Facilitating Communication and Referrals for Families with Lynch Syndrome

by

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A Thesis submitted to the Faculty of Graduate Studies of
The University of Manitoba
in partial fulfilment of the requirements of the degree of

MASTER OF SCIENCE

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ABSTRACT

In the past decade, Manitoba has implemented universal screening for Lynch Syndrome (LS) and established a multidisciplinary clinic for annual follow-up, generating tremendous potential for cancer prevention through the identification of individuals with LS and provision of effective surveillance strategies. However, alerting at-risk individuals to genetic testing and cancer prevention strategies is reliant on communication within families and little is known about the facilitators and barriers facing Manitobans. The current study developed an informational resource to facilitate communication and evaluated the resource using a mixed methods approach. Individuals with LS were recruited through various clinics at the Health Sciences Centre in Winnipeg and at-risk relatives were recruited through snowball sampling. A total of 92 participants provided feedback on the informational resource through an online survey. Responses to the Likert scale questions indicated the informational resource was easy to understand and helped users inform their family members. Logistic regression analysis revealed that individuals age 45 or older were about four times more likely to share information about LS with their relatives. Additionally, fifteen individuals with LS participated in a qualitative interview exploring barriers and facilitators to communicating risk information to relatives. Thematic analysis revealed three major themes impacting communication: perceptions of genetic testing, family dynamics, and level of acceptance towards relatives' autonomy. The numerous subthemes identified were supported by previous literature from other jurisdictions. The results from this study guided proposed revisions to the informational resource and provide recommendations for the development of similar resources for other genetic conditions. The barriers to communication identified in this study should be addressed during genetic counselling sessions to extend the outreach of LS testing and cancer prevention.

ACKNOWLEDGEMENTS

I have a debt of gratitude to the many people who made this project possible. Firstly, I would like to thank the research participants for being open with me about their experiences. I was inspired by your motivation to help others through research and encouraged by your appreciation of this project.

I would like to thank each member of my advisory committee for bringing such valued perspectives to this project. To my supervisor, Dr. Harminder Singh, thank you for your guidance and support throughout this program and transitioning into a new career. To Heidi Rothenmund, your role in the conception of this project was so appreciated and I have you to thank for most of the study recruitment. To Dr. Kirk McManus, thank you for your thoughtful feedback and willingness to also help with other areas of the program like scholarship applications. To Dr. Gayle Restall, thank you for helping me find my way as an interviewer and encouraging me to explore the nuances of the data. To Dr. Kristin Reynolds, thank you for your time spent collaborating on the thematic analysis and your guidance on presenting the findings. To my entire advisory committee, thank you for being available to answer my questions as they arose and for your flexibility and support through these 'unprecedented times'.

Additionally, I benefited from the support and guidance of my program directors, Jessica Hartley and Claudia Carriles, who were there every step of the way. As were my classmates, Cassie and Dorothy, thank you.

A special thank you to my partner, family, and friends for the unwavering love and support.

Lastly, I would like to acknowledge the funding I received through CancerCare Manitoba and the Canadian Institutes of Health Research.

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BSO: Bilateral salpingo-oophorectomy
CT: Cascade genetic testing
CRC: Colorectal cancer
EC: Endometrial cancer
EGD: Esophagogastroduodenoscopy
EPCAM: Epithelial Cell Adhesion Molecule
EUS: Endoscopic Ultrasound
HBOC: Hereditary Breast and Ovarian Cancer syndrome
HNPCC: Hereditary Non-Polyposis Colorectal Cancer
IHC: Immunohistochemistry
IC: Index case
LS: Lynch syndrome
LSFP: Lynch Syndrome Family Package
MLH1: MutL Homolog 1
MMR: Mismatch repair
MRI: Magnetic Resonance Imaging
MRCP: Magnetic Resonance Cholangiopancreatography
MSH2: MutS Homolog 2
MSH3: MutS Homolog 3
MSH6: MutS Homolog 6
MSI: Microsatellite instability
MSI-H: High microsatellite instability
NCCN: National Comprehensive Cancer Network
PMS2:PMS1 Homolog 2

Chapter One: Introduction & Literature Review

Introduction

Lynch syndrome (LS) is an inherited cancer predisposition syndrome accounting for the majority of inherited colorectal and endometrial cancers. Many factors have been reported to impact the uptake of genetic testing for LS. Following a molecular diagnosis of LS, family communication is key to alert relatives of their at-risk status for cancer susceptibility. However, the complexities of the genetic information and family dynamics can prevent effective communication among family members. Additionally, a LS diagnosis can have significant physical and emotional tolls, further complicating the process of informing relatives. In Canada, genetic testing for LS is typically provided by a genetic counsellor trained to help individuals understand and adjust to genetic information. Genetic counsellors aim to facilitate information sharing about LS to at-risk relatives and provision of a family letter is standard practice. However, very limited research has informed the content of family letters and variability exists between published examples with no indication of recipient preferences.

Facilitators and barriers to communication and genetic testing have been described in other jurisdictions but have not been evaluated in Manitoba. Manitobans with LS may have unique perspectives given the contextual landscape. Firstly, individuals can self-refer without a referral from a physician. Secondly, Canada's universal healthcare system provides publicly funded genetic counselling and genetic testing. A specialized multidisciplinary clinic was established in 2018 for individuals with LS in Manitoba. Furthermore, remote genetic counselling appointments have been offered by Telehealth and telephone, even prior to the COVID-19 pandemic, to facilitate individuals distant from the clinic location. Hence, we hypothesized unique facilitators and barriers to communication and genetic testing in Manitoba.

Research Questions

This study explores the experiences of individuals communicating with their relatives about LS and how patient resources for LS can be improved to facilitate information sharing. The specific aims of this study are to 1) evaluate the patient resource provided to individuals with LS, 2) identify any perceived barriers and facilitators to accessing genetic counselling and testing in Manitoba, and 3) suggest improvements to the patient resources and referral system based on the data collected.

Lynch syndrome

LS is an inherited cancer predisposition syndrome first described by Dr. Alfred Warthin in 1913 who recognized an autosomal dominant pattern of colonic, endometrial, or gastric cancer in 33 of 70 members of 'Family G'(Warthin, 1913). In the 1960s, Dr. Henry Lynch began publishing information about other families with similar cancer histories (Boland & Lynch, 2013; Gallon et al., 2021; Lynch et al., 1966, 1967; Lynch & Krush, 1967). At that time, LS was known as Hereditary Non-Polyposis Colorectal Cancer (HNPCC), termed to distinguish LS from Familial Adenomatous Polyposis (Kastrinos & Stoffel, 2014). Eventually, the term HNPCC was abandoned to recognize the additional cancer risks beyond colorectal cancer (CRC) and renamed after Dr. Henry Lynch (Firth & Hurst, 2017; Kastrinos & Stoffel, 2014).

Leading up to the discovery of the molecular etiology of LS in 1993, scientists had recognized loss of heterozygosity in CRC tumour tissue and targeted these loci to try and identify tumour suppressor genes involved in carcinogenesis. Their analysis revealed a high frequency of insertion and deletion variants within the short tandem repeat sequences, called microsatellites. This phenomenon was termed microsatellite instability (MSI). Approximately 12% of CRCs were identified with high microsatellite instability (MSI-H) and a mechanism unique from loss of heterozygosity was suspected for this subset (Aaltonen et al., 1993; Ionov et al., 1993; Thibodeau et al., 1993). In vivo experiments in yeast determined that loss-of-function mutations in the mismatch repair (MMR) genes induced the MSI-H phenotype (Strand et al., 1993). The yeast mutS homolog 2 (*MSH2)* gene was used to map *MSH2* in the human genome and identify a pathogenic variant segregating with MSI-H HNPCC (Fishel et al., 1993; Leach et al., 1993). The remaining human MMR genes were soon identified, including mutL homolog 1 (*MLH1)* (Bronner et al., 1994; Papadopoulos et al., 1994), PMS1 homolog 2 (*PMS2)* (Nicolaides et al., 1994), and mutS homolog 6 (*MSH6)* (Miyaki et al., 1997; Palombo et al., 1995; Papadopoulos et al., 1995).

MMR genes encode proteins which normally function to repair errors in DNA synthesis and double-stranded DNA breaks (Hegde et al., 2014). DNA replication is error prone, but the MMR mechanism is part of the inherent repair systems in place to proofread the newly synthesized DNA and maintain the integrity of the genetic material (Majumder et al., 2018; Tamura et al., 2019).

MMR proteins form heterodimers with specific functions. The heterodimers of MSH2 with MSH6 or mutS homolog 3 (MSH3) are involved in mismatch-pair recognition and initiation of repair. MLH1-PMS2 heterodimers have endonuclease function to excise DNA errors (Tamura et al., 2019). The MMR system is responsible for repairing nucleotide mismatch errors which occur during DNA replication (Hegde et al., 2014; Ryan et al., 2019).

A fifth gene, epithelial cell adhesion molecule (*EPCAM)*, is associated with LS. *EPCAM* is not an MMR gene (as it does not lead to production of an MMR protein), but it is located just upstream of *MSH2*. Deletions in *EPCAM* cause *MSH2* promoter methylation, which inhibits *MSH2* gene expression (Tamura et al., 2019).

Adhering to the central dogma of biology, genes provide a blueprint for the formation of proteins which perform biological functions. A heterozygous mutation in an MMR gene is tolerable as there is sufficient MMR protein activity to maintain the fidelity of the genetic code (Majumder et al., 2018). Cancer develops due to an acquired second mutation which prevents the DNA repair mechanism from functioning and induces MSI (Hegde et al., 2014; Majumder et al., 2018). The subsequent rapid accumulation of mutations leads to tumorigenesis in susceptible tissues, such as the colon or endometrium (Hegde et al., 2014). Individuals with LS have an inherited susceptibility to cancer which is inherited autosomal dominantly.

All classes of mutations can cause LS; nonsense, frameshift, splice, missense, point mutations, exon deletions/duplications and rearrangements have all been known to cause LS (Firth & Hurst, 2017). Frameshift mutations are common in LS associated tumours as insertions/deletions persist due to DNA MMR failure (Majumder et al., 2018).

Estimations of the population prevalence of LS vary across studies. Once believed to affect between 1:2000 and 1:660 (de la Chapelle, 2005), LS is known to be underdiagnosed and an estimated 98% of affected individuals are unaware (Hampel & de la Chapelle, 2011). A study of Canadian, American and Australian populations found 1 in 280 people have LS (Win et al., 2017). Based on the proportion of CRC caused by LS, a prevalence of at least 1 in 200 is estimated (Firth & Hurst, 2017).

Lynch-associated Cancer Risks

LS is the most common cause of inherited CRC and endometrial cancer (EC), accounting for approximately 3% of all CRC and EC (Lynch & de la Chapelle, 1999; Salovaara et al., 2000;

Moreira et al., 2012; Ryan et al., 2019). Early research estimated a lifetime CRC risk up to 80% (Aarnio et al., 1995; Dunlop et al., 1997; Vasen et al., 1996; Watson & Lynch, 2001), which has been proven an overestimation by recent studies (Bonadona et al., 2011; Møller et al., 2018). The inflation in previous studies has been attributed to ascertainment bias of families with prominent cancer histories (E. Stoffel et al., 2009). The National Comprehensive Cancer Network (NCCN), an American not-for-profit alliance of leading cancer centres, assesses the most recent literature to provide LS cancer risk estimates by gene. As illustrated in Table 1, individuals with LS have significantly increased risks for CRC and EC compared to the general population. *MLH1*, *MSH2* and *EPCAM* are the most penetrant genes, associated with up to approximately 60% risk for CRC and EC, followed by *MSH6* with up to almost 50% risk, and *PMS2* around 20% risk (National Comprehensive Cancer Network, 2021). Risks for ovarian, renal pelvis, ureter, bladder, gastric, and small bowel cancer are also significantly increased with certain gene mutations. The risk for biliary tract or brain cancer with LS is below 10% but increased from the general population risk. Female breast cancer and prostate cancer are common among the general population and it is unclear if some LS gene mutations elevate these risks. Benign and malignant skin tumours, such as sebaceous adenocarcinomas, sebaceous adenomas, and keratoacanthomas are associated with the Muir-Torre LS phenotype.

Table 1. Lynch-associated cancer risks. Adapted from the NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Colorectal Version 1.2021 (NCCN.org).

Site	Population Risk (%)	*MLH1* (%)	*MSH2* and *EPCAM* (%)	*MSH6* (%)	*PMS2* (%)
Colorectal	4.2	46-61	33-52	10-44	8.7-20
Endometrial	3.1	34-54	21-57	16-49	13-26
Ovarian	1.3	4-20	8-38	1-13	1.3-3
Renal pelvis and/or ureter	unknown	0.2-5	2.2-28	0.7-5.5	1-3.7
Bladder	2.4	2-7	4.4-12.8	1-8.2	1-2.4
Gastric	0.9	5-7	0.2-9	1-7.9	unknown
Small bowel	0.3	0.4-11	1.1-10	1-4	0.1-0.3
Pancreas	1.6	6.2	0.5-1.6	1.4-1.6	1-1.6
Biliary tract	0.2	1.9-3.7	0.02-1.7	0.2-1	0.2-1
Prostate	11.6	4.4-13-8	3.9-23.8	2.5-11.6	4.6-11.6
Breast (female)	12.8	10.6-18.6	1.5-12.8	11.1-12.8	8.1-12.8
Brain	0.6	0.7-1.7	2.5-7.7	0.8-1.8	0.6-1
Skin*					

*Frequency of skin tumours including sebaceous adenocarcinomas, sebaceous adenomas, and keratoacanthomas are increased among individuals with LS. Gene-specific risk estimates are not available.

Testing for LS

There are various approaches to testing for LS. The two broad categories include tumour testing and germline testing. Only germline testing can diagnose LS, but tumour testing provides screening methods. While tumour testing can only be performed for individuals with cancer, germline testing can be performed on anyone and therefore can be utilized for predictive testing.

Tumour testing is performed by immunohistochemistry (IHC) staining and/or MSI measurements. IHC uses antibodies specific to the MMR proteins to stain for the presence of these proteins in the tumour sample. This method identifies if the MMR proteins are intact or deficient. Deficiency in an MMR protein can predict the MMR gene harbouring a mutation (Tamura et al., 2019). MSI testing quantifies the number of repeated microsatellite sequences. If the number of repeats in the tumour is the same as in normal tissue, the tumour is classified as microsatellite stable and LS would not be expected. If multiple markers show instability, the

tumour is considered MSI-H. This result indicates the genetic integrity has been compromised and LS germline testing should be considered (Tamura et al., 2019).

Sporadic CRCs are MSI-H in 10-15% of cases. The most common cause is the *BRAF*V600E mutation which causes MLH1 deficiency due to *MLH1* promoter methylation. Tumours which are MLH1 deficient undergo *MLH1* methylation analysis or *BRAF*V600E mutation testing to identify sporadic cancers and minimize the number of germline tests required (Capper et al., 2013; Tamura et al., 2019).

Germline testing for LS involves genetic testing on a blood sample. Multigene panel testing using next generation sequencing has been proven to be cost-effective, but other methods including Sanger sequencing and multiplex ligation-dependent probe amplification may be considered at different centres (Tamura et al., 2019).

Historically, family history of cancer was the best way to identify individuals at risk for LS. Several family history-based criteria have been developed to guide approaches for genetic evaluation. The International Collaborative Group on HNPCC developed the Amsterdam criteria, originally revolving around CRC (Vasen et al., 1991), and later revised the criteria to include extra-colonic malignancies (Vasen et al., 1999). The Amsterdam II criteria states LS should be suspected in individuals with three or more individuals on the same side of the family with Lynch-associated cancer, Lynch-associated cancers affecting at least two generations, and at least one diagnosis before age 50. Approximately half of families with LS do not meet these criteria due to reduced penetrance, small family size, or limited family history so centre-specific guidelines have been developed to determine eligibility for germline testing (Strafford, 2012).

In Manitoba, MMR-IHC screening is performed on all CRC diagnosed by age 70, including surgical samples since October 2013 and biopsy specimens since December 2017. Since December 2016, all ECs, including biopsy samples, undergo MMR-IHC. All abnormal MMR-IHC results are forwarded to the Hereditary Cancer Clinic in the Program of Genetics and Metabolism, so patients can receive genetic counselling. If MMR-IHC is intact, MSI testing is considered for individuals diagnosed with CRC or EC before age 50 or who meet the Amsterdam II criteria. An MSI-H result would qualify the individual for germline testing (*Manitoba Cancer Genetic Testing Protocols*, 2019).

Risk Reduction Methods

Cancer screening and prevention strategies are designed to reduce morbidity and mortality from LS. The identification of individuals with LS allows for the initiation of risk reducing strategies, including specialized cancer screening, chemoprevention, and surgery (Kastrinos & Stoffel, 2014; H. V. Petersen et al., 2019; "Practice Bulletin No. 147," 2014). Published recommendations are summarized in Table 2.

Colonoscopy has been proven as an effective screening method for CRC and simultaneously facilitates the surgical removal of polyps or early stage CRC to effectively reduce CRC mortality (de Jong et al., 2006; Kastrinos & Stoffel, 2014). Colonoscopy every three years has been shown to decrease the risk of CRC by over 50% (Järvinen et al., 2000). CRC is known to progress more rapidly (adenoma-carcinoma sequence) in LS than sporadic CRC (Johnson et al., 2006). Increasing the colonoscopy frequency to 1-2 year intervals was shown to further reduce CRC risks from 10% to 6% (Kastrinos & Stoffel, 2014). This led to the recommendation for colonoscopy every 1-2 years starting at age 20-25 years or 2-5 years before the youngest age of CRC diagnosis in the family, whichever occurs first (Kastrinos & Stoffel, 2014; Ladabaum et al., 2015; National Comprehensive Cancer Network, 2021). However, the optimal screening interval continues to be debated as the time since last colonoscopy (<1.5 – >3.5 years) has been shown not to impact the distribution of CRC stages identified (Seppälä et al., 2019). Colonoscopy every 1-3 years has been shown to reduce CRC incidence by approximately 87% and mortality by 94% in LS (Ladabaum et al., 2015). Based on the recent analysis of CRC risk by gene and the finding that CRC risk associated with *MSH6* and *PMS2* is significantly lower than the other LS genes (Table 1), screening recommendations have recently been revised to consider deferring colonoscopy until age 30-35 for individuals with *MSH6* or *PMS2* variants (National Comprehensive Cancer Network, 2021). Most Canadian and American centres continue to initiate colonoscopy screening for patients in their twenties. Prolonged use of daily aspirin has also been shown to reduce CRC incidence (Burn et al., 2011, 2020).

EC prevention is personalized based on factors such as pre- or post-menopausal status and completion of childbearing. The most effective EC prevention strategy is prophylactic hysterectomy, as EC screening has not been proven effective (Gentry-Maharaj & Karpinskyj, 2020; Kastrinos & Stoffel, 2014). Studies assessing transvaginal ultrasound screening found it less effective at detecting EC than symptom monitoring (Dove-Edwin et al., 2002; Rijcken et al.,

2003). Annual endometrial biopsy is recommended by the American and European Cancer Societies despite limited evidence of efficacy (Colombo et al., 2016; Smith et al., 2019). Similarly, effective ovarian cancer screening methods are lacking, and prophylactic bilateral salpingo-oophorectomy may be considered (National Comprehensive Cancer Network, 2021). In Manitoba, LS patients with a uterus and ovaries are referred to the Hereditary Gynecologic Oncology Clinic to discuss these options.

Screening for the additional cancer types associated with LS has not been recommended due to a lack of supporting evidence (National Comprehensive Cancer Network, 2021). The presence of additional risk factors, such as a family history of an extra-colonic/gynecological cancer, factor into the consideration for further surveillance.

Table 2. Surveillance and prevention strategies. Adapted from the NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Colorectal Version 1.2021 (NCCN.org).

Site	Surveillance/Prevention Strategies
Colorectal	Colonoscopy every 1-2 years beginning at age 20-25 if *MLH1/MSH2/EPCAM*, age 30-35 if *MSH6/PMS2*, or 2-5 y prior to the earliest CRC (whichever is earlier) Consider using daily aspirin
Endometrial	Report abnormal uterine bleeding or post menopausal bleeding Consider hysterectomy Consider endometrial biopsy every 1-2 years starting at age 30-35
Ovarian	Consider BSO Report potential symptoms
Urothelial (renal pelvis, ureter, and/or bladder)	Lack of evidence to support surveillance Based on family history, can consider annual urinalysis starting at age 30-35 y
Gastric and small bowel	Lack of evidence to support surveillance Based on the presence of risk factors, consider baseline EGD with stomach biopsy at age 40 and surveillance EGD every 3-5 y
Pancreas	Based on family history, consider annual MRI/MRCP and/or EUS beginning at age 50
Prostate	Consider annual screening starting at age 40
Breast (female)	Follow the population- or family history-based breast cancer screening recommendations
Brain	Report potential symptoms
Skin	Consider skin exams every 1-2 y

BSO: bilateral salpingo-oophorectomy; EGD: esophagogastroduodenoscopy; MRI: magnetic resonance imaging; MRCP: magnetic resonance cholangiopancreatography; EUS: endoscopic ultrasound.

Cascade Genetic Testing

The first person to have genetic testing for LS in a family is often referred to as the index case (IC) (Beard et al., 2020; Katapodi et al., 2017). Universal tumour screening facilitates the identification of individuals with LS who have had cancer, but genetic testing has the potential for a much wider impact (Dicks et al., 2019; Frey et al., 2020; Loh et al., 2019). Targeted genetic testing is available to blood relatives based on the IC's positive test result, called cascade genetic testing (CT) ("ACOG Committee Opinion No. 727," 2018; Bednar et al., 2020; Hampel, 2016). All first-degree relatives (parents, siblings, and children) of someone with LS have a 50% chance of having LS themselves. CT can clarify the genetic status of relatives, including relatives who have no personal history of cancer, to determine which relatives inherited a susceptibility to

developing cancer and would benefit from close surveillance for early detection. Individuals who have negative CT do not require LS cancer surveillance and cannot pass the LS genetic variant to any of their children (Griffin et al., 2020; Hampel, 2016; Marleen van den Heuvel et al., 2020).

Secondary to the potential for personalized cancer prevention, the cost-effectiveness of universal screening is dependent on the uptake of CT (Ladabaum et al., 2011; J. Petersen et al., 2018). Targeted LS testing for a known familial mutation is a fraction of the cost of whole gene sequencing for LS ("ACOG Committee Opinion No. 727," 2018; Kardashian et al., 2012).

CT is traditionally reliant on the IC to inform their relatives about LS (Bednar et al., 2020; Griffin et al., 2020; Hampel, 2016; Marleen van den Heuvel et al., 2020). Relatives who are not aware of their risk for LS cannot make informed decisions about genetic testing or cancer prevention strategies (Mendes et al., 2016). Unfortunately, the process of sharing information with relatives can feel burdensome to the IC (Forrest et al., 2003; Leenen et al., 2016) and many factors impact the decision to disclose genetic information.

Facilitators and Barriers to Communicating About LS with Relatives

There is a body of previous literature describing experiences of disclosing a genetic diagnosis of LS to relatives (K. I. Aktan-Collan et al., 2011; Campbell-Salome & Rauscher, 2019; de Geus et al., 2015; Gaff et al., 2005, 2007; Galiatsatos et al., 2015; Geus et al., 2016; Hunter et al., 2017; Kanga-Parabia et al., 2018; Keogh et al., 2017; Leenen et al., 2016; McCann et al., 2009; McGarragle et al., 2019; J. Petersen et al., 2018; Srinivasan et al., 2020; E. M. Stoffel et al., 2008). Many facilitators and barriers identified by studies examining the communication of genetic information or hereditary cancer risk also apply to LS (Bradbury et al., 2012; Crotser & Dickerson, 2010; Daly et al., 2016; Dean et al., 2021; Forrest et al., 2003; Godino et al., 2016; Hodgson & Gaff, 2013; Lee et al., n.d.; Marleen van den Heuvel et al., 2020, 2020; Montgomery et al., 2013; Ratnayake et al., 2011; Ricker et al., 2018; Seymour et al., 2010; Wiseman et al., 2010). The IC is often conflicted between preventing and causing harm by informing relatives about their risk for LS (Gaff et al., 2007; Seymour et al., 2010). Disclosure of genetic information has been described as a continuous process rather than a single act (Forrest et al., 2003; Gaff et al., 2007). Discussions with relatives are deeply rooted in the family's shared experiences and understanding of cancer, which influence the narrative about cancer risk (Campbell-Salome & Rauscher, 2019; Crotser & Dickerson, 2010; McCann et al., 2009). Family

dynamics, closeness of relationship, and effects of disclosure impact the decision about disclosure (Gaff et al., 2007). Relatives anticipated receptivity to the information and perceived vulnerability, including their current circumstances, and mental and physical health are taken into consideration (Gaff et al., 2007; Hamilton et al., 2005).

