					

	relatives to understand the importance of genetic testing	
III.	**I felt confident that my relatives understood the implications of the information in the family letter for their own health**	

Support

20. Please share your experience with us about your relatives' reaction to hearing the news from you about your family's cancer risk

		Disagree strongly	**Disagree somewhat**	**Uncertain**	**Agree somewhat**	**Agree strongly**
I.	**It was hard for me to talk to my relatives about the risk of hereditary cancer**					
II.	**Some of my relatives relative were angry/upset**					
III.	**Some of my relatives were uninterested when I shared the information about our family's inherited risk**					
IV.	**In general, my relatives were grateful for the information about our family's inherited cancer risk**					
V.	**My relatives encouraged me to share the information with other relatives**					

Distress

21. Were you concerned that sharing genetic cancer risk information would cause distress within the family?

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I worried that communicating the risk of hereditary cancer would bring about conflict in the family**					
II.	**I worried that my family would become anxious or depressed after receiving the information**					

22. We would like to know if you were concerned about confidentiality

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I was concerned about sharing personal medical information with other family members (confidentiality)**					
II.	**I worried that my relatives would not want me to know about their increased risk of cancer**					

SECTION 4 – PREFERRED METHOD OF COMMUNICATING CANCER RISK INFORMATION

The following items (22-25) to be answered by the probands/carriers (i.e., the informers)

23. We would like your feedback on sharing your personal information with your relatives when communicating the risk of hereditary cancer risk to them

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**It would be acceptable to me if my name was shared with my relatives**					

	irrespective of the method that is used to communicate hereditary cancer risk information to them					
II.	**It would be acceptable to me if my genetic test result was shared with my relatives regardless of how they are informed of their cancer risk**					
III.	**It would be acceptable to me if my cancer diagnosis (if applicable) was shared with my relatives when they are being informed of their hereditary cancer risk**					

24. We are interested in your preferences about using a family letter to inform relatives about their hereditary cancer risk and further management. Please choose one response option for each item that follows:

		Disagree Strongly	**Disagree somewhat**	**Uncertain**	**Agree somewhat**	**Agree strongly**
I.	**I prefer to deliver the family letter in person to my relatives**					
II.	**I prefer to deliver the letter to close relatives and to mail the letter to my distant relatives**					
III.	**I would prefer to inform my relatives using the letter in the presence of a health care professional**					
IV.	**I believe that I should share the family letter with my relatives; however, a health care provider should call them afterwards**					

V.	**I feel it is my responsibility to inform my relatives with a family letter; however, a health care professional should send them a follow-up email**					

25. We are interested in your opinions about active contact taken by a healthcare professional to share cancer risk information with your relatives. Please choose one response option for each of the items that follow:

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I believe that my relative should be informed in person by a health care professional of the risk of hereditary cancer**					
II.	**I would like to disclose the information without the involvement of a health care professional**					
III.	**The health care professional should mail the family letter to my relatives**					
IV.	**The health care professional should send an email with information on hereditary cancer risk to my relatives**					
V.	**My relatives should receive a telephone call from a health care professional informing them about the risk of hereditary cancer**					

26. We are interested in your opinion about the use of a mobile health application or a website for communicating the risk of hereditary cancer to your relatives

	Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I. **I would prefer to share the link to a secure mobile health app or a website with my relative that has all the information they need about our family's inherited cancer risk**					
II. **I would prefer if my health care provider shared a link to a secure mobile health app or website with my relative that has all the relevant information they need about our family's inherited cancer risk**					

27. Please share any other thoughts on any other suggestions you might have for informing relatives about inherited risk.

_____

_____

_____

SECTION 5 – THE FAMILY MEDIATED APPROACH – FOR INDIVIDUALS WHO <u>RECEIVED</u> THE FAMILY LETTER

If you received a family letter from another relative, please indicate your level of agreement to the following items

28. We are interested in whether the information in the family letter helped you understand your risk of hereditary cancer and the need for genetic counselling/testing.

Satisfaction with information

	Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly

I.	The information in the family letter was helpful	
II.	The letter should have been more detailed	
III.	Some of the terms used in the letter were not familiar to me; because of this, I did not find the letter useful	

Control

Cognitive control

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	I understood the meaning of the letter for my family's future and me					
II.	I understood what the cause of my own elevated risk was					

Behavioural control

		Disagree strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	I understood I was eligible for genetic counselling					
II.	I understood I could undergo genetic testing to determine if I had a cancer-causing mutation that would put me at an increased risk					
III.	I understood that I could manage my personal inherited					

	cancer risk and what my options were

29. We are interested in your response to being told about your cancer risk by another relative. Please choose one response option for each item:

		Disagree Strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I felt angry/upset about receiving the information**					
II.	**I felt sad**					
III.	**I felt anxious/nervous**					
IV.	**I was concerned**					
V.	**I felt a loss of control**					
VI.	**I was happy that my relative shared the information with me**					
VII.	**I did not care much about receiving the information**					

SECTION 6 – PREFERRED METHOD OF RECEIVING CANCER RISK INFORMATION

The following items to be answered by the relatives (i.e., the 'informed'):

30. How would you like information about hereditary cancer risk to be shared with you?

		Disagree Strongly	Disagree somewhat	Uncertain	Agree somewhat	Agree strongly
I.	**I would prefer if a family letter was provided to me by my relative**					
II.	**I would prefer if my relative contacted me directly to talk about our family's increased cancer risk**					
III.	**I would prefer my relative to inform me of the risk of hereditary cancer with the help of**					

	a health care professional
IV.	**I would prefer that a health care professional contact me directly about my risk of hereditary cancer**
V.	**I would prefer to use a platform such as a secure mobile health app or a website for learning about my risk of hereditary cancer**

SECTION 7 – DEMOGRAPHIC INFORMATION

31. What is your age?

_____

32. What is your marital status?

○ Single ○ Legally married ○ Living Common-law ○ Divorced/Separated

○ Widowed

33. How many children do you have? Please include stepchildren and adopted children and enter 0 if you do not have children.

_____

34. How would you describe your gender?

○ Male ○ Female ○ Non-binary ○ Other, please describe

35. What is the highest level of education you have acquired?

○ Less than high school

○ High school Diploma

○ Trade or College Diploma

○ University, undergraduate degree

- University, graduate degree

36. In what income bracket would you put yourself?

- Low
- Middle
- High

37. In what province or territory do you live? Please choose one: (list out provinces)

38. Do you live in an urban or rural area? Statistics Canada defines urban areas with three sizes of population centres. All areas outside population centres are defined as rural. Please choose one of the following that best describes your residence:

- Small population centre, with a population between 1,000 and 29,999
- Medium population centre, with a population between 30,000 and 99,999
- Large urban population centre, with a population of 100,000 or more.
- Rural area

Please note: The survey items were separated into blocks so that questions that were relevant to each subgroup of study participants (1.the informers who were given a family letter, 2.the informers who were not given a family letter and 3.the informed) were only seen by them.