Common reasons for LS disclosure are to inform relatives of their risk and to encourage genetic testing (Srinivasan et al., 2020; E. M. Stoffel et al., 2008). The availability of genetic testing, targeted cancer surveillance, and the opportunity to empower relatives act as motivators to share information about LS, with the hope that relatives will perceive the information as an opportunity to gain control over health outcomes and facilitate life planning (Campbell-Salome & Rauscher, 2019; Forrest et al., 2003; Montgomery et al., 2013; Srinivasan et al., 2020). Often individuals with LS feel a moral obligation to disclose the information to relatives based on perceived family duties and responsibilities (McCann et al., 2009; Rothstein, 2018; Tarzian, 2018). Relatives who undergo genetic testing, regardless of the genetic test outcome, experience relief from the uncertainty (Godino et al., 2016; Leenen et al., 2016). Relatives who have a negative genetic test result can avoid unnecessary surveillance procedures and resolve the concern of an inherited cancer susceptibility for themselves and their children (Leenen et al., 2016). Those relatives who test positive for LS receive personalized cancer prevention recommendations which have been proven to reduce morbidity and mortality (Järvinen et al., 2009; Leenen et al., 2016; Wagner et al., 2005). Relatives who decline genetic testing are recommended to follow surveillance strategies as if they have LS, but are less likely to adhere than individuals who undergo genetic testing (Wagner et al., 2005). Previous discussions about cancer in the family and preventive options can facilitate the disclosure of LS (Forrest et al., 2003). Females are more likely to be aware of a familial variant and to take on the role of informing other relatives (K. I. Aktan-Collan et al., 2011; Bednar et al., 2020; Galiatsatos et al., 2015; Griffin et al., 2020; McCann et al., 2009; Montgomery et al., 2013; Seymour et al., 2010). Disclosure is more common among relatives who are emotionally close, genetically close (first degree relatives), and geographically close (Seymour et al., 2010; E. M. Stoffel et al., 2008). Additional cited motivators for disclosure are to obtain emotional support and follow physician instructions (E. M. Stoffel et al., 2008). Gene penetrance has not been shown to influence communication and the facilitators and barriers identified have been consistent across families with different genetic variants (Dean et al., 2021, p. 2; Ricker et al., 2018).

Many of the factors that facilitate information sharing, such as individual characteristics, reaction to the role of informant, perceived relevance of the information, anticipated reactions, dynamics of relationships, and cultural factors, can also prevent information sharing depending on the circumstance (Dean et al., 2021; Forrest et al., 2003; Seymour et al., 2010; E. M. Stoffel et al., 2008; Taylor et al., 2019). Individuals being asked to disseminate risk information to their families may concurrently be struggling with their own diagnosis (Caswell-Jin et al., 2018). Time can also impact communication; individuals who recently received a positive genetic test result often experience increased anxiety and depression which tend to return to baseline after six months to one year (K. Aktan-Collan et al., 2001, 2013; Gritz et al., 2005; Meiser et al., 2004). The IC may not feel emotionally or physically able to inform relatives, or may feel concerned about how family members will react ("ACOG Committee Opinion No. 727," 2018; Dean et al., 2021, p. 2; E. M. Stoffel et al., 2008). Anticipated reactions of worry or misunderstanding of the result created hesitation towards disclosure (E. M. Stoffel et al., 2008). Anticipated stigma based on cultural norms can also prevent disclosure. For example, in cultures where being sick and discussing sickness is considered taboo (Mendes et al., 2018; Srinivasan et al., 2020). Many aspects of family dynamics have been identified as significant barriers to communication. Communication patterns are well established within families and some avoid discussing cancer or lack openness in conversation (Crotser & Dickerson, 2010). Physical and/or emotional distance can be a deterrent from disclosing risk information due to discomfort, inconvenience, or lack of means to connect ("ACOG Committee Opinion No. 727," 2018; Dean et al., 2021, p. 2; Griffin et al., 2020; Kohut et al., 2007; McCann et al., 2009; E. M. Stoffel et al., 2008). Perceived authority figures within the family are expected to share the information, preventing other individuals from doing so (Forrest et al., 2003). Disclosure can be delayed until an opportunity arises when the family is together and it feels like the 'right time' (Forrest et al., 2003). Degree of relationship has been shown to impact disclosure rates. A recent study assessing the effectiveness of CT among families with LS or Hereditary Breast and Ovarian Cancer syndrome (HBOC) found that genetic testing results were disclosed to 87% of first-degree relatives, but only 38% of all at-risk relatives (Griffin et al., 2020). These results were consistent with previous studies which found that disclosure of genetic test results for LS were common to first-degree relatives but many second or third-degree relatives were uninformed (J. Petersen et al., 2018; E. M. Stoffel et al., 2008). Concerns about accurately conveying the

information can also prevent disclosure (Dean et al., 2021, p. 2; Griffin et al., 2020). These concerns are heightened by the common lack of awareness about LS. Relatives need to understand the benefits of genetic testing and surveillance to perceive the information as empowering (Srinivasan et al., 2020). Age can deter disclosure when the information is perceived as less relevant for elderly relatives or children are perceived as too young (K. I. Aktan-Collan et al., 2011; Griffin et al., 2020; Kohut et al., 2007; Srinivasan et al., 2020; E. M. Stoffel et al., 2008). Concern about causing worry or creating stress is amplified when relatives are already facing challenging circumstances. Relatives who were recently bereaved or facing cancer are less likely to be included in discussions about hereditary cancer (McCann et al., 2009; Seymour et al., 2010). Concerns about confidentiality have uncommonly been cited as a reason for non-disclosure (E. M. Stoffel et al., 2008).

Genetic Counsellors' Role in Facilitating Communication About LS

The role of a genetic counsellor is to educate individuals and families on genetic contributions to their health and facilitate informed decision making. Genetic counsellors are trained in medical genetics and counselling, equipped to help people adapt to both the medical and psychological implications of a genetic condition (*What Is a Genetic Counsellor?*, 2021). Although genetic counsellors have the skills to discuss LS with individuals at risk, it is up to the individual who has had genetic testing to disclose their results to family members. This family mediated approach without direct contact from a genetic counsellor is widely accepted in the field, although individuals with LS have mixed opinions regarding clinician involvement in sharing information with relatives (Aktan-Collan et al., 2007; Forrest et al., 2003; Seymour et al., 2010). Studies that have piloted a direct contact intervention have reported high levels of satisfaction and a lack of psychological harm due to direct contact from a healthcare provider (Aktan-Collan et al., 2007; Suthers et al., 2006). Two main reasons preventing genetic counsellors' involvement in disseminating information to relatives are resource limitation and patient privacy and confidentiality concerns (Dheensa et al., 2018; Kohut et al., 2007; McCuaig et al., 2018; Ridge et al., 2009; Rothstein, 2018; Schmidlen et al., 2019; Suthers et al., 2006).

All genetic counselling for LS in Manitoba is provided through the Hereditary Cancer Clinic, part of the Program of Genetics and Metabolism located at the Health Sciences Centre in Winnipeg. The Hereditary Cancer Clinic currently includes three genetic counsellors, serving all

of Manitoba, North-Western Ontario, Eastern Saskatchewan, and Nunavut. Over 350 individuals have been identified to have LS through the Hereditary Cancer Clinic (Rothenmund & Khan, 2021) and direct contact from a genetic counsellor to all at-risk relatives would require significant resources. Furthermore, genetic counsellors could not limit their services to families with LS and would have to contact families with other hereditary cancer syndromes if this practice of informing relatives was established. The waitlist for the Hereditary Cancer Clinic is already months to years (depending on urgency), demonstrating limited capacity to increase genetic counsellor involvement per patient. High demand for genetic counselling is not unique to Manitoba; most countries have fewer genetic counsellors than recommended by the Royal College of Physicians and over 60% of the genetic counsellors in the world are located in North America (Abacan et al., 2019).

Genetic counsellors are consistently faced with the duty to protect patient confidentiality versus the duty to warn relatives to prevent harm (Aktan-Collan et al., 2007; Kardashian et al., 2012; Lindor et al., 2006; Mendes et al., 2016; Middleton et al., 2019; H. V. Petersen et al., 2019). Counsellors are bound by a Code of Ethics to maintain patient confidentiality unless imminent risk of serious bodily harm can be averted (*CAGC - Canadian Association of Genetic Counsellors*, n.d.; *CMPA - Genetic Testing — New Options, New Obligations*, n.d.). The Joint Committee on Genomic in Medicine states that "the rule of confidentiality is not absolute. In certain circumstances it may be justified to break confidence where the avoidance of harm by the disclosure outweighs the patients' claim to confidentiality" (Middleton et al., 2019). In the U.S., there have been multiple medical malpractice lawsuits around the duty to warn, leading to the enactment of the Health Insurance Portability and Accountability Act (HIPPA) in 2003 (Rothstein, 2018). Both the American Medical Association Code of Medical Ethics and the National Society of Genetic Counselors Code of Ethics require patient consent before disclosing confidential information (Rothstein, 2018). Although there is the potential to prevent harm by disclosing information about LS to at-risk relatives, there is also evidence that relatives can experience psychological distress by being informed and ultimately the risk for cancer is not imminent.

Genetic counsellors explain the familial implication of genetic testing and encourage patients to inform their at-risk relatives (*CMPA - Genetic Testing — New Options, New Obligations*, n.d.; Hodgson & Gaff, 2013; Kohut et al., 2007). Both the duty to warn and the oath

to protect patient confidentiality are fulfilled by informing the patient of the hereditary risk and the importance of warning their relatives (Hodgson & Gaff, 2013; Rothstein, 2018). Non-directiveness is a pillar of the genetic counselling profession to support patient autonomy (Veach et al., 2007). Genetic counsellor encouragement to inform relatives of their hereditary cancer risk should include a balanced discussion of the risks and benefits (Mendes et al., 2016). Patients rarely report intentions to actively withhold the information from relatives and more often fail to act on their intent to disclose (Clarke et al., 2005; Suthers et al., 2006). Genetic counsellors are recommended to engage their patients in discussions about the challenges they anticipate in disclosing genetic information to relatives and develop strategies and supports to help overcome these challenges (Srinivasan et al., 2020). Based on the proven efficacy of LS cancer surveillance strategies, genetic counsellors are expected to encourage their patients to comply with screening recommendations and encourage their relatives to do the same. This encouragement does not extend to genetic testing. Genetic counsellors are not promoting genetic testing but rather facilitating informed decision making and encouraging cancer prevention strategies (Mendes et al., 2016).

Family Letters are Considered the Standard of Care

To assist patients in discussing LS with their family members, healthcare providers offer written materials, most often in the form of a family letter, which has become standard practice (Dheensa et al., 2018; Geus et al., 2016; H. V. Petersen et al., 2019). A few examples of family letters have been published ("ACOG Committee Opinion No. 727," 2018; Dheensa et al., 2018; Schmidlen et al., 2019; Zordan et al., 2019) and there are fillable template letters available online (*Dear Family Letter*, n.d.; *Resource Center | Individuals*, n.d.; *Talking to Your Family about Your Lynch Syndrome Diagnosis | CDC*, 2020). Published letters include a brief description of the hereditary cancer syndrome, the associated cancer types, and odds of inheritance. The availability of cancer prevention strategies is mentioned without any descriptive details. Family letters encourage the recipient to seek genetic counselling for further information. Some family letters identify the individual who had a positive genetic test result and others omit all identifying information. There is a paucity of research evaluating the content of family letters (Zordan et al., 2019). A standardized letter has not been proposed by any of the professional societies.

Dheensa et al. (2018) identified the limitations of relying on family letters through focus groups with healthcare providers and interviews with patients. Family letters were felt to apply pressure to the patient to disclose the genetic information, and to the recipient to seek genetic counselling. This pressure was perceived both positively towards facilitating communication and negatively due to reduced autonomy and increased anxiety. The authors described letters being distributed in Christmas cards and at funerals, which created family conflict. Letters were also inappropriately distributed to relatives who were not at risk or without permission from the IC. Healthcare providers felt providing patients with a family letter symbolized the end of their involvement and suggested a follow-up appointment six-months after the diagnosis to support patients struggling with disclosure.

Alternative approaches to the family letter have included sending the family letter directly from healthcare provider to at-risk relative. This direct approach was shown to increase the uptake of CT (Evans et al., 2009; Suthers et al., 2006). These studies measured the rate of genetic testing without reporting the uptake of genetic counselling or cancer prevention strategies, limiting the interpretation of their findings. It is unclear if direct contact from a healthcare provider facilitated informed decision making regarding genetic testing and cancer prevention. The use of telephone counselling as an intervention to improve communication was tested by randomized controlled trial and revealed no considerable difference between the intervention and control groups in the proportion of relatives who sought genetic counselling (Hodgson et al., 2016). Motivational interviewing provided by psychosocial workers by telephone was tested as an intervention to improve patient knowledge on which relatives to inform and what information to disclose, and was highly appreciated by the study participants (Geus et al., 2016). The rate of subsequent disclosure was not reported but 59% of participants reported feeling motivated by the social worker to discuss the genetic information with their relatives. Another approach to facilitate communication employed a web-based platform which contacts relatives by email with login instructions to securely access confidential files with genetic information (*Kintalk UCSF*, n.d.). The impact of this tool on cascade testing and decision making is currently under review (Kim et al., 2021). An intervention developed for HBOC, called the Sharing Risk Information Tool (ShaRIT), is a binder given to each patient containing their personalized medical report, family pedigree, gene mutation report, personalized recommendations for surveillance and prevention, family letter, fact sheet, genetic counselling

contact information, support websites and brochures (Kardashian et al., 2012). This tool was developed at the University of California San Francisco Cancer Risk Program and found to be both feasible and useful for sharing information at that site, however uptake of this tool has not been reported or evaluated by other sites. Despite the various supplemental and alternative approaches to facilitating communication, the family letter remains the most widely used tool and the standard practice among genetic counsellors.

Facilitators and Barriers to Cascade Testing

Studies have found only about 40% of at-risk relatives undergo CT for hereditary cancer syndromes (Griffin et al., 2020; Ramsoekh et al., 2007; Seppälä et al., 2017; Sharaf et al., 2013; Suthers et al., 2006). Reasons for declining CT have included limited knowledge of genetic testing and lack of trust of the results, lack of perceived benefit, being content without having genetic testing, and anticipating negative outcomes as a result of genetic testing, including insurance problems (Caswell-Jin et al., 2018; Hadley et al., 2003; Keogh et al., 2017; Leenen et al., 2016). Most at-risk relatives who chose to decline do so without consulting a genetic counsellor (Kanga-Parabia et al., 2018; Keogh et al., 2017; Seppälä et al., 2017). A recent study found that most at-risk individuals who were aware of their familial variant but had not had genetic testing had no intention to take action in the next six months (Bednar et al., 2020). The study used the transtheoretical model as a framework to understand health behaviours over time and considered these individuals to be in the precontemplation stage, meaning no action was being considered. This result suggests that communication and accessibility to genetic testing may not influence decisions to decline. Although individuals are aware of the familial variant, they may lack information about the treatment and management options for LS (Bednar et al., 2020).

Sweeny et al. (2014) performed a systematic review of the literature on predictors of genetic testing. They found that generally, individuals are more likely to accept genetic testing who are more worried about developing cancer, perceive greater control over disease management and prevention, perceive genetic testing as socially acceptable, perceive greater benefit from genetic testing, and perceive fewer barriers to genetic testing. Perceived risk for CRC has inconsistently predicted interest in genetic testing, however the general trend across genetic conditions is that people who perceive their risk as higher are more motivated to pursue

genetic testing to clarify their risk. Individuals who have an optimistic disposition and have low depressive scores are more likely to proceed. Sociodemographic characteristics were found to be less consistent predictors of genetic testing, as different studies found conflicting results or no relationship. There is limited evidence to suggest that gender, education level, employment status, income, age, marital status, parental status, religion, or spirituality can predict genetic testing (Sweeny et al., 2014).

Outside of Canada, many studies have found cost to be a prohibitive barrier to genetic testing (Caswell-Jin et al., 2018; Courtney et al., 2019; Frey et al., 2020; Rahma et al., 2020; Ramirez et al., 2015; Steffen et al., 2017). The universal healthcare system mitigates this barrier for Canadians, but other barriers to genetic testing have been identified. The need for pretest genetic counselling before genetic testing can complicate the process and is contrary to the idea that genetic testing only requires a simple blood test ("ACOG Committee Opinion No. 727," 2018). A recent study performed a trial of "facilitated CT" where genetics professionals contacted at-risk relatives by telephone to disclose the familial genetic variant, provide telephone counselling, and offer genetic testing through a mailed saliva kit (Frey et al., 2020). In this sample, almost 60% of at-risk relatives had genetic testing. The intervention simultaneously addressed barriers of family-mediated communication and convenience. The outreach of genetic services is suggested to be poor based on the low awareness of the availability of genetic services among the general population (Allen et al., 2019). Family physicians have reported a lack of confidence in discussing LS with patients (Barrow et al., 2015).

Some of the interventions to help facilitate communication of genetic information have increased the uptake of CT (Evans et al., 2009; Frey et al., 2020; Suthers et al., 2006). Provision of a family letter was found to double the rate of CT (Griffin et al., 2020). The enactment of Bill S-201 in Canada facilitates genetic testing by addressing concerns about insurance discrimination. The Genetic Non-Discrimination Act was passed in 2017 which prevents insurance companies or employers from accessing genetic testing results (*Legislative Summary of Bill S-201*, n.d.). This federal law was challenged and recently upheld by the Supreme Court of Canada (Stefanovich, 2020).

A previous Canadian study illuminated the need for coordinated care centres for LS patients (Watkins et al., 2011), which has since been established in Manitoba. In February 2018, CancerCare Manitoba opened the Hereditary Gastrointestinal Cancer Clinic (also known as the

Lynch clinic), one of the first in Canada (*Helping Save Lives*, 2018). The multidisciplinary clinic includes a medical oncologist, a gastroenterologist, and a genetic counsellor providing coordinated care. Patients with LS can receive regular follow-up for the latest screening and prevention recommendations, as well as supportive discussions about notifying other relatives.

Study Rationale

The current study combines areas of research in communication about genetic conditions and uptake of CT to provide a broadened understanding of seemingly low CT rates given the efficacy of LS cancer prevention strategies. Studying facilitators and barriers of both communication and genetic testing allows better identification of the foremost challenges overall. Although there is a body of literature identifying challenges in communicating genetic information, literature also suggests that almost all first-degree relatives are informed about LS, yet a significant proportion decline genetic testing. It remains unknown if family-mediated communication is effective and relatives are making an informed choice to decline genetic testing, or if relatives are partially informed and declining CT with limited understanding. This study will also determine if relatives wish to have genetic testing but face barriers that make CT inaccessible.

The family letter seems to be the most widely used tool to facilitate communication of genetic information, yet literature review revealed a surprising lack of recommendations to optimize the family letter. This study addresses this gap in the literature by gathering user feedback on a modified informational resource inspired by published family letters and providing suggestions for improvement. The informational resource developed through this study is called the Lynch Syndrome Family Package (LSFP) and contains a cover letter, two pages of information, and a self-referral form for genetic counselling (See Appendix A). Individuals receiving the LSFP have an opportunity to identify their most pressing questions and concerns and assess if they are adequately addressed. Additionally, this study will identify the patient demographics most likely to utilize the LSFP. The findings can be implemented beyond LS towards improving patient resources for other hereditary conditions.

Understanding the facilitators and barriers impacting communication and CT for Manitobans with LS will allow clinicians at the Lynch Clinic to tailor their approach. Similarly, the LSFP can be tailored to highlight the information considered most valuable by individuals

with LS. These findings will improve patient care for individuals with LS and their relatives by facilitating informed decision making though improved communication and accessibility to genetic counselling. Results from this study have the potential to initiate earlier surveillance of individuals at-risk for LS, which may prevent new cases of LS-related cancers and subsequently decrease related mortalities.

Chapter 2: Methods

Study Design

The framework of this study is a mixed-methods design. The quantitative method assumes a positivist paradigm and seeks to find trends and generalizations. The qualitative method assumes an interpretivist paradigm and elicits details and depth. Using pragmatism, our mixed-methods design utilizes both approaches to address the research aims (Glogowska, 2011). The quantitative and qualitative data will be combined through convergent design (QUAN + QUAL) to obtain a more complete understanding of the research questions (Creswell & Clark, 2017) (Figure 1).

The study was approved by the University of Manitoba Bannatyne Campus Health Research Ethics Board (Approval number HS23886/H2020:204)(See Appendix B).

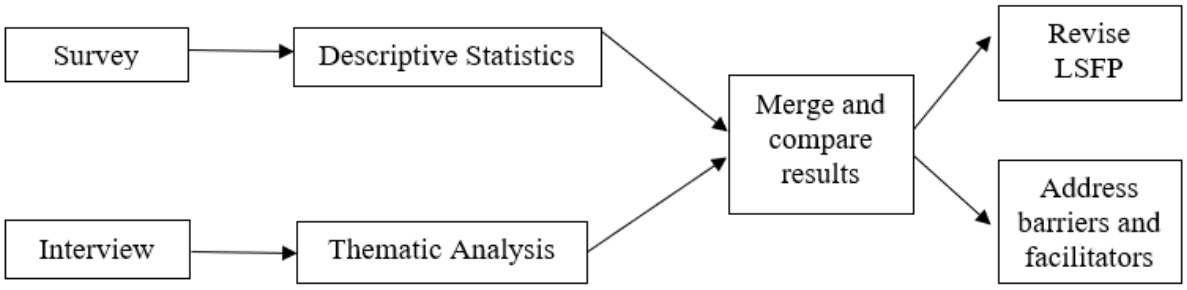

Figure 1. Convergent design. Adapted from Creswell & Clark (2017).

LSFP Development

The LSFP was developed through collaboration with the research team, genetic counsellors and geneticists at the Hereditary Cancer Clinic, physicians at the Lynch Clinic, and a genetic counsellor at the Hereditary Cancer Program in British Columbia. Aspects of previously published family letters ("ACOG Committee Opinion No. 727," 2018; Dheensa et al., 2018; Schmidlen et al., 2019; Zordan et al., 2019), genetic counsellor family letters from the Hereditary Cancer Clinic, and the family letter from the Hereditary Cancer Program in BC guided the development of the LSFP. The family letters referenced were not previously evaluated, but an expert in plain language was involved in the development of the BC Cancer letter. The LSFP is

at an eighth-grade reading level according to the Flesch-Kincaid, SMOG Index, Automated Readability Index, and Linsear Write Formula. Two individuals with LS partnered with this study to provide feedback on the LSFP during development.

Participants

The study population included individuals with LS and their relatives, which included two groups: 1) individuals who had a molecular diagnosis of LS, and 2) individuals related to someone with LS but not known to have LS themselves. Individuals in the first group would have undergone genetic counselling and genetic testing. The second group included individuals who have not had genetic counselling, had genetic testing with a negative result, or declined genetic testing following their counselling appointment. Participant eligibility was based on the meeting all five of the following criteria (Table 3).

Table 3. Participant inclusion criteria

Inclusion Criteria
✓ You have LS or are related to someone with LS
✓ You received a LSFP
✓ You are at least 18 years old
✓ You speak and read English
✓ You can provide informed consent

Recruitment

Individuals with LS (Group 1) were recruited prospectively from the clinics which specialize in caring for this population, including the Hereditary Cancer Clinic (at the Program of Genetics & Metabolism), the Hereditary Gastrointestinal Cancer Clinic (at CancerCare Manitoba) and the gastroenterology clinics (at Health Sciences Center). All genetic testing for LS in Manitoba is coordinated by the Hereditary Cancer Clinic, located in Winnipeg. Individuals with LS are followed by the Hereditary Gastrointestinal Cancer Clinic (also known as the Lynch Clinic) at CancerCare Manitoba for ongoing management. Routine endoscopy screening for individuals with LS is performed by endoscopy physicians (gastroenterologists, surgeons and a few family physicians). Health care providers involved include genetic counsellors, geneticists, oncologists, and gastroenterologists/surgeons (henceforth called “clinicians”). Clinicians

identified potential study participants using the eligibility criteria above (Table 3) and provided their patients with the LSFP. Clinicians introduced the study and documented consent for the student researcher to contact potential participants by phone.

Using the consent to contact forms (See Appendix C), the student researcher telephoned individuals using a prepared script (See Appendix D) to provide information about the study. Those who agreed to provide their email address were sent an invitation email (See Appendix E) with the survey link and the LSFP attached. Recipients were asked to complete the survey and forward the email to their relatives so they could also participate in the online survey. Individuals were also invited to participate in a qualitative interview. Those who were willing were asked pre-screening questions to allow for purposive sampling (described in a later section). The student researcher attempted to contact each potential participant by phone once per week, up to three attempts. Participants who agreed to take the survey received up to three reminder emails at least one week apart (See Appendix F).

The online survey had a field where participants could indicate if they were willing to participate in an interview and provide their email address. This allowed individuals with LSanother opportunity to opt in for an interview if they changed their mind since speaking to the student researcher by phone. It also allowed untested relatives (Group 2) the opportunity to opt in for an interview without recruitment by the student researcher. The student researchers' contact information was also provided to schedule an interview.

Relatives who were provided the LSFP by someone with LS had the option to refer themselves to the Hereditary Cancer Genetic Clinic using the Self-Referral Form. Following the receipt of a self-referral form, clinicians contacted the individual to introduce the study and ask consent for the student researcher to contact them. The student researcher then called the potential participant as described above.

Individuals selected for an interview were contacted for scheduling and given the option to interview by phone or video conference. Individuals who did not respond to the interview invitation were excluded. The interview consent form (See Appendix G) was provided by email/mail.

Approximately 10 potentially eligible participants with LS were expected to present to the relevant clinics each month, for a total of 70 eligible participants during the recruitment period (June 2020-February 2021). Unpublished data from the Hereditary Cancer Genetics Clinic

suggests that on average each individual with LS has four relatives eligible for CT. Based on this finding, a study population of 350 individuals was predicted with relatives included. The recruitment process is outlined in the flowchart below (Figure 2).

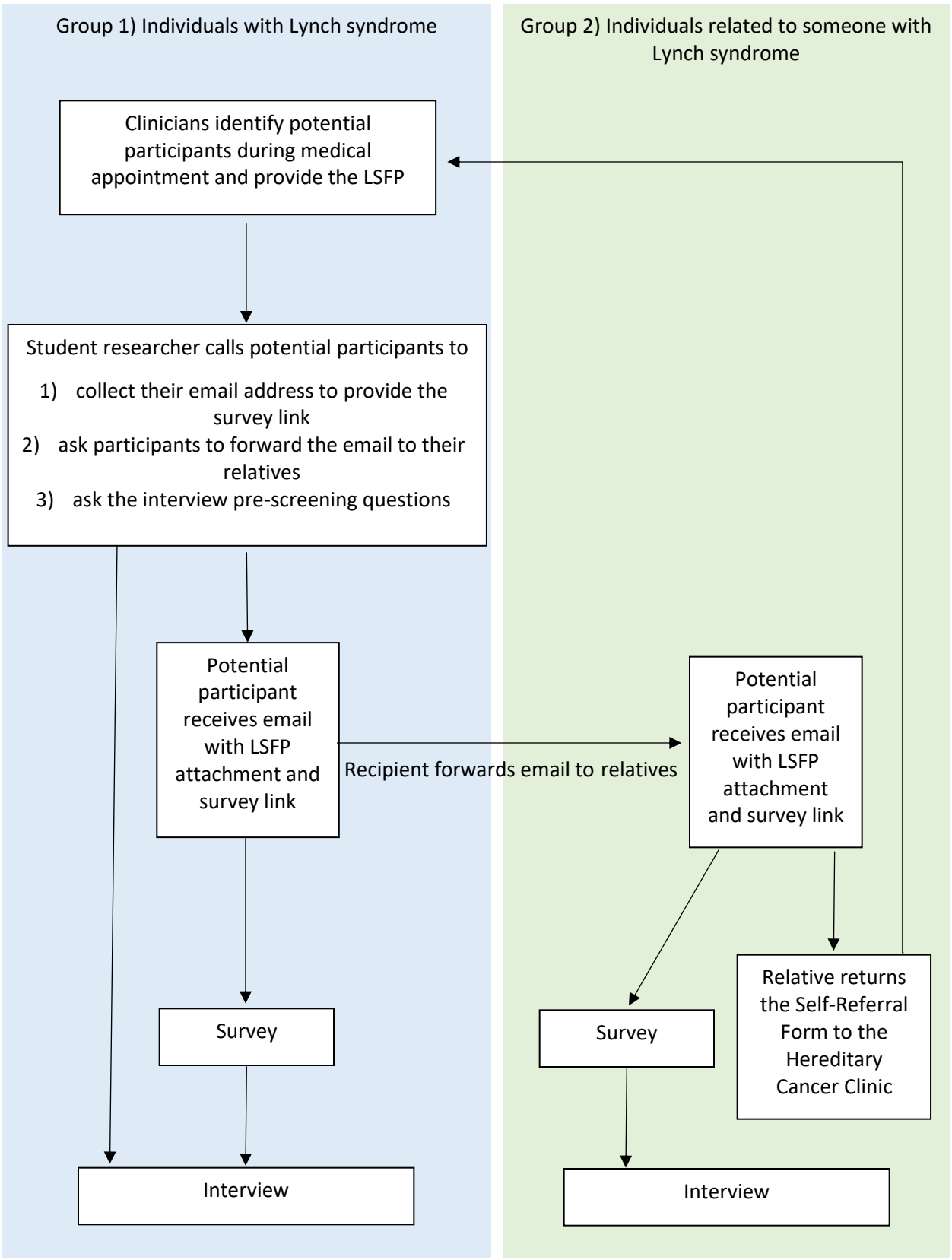

Figure 2. Recruitment strategy for survey and interview participants.

Compensation

Interview participants were offered a $25 gift card to Amazon.ca, or a major box store of their choice if they did not have computer access. Amazon gift cards were delivered electronically, and other gift cards were mailed.

Five months into the recruitment period, less than 30 surveys had been completed and no relatives (Group 2) had been recruited. Therefore, after approval of the amendment by HREB, a $20 incentive was added for completing the survey. All participants recruited after October 2020 were offered compensation for their time, in the form of Amazon.ca gift cards. Individuals who had already completed the survey without compensation could not be contacted due to the anonymity of their response, however if anyone had contacted the student researcher, they would have received compensation.

Survey

Instrument

Survey data was collected and managed using REDCap electronic data capture tools hosted at the University of Manitoba (P. A. Harris et al., 2009, 2019). One survey instrument was used for both groups, however some questions were branched based on responses (See Appendix H). Participants who indicated they had LS were asked 26 questions, and participants related to someone with LS had an additional 5 questions. The first page of the survey was informed consent disclosure. At the end of the survey, 12 demographic questions were asked. The survey anonymously collected opinions about the format and content of the LSFP to guide improvements. Survey questions explored what actions individuals took in response to receiving the LSFP. A five-item Likert scale was used to measure responses. Survey questions were developed based on previously published questionnaires (Bernstein et al., 2019; Dinchong, n.d.; Nemoto & Beglar, n.d.; Schmidlen et al., 2019; Streiner et al., n.d.). Data collection occurred from June 2020 – February 2021.

Data Analysis

Statistical analysis was performed by Casandra Dolovich, a statistician with the Department of Internal Medicine, using Statistical Analysis Software (SAS), version 9.4. Descriptive statistics, including means and percentages, were performed to summarize participant sociodemographic characteristics and responses to questions about information

preferences and impressions of the LSFP. The 95% confidence intervals around the mean were used to compare responses between those who shared the LSFP with relatives and those who did not, and between those who received the LSFP from a relative versus a healthcare provider. Confidence intervals are recommended for these types of comparisons to illustrate the magnitude of difference (Bernstein et al., 2020; Cummings & Koepsell, 2010; Gardner & Altman, 1986). Additionally, the Wilcoxon rank sum test was performed to determine statistical significance. The chi-square test was used to compare which relatives participants informed about LS and how the information was shared. Statistical significance was determined based on a p-value of <0.05.

Logistic regression analysis was performed to identify predictors of sharing information about LS with relatives. Participant characteristics (age, gender, education, employment, income, marital status, childbearing status, cancer history, impression of LSFP, and gene mutation) were explored by unadjusted logistic regression analysis. Based on the qualitative interview findings and unadjusted results (p-value <0.05), age, gender, marital status, cancer history, and gene mutation were selected for the multivariable logistic regression analysis.

Interview

Selection Criteria

Between recruitment calls and survey respondents, 59 individuals indicated they would be willing to participate in a qualitative interview and were telephoned or emailed by the student researcher to collect sociodemographic characteristics as a method of pre-screening (Table 4). Responses were provided by 24 individuals. Responses to question 11 determined if participants fell into Group 1 (known to have LS) or Group 2 (relative of someone with LS who has not had genetic testing). The goal was to interview an equal number of participants from each group. However, no one from Group 2 agreed to participate in an interview. Purposive sampling (Palinkas et al., 2015) was used to select 15 interview participants from Group 1 based responses to the pre-screening questions. The purposive sampling method aimed to include diversity within the study sample based on age, gender, geographic location, ethnicity, education level, employment status, income, marital status, childbearing status, cancer history, time since genetic testing for LS, and family experience with LS. Since interviews and recruitment occurred concurrently, the first participants were selected before pre-screening data was available from all 24 individuals. These early participants were selected based on the eligibility criteria (Table 3)

and the timing of their recruitment. Subsequent participants were selected to complement the characteristics of those already included in the sample. For example, the first individuals who indicated they were willing to participate in an interview near the beginning of the recruitment period were women, so the first man to agree was interviewed. Responses to the pre-screening questions were tabulated in an excel worksheet to identify sociodemographic groups that were missing and individuals who fit those descriptors were invited to interview. Interviews were preformed until data saturation was reached, defined by a lack of new emergent themes (Francis et al., 2010).

Table 4. Purposive sampling criteria.

Questions
1. How old are you?
2. What is your gender?
3. What province or territory do you live in?
4. Do you live in an urban or rural community?
5. What is your ethnic background?
6. What is your highest level of education?
7. What is your current employment status?
8. Is your combined annual household income more or less than $68, 000?
9. What is your marital status?
10. Do you have children?
11. Have you had/when did you have genetic testing for LS?
12. Have you ever been diagnosed with cancer? If yes, what type of cancer?
13. How many of your relatives are known to have LS? And how large is your family?

Instrument

Participant consent was obtained at the beginning of each interview (See Appendix I). A semi-structured interview guide was developed to explore the barriers and facilitators to accessing genetic counselling and testing for LS in Manitoba. Additionally, we aimed to assess the emotional reactions to the LSFP and what actions were taken in response to the LSFP. The interview guide was developed by referencing previously published studies (Dinchong, n.d.; Hansen, 2019; Schmidlen et al., 2019; Tolotti et al., 2020). After the first interview, Dr. Gayle Restall (GR), a member of the advisory committee with qualitative research expertise reviewed the audio recording and provided feedback to the student researcher. This feedback was incorporated into subsequent interviews. The guide consisted of 11 open-ended questions and

prompts to probe each question further (See Appendix J). The interview guide evolved based on completed interviews. For example, participants were asked, “Can you suggest any other tools (in addition to the LSFP) that we could use to make things easier for people?”. Participants were probed using suggestions from previous participants: “One suggestion has been to provide pamphlets about LS in doctors office waiting rooms. What do you think about that idea? Can you suggest anything else?”

Data Collection

All interviews were performed by the student researcher. Participants were given the option to interview by phone or online with video using the BlueJeans platform (*Blue Jeans Network*, 2021). Most participants (13/15) chose to participate by phone. All interviews were audio recorded. The average length of an interview was 45 minutes (range 19-65 min). The student researcher reflexively journaled before and after the interview. Feelings, expectations, and biases were noted, as well as other events of the day which may have been impactful. Prior to the first interview, the student researcher received guidance on qualitative interviewing skills and techniques from a team member with expertise in qualitative research (GR). The deidentified audio recording of the first interview was reviewed by GR with the student researcher.

Data Analysis

Interviews were transcribed verbatim by the student researcher and TranscriptHeroes, a professional transcription service. Thematic analysis (Braun & Clarke, 2006) was used to inductively code transcripts, using Dedoose software (*Dedoose*, 2020). The student researcher used open coding for the first pass (Ravitch & Carl, 2016). To ensure validity, a team member with qualitative research expertise, Dr. Kristin Reynolds, independently coded two transcripts. Initial codes were similar between researchers and any differences in coding were resolved through discussion. The codebook was updated accordingly, and subsequent transcripts were coded by the student researcher using the validated thematic structure. The codebook was revised iteratively as new themes emerged and prior interviews were re-coded. Another interrater reliability check with a team member occurred after all transcripts were coded to verify the emergent themes.

Chapter 3: Qualitative Findings

Overview

As described in the previous chapter, purposive sampling was used to include diversity among the 15 qualitative interview participants. Sociodemographic characteristics reported by participants are summarized in Table 5. Men and women were equally represented, as were individuals with and without a personal diagnosis of cancer, and individuals with an annual household income above and below the provincial median (Government of Canada, 2017). Inclusion of ethnic diversity was not achieved, with 86% of participants reporting their ethnicity as White.

Of the 15 interview participants, 8 were the first person in their family to find out they have LS, referred to as the IC. Seven were informed by a family member about LS and confirmed their genetic status through CT (i.e. the performance of genetic testing in blood relatives of individuals who have been identified with specific genetic mutations). The major difference between these two groups is the family awareness of LS. Individuals who were the IC described the challenges of explaining LS to their relatives who were learning about it for the first time. Individuals who had CT described an entire generation of their family already informed about LS. These participants were often accompanied by parents or siblings throughout the process of learning about LS and genetic testing. Despite these differences, the emergent themes were described by participants in both groups. Descriptive information as reported by participants is summarized in Table 6. During the consent process, all participants agreed to the use of a pseudonym assigned by the student researcher.

Data saturation was reached after 12 interviews; novel themes did not emerge in the final three interviews. Interviews gathered information about participant motivations for having genetic testing, reactions to learning they had LS, considerations for telling relatives, and feedback on accessing healthcare related to LS in Manitoba and on the LSFP. Using thematic analysis, the details of participant experiences revealed facilitators and barriers to communicating about LS within families, plus strengths and weaknesses of the LS-related Manitoba health system and the LSFP.

The thematic framework of communication about LS within families is outlined in Figure 3. Three main themes emerged: family dynamics, autonomy, and perceptions of genetic testing.

Family dynamics were shown to be complex and greatly impacted participant experiences to either facilitate or hinder communication about LS. Six sub-themes were identified within family dynamics, outlined in Figure 3. All participants recognized the autonomy of their relatives to make their own decision about genetic testing, but acceptance levels varied among participants, described within the sub-themes of acceptance and frustration. Perceptions of genetic testing coloured the conversations participants had with their relatives and were organized into risks/hesitations and benefits/motivators of genetic testing. Four subthemes emerged within the perceived risks and hesitations towards genetic testing. The two major benefits and motivators for genetic testing were the perception that knowledge is power and the perceived duty to share the information about LS. The belief that knowledge is power motivated all participants to have genetic testing and was further analyzed into three sub-themes. All themes and sub-themes collectively shaped the way information about LS was shared with at-risk relatives and illuminate the many factors individuals with LS are balancing.

Feedback was solicited on the experiences accessing healthcare related to LS in Manitoba and on the LSFP specifically (

Figure **4**). All participants indicated that genetic testing for LS is accessible and were satisfied overall with the LS-related care they received in Manitoba. Two suggestions for improvement emerged: (1) increasing the availability of Canadian online resources and (2) increasing awareness of LS among family physicians and the general public. Additionally, participants assessed the LSFP positively. The most common suggestion to improve the LSFP was to add links to online resources for further reading.

Table 5. Sociodemographic characteristics of interview participants.

	n	(%)
Total interview participants	15	(100)
Age		
18-29	2	(13)
30-44	4	(27)
45-59	5	(33)
60-74	4	(27)
Population		
Urban	9	(60)
Rural	6	(40)
Gender Identity		
Woman	7	(47)
Man	8	(53)
Ethnic Background		
East Indian	1	(7)
Métis	1	(7)
White	13	(86)
Education		
>High school	10	(67)
High school or less	5	(33)
Employment Status		
Employed	10	(67)
Not Employed	5	(33)
Annual Household Income		
<$68,000	7	(47)
≥$68,000	8	(53)
Marital Status		
Single	4	(27)
Married	11	(73)
Parental Status		
Have children	10	(67)
None	5	(33)
Personal Cancer Diagnosis		
Yes	7	(47)
No	8	(53)
Time Since LS Diagnosis		
3 years or less	8	(53)
More than 3 years	7	(47)

Table 6. Descriptive characteristics of interview participants.

Pseudonym	Case within the Family	Year of Genetic Testing
Jeff	IC	2000
Sarah	IC	2002
Jessica	IC	2014
Ben	IC	2014
Mike	CT	2015
Daniel	CT	2015
Sofia	CT	2017
Mandy	IC	2018
Liam	CT	2018
Janice	IC	2019
Armaan	IC	2019
Randy	CT	2019
Erica	IC	2019
Jacob	CT	2019
Emma	CT	2020

IC = index case (the first person in the family to have genetic testing for LS), CT = cascade testing (someone else in the family had a positive genetic test for LS and informed the participant)

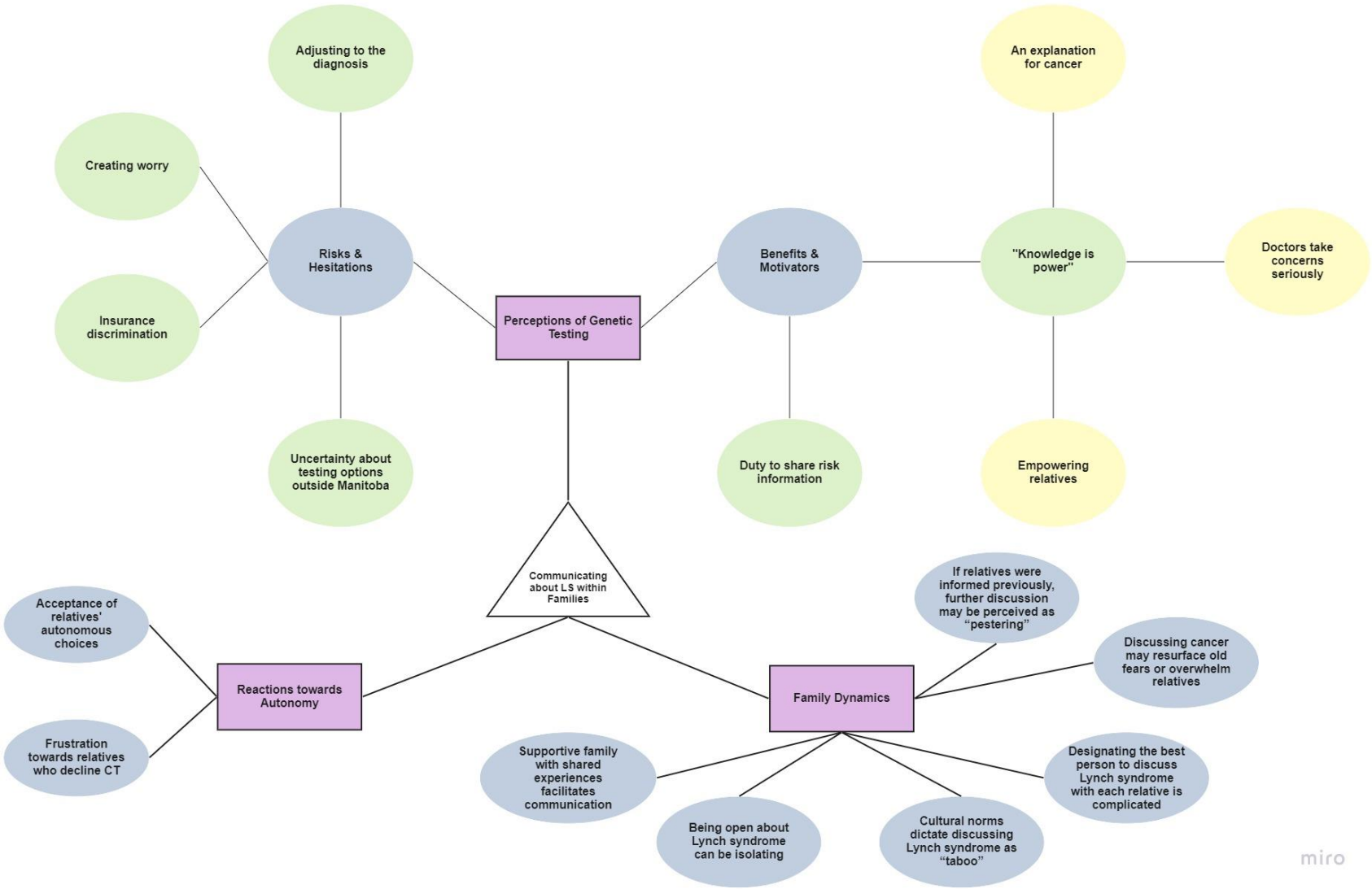

Figure 3. Thematic framework of communicating about LS within families. The main themes are perceptions of genetic testing, reactions towards autonomy, and family dynamics, shown in purple. Sub-themes stem radially from their parent theme, represented by the different colours.

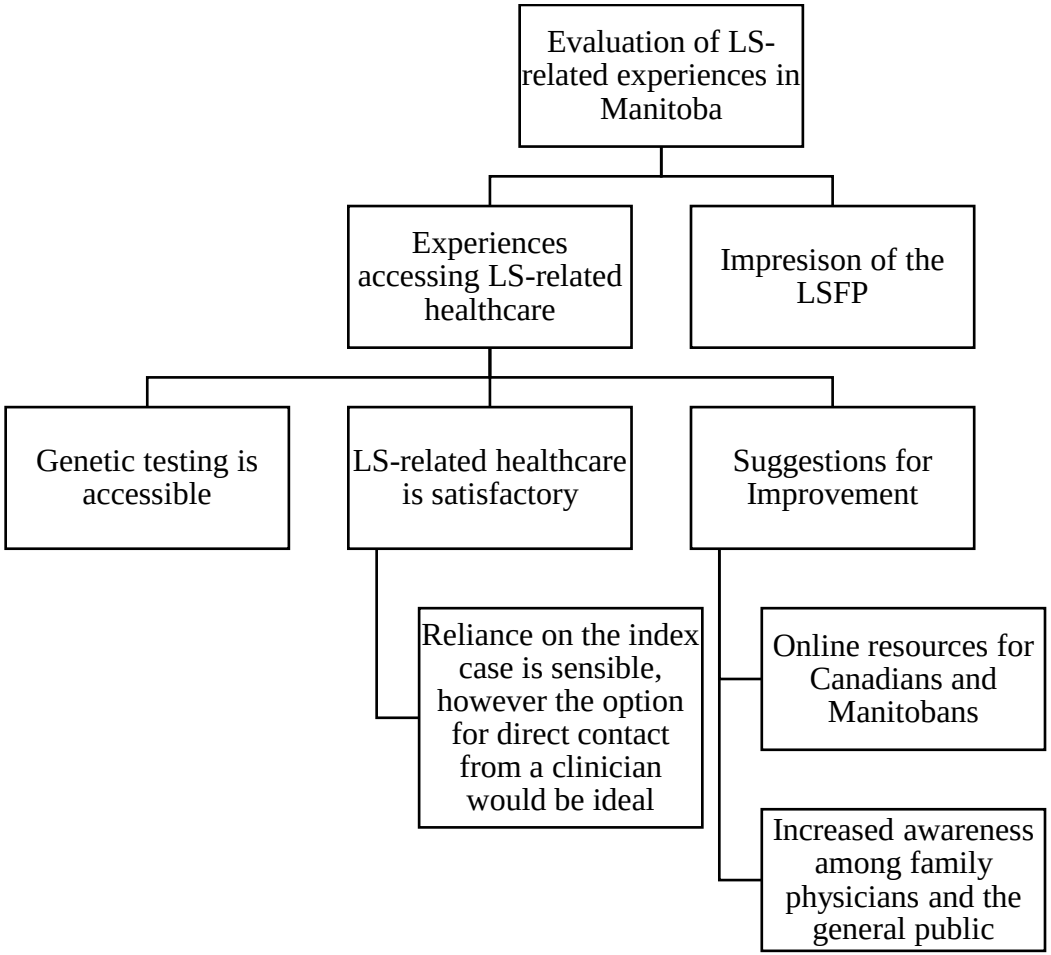

Figure 4. Thematic framework of the evaluation of LS-related experiences in Manitoba.

Communicating about LS within Families

Perceptions of Genetic Testing

All participants ultimately decided to proceed with genetic testing, but many risks and benefits factored into their decision. Participant experiences learning about LS, their perception of the most significant risks and benefits of genetic testing, and the impact of having a positive genetic test result for LS all to pursue genetic testing contributed to participant perspectives and how they conveyed the experience to relatives. Personal perceptions of genetic testing also impacted the way participants expected their relatives to react to their disclosure and acceptance towards their relatives' decision whether to pursue genetic testing and/or cancer prevention strategies.

Risks & Hesitations

Although all participants chose to proceed with genetic testing, some discussed their personal hesitations. Those who had relatives who declined genetic counselling and testing hypothesized why. A general fearfulness was described. Specific concerns were explored throughout the interviews, including privacy, insurance, stigma, and uncertainty.

Adjusting to the diagnosis. Among the spectrum of responses to learning about LS, some participants discussed their difficulties accepting their genetic test results. Some participants proceeded with genetic testing in hopes of a negative result and were forced to face their "worst case scenario" (Liam, CT, 2018). The following excerpt illustrates some of the challenges in coming to terms with LS:

> It did take me a little while to absorb the fact that I really have this and it is permanent. Because to say have a surgery and then it's over and that's it. I kind of downplayed it, oh, it's a just a hysterectomy. Well, if it were just a hysterectomy, people recover from it and they go on with their life. So in a way this felt like a bit of a weight. This is hanging over me. This is permanent and this is always going to be a concern. (Janice, IC, 2019)

The participants who described challenges adjusting to their diagnosis of LS chose to inform relatives about LS, perhaps partially as a way of reaching out for support.

Two participants admitted to feeling stigmatized by their diagnosis of LS. Liam (CT, 2018) said, "At the very beginning I would definitely kind of say I was a little bit ashamed of it (LS), in a weird way. I honestly couldn't tell you why. I felt like oh, there's something wrong with me". Stigma surrounding LS could prevent affected individuals from disclosing the information to others, or delay disclosure until the individual feels more comfortable. For

example, Sarah (IC, 2002) cited her experience feeling stigmatized as her reason for why she "was very selective on who [she] told."

Creating worry. Some participants theorized that their relatives chose not to have genetic testing because they were not prepared to attend cancer screening or make preventive lifestyle changes. For these individuals, knowing about LS would only create worry, without the benefit of cancer prevention:

> My sister doesn't really want to do it (genetic testing) because she figures if she's going to get cancer anyways, it'll happen, and she won't have to worry about it everyday. Cause she feels like it might make her more paranoid. (Emma, CT, 2020)

Janice (IC, 2019) described the perception that genetic testing is life changing and a positive test result is "just going to hang over them." Participants recognized that the main motivator for parents to have genetic testing was for their children and individuals without children may feel less urgency:

> I watched my little brother do the same thing, thinking to himself, well I'm not married, I'm not having any kids right now, all I'm worried about is myself, if it happens it happens kind of thing… Until my brother had his own children, [then he] started taking it more seriously. (Sarah, IC, 2002)

Some participants had relatives who had colonoscopy procedures regularly to screen for cancer without genetic testing. One participant stated that their relative indicated they would prefer to have regular colonoscopies than have genetic testing to clarify their inherited cancer risk. Other relatives were unphased when participants informed them about LS because they were already receiving screening. It was unclear if these relatives are aware that a negative genetic test result could mitigate their need for frequent colonoscopy screening. Some participants seemed dissatisfied with relatives receiving screening without genetic testing and would recommend their relatives proceed with genetic testing. For example, Sarah (IC, 2002) said, "I have a sister that thinks that she's just healthy either way, so she doesn't have to be genetically tested. [Laughs] She does go for colonoscopies, so she thinks that's good enough."

Insurance discrimination. Some participants discussed the risk of insurance discrimination as a consideration when deciding to have genetic testing. Ultimately, participants agreed that the benefit of cancer prevention outweighed the risk of insurance discrimination. However, some participants still factored insurance risk into their decision and hypothesize that this could be a deterrent for some of their relatives:

> I wanted to make sure that I had adequate life insurance and that I was, you know, not getting myself into a position where I would be uninsurable or whatever in the future. That was an even more substantial concern for my children when we went to get them tested. (Ben, IC, 2014)

As mentioned in the LSFP, the Genetic Non-Discrimination Act was enacted in 2017 to protect Canadians from insurance or employment discrimination based on genetic test results. The interview guide did not specifically address the law, but many participants indicated they were unfamiliar with the law after reading about it for the first time in the LSFP. Some individuals recognized the limitations of the law such that a family history of cancer, regardless of genetic testing, can impact insurance availability. Sarah (IC, 2002) was concerned that "even if my son doesn't do it (genetic testing) … because I have had cancer, they're probably going to deny him [insurance]." Uncertainty was common, which created hesitation towards genetic testing for some and acted as motivation for others. Those who expected to be denied insurance based on their family history of cancer were less concerned about genetic test results impacting their insurance. Some participants mentioned concern or uncertainty about the implications of genetic testing on their insurance but felt it was not an important factor in their decision because they felt genetic testing would have significant benefit for their family.

Uncertainty about testing options outside Manitoba. Participants with relatives outside of Manitoba described specific challenges accessing genetic testing based on location and differing health systems. Participants described providing their relative with information about LS, but when their relative presented the information to their family doctor, the doctor was unclear on how to proceed. For example, Jessica (IC, 2014) has family living abroad and she recalled "[the doctor] didn't know what they wanted. And then it just fell by the wayside, and then they moved, so, yeah, nothing has been done to date." Erica (IC, 2019) had relatives trying to access genetic counselling in another province and she found "it can be up to four years [wait] to get in there." Most participants with relatives outside Canada considered cost to be a potential barrier for their relatives:

> I know my mom has talked about it with them, but they don't live in Canada and I don't think they have access to the testing or, I'm sure it's not free. So none of them have actually done it. (Sofia, CT, 2017)

One participant described the healthcare system where his relatives live as unreliable, saying "we are not 100% sure that the testing will be accurate. …I don't have a faith [in] them. … [Some

healthcare providers prioritize] making money and they don't bother about the lives of people" (Armaan, IC, 2019). He saw no purpose in accessing healthcare he cannot trust:

> If they (my relatives) had been in this country then I would have certainly shared [information about LS] with them; I [would] have told somebody like you to give them a call about that, to tell them. But in our country, I don't think so. (Armaan, IC, 2019)

Benefits & Motivators

"Knowledge is power". Despite the various concerns described above, all participants chose to have genetic testing, and many reported a complete lack of hesitation towards genetic testing:

> I knew I needed to do it (genetic testing). I wasn't psyched that I might have the LS, but there was no hesitancy as far as going to get the test done. Yeah, I know some of my cousins did hesitate and that didn't turn out too well for them, so looking back, I'm glad I took the proactive approach, that's for sure. (Daniel, CT, 2015)

All participants described genetic testing as a step towards gaining more control over their cancer risk and empowering them to take steps towards cancer prevention. These perceptions translated to motivators of informing relatives in the hope relatives can receive the same benefits.

Many participants described mixed feelings towards receiving their genetic test result confirming they have LS. Although genetic testing confirmed an inherited risk of developing cancer, participants recognized that having this information allowed them to receive targeted cancer prevention:

> You get to know, so you can do things beforehand to make sure that it (cancer) doesn't happen, or you're constantly monitored. So it's scary, but it's kind of good, you know, in a way. So, I think it's great to know, but it's like "darn." (Jessica, IC, 2014)

Participants considered the benefits of genetic testing to be worthwhile and felt it was better to know than not:

> From my perspective I wanted to know because I didn't want to be ignorant to the fact and I don't want to have to go through any future complications from something, or surgery. So, the more info, the more that I can do to prevent something like that, it was better for me. (Randy, CT, 2019)

Many participants quickly adjusted to learning they had LS and felt it minimally impacted their daily lives besides attending cancer surveillance appointments. The perceived utility of genetic testing was to arrange appropriate cancer prevention and for many that was the main outcome:

> In my normal life, I really don't worry about it too much. I just know that – well I know what to expect on a yearly basis going for my screening and stuff like that. You know, it's

> not fun, obviously, but it's just something you've got to go about – you've got to get done. I don't really let it bother me whatsoever. (Randy, CT, 2019)

An explanation for cancer. Participants who have had cancer or a significant family history of cancer found some relief in learning they had LS. Genetic testing provided an answer for why they or their family members had cancer and clarified their cancer risk. Sarah (IC, 2002) described learning about LS as an "aha moment". Based on their cancer history, learning about LS was not surprising:

> There was no similarity in the way we lived or anything. The only thing it could be was hereditary. …Even without any genetic testing we knew there was a problem with the family. … It sort of confirmed is about all. (Jeff , IC, 2000)

There was also relief in knowing that LS does not equate to a cancer diagnosis:

> I think I was more worried that they were trying to tell me I had still had some other medical problem. So, in a way, I was kind of relived. I know it sounds strange, but because they got all the cancer in the surgery, so I was just kind of relieved to know that this was a genetic hereditary situation, rather than I still had an actual problem, physically. (Janice, IC, 2019)

Doctors take concerns seriously. Participants discussed how being diagnosed with LS not only enabled them to begin thorough cancer screening regimens, but also made them feel like their doctors were taking their concerns seriously. Genetic testing provided justification for individuals at risk for cancer to have their concerns addressed by their doctors:

> The doctors have more opportunity to say, you know what, this person does have LS, we need to look at things a little more deeply. Which to me, it's a good thing. I'm not here this extra 20 years if they wouldn't have taken me seriously on a number of different occasions. Right? (Sarah, IC, 2002)

Empowering relatives. The belief that knowledge is power motivated many individuals to share information about LS with their relatives. Participants understood that knowledge about LS could provide opportunities for cancer prevention. Jacob (CT, 2019) was motivated to inform his children about LS "so that they have the chance to catch something early rather than letting it get away on them." Many participants presumed their relatives would share their perspective and be grateful to learn about LS. Regarding sharing information about LS with relatives, Mike (CT, 2015) thought "overall it would be well received… I would hope that they would see this as a gesture or an act of love, me wanting what's best for them." By sharing this information, participants felt they were empowering their relatives to prevent future diagnoses of cancer. Participants felt the burden of increased surveillance was insignificant compared to a cancer diagnosis:

> I didn't quite understand why somebody would not want to know that (if they have LS) when it's just simple, a test, and then you go for your screening, like colonoscopy every year, whatever you have to do. It's just a small inconvenience basically. (Randy, CT, 2019)

Interestingly, one participant who chose not to inform relatives about LS believed "it's good to tell somebody if they can save themselves" (Armaan, IC, 2019). This participant expected his relatives not to believe him if he informed them about their risk for LS and expected they would not take the initiative to "save themselves". Furthermore, he anticipated negative reactions if he shared the information with his relatives, such as anger and blame. Evidently, many factors intersect when deciding whether to share information about LS with relatives and the perceived power of the knowledge is weighed against the many other factors identified, including family dynamics, cultural expectations, and perceived hesitations towards genetic testing.

Duty to share risk information. Many participants felt an obligation to share information about LS with their relatives, distinct from the motivation of sharing perceived benefits of cancer prevention (positive reinforcement), as the obligations stems from avoiding guilt (negative reinforcement). Once participants learned about the hereditary nature of LS, they felt responsible to warn their relatives of their risk and feared considerable guilt if they did not pass the information on. For example, Mandy (IC, 2018) discussed informing her relatives about LS "because I would've felt responsible for not informing them if something happened." A subsequent illustration of this theme is the experience of Janice (IC, 2019) who shared information about LS with her relatives to avoid "feeling guilty if one of them got cancer and it could have been prevented or caught at an early stage. [She didn't] want to carry that around with [her]."

Family Dynamics

The hereditary nature of LS necessitates the consideration of the involvement of relatives and consequently family dynamics emerged as a significant theme. Family dynamics impacted many participant experiences with LS along their journey, from learning about LS for the first time, navigating whether or how to tell family members, adjusting to the diagnosis with the support or lack of support from relatives, and adhering to surveillance and prevention recommendations. One participant was adopted and described very limited contact with her biological relatives, which made informing them about LS more difficult and less of a priority.

Supportive family with shared experiences facilitates communication

The CT group first learned about LS from a relative who could relate to the experience. Liam (CT, 2018) remembered learning about LS from his mother, who was able to anticipate his reaction and provide the reassurance he needed because she knew him so well. Daniel (CT, 2015) discussed how his mother broke the news about LS to him and his siblings together, and how they all perceived genetic testing as beneficial and decided to go through the process together. Many participants acknowledged that broaching the topic of an inherited cancer risk with relatives can be difficult, but those whose families had open discussions about cancer in the past found it easier. To quote Jeff (IC, 2000), "We've got so much of it (cancer), there's not a secret at all. We discuss it like just anything that's going on that day." Mike (CT, 2015) emphasized the benefit of having supportive relatives who understand the experience of having a colonoscopy. Families could support one another through shared experiences with cancer and cancer screening.

Being open about LS can be isolating

Most participants described supportive reactions from their relatives, but unsupportive family members were extremely impactful. Many participants described their vulnerability when discussing LS with their family and those who were met with unsupportive reactions discussed how isolating that felt. One participant believed her relatives distanced themselves as a mechanism to cope with their concern, stating "it's easier to kind of let go than to be really close to someone and let them go" (Sarah, IC, 2002). Another participant had a particularly strained family dynamic which impacted her experience with LS:

> I swear that I'm so frustrated with the whole thing that me and them (my family) have not even been talking for two months already. And our last conversation was the fact that they still will not even consider this information about LS. I no longer want to discuss this with them, considering I just had my own surgery. I had to learn of this condition and absorb it and so on, and then to top it off they mock me about the whole thing. They haven't been very nice about the whole thing. And that actually has bothered me probably more than even finding out I had LS. (Janice, IC, 2019)

Cultural norms dictate discussing LS as "taboo"

Family dynamics can be shaped by the broader culture the family identifies with, and some families have their own culture (attitudes, values, goals and practices) in which their family dynamics contribute. A few participants discussed how it would be perceived as unacceptable to

openly discuss LS in their family. Armaan (IC, 2019) expected his relatives to perceive information about LS as pointing blame:

> Our culture is different from Canada. If we talk to someone like that, "I have a problem, you have a problem", then they might get a negative thing about us that you are saying [something] negative – you got something and you are just trying to put on us too.

Armaan felt initiating a conversation about LS would strain family relationships and would not be worthwhile because he would not expect his relatives to be interested. Another participant chose to discuss LS with her relatives and was met with discomfort and avoidance. She said, "I don't know if it was just our upbringing, that's the way you dealt with things. I think that could be culturally, in a society where you don't talk about things and it won't happen" (Sarah, IC, 2002).

Designating the best person to discuss LS with each relative is complicated

One hesitation that arose when discussing LS with more distantly related family members was the fear of "stepping on toes" (Sarah, IC, 2002). In some cases, participants were not sure if their distant relatives were informed about LS but knew of other intermediate relatives who were informed. These participants wanted their distant relatives to be informed but felt the intermediate relatives should be responsible for passing on the information. Some participants felt that parents should be responsible for informing their children and that speaking directly to someone else's children, regardless of their age, would be disrespectful. Concern arose around the potential harms of telling someone else's children about LS, including a child having negative feelings towards their parent for withholding the information and "causing a family scene" (Sarah, IC, 2002). These concerns are illustrated by the following quote:

> I wonder if I was presenting this information and they didn't have their parents present this information, like I guess I wonder how they would feel towards their parent. Cause if this was something that was readily available for a number of years and they weren't doing it and now you know I'm presenting it to them saying, "hey this could be in your best interest," they could see it as like well why didn't my mom or dad or whoever, why didn't they pass it on to me? (Mike, CT, 2015)

Some parents hesitated to discuss LS with their own children because of the guilt of possibly passing down LS. Mandy (IC, 2018) said, "It's illogical, but I felt responsible. And I know, I don't know for sure if my mother had LS, but she did have the same type of cancer. And I don't blame her, but I do blame myself." Despite feelings of guilt among parents, all participants chose to tell their children or intended to tell their children about LS when they

consider them old enough. Most parents of young children did not have a specific age they were waiting for to discuss LS, but rather plan to answer honestly when their children begin noticing and questioning their cancer surveillance procedures.

In some families, communication was facilitated by the "matriarch of the family" (Erica, IC, 2019), a person in their family who stayed in contact with all their relatives. It was expected that relatives would be receptive to information from this appointed female leader, and that she would keep track of everyone in the family. Some participants only discussed LS with this relative and relied on her to disseminate the information.

Discussing cancer may resurface old fears or overwhelm relatives

Almost half of participants had cancer themselves, and all participants had dealt with cancer in their family. Consequently, participants recognized that sharing information about LS could be upsetting for their relatives who have experienced the fear of losing a loved one to cancer. One participant delayed discussing LS with a relative who was currently facing a cancer diagnosis, saying "I don't want to mention any other cancer to her. She's sort of on the edge right now" (Jeff, IC, 2000). Other participants who had previously had cancer discussed how difficult their diagnosis was on their children. Some parents were hesitant to discuss LS for fear of resurfacing those cancer worries:

> It was a really big time in our lives, and I know that my youngest went through, and we're still going through, some issues around that, and I just don't want to bring up some memories for them and make them scared that something might happen to me again. (Jessica, IC, 2014)

If relatives were informed previously, further discussion may be perceived as "pestering"

Some participants chose not to discuss LS with relatives who they believed were informed by another family member. Most participants among the CT group indicated the previous generation was already aware. These participants did not feel obligated to share information about LS in their families, but those who have children feel it will be their responsibility to inform their children when they become old enough. Some participants did not forward any new information about LS, such as the LSFP, to relatives who were previously informed. These participants discussed that if relatives were already informed, it is their choice to seek out any further information. Autonomous decision making was a common theme which intertwined with family dynamics. Many participants felt uncomfortable sending further information unsolicited, as demonstrated by the following quote:

> I don't have the type of relationship with the other cousins to follow-up and sort of, you know. It would be seen as pestering if I went back to them now and said, "Hey just to confirm you did get tested, right?" (Ben, IC, 2014)

Reactions towards Autonomy

Following disclosure of LS information to relatives, participants had limited control over whether their relatives sought genetic counselling. All participants recognized the autonomy of their relatives to make their own decisions about genetic testing and cancer prevention, but acceptance towards relatives' decisions varied. Reactions towards autonomy impacted future communication about LS following the initial disclosure. Most participants were motivated to share information about LS with their relatives by any or all of two main reasons: (1) they hoped their relatives would take action to prevent cancer, and (2) they felt it was their duty to pass on the information and, in doing so, unload their burden of responsibility. Those participants who hoped their relatives would pursue genetic testing and cancer prevention strategies felt extremely frustrated if they perceived their relatives were not concerned. Others felt their duty was done after sharing the information and felt the outcome was no longer in their hands. Those who accepted their relatives' decision were reluctant to press the issue by providing further information, and those who were frustrated by the decision reacted by persistently providing information. Family dynamics remained prevalent throughout this theme and impacted the level of involvement participants found acceptable in their relatives' decisions.

Acceptance of relative's autonomous choices

No participant regretted their decision to have genetic testing and all perceived the decision for their relatives to pursue genetic testing as positive. Even so, some participants were comfortable with leaving the decision up to their relatives and perceived either outcome (having genetic testing or not) as positive if their relative was informed. Among participants there were variable levels of acceptance. A few participants had no reservations leaving the choice up to their relatives, believing "they are aware and they can make their own decisions" (Sofia, CT, 2017). Some participants accepted their relatives' choice not to have genetic testing despite disagreeing with it:

> Whether I like it or not I'm not going to start telling younger guys what to do or how do deal with their – it's their decision. Like, I can give them the information. If they want to use it great, if they don't that's great for them too. That's up to them. (Jeff, IC, 2000)

Frustration towards relatives who decline CT

Some found their relatives were not receptive to the information, which was troubling for participants who hoped their relatives would take preventive action. These participants had the goal of ensuring their relatives have genetic testing and perceived not having genetic testing as an act of avoidance, fear, ignorance, or denial. Sharing information, like the LSFP, was a means of motivating relatives to pursue genetic testing and cancer prevention. A common feeling among participants with relatives who have not had genetic testing was frustration, exemplified by the following quote:

> To me, [convincing my daughter to have genetic testing is] something that I need to do because it could be a life and death situation in the future for her… I can only do my best and it's just, well you can probably hear my little frustration in my voice talking about it, it's frustrating when you know it's important. I know it's important, I just wish that she and my other son knew it was important to get the testing done. (Jacob, CT, 2019)

Some participants suspected their relatives threw the information away without reading it. One participant mentioned that it does not matter how the information is presented, on a piece of paper or by email, if relatives are not interested in reading the information they simply will not (Sarah, IC, 2002). Erica (IC, 2019) plans to inform her extended family about LS once she has determined which side of the family is affected, but she expects "some [of her relatives] would choose to ignore it".

One participant described a strained family dynamic where she was not in contact with some of her relatives. She hoped the relatives she was in contact with would pass on the information, but the following excerpt illuminates the limitations of this method:

> I had said point blank, "If you loved your children and your grandchildren, share this information with them". And nothing can budge their attitude. Of course, going back to my family, it's people like them that, if they were the ones that found out they had LS, would they share that information? Would I have found out from them? Probably not. So some people may not want to share their cancer risk. If they don't even want to hear about it, why would they share it, right? (Janice, IC, 2019)

Some participants believed that not everyone took the risk seriously when they shared the information about LS. Some relatives who considered themselves to be healthy were reportedly in disbelief and saw no need to inconvenience themselves with the information. "Their outlook is sort of like oh we're all healthy, whatever" (Erica, IC, 2019). The following passage demonstrates the scepticism Sarah (IC, 2002) faced when she told her sister about LS:

> She plays the card that she's not the chosen one, you know? That she lives a healthy lifestyle. I don't think it's any different than mine. I don't know, but in her mind I guess she's just not … How can I say this? It's not going to happen to her. You know, when you don't think about it you don't, I guess, create it or bring it on to you, right. I think that's what her thinking is.

Some relatives struggled with accepting the new information which had changed since they last consulted a healthcare provider. For example, Janice (IC, 2019) found "because my parents had cancer [and] they were never approached about LS, they look at me like they don't buy into any of this. They don't believe it. They aren't taking this seriously." She believed their strained family dynamic also impacted her parents' distrust.

Evaluation of LS-related experiences in Manitoba

Experiences accessing LS-related healthcare

Genetic testing is accessible. Among our participants, no common barriers to accessing genetic services were identified in Manitoba. The most common challenge acknowledged by participants was waiting for their genetic testing results. The Hereditary Cancer Clinic typically quotes a turnaround time of 3-4 months, although one participant reportedly waited close to a year. The following quote exemplifies the common challenge of coping with the unknown while waiting for genetic test results:

> The only disappointment I have had is that getting the test results is a very lengthy process and that was hard to go through. So that would be my only recommendation in the whole system if it was — 'cause it's hard to live with that limbo, you know? At least once you know, even if it's a positive, at least you know. (Mandy, IC, 2018)

Participants could not foresee any barriers preventing their relatives from accessing genetic services in Manitoba. Many reported that provincial health coverage made genetic testing accessible to them. Forty percent of participants reported living in rural Manitoba and although the Hereditary Cancer Clinic is located in Winnipeg, no one identified distance from the clinic as a challenge. When asked directly if having the only genetics clinic located in Winnipeg created a challenge, one participant replied, "No, that's just a fact of living here" (Erica, IC, 2019).

LS-related healthcare is satisfactory. Overall, participants had overwhelmingly positive impressions of the healthcare they received related to LS. Most participants had no suggestions for improvement. The Lynch Clinic was recognized as a useful touchpoint to stay up to date on recommendations from the latest research and ensure screening recommendations are being

followed. Emma (CT, 2020) illustrated this theme by stating, “I really like that there is a clinic that’s specifically for this because if there’s any problems, I have somebody to call that actually knows what they’re talking about.” Participants felt reassured by the regular follow up with a specialized team, including Janice (IC, 2019) who said, “I’ve got two follow-ups a year so I feel like I’m in really good care. That if anything were to happen, at least it would be an early detection.” Furthermore, many participants noted that their surveillance and follow-up was arranged for them well in advance:

> I've had a relatively easy experience with it. So as far as the whole process of – from day one, it's all been good. And I know at HSC they're – they've got everything – my appointment for next June's already booked. So I'm happy with that. (Randy, CT, 2019)

Mandy (IC, 2018) summarized the sentiment shared by many participants when she said, “I give the whole system an A.”

Reliance on the index case is sensible, however the option for direct contact from a clinician would be ideal. Participants were understanding of the necessity for their involvement in sharing information about LS with their relatives. Participants agreed the current system is sensible and identified various reasons why they were best suited to share the information with their relatives, such as their ability to personalize the information for their relative, protecting their privacy and confidentiality, and respecting their relative’s right not to know. Liam (CT, 2018) thought it would be easier on relatives to learn about LS from a family member whom they have a relationship with, rather than “from just a faceless health care professional.” Regarding privacy, Sarah (IC, 2002) agreed with the current practice because “if it comes from me it comes from me, I am sharing what I need to share.” Participants also recognized that logistically it would require significant healthcare resources to contact the relatives of each person with LS. Like Sofia (CT, 2017) noted, “every person that is diagnosed has so many relatives, it can’t be the responsibility of the healthcare provider to let everybody know about it (LS).”

All participants agreed that direct contact from a clinician would make their relatives take the information more seriously; however, opinions on whether the impact would be positive or negative were mixed. Some participants felt that direct contact from a healthcare provider would create unwanted stress for their relatives:

> I think it should be the way it is now; the family should inform the rest of the family and then the rest of the family can decide whether or not they want to do the test. Just for – the simple fact is, if the doctor, I think, were to tell the patient that there is a possibility

> they might have it and that they could be at risk for more cancers, it might make them a little bit more paranoid and scared. Whereas having a family member talk to you will give them the choice whether or not they want to do it. (Emma, CT, 2020)

The participants who would consider direct contact between a healthcare provider and their relative to be ideal tended to be more directive in urging their relatives to have genetic testing. These participants thought direct contact from a healthcare provider would help facilitate their goal of genetic testing for their relatives:

> If the Lynch Clinic, the authority, could be able to send it directly to, let's say, my two children that haven't been tested yet. That would be a nice touch because not only have I let them know but now somebody professionally has let them know that they're eligible for testing, type thing. Yeah, I think it would be more helpful and maybe they would take an entirely different view and go get tested when it's coming from a professional body. (Jacob, CT, 2019)

Jessica (IC, 2014) added to this perspective by noting "sometimes the kids don't believe their parents, you know, and sometimes kids getting some information from other people is a little bit more meaningful." Participants with this perspective also recognized the resource limitations, but hypothetically speaking would appreciate this type of service on an opt-in basis.

Suggestions for Improvement

Online resources for Canadians and Manitobans. When asked about suggestions for improvement, many participants indicated an informational webpage specific to Manitobans would be valued. Many participants sought information about LS online and reported the information they found was typically published in the United States. The distinctive differences between the Canadian and American healthcare systems made participants feel that much of the information available online was not relevant to them:

> Information is probably the hardest thing to get, and that's again because whenever you look up something you always get from, like American sites, like the CDC, and it's not really the most useful thing for me. Like, I want to know oh, what are my options in Manitoba? Not what are my options in America. So I think that the healthcare system could do better by supplying people with LS with a local – like, local sources or sources that are more relevant to them. (Liam, CT, 2018)

Most participants agree online resources are most convenient to access and suggest the best platform to make information available would be online. Erica (IC, 2019) thought "people do use online for a lot especially – and I'm older, I use it. I think that's for sure with all young people." In contrast, one participant did not have internet access, highlighting the need to maintain paper

options even if the majority prefer online access. The interview findings suggest a need for local online informational resources in addition to the LSFP.

Increased awareness among family physicians and the general public. All participants indicated they were satisfied with the care they received from LS specialists; however, many participants felt their family physicians lacked awareness about LS. For example, Erica's (IC, 2019) "GP didn't know what it was" and Sofia (CT, 2017) noticed "there's not a lot of people that actually know what it is. Yeah sometimes I'll say I have it and, even health care providers, they're like, 'oh well what is that?'." Many participants shared experiences of self-advocacy, providing their family physicians with information to ensure their physician referred them for appropriate screening:

> I had gone and done research myself, right, so my primary physician didn't know anything about Lynch. She does now but she didn't [laughs]. And the variant that I have, there's also a skin cancer component to it and so I needed her to send me to a dermatologist and she, you know, once I explained why it was fine but had I not gone and done the research and figured that out for myself she wouldn't have figured that out. (Ben, IC, 2014)

Some participants noticed improved awareness in recent years; however, many participants were laden with the necessity to provide their family physician with information about LS in addition to informing relatives, adjusting to their diagnosis, and attending cancer surveillance.

Participants would not expect the average person to be familiar with LS but perceived many benefits of increasing awareness among the general population. Familiarity with LS would ease the burden on individuals with LS trying to explain it to their relatives. As Ben (IC, 2014) pointed out, if "more of the general population knew about LS then the, you know, 'Hey cousin it turns out I've got LS, you should probably go get tested' conversation would be a lot easier." Additionally, participants expect their relatives may take the information more seriously if they have heard of LS before from a credible source:

> I think there has to be another step in that whole process, and to me I think it's about the awareness, a campaign. You know? I don't know. Something along that line that kind of triggers, 'Oh yeah, I remember [someone] told me something about that, oh maybe I should look into that.' You know what I mean? Like even though I may have said something, I'm too close to them to say something sometimes. Sometimes, you know, your family member is too invested to make you aware of these things. And sometimes it takes a stranger or someone else that they don't know. (Sarah, IC, 2002)

Beyond increased awareness about LS, Sarah (IC, 2002) discussed a lack of awareness of genetic counselling, making the entire process feel foreign. To quote Sarah (IC, 2002), "When I

think back to when my surgeon said to me, 'You should do genetic counselling', I didn't know what it was. I had no idea what it pertained; I had no idea what any of that information is." An increased awareness of genetic counselling would help individuals to know what to expect as they organize their next steps and gather more information about their options. Emma (CT, 2020) suggested "maybe they (doctors) could have like a little pamphlet, like they do with some other things, just to give to the person the information on how to get to genetics". Similarly, Randy (CT, 2019) proposed "a pamphlet like that even sitting in a, say a waiting room in a doctor's office. …And then they can get more information just by looking at that."

Impression of the LSFP

The LSFP left an overall positive impression on all participants and many did not have any suggestions for improvement. Participants found the LSFP easy to understand, concise, and felt the appropriate information was included. The following quote exemplifies some of the positive feedback provided:

> I think it's concise enough without being, like, without hiding information. So I think it was well written. I don't think it, in my opinion, it doesn't need to be added to or reduced at all. To me it's a good amount of information that both addresses the concern of like what's actually going on and also you know it does address a bit of the emotional side too and the effect that it could have on your well being. I think it's good. It provides the information, so there's good truth that's put in there, but it also – there's some grace in how it's presented so it's not harsh. (Mike, CT, 2015)

Some participants provided minor suggestions, including specifying the mode of inheritance (dominant), adding a more complete list of associated cancer types and risk percentages, adding lifestyle recommendations, and adding images to visually break up the text. One participant was disappointed that the LSFP felt less personal than the family letter provided previously by their genetic counsellor and felt the LSFP needed more information for relatives outside of Manitoba. Another participant lacked clarity on the age of onset for LS-related cancer risk and found the explanation in the LSFP vague. The most common suggestion was to add website links to the LSFP which readers could visit for further information:

> One thing I would personally add to this thing would be another section just with links on further readings and then to just point people into the right direction if they want to learn even more. Because Google is not always the most reliable thing. (Liam, CT, 2018)

A link with more information regarding the Genetic Non-Discrimination Act would be particularly helpful, as multiple participants reported they had never heard of it before.

When asked about the preferred format of the LSFP, participants chose a combination of on paper, as an email attachment, and on a website. Many participants liked having a hard copy for their own records but sent the LSFP as an email attachment to relatives. Those who recommended a website mentioned the convenience of accessing it anytime. The main limitation of a website would be the inability to tailor it to the individual, so it would not specify the gene mutation. Most participants indicated it would be most convenient if available in all three formats.

Chapter 4: Quantitative Results

Overview

Clinicians obtained consent from 111 eligible patients to contact for study recruitment. The number of eligible individuals who declined to be contacted was not recorded, however clinicians reported very few instances and estimated less than five. Therefore, we expect the 111 individuals who provided consent are representative of individuals newly diagnosed with LS or attending LS-related follow-up during the recruitment period. Of the 111 individuals contacted, 17 could not be reached or did not respond to three voicemail messages.

A total of 96 questionnaires were submitted using the online REDcap platform. One participant completed the survey by phone with the student researcher recording the responses in REDcap. The option to mail paper surveys was provided and one individual chose this method, but the survey was not returned. One respondent did not meet eligibility criteria (did not receive a LSFP) and three participants were excluded due to largely incomplete responses, providing a total of 92 responses for analysis. Participants were asked to forward the study recruitment email, with the LSFP attached, to their relatives. Eighty-six percent (79/92) of respondents indicated they received the LSFP from a healthcare provider and the remaining 14% (13/92) received the LSFP from a relative. The response rate among participants introduced to the study by a healthcare provider was 71% (79/111). Almost all respondents had genetic testing for LS (96%, 88/92), including 9/13 of the participants who received the LSFP from a relative. Of the 88 participants who had genetic testing, 85 had a positive result which confirmed LS, 1 had a negative result, and 2 were still waiting for their genetic test results. Most participants (79%) received their genetic test results over a year ago and those who received their results in the last year included 11% in the last 7-12 months, 5% in the last 4-6 months, and the rest (5%) within the last three months. The full questionnaire is available under Appendix H.

The sociodemographic characteristics of participants are presented in Table 7. Participants represented diverse age groups from young adults to individuals over age 75. The majority of participants live in a city with a population over 100,000 (60%), identify as women (60%), are of White ethnicity (78%), completed post-secondary education (75%), are employed (68%), have an annual household income greater than the provincial median (59%), are married (58%), and have children (60%). Forty-three percent of participants have had cancer.

Table 7. Sociodemographic characteristics of survey participants

	n	(%)
Total Survey Participants	92	(100)
Age (years)		
18-30	21	(23)
31-45	24	(26)
46-60	25	(27)
61-75	18	(20)
>75	4	(4)
Population of Town/City of Residence		
>100,000	55	(60)
7,000 -100,000	11	(12)
<7,000	25	(27)
Prefer not to say	1	(1)
Gender Identity		
Women	60	(65)
Man	29	(32)
Gender-fluid	1	(1)
Prefer not to say	2	(2)
Ethnic Background *		
Black	1	(1)
French Canadian	9	(10)
Jewish	1	(1)
Mennonite	15	(16)
Metis	4	(4)
South Asian	2	(2)
White	72	(78)
Prefer not to say	4	(4)
Education		
Did not complete high school	3	(3)
High School	20	(22)
College	30	(33)
Undergraduate University	23	(25)
Graduate or Professional Program	16	(17)
Employment Status		
Not working	9	(10)
Part-time	17	(18)
Full-time	46	(50)
Retired	19	(21)
Prefer not to say	1	(1)
Annual Household Income		
<$68,000	20	(22)
≥$68,000	54	(59)
Prefer not to say	18	(19)

Marital Status		
Single	25	(27)
Common law	7	(7)
Married	53	(58)
Widowed	2	(2)
Separated	2	(2)
Divorced	2	(2)
Prefer not to say	1	(1)
Parity		
Has children	55	(60)
No children	37	(40)
Personal Cancer Diagnosis		
Yes	40	(43)
No	52	(57)

*Participants were asked to check all that apply, for a total of 108 responses by 92 participants. Seventy-nine participants (86%) selected a single ethnic background, 11(12%) selected 2 ethnicities, 1(1%) selected 3 ethnicities, and 1(1%) selected 4 ethnicities.

Impression of the LSFP

Eighty-nine percent of respondents were familiar (46/92) or very familiar (36/92) with the information in the LSFP. Most had previously received information about LS from a healthcare provider in another format (68%, 63/92).

Eighty-five percent of respondents (78/92) indicated the amount of information in the LSFP is just right. Twelve percent indicated the amount of information is too little (10/92) or much too little (1/92). Three percent (3/92) indicated the LSFP contains too much information, and none of the respondents selected “Way too much”.

The survey included 11 Likert scale questions to gather impressions of the LSFP. Questions assessed whether the information in the LSFP was clear, easy to understand, convenient, trustworthy, and helped participants tell their relatives about LS. Participants were asked if receiving the LSFP made them feel informed, overwhelmed, worried, in control, able to cope, and if they felt it was an invasion of their privacy. Each question contained five possible responses: (1) strongly disagree, (2) disagree, (3) neutral, (4) agree, and (5) strongly agree. The mean and 95% confidence interval were calculated for each question. As illustrated in Figure 5, respondents agreed or strongly agreed that the LSFP is clear, easy to understand, trustworthy, helpful, convenient, informative, and felt able to cope with the information. Most respondents did not perceive the LSFP as overwhelming or worrying. Respondents reported that the LSFP gave them a sense of control. Most participants disagreed that receiving the LSFP felt like an invasion of privacy. The narrow confidence intervals in Figure 5 demonstrates the lack of variability among responses. Not a single respondent selected “disagree” or “strongly disagree” when asked if the LSFP is clear, seems trustworthy, helps inform relatives, is convenient, informative, a good way to share the information, and if they understood why they received the LSFP. Similarly, no one disagreed or strongly disagreed with the statements, “I understand why I received the LSFP” and “I felt able to cope with the information from the LSFP”. Only 2% (2/92) of respondents indicated the LSFP was not easy to understand and 3% (3/92) disagreed that the LSFP provided a sense of control. A single participant (1/92) felt that the LSFP was an invasion of privacy. The most varied responses were regarding feeling worried and overwhelmed by the LSFP. In response to “The amount of information in the LSFP left me feeling worried”, 17% agreed or strongly agreed, 33% were neutral, and 50% disagreed or strongly disagreed.

Similarly, 17% agreed or strongly agreed, 30% were neutral, and 53% disagreed or strongly disagreed in response to “The LSFP left me feeling overwhelmed”.

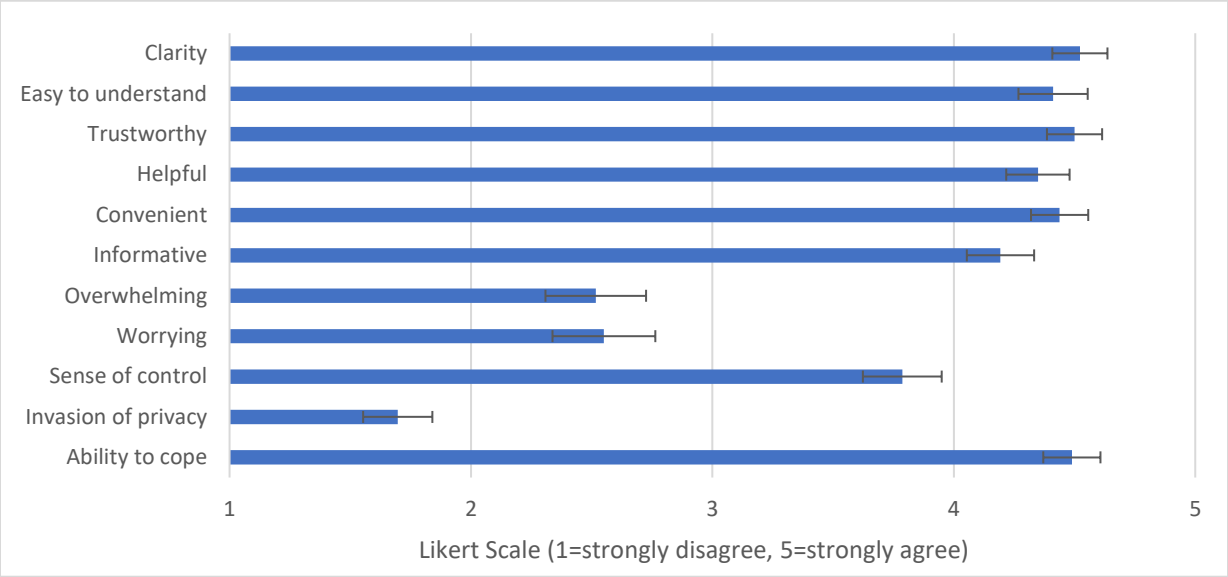

Figure 5. Overall Impression of the LSFP (n=92). The error bars indicate the 95% confidence interval around the mean.

Perhaps the most important indicator to assess the LSFP is the proportion of people who actually used it. Participants were roughly split into thirds: 29% (27/92) reportedly passed on the LSFP to their relatives, 38% (35/92) indicated they had not passed the LSFP to any relatives yet but plan to, and 32% (30/92) had no intention of using the LSFP. The reasons for not using the LSFP are explored in the next section (Figure 9), but no one indicated their opinion of the LSFP deterred them from using it. Responses to the Likert scale questions were stratified to compare (1) those who passed or plan to pass the LSFP on to relatives with (2) those who did not share the LSFP with anyone. P-values were calculated using the Wilcoxon rank test sum and considered significant if $p<0.05$. Although both groups assessed the LSFP positively, those who did not use the LSFP had a weaker understanding of why they received the LSFP ($p=0.018$) and were less agreeable that the LSFP was a good way to share the information ($p=0.016$). Figure 6 compares the appraisal of the LSFP between groups. Although both groups assessed the LSFP positively, those who did not use the LSFP found it significantly more overwhelming ($p=0.0094$) and felt less sense of control from the LSFP ($p=0.028$). Comparison of the 95% confidence intervals demonstrates a small magnitude of difference between groups.

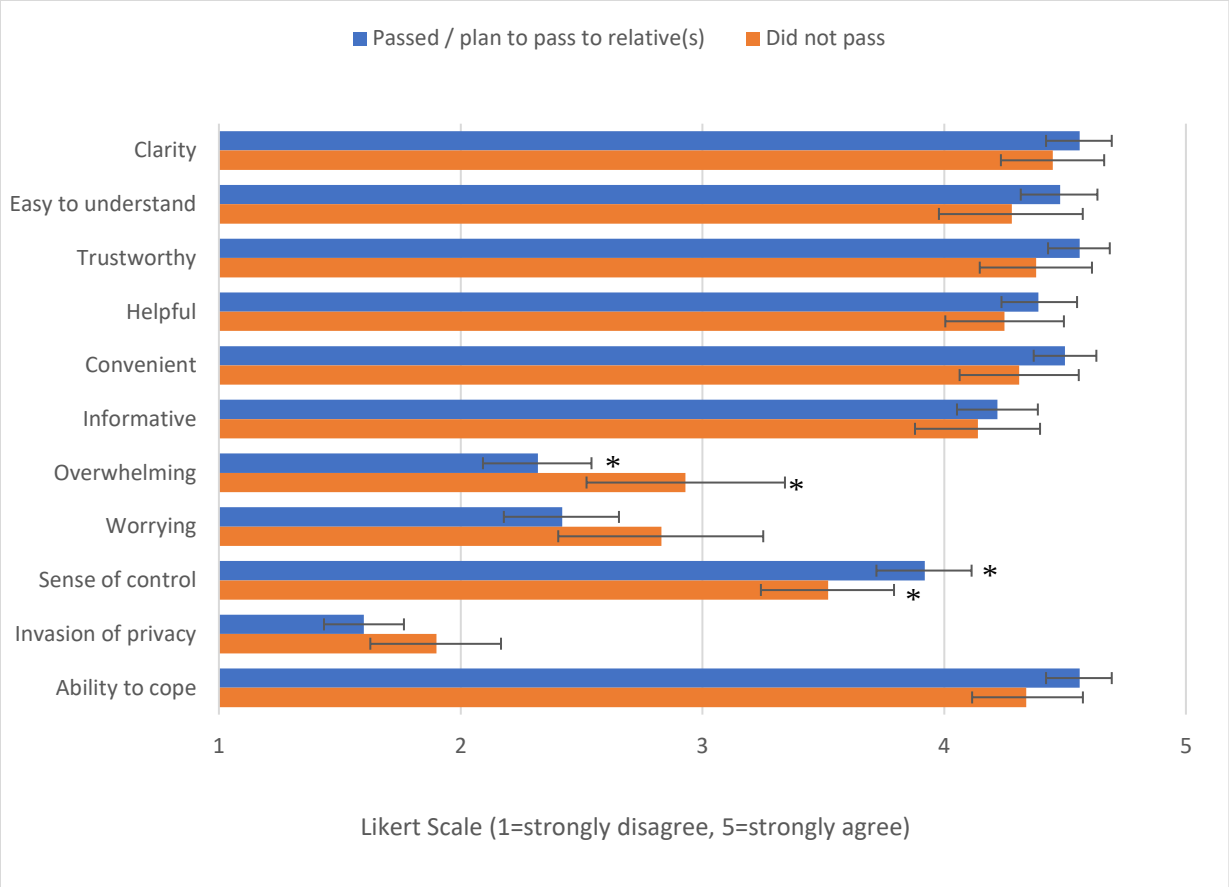

Figure 6. Assessment of LSFP was similar between participants who used or plan to use it (n=62) and those who did not (n=30). The error bars indicate the 95% confidence interval around the mean. Significant differences ($p<0.05$) between those who passed or plan to pass the LSFP to relatives and those who did not are indicated with an asterisk.

Most participants received the LSFP from a healthcare provider (86%, 79/92), as opposed to from a relative (14%, 13/92). Despite the limited sample size that received the LSFP from a relative, responses were stratified to determine if participants assessed the LSFP differently based on who they received it from. The results indicated that receiving the LSFP from a healthcare provider versus a relative did not impact the recipients impression of the LSFP (Figure 7). Responses from those who received the LSFP from a relative were more variable, especially in response to feeling overwhelmed and worried by the LSFP, illustrated by the wider confidence intervals.

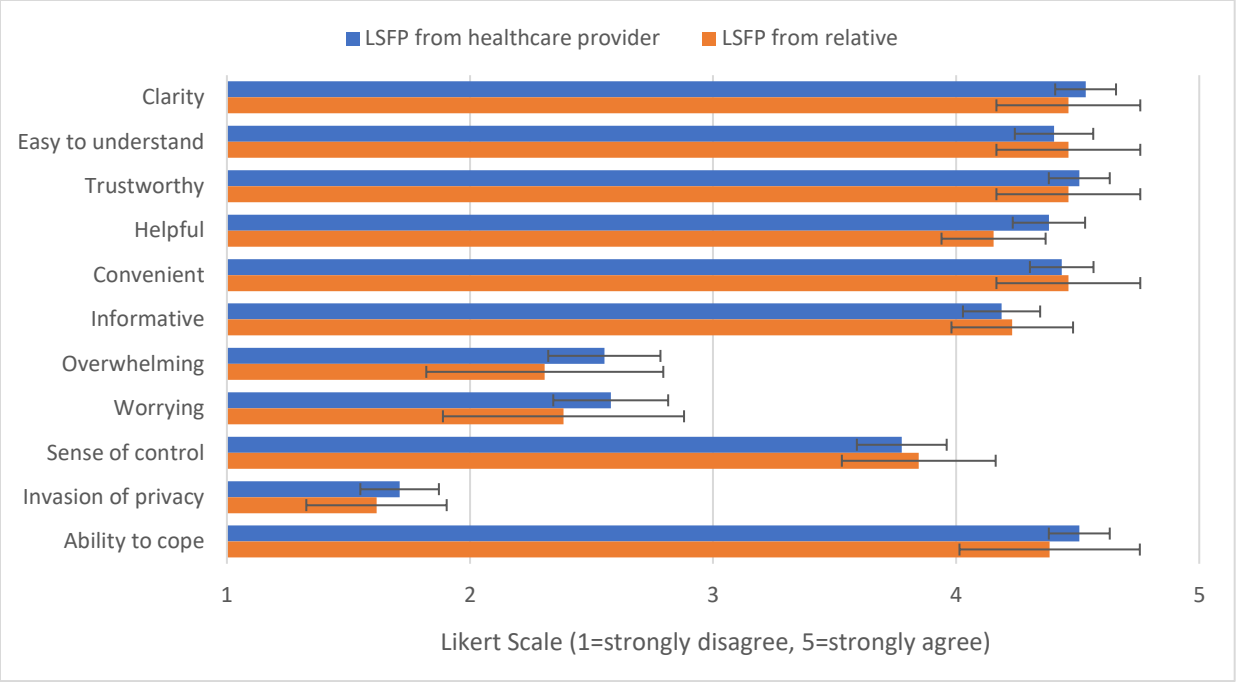

Figure 7. Impression of the LSFP was not impacted by who provided the LSFP: a healthcare provider (n=79) or a relative (n=13). The error bars indicate the 95% confidence interval around the mean.

The subset who received the LSFP from a relative (n=13) were asked five additional Likert scale questions (Figure 8). All respondents were glad their relative provided information about LS (10/13 strongly agree, 3/13 agree). Among this group, nine already had genetic counselling and the remainder indicated interest in an appointment for genetic counselling.

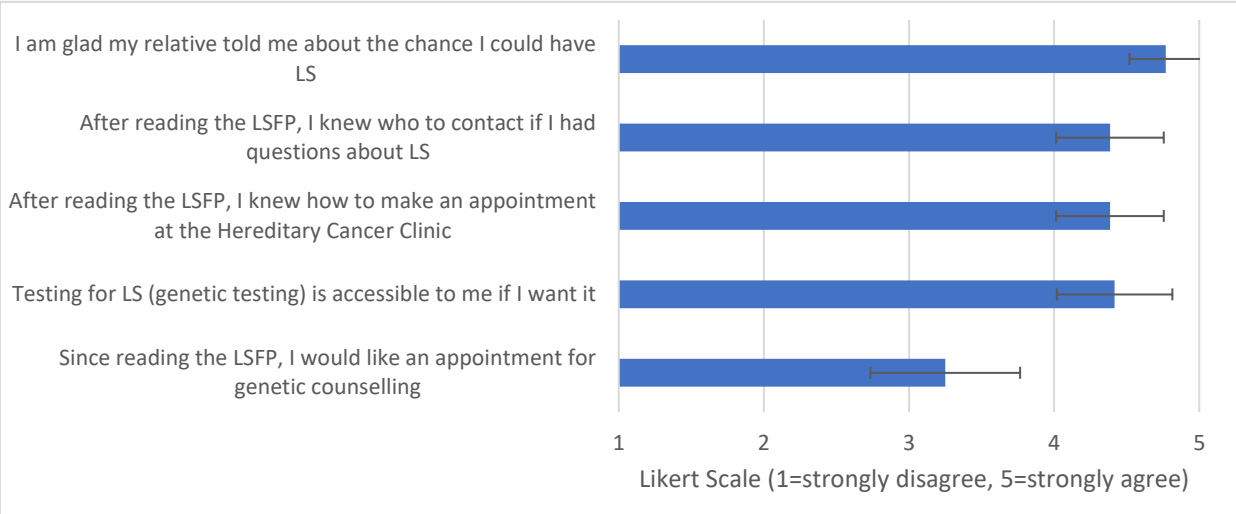

Figure 8. Impression of LSFP gathered from participants who received the LSFP from a relative (n=13). The error bars indicate the 95% confidence interval around the mean.

Participants were asked about their preferred format of the LSFP and were able to select multiple responses. About two thirds of participants would like the LSFP to be available by email (71%), on a website (68%), and on paper (63%), indicating the desire to have all three options available. Only 21% selected an app for smartphones and 17% an online video. No other formats were suggested in the open text field provided.

Predictors of sharing information about LS

Logistic regression analysis was performed to identify predictors of use of the LSFP and predictors of informing relatives about LS without using the LSFP. Univariable analysis identified two predictors of LSFP use: age and gene mutation (Table 8). Participants age 45 or older were about three times more likely to use the LSFP. The LS-associated genes were grouped based on cancer risk. Individuals with a pathogenic variant in *MLH1/MSH2/EPCAM* have a higher CRC risk than *MSH6/PMS2*. Participants with a pathogenic variant in *MLH1/MSH2/EPCAM* were only two thirds as likely to use the LSFP as participants with a pathogenic variant in *MSH6/PMS2*, although the difference was not statistically significant. In other words, participants with less severe CRC risk were somewhat more likely to use the LSFP. Thirty-two percent of respondents were unsure which gene caused their LS and this group was significantly less likely to use the LSFP. Three predictors of informing relatives about LS without the LSFP were identified using univariable analysis: age, marital status, and cancer history (Table 8). Participants age 45 or older were seven times more likely to have informed their relatives about LS without using the LSFP than participants under age 45. Married participants were four times more likely than single participants to have informed their relatives about LS without using the LSFP. Participants who have had cancer were four times more likely to have informed their relatives about LS without using the LSFP than participants who have never had cancer.

Table 8. Univariable logistic regression analysis: Predictors of sharing information about LS with relatives, with and without the LSFP.

	Passed/planned on passing the LSFP to relatives[1]	Told relatives about their risk for LS without the LSFP[2]
Predictor	Unadjusted Odds ratio (95% CI)	Unadjusted Odds ratio (95% CI)
Age		
(0=44 or younger, 1=45 or older)	**2.96 (1.19 - 7.38)***	**7.4 (2.91 - 18.83)***
Gender		
(0=male, 1=female)	1.13 (0.46 - 2.81)	1.02 (0.43 - 2.42)
Education		
(0=postsecondary, 1=high school or less)	1.51 (0.53 - 4.34)	1.00 (0.39 - 2.59)
Employment		
(0=not employed, 1=employed)	2.36 (0.84 - 6.62)	2.15 (0.85 - 5.45)
Income		
(0=<$68,000, 1=≥$68,000)	0.92 (0.31 - 2.67)	0.54 (0.19 - 1.56)
Marital status		
(0=single, 1=married/common law)	1.69 (0.62 - 4.59)	**3.95 (1.46 – 10.66)***
Childbearing status		
(0=no, 1=yes)	2.23 (0.92 - 5.43)	2.06 (0.88 - 4.81)
Cancer history		
(0=no, 1=yes)	2.33 (0.92 - 5.89)	**4.09 (1.66 - 10.09)***
Impression of LSFP informational content		
(0=just right, 1=too much/too little)	0.59 (0.19 - 1.9)	3.31 (0.86 - 12.79)
Gene mutation		
(0= *MSH6/PMS2*, 1=*MLH1/MSH2/EPCAM*)	0.62 (0.19 – 2.09)	0.73 (0.25 – 2.14)
(0= *MSH6/PMS2*, 1=not sure)	**0.28 (0.08 – 0.96)***	0.41 (0.13 – 1.25)

[1]Survey Q7. Did you pass the LSFP on to any relatives? (n=62 yes/planned to).

[2]Survey Q9. Did you tell any relatives about their risk for LS without showing them the LSFP? (n=52 yes).

*Statistically significant if confidence interval does not cross 1.

The significant predictors from the univariable analysis ($p<0.05$), plus gender, were included in the multivariable analysis. Using the adjusted odds ratios, age was no longer a significant predictor of LSFP use. Gene mutation was the sole statistically significant predictor of LSFP use identified (Table 9). Participants who were unsure which gene caused their LS were less likely to use the LSFP. Age was the sole predictor of informing relatives about LS without using the LSFP (Table 9). Participants age 45 or older were four times more likely to inform

relatives about LS without the LSFP. Although marital status and cancer history were significant predictors using univariable analysis, the adjusted odds ratios were not significant.

Table 9. Multivariable logistic regression analysis for factors associated with sharing information about LS with relatives, with and without the LSFP.

	Passed/planned on passing the LSFP to relatives[1]	Told relatives about their risk for LS without the LSFP[2]
Predictor	Adjusted Odds ratio (95% CI)	Adjusted Odds ratio (95% CI)
Age		
(0=44 or younger, 1=45 or older)	2.68 (0.78 – 9.17)	**4.39 (1.30 – 14.83)***
Gender		
(0=male, 1=female)	1.14 (0.40 – 3.24)	0.90 (0.31 – 2.64)
Marital status		
(0=single, 1=married/common law)	0.98 (0.31 – 3.07)	2.34 (0.70 – 7.82)
Cancer history		
(0=no, 1=yes)	1.53 (0.47 – 4.96)	2.16 (0.65 – 7.18)
Gene mutation		
(0= *MSH6/PMS2*, 1=*MLH1/MSH2/EPCAM*)	0.69 (0.19 – 2.47)	0.79 (0.23 – 2.76)
(0= *MSH6/PMS2*, 1=not sure)	**0.25 (0.07 – 0.92)***	0.30 (0.08 – 1.13)

[1]Survey Q7. Did you pass the LSFP on to any relatives? (n=62 yes/planned to).

[2]Survey Q9. Did you tell any relatives about their risk for LS without showing them the LSFP? (n=52 yes).

*Statistically significant if confidence interval does not cross 1.

The logistic regression analysis did not identify gender as a significant predictor of LSFP use. However, among the participants who received the LSFP from a relative, 77% (10/13) received the LSFP from a female relative (mother (n=3), sister (n=3), daughter (n=1), aunt (n=3)). The LSFP was provided by one father and two brothers. The limited sample size does not provide statistical power for analysis.

Most respondents either passed on the LSFP to their relatives (29%, 27/92) or plan to pass the LSFP to their relatives (38%, 35/92). The remaining 32% (30/92) were asked “What made you decide not to pass the Lynch Syndrome Family Package on to any relatives?” and their responses are described in Figure 9. Participants could select multiple responses and 32 responses were selected in total (28 participants selected 1 response, 2 participants selected 2 responses). Most indicated they did not use the LSFP because their relatives had previously been informed by either the respondent (47%, 14/32) or another relative (30%, 9/32). Five participants

selected “Another reason” and provided a free text response. One of the five indicated another relative shared the information already. The other four indicated their relatives were already informed but did not indicate by whom. Therefore, all “Another reason” responses can be grouped together with those who already informed their relatives and those whose relatives were already informed by someone else, which together accounts for 88% (28/32) of responses. Two respondents (6%) do not have any relatives who are at risk for LS. The remaining 6% of responses includes 3% (1/32) who do not have their relatives’ contact information and 3% (1/32) in limited communication with their relatives. Both these responses were provided by the same participant. Most participants shared or plan to share the LSFP, and among the participants who have no intention of sharing the LSFP, only 3% (1/30) have a relative/relatives who may be unaware about their risk for LS. Ultimately, our results indicate that almost all at-risk relatives have been informed about LS. Only one participant reported limited contact as a barrier to sharing the LSFP.

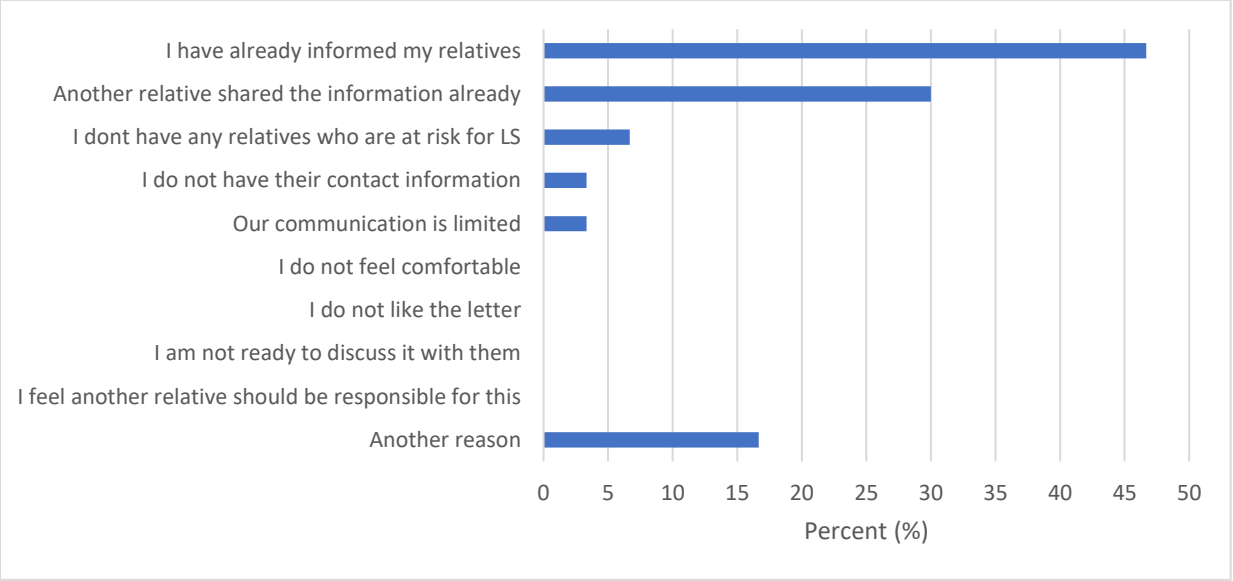

Figure 9. Reasons for not using the LSFP (n=32).

Reasons for not using the LSFP suggest that disclosure rates are higher than LSFP use. To assess the proportion of individuals who shared information about LS with their relatives, we cross analyzed two questions: “Did you pass the LSFP on to any relatives?”, and “Did you tell any relatives about their risk for LS without showing them the LSFP?”. Sixty-eight percent of respondents indicated they have shared information about LS with at least one relative. Twelve

percent (11/92) used the LSFP and did not tell any relatives about LS without the LSFP. Seventeen percent (16/92) shared information about LS both with and without using the LSFP. Twenty two percent (20/92) have previously shared information about LS with their relatives and intend to pass on the LSFP. An additional 16% (15/92) plan to share the LSFP and have not otherwise shared information about LS with their relatives. Seventeen percent (16/92) told relatives about LS without the LSFP and do not intend to share the LSFP. Fifteen percent (14/92) have not told relatives about LS and do not intend to share the LSFP. These last two groups were combined to analyze reasons for not using the LSFP (Figure 9).

The chi-square test was used to study the relationship between who participants informed about LS (which relatives) and how participants shared the information (with the LSFP or without). Twenty-nine participants provided 60 responses indicating the various relatives they provided with a LSFP. Thirty-five participants provided 62 responses indicating the relatives they plan to provide with a LSFP in the future. Fifty-one participants provided 111 responses indicating the relatives they informed about LS without using the LSFP. The proportion of responses for each relative was similar across the three information sharing methods (Figure 10). For example, parents were selected among 7% of responses (4/60) to, “Who did you give the LSFP to?”, 10% of responses (6/62) to, “Who do you plan to give the LSFP to?”, and 10% of responses (11/111) to, “Who did you tell about LS without giving the LSFP?”. A lack of association was observed between which relatives participants informed about LS and how the information was shared ($p=0.60$). Comparing how information was shared between first-degree relatives and more distant relatives similarly revealed a lack of association ($p=0.45$). Information about LS and the LSFP were not being disproportionately shared or withheld from certain relatives.

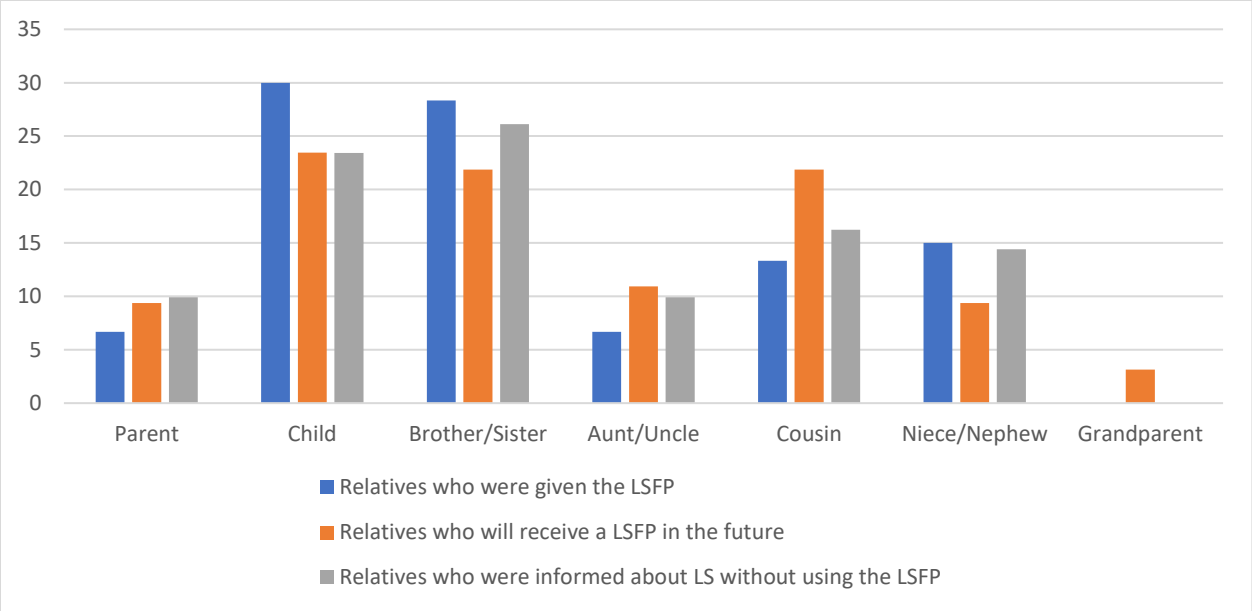

Figure 10. There is no significant difference between who participants informed about LS (which relatives) and how participants shared the information (with the LSFP or without) (p=0.5998).

Most participants (83/92, 90%) indicated they sought out more information about LS. Among this group, the most common source of information was from an internet search (81%), followed by a geneticist or genetic counsellor (54%), colonoscopy physician (39%), and family physician / nurse (31%). Pamphlets or brochures were used by 18%, academic journals by 13%, and books by 7%. Discussion with a family member or friend, support group, or seminar occurred among 19%, 8%, and 5% respectively. Social media was rarely used as an information resource; 6% used Facebook, 6% used YouTube, 1% used Instagram, 1% used Twitter, and 1% used podcasts. A Naturopath was consulted by 1%.

Chapter 5: Synthesis of Qualitative and Quantitative Findings

Overview

The survey gathered targeted information on opinions and use of the LSFP, while the interviews contextualized broad experiences with LS and the decisional factors impacting communication with relatives. The qualitative findings from the interviews also explored the nuances impacting participant perceptions and use of the LSFP. Although not meant to be generalizable, the qualitative findings provide further explanation of the survey results by illuminating some of the participant experiences which shaped the survey responses.

Experiences accessing LS-related healthcare

Survey respondents who received the LSFP from a relative (n=13) were asked if genetic testing is accessible to them. Most (6/13) strongly agreed, 5/13 agreed, 1/13 was neutral, and one participant did not provide a response. Participants who received the LSFP from a healthcare provider were not asked about accessibility of genetic testing as everyone in this group had genetic testing. Although the limited sample size does not allow for generalizability, the qualitative findings also support that accessibility of genetic testing is not a significant barrier impacting genetic testing rates in Manitoba. To quote a participant, “I don't see that (accessibility) being an issue. No, I think it's just a matter of them (my relatives) wanting to or not” (Randy, CT, 2019).

Impression of the LSFP

Between both the survey and interview responses, impressions of the LSFP were consistently positive. The survey demonstrated a positive consensus with narrow confidence intervals among the 92 respondents. Interview participants were asked open-endedly for suggestions to improve the LSFP and most participants responded by commending the LSFP and denying any need for improvement.

Regarding privacy and the LSFP, survey respondents and interview participants generally did not perceive the LSFP as an invasion of privacy. On the Likert scale, the mean response to “The LSFP feels like an invasion of my privacy” was 1.7 (95% CI 1.55-1.84), where 1=strongly disagree and 2=disagree. Only one survey respondent felt that the LSFP was an invasion of

privacy and none of the interview participants expressed privacy concerns. One interview participant elaborated by saying "I think if somebody's willing to share this information, they wouldn't feel like it's an invasion of privacy because they're already actively telling someone about themselves" (Liam, CT, 2018). This quote illustrates the potential bias in the sample population, considering only 15% of survey respondents indicated they have not shared and do not intend to share information about LS with their relatives. Correspondingly, most interview participants chose to discuss LS with their relatives and privacy concerns did not emerge as a sub-theme among risks and hesitations towards genetic testing. One participant reported they were not concerned about their privacy because they "would rather help people" (Erica, IC, 2019). This quote suggests that concerns regarding privacy are present, however they are not weighed heavily compared to the potential for cancer prevention.

Participants were asked about their preferred format of the LSFP and there was concordance between survey and interview responses. Participants indicated the LSFP should be available by email, on a website, and on paper. One interview participant did not have internet access, which demonstrated the need to continue offering hardcopies at clinic visits or by mail. However, many interview participants chose to share the LSFP as an email attachment and indicated an electronic version of the LSFP would be convenient. A desire for the development of informational resources in other formats, like an app or video, was lacking among both participant groups.

Sharing information about LS

The multivariable regression analysis identified the known gene mutation as the only independent predictor of LSFP use. Participants who were unsure which gene caused their LS were less likely to use the LSFP than those who knew which genetic variant they carried. The interview guide and pre-screening questions did not specifically address genetic variants, however "knowledge is power" emerged as a theme. Feeling knowledgeable about LS can facilitate information sharing, as illustrated by the following quote:

> I felt like I had a good handle on what I was talking about, right. That didn't necessarily make it easier to send the letter to somebody saying, you know, "Hey you should, you know, you should think about going and getting tested to see if you have a predisposition for cancer", right, particularly my cousins who have little kids, right, I mean taking that

> message to them was not, you know, it's not an easy message to send but … but having good information behind it helped. (Ben, IC, 2014)

Uncertainty regarding the specific gene involved indicated a gap in knowledge which acted as a barrier to informing relatives. Integrating the data suggests participants who were unsure about their genetic variant felt they had insufficient information to address the topic with relatives. Additionally, the genetic variant must be known to coordinate CT for individuals who do not otherwise meet criteria for genetic testing with a multi-gene panel. The LSFP has a fillable field for the healthcare provider to write in the genetic variant, meant to help overcome this barrier. Interestingly, education level was not found to impact information sharing about LS, with or without the LSFP.

The survey collected reasons why participants chose not to use the LSFP by providing a list of reasons and asking participants to select all which apply. There was also a free text response for participants to add reasons which were not included in the selection. Most respondents who did not use the LSFP indicated their relatives were already informed, which was also a common reason for not sharing information among interview participants. Additional decisional factors were provided by interview participants which did not appear among the survey selections or the free text responses, many of which fall under the theme of family dynamics. Reasons identified qualitatively which were not mentioned in the survey include feeling isolated by unsupportive reactions, conforming to cultural expectations, and struggling to accept the diagnosis or overcome stigma. Some interview participants were hesitant to discuss LS with distant relatives because they felt it should come from a parent or close relative. Contrastingly, one of the survey selections stated, "I feel another relative should be responsible for this" and no one selected this response. The survey as compared to the interview was more focused on the LSFP which could account for the difference in responses. The main reason participants chose not to share the LSFP was if their relatives were informed previously, and the additional factors hindered participants from generally discussing LS with relatives.

LSFP aside, participants age 45 or older were four times more likely to inform relatives about LS according to the multivariable logistic regression analysis. Although age was not explicitly discussed, qualitative interviews revealed that none of the interview participants younger than age 45 had informed relatives about LS. All but one of the interview participants under age 45 had CT, meaning another relative informed them about LS. These participants discussed how the IC in their family was someone from the previous generation. Since their

family already knew about LS, these participants did not choose to share information with most of their relatives. Interview participants in this age group often shared information with their siblings who had not had genetic testing, but their siblings had previously been informed about LS by another relative. Correspondingly, survey participants indicated a common reason not to share information about LS was knowing a relative was already informed. Other characteristics that correlate with age, including having children and cancer, emerged as qualitative subthemes impacting communication. However, when these factors were analyzed in the survey analysis, they were not independent predictors of sharing information about LS. The interview findings provide some insight into why childbearing status was not a good predictor. Although many interview participants identified informing their children as their main motivator for having genetic testing, cancer prevention recommendations begin in adulthood. Half of the interview participants under age 45 had children, but they all considered their children to be too young to be informed about LS or have genetic testing. Regarding cancer history, qualitative findings illuminated how a personal history of cancer can act as both a facilitator and barrier in sharing information with relatives. Cancer survivors were motivated to share information about LS with relatives for the benefit of cancer prevention, but these conversations were often challenging. Cancer survivors worried about resurfacing the fear their family had experienced. Participants thought discussing LS with relatives would bring up their worries about cancer risk for relatives and for themselves.

Survey analysis found that gender was not an independent predictor of sharing information about LS. One interview participant reported that gender impacted the actions relatives took after learning about LS. This participant reported that her female relatives were more motivated to attend genetic counselling versus her male relatives, who had more difficulty accepting the information about LS and delayed seeking medical attention. Men were thought to be more hesitant, “I don’t know why. maybe because females are more nurturing and we just want everything to be right” (Sarah, IC, 2002). The survey data suggested that the LSFP was more often provided by a female relative, however the small sample of respondents who received the LSFP from a relative (n=13) limited statistical power.

Chapter 6: Discussion

The aim of this research was to identify facilitators and barriers to communicating about LS with relatives, with the future goal of increasing the uptake of cancer prevention among families with LS. The LSFP was developed as a tool to facilitate information sharing and evaluated through this project. The research findings provide recommendations for healthcare providers to improve patient care for individuals with LS. Proposed changes to the LSFP are outlined based on participant feedback.

Facilitators and Barriers to Communicating about LS with Relatives

The three main themes found to impact communication were family dynamics, reactions towards autonomy, and perceptions of genetic testing. Perceived facilitators and barriers to genetic testing were embedded within the facilitators and barriers to communication identified in this study, as perceptions of genetic testing shaped the narrative between relatives. Individuals with LS are not impartial informants; their personal experiences with genetic testing influenced the way they framed the information to relatives. The qualitative findings were organized to reflect the narratives described by participants and both barriers and facilitators are encompassed by each theme. Below, the subthemes are organized into barriers and facilitators of communication (Table 10). Perceptions of genetic testing included benefits and motivators of genetic testing, and risks and hesitations towards genetic testing. Perceived benefits and motivators of genetic testing facilitated communication about LS because the IC wanted their relatives to receive the same benefits of genetic testing they experienced. This finding fits within the commonly cited reason for disclosure where individuals with LS hope to empower their relatives with knowledge to make informed health decisions (Forrest et al., 2003; Montgomery et al., 2013; Srinivasan et al., 2020). Perceived risks and hesitations towards genetic testing create hesitations towards disclosure. For example, some participants described difficulty adjusting to their genetic test results and felt stigmatized by the diagnosis of LS. Other studies measuring anxiety and depression have found levels peak around the time of being diagnosed with LS and gradually return to baseline with time (K. Aktan-Collan et al., 2001, 2013; Gritz et al., 2005; Meiser et al., 2004). Individuals may need time to overcome these emotions before feeling able to disclose the information to relatives. The survey analysis did not assess time since genetic testing as a predictor of sharing information about LS with relatives. Our findings also suggest

that uncertainty about testing options outside Manitoba can prevent communication. Informants anticipate the questions their relatives will have and feel a sense of pressure to have the answers. This finding is aligned with previous studies which found that concerns about accurately conveying the information can prevent disclosure (Dean et al., 2021; Griffin et al., 2020).

Open and supportive family dynamics facilitated communication by reassuring the IC that the information would be received warmly and appreciated. In support of this finding, other studies have found that families who have a history of discussing cancer openly and are emotionally close have fewer concerns disclosing genetic information (Forrest et al., 2003; Seymour et al., 2010; E. M. Stoffel et al., 2008). However, family dynamics have also been found to prevent disclosure. Even some participants who disclosed their genetic status did not feel comfortable providing further information as it became available because they did not feel they had "that kind of relationship" and worried it would be perceived as "pestering". Some participants thought that LS disclosure would be perceived as unacceptable in their family, considered taboo, and could cause them to feel isolated, which is supported by previous research (Mendes et al., 2016; Srinivasan et al., 2020). Designating the best person to discuss LS with each relative complicated disclosure. Some participants worried about creating family conflict by disclosing directly to someone else's child, for example a niece, nephew, or cousin, if they have not been informed by their parent. This phenomenon has been previously described as "authority within a family" (Forrest et al., 2003) where the responsibility is designated to parents or can be extended vertically in the family tree such that a grandparent would be thought to have more authority than an aunt or uncle. Perceptions of authority and responsibility within families likely contribute to the decreased disclosure to second and third-degree relatives seen in previous studies (J. Petersen et al., 2018; E. M. Stoffel et al., 2008). Some participants who had a personal history of cancer described how difficult the experience was on their relatives, particularly their children. Relatives were worried and fearful of losing their loved one to cancer. Understandably, the IC wanted to avoid resurfacing those cancer fears and avoid creating worry for their relatives, which prevented disclosure. This finding was consistent with the avoidance described in previous studies (Seymour et al., 2010; E. M. Stoffel et al., 2008).

Reactions towards relatives' autonomy impacted the likelihood that the IC would provide information about LS more than once. Individuals who were frustrated by their relative's choice not to attend genetic counselling or proceed with genetic testing were more likely to repeatedly

provide information about LS, versus individuals who preferred to leave the decision up to their relatives and accept their choices without influencing them. This finding highlights a gap in research methodology in the area as most prior studies explore facilitators and barriers to the disclosure of genetic information, without addressing subsequent discussions.

Table 10. Facilitators and barriers to communicating about LS with relatives.

Facilitators
Providing an explanation for cancer
Feeling that doctors take concerns more seriously
Empowering relatives
Feeling a duty/obligation to share
Having open and supportive family dynamics
Barriers
Relatives were previously informed
Fear of creating worry/resurfacing old worries
Deciding who the information should come from
Cultural sensitivities to sharing health information within families
Uncertainty about testing options outside Manitoba
Difficulty adjusting to the diagnosis
Concern regarding insurance discrimination

One in five survey respondents did not share information about LS with their relatives. The most common reason for non-disclosure was that another relative shared the information already. Other reasons for non-disclosure included not having any relatives at risk for LS, not having their contact information, and having limited communication. Previous studies have collected reasons for non-disclosure with few consistently identified specific factors. An American study from 2008 found the most common reasons for non-disclosure in families with LS were not wanting to cause worry, not having a close relationship, and believing their relative would not understand the meaning of the result (E. M. Stoffel et al., 2008). Another American study from 2020 included individuals with LS or HBOC and found the most common reasons for non-disclosure were perceiving relatives as too young, having conflict in the family, and concerns about the cost of genetic testing (Griffin et al., 2020). The findings from these studies

and ours are difficult to compare because the list of reasons available for participants to select from varied. However, lack of a close relationship was a common deterrent in all three groups.

Our findings support the use of an informational materials to facilitate communication given the positive appraisal of the LSFP and that most participants would choose to share it with relatives. Information preferences were evaluated and about two thirds of respondents indicated the information should be available by email, on a website, and on paper. A recent American study provided four different types of informational materials to aid disclosure of LS or HBOC: a family letter, links to four websites, a brochure, and links to two 2-minute informational videos (Griffin et al., 2020). They found that the family letter was viewed most often (89%), followed by brochures (56%), websites (55%), and videos (53%). No material was perceived as significantly more helpful than the others. Among published informational materials, the LSFP is most comparable to a family letter. Our study did not provide educational materials in addition to the LSFP but asked participants about other information sources accessed. Eighty-one percent of respondents had done an internet search, 18% read a pamphlet or brochure, and 6% watched videos on YouTube. Contrary from Griffin et al.'s findings, our results suggest that informational websites are more helpful than brochures or online videos. The findings from both studies support the use of family letters.

Griffin et al. (2020) found that rates of disclosure to relatives were quite high among families with LS and HBOC, but only a minority of relatives proceeded with CT. The research group suggested that barriers must exist preventing relatives from undergoing CT. Disclosure rates were also high in our study and the most common reason for nondisclosure was that the relative was previously informed, indicating even higher rates of LS awareness. Although our study did not quantify the uptake of CT, many participants spoke of relatives who had declined CT. Participants believed that genetic testing was accessible to relatives if they were interested and felt that declining was a personal choice based on fear or avoidance. The need for increased awareness of LS among the general public as well as among family physicians was identified as a main area for improvement. Griffin et al. (2020) found that CT rates were lower among families with LS compared to HBOC, attributed to the greater awareness of HBOC. There have been considerable improvements to LS testing in the last decade, but LS awareness seems to be lagging. Universal screening for LS first began in 2013 for CRC cases in Manitoba. Relatives who had CRC prior to 2013 may not have been informed about LS from a healthcare provider,

which contributes to reactions of disbelief from relatives. Increased awareness is thought to improve the perceived credibility of the information provided by individuals with LS.

Our findings suggest that most relatives are aware of their risk for LS but there is a hesitancy to share unsolicited informational materials after the first disclosure. Furthermore, previous studies have found that most relatives who decline CT do so without attending genetic counselling. It has been suggested that patients only remember half the information from a genetic counselling appointment and after they share that portion of the information with a relative, the amount of information accurately conveyed lessens further (Jacobs et al., 2015). Rather than relatives being uninformed, it seems many relatives who are declining CT could be making the decision underinformed. Participants felt an emphasis on the effectiveness of cancer prevention strategies would be important when sharing information about LS.

Impression of the LSFP

The feedback provided on the LSFP was almost unanimously positive. Social and/or authoritative pressures must be considered in the interpretation of these findings. Some interview participants referred to the LSFP as “your letter”, indicating their awareness of the researcher’s involvement in the development of the LSFP. The researcher responded to these cues by encouraging honest feedback and criticisms, however the researcher’s position in the study may have impacted responses of participants. The quantitative portion of the study mitigated this pressure by providing anonymity and the survey feedback was also predominantly positive.

One of the main goals in developing the LSFP was to make the reading level accessible. An expert in plain language was involved in the development of the family letter at BC Cancer, which prompted the consultation with Jennifer Nuk, a genetic counsellor at the Hereditary Cancer Program in British Columbia. The LSFP is at an eighth-grade reading level according to the Flesch-Kincaid, Simple Measure of Gobbledygook Index, Automated Readability Index, and Linsear Write Formula. Both survey and interview participants indicated the LSFP was easy to understand and many interview participants commented that the LSFP was easier to understand than other family letters they had received previously.

Many of the suggestions provided by study participants had been considered during the development of the LSFP but were removed as challenges arose. Drafts of the LSFP previously included links to webpages with further information about LS but were not authorized for

inclusion in the study version. The need to thoroughly evaluate the content of linked webpages prevented the addition of links in the LSFP. Additionally, links required approval by the Health Sciences Centre, but the approval process was unfamiliar to the student researcher and team collaborating on the development of the LSFP. Similarly, the team discussed adding links to the Genetics & Metabolism webpage (*Hereditary Cancer Service*, 2021) with information about LS. The Conditions of Use published on the Health Sciences Centre website states, "HSC Winnipeg does not review or control, and is not responsible for, any information which is created or supplied by a third party" (*Conditions of Use*, 2021), suggesting the addition of links to the Genetics & Metabolism webpage is a feasible options. The findings from this study suggest that individuals with LS would value access to additional online resources and will prompt further attempts for approval.

Many participants searched for LS information online and found the results were mainly from American medical centres such as Mayo Clinic or the Center for Disease Control and Prevention. The main concern about the lack of Canadian-centred information was uncertainty regarding the relevance of the genetic testing and cancer screening recommendations. Participants emphasized the difference between the Canadian and American healthcare systems and implied that Americans who can afford it have more options for cancer prevention than Canadians. Many participants could not find information on the screening and prevention recommendations followed in Canada and the lack of information contributed to concerns and questions about if they were receiving the appropriate care. Comprehensive Canadian online resources exist, but none of the interview participants were familiar with them, suggesting they are not easily accessible. The Manitoba Hereditary Cancer webpage (*Hereditary Cancer Service*, 2021) includes two links with information about LS. The first is a downloadable PDF pamphlet with information about genetic testing, cancer screening, LS features, causes, inheritance, and associated cancer risks. However, the cancer risks reference the NCCN guidelines from 2014 and require updating. The second is a downloadable document explaining LS screening in Manitoba and the referral process to the Hereditary Cancer Clinic. The BC Cancer Clinic website (*Hereditary Cancer*, 2021) has a list of resources which includes a 15 page booklet called Understanding LS. This booklet could be helpful to individuals seeking very detailed information and could compliment the simplified LSFP. Mount Sinai Hospital in Toronto has a webpage with information about LS which includes cancer screening guidelines (*What Are the*

Cancer Screening Guidelines for LS?, 2021). Although these resources exist, our findings suggest they are not easily accessible, which supports the inclusion of links in the LSFP.

Some participants suggested including a table in the LSFP with the LS-associated cancer types and risk percentages. There are many views to consider when determining the appropriate level of information to include in informational materials. The purpose of the LSFP is to facilitate information sharing so it may seem intuitive to include as much information as possible. However, previous research indicates that many people struggle with health literacy (Davis et al., 2002; Tea et al., 2018). Participants identified the amount of information and comprehension level as strengths of the LSFP and discussed how more densely worded letters are easily overwhelming and could discourage relatives from reading the letter at all. Family letters must also consider the 'right not to know' when determining the appropriate amount of information to include. The right not to know has long been debated (Davies, 2020; J. Harris, 2020; Wilcke, 1998; Wilson, 2005) and although it is outside the scope of the current study to take a stance on whether not knowing about LS should exist as a right, one can appreciate that some people would prefer not to know their genetic information. Individuals who attend genetic counselling are supported if they choose to decline genetic testing and similarly individuals who prefer not to know the details of their risk for cancer should be respected. Although previous studies suggest most individuals who decline CT do so without consulting a genetic counsellor (Kanga-Parabia et al., 2018; Keogh et al., 2017; Seppälä et al., 2017), the family letter is not meant to replace the need for genetic counselling. To address the needs of both those who want to avoid information and those who are anxious to learn more as soon as possible, the proposed solution is to add a link on the LSFP to a table with the associated cancer types and risks. The table could be included as an additional page of the LSFP provided on paper in the clinic so that patients could choose to include it with the LSFP when distributing to relatives. The table from the NCCN guidelines (National Comprehensive Cancer Network, 2021) is the preferred choice as it is frequently updated to reflect current research, however it is password protected and therefor not accessible to most patients and an alternative table has been proposed (*Cancer Risk Lynch Genotypes - UpToDate*, 2021). Efforts should be made to have all the online information be available in hard copies to increase equity and make the information as accessible as possible. Below is the suggested addition to the LSFP of links for further reading, of which the table of

cancer risks is amenable to printing. Links will require evaluation and approval before being added to the LSFP.

Links for further reading:

Canadian informational webpages:
https://wrha.mb.ca/genetics-and-metabolism/hereditary-cancer-service/
https://tinyurl.com/bccancerlynch
https://www.zanecohencentre.com/gi-cancers/diseases/ls

Information on the Genetic Non-Discrimination Act:
https://ccla.org/genetic-non-discrimination-act-overview/

Lynch Syndrome International:
https://lynchcancers.com/

Table of cancer risks:
https://tinyurl.com/risktable

Figure 11. Proposed addition to the LSFP based on participant suggestions.

Governing policies limit communication between clinicians and patients via email due to privacy and confidentiality concerns, because of institutional concerns that the security of information shared by email cannot be guaranteed and is believed to be better with regular mail. However, most study participants would like the LSFP to be available by email for the convenience of forwarding it to their relatives. Interview participants indicated privacy and confidentiality was not a significant factor in their decision to share the LSFP with relatives. Genetic counsellors in the Hereditary Cancer Clinic have consent forms to facilitate informed decision making when patients wish to pursue genetic testing or permit the clinic to disclose personal health information to other relatives to facilitate their care. Like email, these procedures have inherent risks but patients who perceive the benefit as worthwhile can choose to proceed. The research findings indicate that some individuals with LS would opt to receive the LSFP by email if given the choice. The findings provide a motive to reconsider the email policy to facilitate information sharing. Furthermore, the COVID-19 pandemic has caused many healthcare encounters to become virtual, which limits the opportunity for clinicians to provide paper copies of the LSFP during an appointment. Allowing the LSFP to be emailed provides an option for the patient to receive the LSFP without delay. The current restrictions requiring the

LSFP to be provided on paper are limiting and archaic considering the available infrastructure to distribute the LSFP electronically. The electronic medical record used by the Genetics program and others have infrastructure to send what are considered more secure emails and are likely to be used in future.

Genetic Counselling Considerations

Many of the barriers identified in this study can be addressed in a genetic counselling session. Participants indicated that the best time to discuss implications for family members would be a few months after receiving their positive genetic test result. This could imply that a follow up visit with a genetic counsellor or another trained health care provider is essential to discuss this issue, which supports the Lynch Clinic model After determining which relatives have been informed about LS and who has had genetic testing, there may be an opportunity for further discussion around those relatives who have not yet had genetic testing. Our results indicated that participants were often reluctant to share information with relatives who were already aware of their risk for LS. Genetic counsellors can use the LSFP as a tool to ask their patients if they think their relatives are aware of all the information outlined in the LSFP. This could help determine if their relative is making an informed decision about declining genetic testing. If patients identify relatives who have only received limited information about LS, patients may feel more motivated to share the LSFP with those relatives. Dissemination of the LSFP, which has information on LS, could help address some of the misconceptions among relatives, such as the belief that cancer is inevitable therefore there is no benefit of knowing LS gene status.

Fear of creating worry was identified as another common barrier to family communication. Our data on the LSFP could be used to reassure patients that most people who received a LSFP did not report feeling worried and many people felt empowered by the information to take control over their cancer risk.

Another common barrier to family communication was determining who the appropriate relative was to disclose the information. Genetic counsellors can address this with their patients by helping patients identify the appropriate informants in their family and encouraging them to share the LSFP with those relatives who could then pass along the LSFP to others.

The limitations in overcoming all barriers must be acknowledged. Certainly not everyone who receives a LSFP may read or respond to it. In cultures where discussing cancer risk is considered taboo, hesitations may be too deeply engrained to address in a single counselling session. Lack of trust in the healthcare system was reported by one participant and although this participant was referring to healthcare systems outside of Canada, the same could prevent some patients within Canada (marginalized groups and those who have experienced institutional discrimination) from engaging with the genetic counselling process. This likely contributes to lower testing rates in underprivileged populations. Genetic counsellors cannot be expected to know the availability of genetic counselling around the world but can direct their patients to resources with more information or seek out the relevant information as needed.

Limitations

The study aimed to recruit two participant groups: 1) individuals who had a molecular diagnosis of LS, and 2) individuals related to someone with LS but not known to have LS themselves. Ninety-two percent of survey respondents (85/92) and all interview participants had a molecular diagnosis of LS (Group 1). The survey respondents representing Group 2 included three individuals who had genetic testing (two were awaiting test results and one had a negative result) and four individuals who had not had genetic testing. The survey did not assess who attended genetic counselling and although everyone who had genetic testing presumably had genetic counselling, it is unknown if the four respondents who declined genetic testing sought genetic counselling previously. Use of the self-referral form was difficult to track because individuals could phone the Hereditary Cancer Clinic to self-refer and there would be no record of LSFP use. Only one self-referral form was received by mail. Per the recruitment strategy, a genetic counsellor phoned the individual who self-referred to offer a genetic counselling appointment and introduce the study. The individual provided consent to contact but did not respond to three voicemail messages and therefore was not recruited for the study. Feedback on the LSFP was desired from Group 2, especially from at-risk relatives who had not had genetic counselling yet, to gain the perspective of people learning the information for the first time. The feedback received was mostly from people who were already familiar with the information, which could impact their impression of the LSFP. The small Group 2 sample did not allow for statistical analysis to compare feedback between groups. The major drawback of having all

interview participants from Group 1 was that none of their experiences with barriers to genetic services prevented them from having genetic testing. Of the four survey respondents who had not had genetic testing, no one indicated they would be willing to participate in an interview. Our sample is biased by the shared perspective among participants that the benefits of genetic testing outweigh the risks. There is also potential of reporter bias as Group 1 participants reported the opinions of their Group 2 relatives. Our recruitment strategy relied on Group 1 participants to recruit their relatives. Group 2 participants were expected to be reluctant to participate in this study given some may be avoiding facing LS. The $20 incentive for surveys and $25 incentive for interviews was not sufficient to overcome the recruitment challenges. Contrastingly, the response rate was high at 71% among participants introduced to the study by a healthcare provider.

Given that cultural norms were found to impact communication about LS, the lack of diversity of ethnic backgrounds among the interview participants was another limitation. Thirteen of the fifteen interview participants were of White ethnicity. Qualitative findings are not meant to be generalizable, but there are likely barriers and facilitators to communicating among other ethnic backgrounds which are missing from our findings.

Future Directions

The results from this mixed-methods study have guided the improvement of the LSFP to make it as useful as possible in facilitating communication. This study also identified barriers to communication which clinicians can assess and counsel to better support patients with LS. The specialized Lynch Clinic in Manitoba creates more opportunities to counsel about CT and utilize these findings. Future studies should quantitatively assess rates of genetic counselling and uptake of CT in Manitoba to determine if attendance at the Lynch Clinic impacts these numbers. The uptake of genetic counselling and testing could be compared to other jurisdictions that do not have a specialized Lynch Clinic.

The interview guide did not address experiences with cancer surveillance, such as colonoscopy or prophylactic hysterectomy. These experiences likely also contribute to the narrative shared about LS. Future studies should explore experiences with cancer prevention to determine the impact on communication, decisions to attend genetic counselling, uptake of CT, and adherence to the recommended surveillance strategies.

Our findings suggest that patient knowledge about their genetic variant may facilitate communication as individuals who could not recall their LS-gene were less likely to share information about LS. A recent study found that gene penetrance did not impact communication among breast cancer genes (Dean et al., 2021), however LS cancer risks have only recently been broken down by gene and are not classified into high or moderate risk genes the same way as breast cancer. If later onset cancer surveillance becomes common practice for the lower penetrant LS genes, studies should assess the impact on at-risk families.

In the hope of accommodating higher volumes of genetic counselling, many creative interventions and approaches have been trialed in other studies. The Hereditary Cancer Clinic already offers group counselling for individuals who have had breast or ovarian cancer and are eligible for genetic testing. Future studies should assess the group counselling model for individuals with a history of CRC or EC. The results from this study indicate a desire for the convenience of online resources, including a desire for the LSFP to be available by email. Future studies should consider developing an online referral system. If the LSFP was distributed electronically, the self-referral form could include a link where at-risk relatives could sign up to be contacted by the genetics team, just as they would be if they returned the self-referral form by mail. Implementing this type of system would enable researchers to easily quantify the interest in genetic counselling, the proportion of at-risk relatives who proceed with CT, and the efficiency of group counselling for these patients.

All interview participants understood why they were asked to inform their relatives about LS and found the current system for information sharing sensible, but many participants desired the option for a clinician to contact their relatives directly. Future studies should review the literature to assess the feasibility and acceptance of direct contact models at other centres to develop a Manitoba model.

Chapter Seven: Concluding Remarks

In summary, an informational resource called the LSFP was developed to facilitate communication about LS within affected families. Individuals with LS were informed about this study by their LS-related healthcare providers between June 2020 and February 2021 and their relatives were recruited by snowball sampling during the same period. The response rate was high at 71%. Participants were asked to provide feedback on the LSFP by completing a survey which demonstrated that approximately two thirds of participants shared the LSFP with their relative(s) and the LSFP was unanimously perceived as clear and helpful. Most participants appreciated the simplified presentation of the LSFP and the most common suggestion for improvement was to add links for further reading, particularly to Canadian websites. In addition to hard copies, participants desire the LSFP to be available electronically for convenience. Participants were also asked to complete a qualitative interview exploring their experiences, from first learning about LS to present, to identify barriers and facilitators to informing at-risk relatives and accessing genetic services. Manitobans with LS are distinct from other jurisdictions given their access to a multidisciplinary Lynch Clinic, publicly funded genetic counselling and testing, and the ability to self-refer for genetic counselling without a physician. Nevertheless, the identified facilitators and barriers to communication were consistent with previous studies and demonstrated that many factors impact the decision to disclose genetic information to relatives, including personal perceptions of genetic testing, family dynamics, and acceptance of relatives' autonomy to decide for themselves about pursuing further information, genetic testing, and/or cancer prevention strategies. All interview participants believed that genetic counselling was accessible to their relatives, although some described long wait times. Strategies to facilitate information sharing include increasing LS awareness among family physicians and the general public, addressing the prominent barriers for each patient through supportive counselling, and offering direct contact between clinicians and at-risk relatives on an opt-in basis. The Lynch Clinic is uniquely suited to provide genetic counselling with a focus on relatives after the individual with LS has had time to adjust to their own condition.

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APPENDIX

Appendix A: LSFP

Program of Genetics & Metabolism,
HSC Winnipeg
FE229 820 Sherbrook Street
Winnipeg, MB R3A 1R9
P: (204) 787-2494
F: (204) 787-1419

Date

Name
Title
Organization
Street Address
City, PR PoS tAl

Information for your family members about Lynch syndrome and genetic testing

Please find enclosed an information sheet about Lynch syndrome and a self-referral form. The information sheet is intended to help you explain Lynch syndrome to your relatives. The self-referral form had instructions to help your relatives make an appointment in Genetics if they are interested. We recommend that these forms be shared with your:

1. Mother
2. Father
3. Children
4. Brother(s) & sister(s)
5. Niece(s) & nephew(s)
6. Aunts and uncles on your mother's side of the family
7. Cousins on your mother's side of the family
8. Aunts and uncles on your father's side of the family
9. Cousins on your father's side of the family
10. Other:_____

Please contact me if you have any questions or concerns.

Sincerely,

[Name of Genetic Counsellor]

Genetic Counsellor
Hereditary Cancer Clinic

Shared health Soins communs Manitoba

Program of Genetics & Metabolism,
HSC Winnipeg
FE229 820 Sherbrook Street
Winnipeg, MB R3A 1R9
P: (204) 787-2494
F: (204) 787-1419

Lynch Syndrome Information for Families

A relative of yours has Lynch syndrome. This means that you and other relatives may also have Lynch syndrome.

What is Lynch syndrome?

- People with Lynch syndrome have a much higher risk for cancer than the average person.
- It is inherited, so this increased risk for cancer runs in the family.
- There is an increased risk for several types of cancer, but the most common types are colorectal and uterine (also known as endometrial) cancer.
- It affects both men and women.
- People with Lynch syndrome often develop these cancers at younger ages, but almost all of these cancers are diagnosed in adults.
- Not everyone with Lynch syndrome will get cancer.

How Lynch syndrome runs in families

- All siblings and children of someone with Lynch syndrome have a 50% chance to have Lynch syndrome.
- Other relatives on the same side of the family (parents, grandparents, grandchildren, nieces/nephews, aunts/uncles, cousins) may also have Lynch syndrome.
- People with Lynch syndrome can still pass it on to their children, even if they have not had cancer.

Testing for Lynch syndrome

- Relatives can be tested using a blood sample. You will need to have a genetic counselling appointment before the blood test.
- This test is optional. You can make a genetic counselling appointment to learn more information and then decide if you want testing.
- This blood test is not part of a research study.
- This test can be done whether you have had cancer or not. You should not wait to have symptoms of cancer first.

- Since the risk of cancer usually starts in adulthood, the test is offered to relatives once they are mature enough to provide informed consent.
- There is no charge for this test if you have a provincial health card. Coverage options may vary if you live outside of Canada.
- In Manitoba, it is not necessary to travel to our clinic in Winnipeg. Appointments are available in-person or by Telemedicine.
- Your test results are kept confidential. We do not share your test results with your family members without your consent.
- There is a law in Canada called the *Genetic Non-Discrimination Act of 2017* regarding genetic information and insurance coverage.

Why would someone want to know if they have Lynch syndrome?

- It could explain why there is a personal or family history of cancer.
- For family members who test positive for Lynch syndrome, there are tests (like a colonoscopy) to help prevent some of these cancer types or to try to find them as early as possible. Some of these tests would start at age 20-25.
- There are also some other options for preventing cancer. This might include the option of preventive surgery.
- For family members who test negative for Lynch syndrome, they have cancer risks similar to the average person and may not need to have these extra tests.
- Some people want to be able to inform relatives about their cancer risks.
- Not everyone wants to know if they have Lynch syndrome. It is a personal decision.
- There is a specialized clinic in Manitoba for people with Lynch syndrome.

What to expect from an appointment in the Hereditary Cancer Clinic:

- A review of your medical history and your family history of cancer.
- More information about Lynch syndrome.
- A discussion about the potential benefits and harms of genetic testing.
- You may choose to have genetic testing or not.
- Recommendations to lower your cancer risk.
- There is a waitlist for these appointments which can often be a few months.
- This information can cause anxiety and stress. Medical professionals are here to support you.

If you would like to book an appointment in our clinic to find out more, please see the instructions provided on the *Self-Referral Form for Family History of Lynch Syndrome*.

Program of Genetics & Metabolism,
HSC Winnipeg
FE229 820 Sherbrook Street
Winnipeg, MB R3A 1R9
P: (204) 787-2494
F: (204) 787-1419

Self-Referral Form for Family History of Lynch Syndrome

How to make an appointment for genetic counselling:

If you live in Manitoba, you can make an appointment by one of the following options:

- Take this letter to your family doctor and ask for a referral.
- **Call** our clinic at *204-787-4267*. Please provide the information outlined on the form below.
- Complete the form below and **mail** it to:
  Hereditary Cancer Clinic
  Health Sciences Centre
  FE229 -820 Sherbrook Street
  Winnipeg, MB R3A 1R9
- Complete the form below and **fax** it to *204-787-1419*.

If you live outside of Manitoba, we suggest that you take this letter to your family doctor to be referred to your local Genetics clinic.

My relative has Lynch syndrome. I would like an appointment.

Full Name:_____ Date of birth:_____

Health card number: _____ Phone number: _____

Address:_____

My family physician is:_____ ☐I do not have a family physician.

Name of relative:_____ Their date of birth: _____

Gene: _____; mutation: _____ Genetic Counsellor: _____

Appendix B: Health Research Ethics Board Approval Certificate

Research Ethics Bannatyne
P126-770 Bannatyne Avenue
Winnipeg, MB R3E 0W3
T: 204 789 3255
F: 204 789 3414
bannreb@umanitoba.ca

University of Manitoba | Research Ethics and Compliance

HEALTH RESEARCH ETHICS BOARD (HREB)
CERTIFICATE OF FINAL APPROVAL FOR NEW STUDIES
Full Board Review

PRINCIPAL INVESTIGATOR:	INSTITUTION/DEPARTMENT:	ETHICS #:
Dr. Harminder Singh	U of M and HSC/Internal Medicine/ Gastroenterology	HS23886 (H2020:204)
HREB MEETING DATE: April 27, 2020	**APPROVAL DATE:** June 11, 2020	**EXPIRY DATE:** April 27, 2021
STUDENT PRINCIPAL INVESTIGATOR SUPERVISOR (if applicable): NA		

PROTOCOL NUMBER:	PROJECT OR PROTOCOL TITLE:
NA	Facilitating Communication and Referrals for Families with Lynch Syndrome
SPONSORING AGENCIES AND/OR COORDINATING GROUPS: Department of Biochemistry and Medical Genetics, University of Manitoba; CancerCare Manitoba Infrastructure Grant (Pending)	

Submission Date(s) of Investigator Documents:	REB Receipt Date(s) of Documents:
April 6 and June 6, 2020	April 6 and June 6, 2020

THE FOLLOWING ARE APPROVED FOR USE:

Document Name	Version(if applicable)	Date
Protocol:		
Protocol	V. 1.0	30-Mar-2020
Consent and Assent Form(s):		
Research Participant Information and Consent Disclosure (Paper Survey)	V. 1.1	19-May-2020
Research Participant Information and Consent Disclosure (Online Survey)	V. 1.1	19-May-2020
Research Participant Information and Consent Form (Individual Interview)	V. 1.1	19-May-2020
Consent to Contact by Telephone	V. 1.0	31-Mar-2020
Other:		
Telephone Script (Lynch Syndrome)	V. 1.1	19-May-2020
Telephone Script (Relatives)	V. 1.1	19-May-2020
Telephone Script (Survey Completed)	V. 1.1	19-May-2020
Study Information Sheet	V. 1.1	19-May-2020
Recruitment Email	V. 1.1	19-May-2020
Lynch Syndrome Family Package	V. 1.1	19-May-2020
Survey	V. 1.1	31-May-2020
Interview Guide	V. 1.0	31-Mar-2020
Master List	V. 1.0	31-Mar-2020

CERTIFICATION
The University of Manitoba (UM) Health Research Board (HREB) has reviewed the research study/project named on this ***Certificate of Final Approval*** at the ***full board meeting*** date noted above and was found to be acceptable on ethical grounds for research involving human participants. The study/project and documents listed above was granted final approval by the Chair or Acting Chair, UM HREB.

HREB ATTESTATION
The University of Manitoba (UM) Health Research Board (HREB) is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement 2, and the applicable laws and regulations of Manitoba. In respect to clinical trials, the HREB complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations of Canada and carries out its functions in a manner consistent with Good Clinical Practices.

QUALITY ASSURANCE
The University of Manitoba Research Quality Management Office may request to review research documentation from this research study/project to demonstrate compliance with this approved protocol and the University of Manitoba Policy on the Ethics of Research Involving Humans.

CONFLICT OF INTEREST
Any Principal or Co-Investigators of this study who are members of the UMHREB did not participate in the review or voting of this study.

CONDITIONS OF APPROVAL:

1. The study is acceptable on scientific and ethical grounds for the ethics of human use only. ***For logistics of performing the study, approval must be sought from the relevant institution(s).***
2. This research study/project is to be conducted by the local principal investigator listed on this certificate of approval.
3. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to the research study/project, and for ensuring that the authorized research is carried out according to governing law.
4. **This approval is valid until the expiry date noted on this certificate of approval. A Bannatyne Campus Annual Study Status Report** must be submitted to the REB within 15-30 days of this expiry date.
5. Any changes of the protocol (including recruitment procedures, etc.), informed consent form(s) or documents must be reported to the HREB for consideration in advance of implementation of such changes on the **Bannatyne Campus Research Amendment Form.**
6. Adverse events and unanticipated problems must be reported to the REB as per Bannatyne Campus Research Boards Standard Operating procedures.
7. The UM HREB must be notified regarding discontinuation or study/project closure on the **Bannatyne Campus Final Study Status Report.**

Appendix C: Consent to Contact Form

University of Manitoba
Rady Faculty of Health Sciences
Max Rady College of Medicine
Biochemistry and Medical Genetics

336 – 745 Bannatyne Avenue
Winnipeg, Manitoba
Canada R3E 0J9
Telephone (204) 789-3593
Fax (204) 789-3900
bmgadmin@umanitoba.ca

Consent to Contact by Telephone

Name of study: *Facilitating Communication and Referrals for Families with Lynch Syndrome*

Student Researcher: Natasha Osawa, Genetic Counselling Trainee (204-789-3774; osawan@myumanitoba.ca)

Supervisor: Dr. Harminder Singh (204-789-3369; Harminder.Singh@umanitoba.ca)

The purpose of this study is to obtain feedback from patients on a referral form and information sheet about Lynch syndrome in order to make improvements. Participants would be asked to complete a 15-minute anonymous survey and may be asked for a telephone interview.

Patients are eligible to participate in this study if they are:

- ✓ at least 18 years old
- ✓ fluent in English

AND either (check one):

- ☐ a known carrier of a pathogenic or likely pathogenic mutation in the following Lynch syndrome **gene:** **; mutation:** , OR
- ☐ a relative of an affected individual seeking an appointment using the Lynch Syndrome Referral Form

I, _____ confirm that I discussed this study with
(name of clinician)

_____, _____ who meets the above
(name of patient) (DOB)

eligibility criteria and agreed to be contacted by telephone at _____.

Best time to contact the potential participant: ☐ Morning ☐ Afternoon ☐ Evening

Signature:_____ **Date**:_____

Appendix D: Phone Script

TELEPHONE SCRIPT
Individuals with Lynch Syndrome who gave Consent to Contact via Clinician

Hello, may I speak with ___?

If the potential participant is not available and someone else answers the phone: My name is Natasha, I am calling about a research study at the University of Manitoba. Is there a better time for me to call back? I can be reached at **(204) 789-3774**.

If it goes to voicemail: Hello, this message is for _____. My name is Natasha, I am calling about a research study at the University of Manitoba. Please give me a call back at **(204) 789-3774**.

My name is Natasha Osawa, I am a researcher with the Faculty of Health Sciences at the University of Manitoba. You recently spoke with name of healthcare provider at name of clinic and you indicated that you are willing to be contacted regarding this study. Is now an okay time for you to talk about this more? How are you doing today? *Establish rapport*

I'll explain more about this research study. Our group is working to improve the information materials provided to families about Lynch syndrome. The *Lynch Syndrome Family Package* has been developed and distributed to help individuals with Lynch syndrome share information with their relatives. We are asking for opinions on the package by survey and interviews. Your participation will lead to improved information materials for individuals and their families about Lynch syndrome.

May I email you the *Lynch Syndrome Family Package* and a link to the online survey? Or, if you prefer paper, I can send everything by mail with a return envelope for the survey.
Email address / address: _____

(If electronic:) The package I send you will include the *Lynch Syndrome Family Package* as an attachment and the link to the online survey. Only two questions will be visible at the beginning, you will need to answer yes to both for the rest of the questions to appear. Please consider forwarding the email on to your relatives so they can read the letter and complete the survey.

We are offering a $20 Amazon gift card to everyone who completes the survey as a token of our appreciation. After submitting the survey, a new page will appear where you can leave your email address to receive the electronic gift card. Your email address will not be linked to your survey responses.

Through interviews, we hope to learn more about how people respond to learning about Lynch syndrome in their family, what information is most important for families to know, how they'd like to receive this information, and if there are any barriers people are facing which make it harder to get genetic testing. We hope that the results will help improve the way relatives are referred to the Hereditary Cancer Clinic with a family history of Lynch syndrome. Participating in this interview is optional and may take up to 1 hour.

Would you consider participating in an interview?

Are you willing to answer some demographic questions? I ask these questions as pre-screening questions to select who I will interview. My goal is to include people with diverse backgrounds and experiences in the study, so I am hoping to find people who answer these questions differently from the people I have already interviewed. If we do proceed with an interview in the future, your answers to these questions will be linked to the interview. If there are any questions you would prefer not to answer, please let me know and we can skip the question.

1. How old are you?
2. What is your gender?
3. What province / territory do you live in?
4. Do you live in an urban or rural community?
5. What is your ethnic background?
6. What is your highest level of education?
7. What is your current employment status?
8. Is your combined annual household income more or less than $68, 000?
9. What is your marital status?
10. Do you have children?
11. Have you had genetic testing for Lynch syndrome? – yes, based on consent to contact form
    a. WHEN
12. Have you ever been diagnosed with cancer?
    a. TYPE
13. How many of your relatives are known to have Lynch syndrome?
    And how large is your family?
    (How many siblings/aunts/uncles/cousins do you have?)

Thank you, those are all the questions I had.

(If a good fit for the study, proceed to schedule interview)

I will send you a consent form which describes the interview process. We will go over the consent form together at the beginning of the interview. It would be great if you could read it over beforehand in case you have any questions. You don't need to return the form to me, it is for your records.

We can schedule the interview by telephone or by computer using a video call software called Bluejeans. Which would you prefer?
Phone number:_____ / email address:_____

When would be a convenient time to schedule the interview?
Date and time for interview: _____

Any questions? Thank you so much for choosing to participate in this study. I look forward to speaking with you again soon.

Appendix E: Recruitment Email

SUBJECT: Lynch Syndrome Study

ATTACHMENT: *Lynch Syndrome Family Package*

Dear ___,

It was a pleasure speaking to you on the phone recently. As I mentioned, our group is working to improve the patient resources about Lynch syndrome. We would really appreciate your feedback.

Attached is our *Lynch Syndrome Family Package*. The Program of Genetics and Metabolism developed this package for people with Lynch syndrome to share with their relatives. The package includes information about Lynch syndrome and a referral form for relatives who want to make an appointment with the Hereditary Cancer Clinic.

After you read the package, please complete the survey at the link below. The survey will take about 15 minutes and all answers will remain anonymous.

https://is.gd/lynchsyndrome

Once you submit the survey, there will be a field where you can leave your email address to receive a $20 electronic gift card to Amazon, as a token of our appreciation for your time.

We are also conducting individual interviews by phone or video call. If you are willing to be interviewed, you can leave your email address at the end of the survey, or contact the student researcher by phone or by replying to this email.

Finally, please consider forwarding this email to your relatives so they can participate and provide feedback on this package.

Thank you for your participation!

Sincerely,

Natasha Osawa

Student Researcher
Genetic Counselling Program
Biochemistry and Medical Genetics
336 – 745 Bannatyne Avenue
Winnipeg, Manitoba
Canada R3E 0J9
Telephone: (204) 789-3774
osawan@umanitoba.ca

Rady Faculty of Health Sciences | University of Manitoba

Appendix F: Reminder Email

SUBJECT: Lynch Syndrome Survey

ATTACHMENT: *Lynch Syndrome Family Package*

Hello again,

We would really appreciate your feedback on the Lynch Syndrome Family Package. If you haven't already done so, please click the link below to access the online survey.

https://is.gd/lynchsyndrome

Once you submit the survey, there will be a field where you can leave your email address to receive a $20 electronic gift card to Amazon, as a token of our appreciation for your time.

If you have already completed the survey, sorry to bother you again. You can let us know by replying to this email and we won't send any further reminders.

Thank you for your participation!

Sincerely,

Natasha Osawa

Student Researcher
Genetic Counselling Program
Biochemistry and Medical Genetics
336 – 745 Bannatyne Avenue
Winnipeg, Manitoba
Canada R3E 0J9
Telephone: (204) 789-3774
osawan@umanitoba.ca

Rady Faculty of Health Sciences | University of Manitoba

Appendix G: Survey Consent Disclosure

Study Title: *Facilitating Communication and Referrals for Families with Lynch Syndrome*

Principal Investigator: Natasha Osawa, BSc, Genetic Counselling Student, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba

Supervisor: Harminder Singh, MD, MPH, FRCPC, Gastroenterologist, Associate Professor, Department of Internal Medicine, Rady Faculty of Health Sciences, University of Manitoba

Advisory Committee: Kirk McManus, PhD; Heidi Rothenmund, CGC; Gayle Restall, PhD; Kristin Reynolds, PhD; Christina Kim, MD

Study Description: Our group is working to improve the information materials provided to families about Lynch syndrome. We are asking for your opinions in the attached survey. The survey will take about 15 minutes to complete. Your participation and opinions will lead to improved information materials.

Your participation is completely voluntary. Your decision whether or not to participate will have no affect on your current or future healthcare.

You are **not** required to provide any **personal information such as your name, address or telephone number**. The survey system will not record your email address or IP (internet protocol) address. If you agree to participate in the survey, please note that you must complete the survey in one sitting. Also, you will not be able to withdraw your response once submitted as we cannot link the survey responses back to you.

Once you submit the survey, there will be a field where you can leave your email address to receive a $20 electronic gift card to Amazon, as a token of our appreciation for your time. Your email address will not be linked to your survey responses.

If you are willing to be interviewed at a later date, please provide your contact information at the end of the survey. Your contact information will be kept separate from your survey responses.

The risks of participating include potentially feeling upset or emotional as a result of speaking about your experiences with Lynch syndrome.

There will be no direct benefit to you for your participation in the study. We hope that the results will help improve patient resources and the way relatives are referred to the Hereditary Cancer Clinic with a family history of Lynch syndrome.

We will send you a reminder email every two weeks, up to three times total, asking you to complete the survey.

Questions: If you have any questions or concerns about the study, you may contact the student researcher, Natasha Osawa, at 204-789-3774 or osawan@myumanitoba.ca. You may also contact the supervisor of the study, Dr. Harminder Singh, at 204-789-3369 or Harminder.Singh@umanitoba.ca.

If you have questions about your rights as a research study participant, contact the University of Manitoba Research Ethics Board by at 204-789-3389.

The study is funded by the University of Manitoba. This study and survey have been approved by the University of Manitoba Health Research Ethics Board. By continuing on and completing the survey, you are consenting to participate in this survey.

Appendix H: Survey Instrument

1. Did you receive a *Lynch Syndrome Family Package* (see the attached PDF example)?

   - Yes
   - No

If 'No' was selected, please read the Lynch Syndrome Family Package (PDF attached) before continuing the survey.

2. Are you age 18 or older?
   - Yes
   - No

If 'No' was selected: You need to be at least 18 years old to participate in this survey. Please do not answer the remaining questions and submit the survey now.

3. Have you had genetic testing for Lynch syndrome?
   - Yes
   - No

   If you answered 'YES' to question 3, what was your genetic test result?
   - Positive for Lynch syndrome.
   - Negative for Lynch syndrome.
   - Still waiting for test results.

   If you answered 'POSITIVE FOR LYNCH SYNDROME', when did you receive your positive genetic test result for Lynch syndrome?
   - Within the last 3 months
   - 4-6 months ago
   - 7-12 months ago
   - Over a year ago

4. In the past, have you received information about Lynch Syndrome from a healthcare provider in another format?
    - Yes
    - No

   If you answered 'YES' to question 4, *This survey is only asking your opinion of the current version of the Lynch Syndrome Family Package. Please click on the attachment (*Lynch Syndrome Family Package.pdf) *at the top of the survey to see this version.*
5. Who gave you the *Lynch Syndrome Family Package*?
    - A healthcare provider
    - A relative

   If you answered 'A HEALTHCARE PROVIDER' to question 4, which provider gave you the *Lynch Syndrome Family Package*?
    - Genetic counsellor / Geneticist
    - Colonoscopy Physician
    - Oncologist
    - Another healthcare provider:_____
    - Unsure

   If you answered 'A RELATIVE' to question 4, which relative gave you the *Lynch Syndrome Family Package*?
    - Mom
    - Dad
    - Brother
    - Sister
    - Son
    - Daughter
    - Aunt
    - Uncle
    - Niece
    - Nephew
    - Cousin
    - Grandparent
    - Another relative: _____
6. Which one of the following Lynch syndrome genes was found to have a mutation in your family?
    - MLH1
    - MSH2
    - MSH6
    - PMS2
    - EPCAM
    - Not sure
7. Did you pass the *Lynch Syndrome Family Package* on to any relatives?
    - Yes
    - Not yet, but planning to
    - No

   If you answered 'YES' to question 7, who did you give the *Lynch Syndrome Family Package* to? *Check all that apply.*

- ☐ Parent
- ☐ Child
- ☐ Brother / sister
- ☐ Aunt / uncle
- ☐ Cousin
- ☐ Niece / nephew
- ☐ Grandparent
- ☐ Another relative:

If you answered 'NOT YET, BUT PLANNING TO' to question 7, who do you plan to give the *Lynch Syndrome Family Package* to? *Check all that apply.*

- ☐ Parent
- ☐ Child
- ☐ Brother / sister
- ☐ Aunt / uncle
- ☐ Cousin
- ☐ Niece / nephew
- ☐ Grandparent
- ☐ Another relative:

If you answered 'NO' to question 7, What made you decide not to pass the Lynch Syndrome Family Package on to any relatives? *Check all that apply.*

- ☐ I do not have their contact information
- ☐ Our communication is limited
- ☐ I do not feel comfortable
- ☐ I do not like the letter
- ☐ I am not yet ready to discuss it with them
- ☐ I do not wish to inform them about this
- ☐ I feel another relative should be responsible for this
- ☐ I have already informed my relatives
- ☐ Another relative shared the information already
- ☐ I don't have any relatives who are at risk for Lynch syndrome
- ☐ Another reason:_____

8. How many adult children and adult siblings (over age 18) do you have? _____
9. Did you tell any relatives about their risk for Lynch syndrome without showing them the *Lynch Syndrome Family Package*?
   - o Yes
   - o No

   If you answered 'YES' to question 9, which relatives did you tell about their risk for Lynch Syndrome without showing them the *Lynch Syndrome Family Package*? *Check all that apply.*
   - ☐ Parent
   - ☐ Child
   - ☐ Brother / sister
   - ☐ Aunt / uncle
   - ☐ Cousin

- ☐ Niece / nephew
- ☐ Grandparent
- ☐ Another relative: _____

10. The amount of information in the *Lynch Syndrome Family Package* is:
    - o Much too little
    - o Too little
    - o Just right
    - o Too much
    - o Way too much
11. The information in the *Lynch Syndrome Family Package* is clear.
    - o Strongly disagree
    - o Disagree
    - o Neutral
    - o Agree
    - o Strongly agree
12. The information in the *Lynch Syndrome Family Package* is easy to understand.
    - o Strongly disagree
    - o Disagree
    - o Neutral
    - o Agree
    - o Strongly agree
13. The information in the *Lynch Syndrome Family Package* seems trustworthy.
    - o Strongly disagree
    - o Disagree
    - o Neutral
    - o Agree
    - o Strongly agree
14. I understand why I received the *Lynch Syndrome Family Package*.
    - o Strongly disagree
    - o Disagree
    - o Neutral
    - o Agree
    - o Strongly agree
15. The information in the *Lynch Syndrome Family Package* helps me tell my relatives about Lynch syndrome.
    - o Strongly disagree
    - o Disagree
    - o Neutral
    - o Agree
    - o Strongly agree
16. How familiar to you or new to you is the information in the *Lynch Syndrome Family Package*?
    - o Very familiar
    - o Familiar
    - o Unsure
    - o New

- Very new

17. The *Lynch Syndrome Family Package* is a convenient way to share information with relatives.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
18. The *Lynch Syndrome Family Package* left me feeling informed.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
19. The *Lynch Syndrome Family Package* left me feeling overwhelmed.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
20. The *Lynch Syndrome Family Package* left me feeling worried.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
21. The *Lynch Syndrome Family Package* gave me a sense of control.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
22. The *Lynch Syndrome Family Package* feels like an invasion of my privacy.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
23. I felt able to cope with the information from the *Lynch Syndrome Family Package*.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
24. The *Lynch Syndrome Family Package* is a good way to share this information.
    - Strongly disagree

- Disagree
- Neutral
- Agree
- Strongly agree

25. I would like the *Lynch Syndrome Family Package* to be available by:
    - ☐ Letter (on paper)
    - ☐ Email
    - ☐ Website
    - ☐ Online video
    - ☐ An app for smartphones
    - ☐ Another format: _____
26. I looked for more information about Lynch syndrome through: *Select all that apply.*
    - ☐ Internet search
    - ☐ YouTube
    - ☐ Facebook
    - ☐ Twitter
    - ☐ Instagram
    - ☐ Podcast
    - ☐ Academic journal
    - ☐ Book
    - ☐ Pamphlet / brochure
    - ☐ Seminar
    - ☐ Support group
    - ☐ Geneticist / genetic counsellor
    - ☐ Colonoscopy Physician
    - ☐ Oncologist
    - ☐ Family doctor / nurse
    - ☐ Family / friend
    - ☐ Another resource: _____

If you answered 'A RELATIVE' to question 4:

27. I am glad my relative told me about the chance I could have Lynch syndrome.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
28. After reading the *Lynch Syndrome Family Package*, I knew who to contact if I had questions about Lynch syndrome.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree

29. After reading the *Lynch Syndrome Family Package*, I knew how to make an appointment at the Hereditary Cancer Clinic.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
30. Testing for Lynch syndrome (genetic testing) is accessible to me if I want it.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
31. Since reading the *Lynch Syndrome Family Package*, I would like an appointment for genetic counselling.
    - Strongly disagree
    - Disagree
    - Neutral
    - Agree
    - Strongly agree
32. Please provide any additional comments here:_____

Demographics

1. Please select your age:
    - 18-30
    - 31-45
    - 46-60
    - 61-75
    - Above 75
    - Prefer not to say
2. Do you live in Manitoba?
    - Yes
    - No
    - Prefer not to say
3. Do you live in a city or smaller community?
    - Large city with a population over 100, 000
    - City or town with a population between 7, 000 and 100, 000
    - Smaller community with a population less than 7, 000
    - Prefer not to say
4. Which gender do you identify with?
    - Woman
    - Man
    - Gender-fluid, non-binary, and/or Two-Spirit
    - Prefer not to say
5. What is your ethnic background? *Please check all that apply.*

- Arab
- Black
- Chinese
- Filipino
- First Nations
- French Canadian
- Hutterite
- Inuk (Inuit)
- Japanese
- Jewish
- Korean
- Latin American
- Mennonite
- Metis
- South Asian (e.g. East Indian, Pakistani, Sri Lankan, etc.)
- Southeast Asian (e.g. Vietnamese, Cambodian, Laotian, Thai, etc.)
- White
- West Asian (e.g. Iranian, Afghan, etc.)
- Another ethnicity:_____
- Prefer not to say

6. What is your highest level of education?
    - Did not complete high school
    - High school
    - College
    - Undergraduate university
    - Graduate or professional program
    - Prefer not to say
7. What is your current employment status?
    - Not working
    - Part-time
    - Full-time
    - Retired
    - Prefer not to say
8. What is your combined household income per year?
    - Less than $68, 000
    - $68, 000 or more
    - Prefer not to say
9. What is your marital status?
    - Single
    - Common law
    - Married
    - Widowed
    - Separated

- Divorced
- Prefer not to say

10. Do you have children?
    - Yes
    - No
    - Prefer not to say
11. Have you ever been diagnosed with cancer?
    - Yes
    - No
    - Prefer not to say
12. If yes, what type of cancer? *Check all that apply.*
    - ☐ Colorectal cancer
    - ☐ Endometrial or uterine cancer
    - ☐ Stomach cancer
    - ☐ Ovarian cancer
    - ☐ Small bowel cancer
    - ☐ Urothelial (bladder or ureter) cancer
    - ☐ Brain cancer
    - ☐ Pancreatic cancer
    - ☐ Breast cancer
    - ☐ Prostate cancer
    - ☐ Another type of cancer:_____
    - ☐ Prefer not to say

SUBMIT

Thank you for participating in our study. Your opinions will help us improve the Lynch syndrome resources available to patients in the future.

- ☐ Check this box and provide your email address below if you would like to receive a $20 electronic gift card to Amazon.
- ☐ Check this box and provide your email address below if you would be willing to be interviewed at a later date. The researcher will email you to give you more information about the interview.

Your email address will not be linked to your survey responses. All survey responses will remain anonymous. If you provide your contact information,

Email address:

Appendix I: Interview Participant Informed Consent Form

Study Title: *Facilitating Communication and Referrals for Families with Lynch Syndrome*

Principal Investigator: Natasha Osawa, BSc, Genetic Counselling Student, Department of Biochemistry and Medical Genetics, Rady Faculty of Health Sciences, University of Manitoba

Supervisor: Harminder Singh, MD, MPH, FRCPC, Gastroenterologist, Associate Professor, Department of Internal Medicine, Rady Faculty of Health Sciences, University of Manitoba

Advisory Committee: Kirk McManus, PhD; Heidi Rothenmund, CGC; Gayle Restall, PhD; Kristin Reynolds, PhD; Christina Kim, MD

You are being asked to participate in a research study involving an individual interview. Please take your time to review this consent form and discuss any questions you may have with the study staff before you make your decision. Please ask the study staff to explain any words or information that you do not clearly understand.

PURPOSE OF STUDY
This research study is being conducted to study how people respond to learning about Lynch syndrome in their family, what information is most important for families to know, how they would like to receive this information, and if there are any barriers people are facing which make it harder to get genetic testing. We hope that this study will improve the referral process of individuals with a family history of Lynch syndrome to the Hereditary Cancer Clinic.

PARTICIPANT SELECTION
You are being invited to participate because you or your relative had an appointment with the Hereditary Cancer Clinic about Lynch syndrome. You are eligible to participate in this study if you have Lynch syndrome or are related to someone with Lynch syndrome, you are at least 18 years old, and you are fluent in English. Previously, you answered pre-screening questions and were selected to interview based on your responses, which will be linked to this interview. A total number of approximately 20 participants will be asked to interview.

STUDY PROCEDURES
You will be interviewed by the student researcher, Natasha Osawa, by phone or by video conference. Interviews are expected to last approximately one hour. You will be asked questions about your experience learning about Lynch syndrome, communicating with relatives, and accessing genetic testing. These questions will help us better understand the needs of families with Lynch syndrome in order to improve the resources provided to patients by the Hereditary Cancer Centre. Interviews will be audio recorded and the student researcher may also take notes during the interview. The recording will be transcribed by the research team for further qualitative analysis.

POTENTIAL RISKS AND BENEFITS OF PARTICIPATING
The risks of participating are minimal; speaking about your experiences with Lynch syndrome may be upsetting or emotional. You do not have to answer any question that makes you feel uncomfortable or that you find too upsetting. Should you need any additional help or support, we will refer you to Klinic Crisis Line or help you find other counselling help.

There will be no direct benefit to you for your participation in the study. We hope that the results will help improve the way relatives are referred to the Hereditary Cancer Clinic with a family history of Lynch syndrome in the future.

SAFETY

Your confidentiality may be broken if you describe one of the following:

1. You say something about harming yourself or others
2. You tell me about the abuse or neglect of a child
3. You report inappropriate or incompetent practice of a healthcare professional

COST

There is no cost to you to participate in the study, aside from the time it takes to conduct the interview.

PAYMENT

You will receive a $25 Amazon gift card as a gesture of appreciation for your participation.

CONFIDENTIALITY

We will do everything possible to keep your personal information confidential. Your name will not be used at all in the study records. A list of names and addresses of participants will be kept in a secure file in case we need to contact you with regards to the study. If the results of this study are presented in a meeting, or published, nobody will be able to tell that you were in the study. Please note that although you will not be identified as the speaker, your words may be used to highlight a specific point. The collection and access to personal information will comply with provincial and federal privacy legislations.

Audiotapes of the interview will be typed and used to prepare a report. The audiotapes and typed notes will be kept for 18 months after the study ends in a secure locked file cabinet and office. Only the research staff and the Genetic Counselling Program Director will have access to them.

The University of Manitoba Health Research Ethics Board may review records related to the study for quality assurance purposes.

We may wish to quote your words directly in reports and publications resulting from this. With regards to being quoted, please check yes or no for each of the following statements:

Researchers may publish documents that contain my quotations under the conditions below:	
☐ Yes ☐ No	I agree to be quoted directly if my name is not published (anonymously).
☐ Yes ☐ No	I agree to be quoted directly if a made-up name (pseudonym) is used.

VOLUNTARY PARTICIPATION AND WITHDRAWL

Your decision to participate in this study is voluntary. You may refuse to participate or withdraw from the study at any time, within three months following the interview, by contacting the student researcher, Natasha Osawa. If you withdraw from the study, all data you provided will be destroyed. Your decision not to participate or to withdraw from the study will not affect your medical care.

RESEARCH CONTACTS

If you have any questions or concerns about the study, you may contact the student researcher:

Natasha Osawa
Telephone: 204-789-3774
Email: osawan@myumanitoba.ca

You may also contact the supervisor of the study:

Dr. Harminder Singh
Telephone: 204-789-3369
Email: Harminder.Singh@umanitoba.ca

If you have questions about your rights as a research study participant, contact the University of Manitoba Research Ethics Board at 204-789-3389.

CONSENT SIGNATURES

1. I have read all 3 pages of the consent form.
2. I have had a chance to ask questions and have received satisfactory answers to all of my questions.
3. I understand that by giving my consent I have not waived any of my legal rights as a participant in this study.
4. I understand that my records, which may include identifying information, may be reviewed by the research staff working with the Principal Investigator and the agencies and organizations listed in the Confidentiality section of this document.
5. I understand that I may withdraw from the study at any time and my data may be withdrawn prior to publication.
6. I understand I will be provided with a copy of the consent form for my records.
7. I agree to participate in the study.
8. I am providing verbal consent to the researcher to sign on my behalf.

Participant printed name: _____ Date _____
(day/month/year)

Participant phone number: _____

I, the undersigned, have fully explained the relevant details of this research study to the participant named above and believe that the participant has understood and has knowingly given their verbal consent

Printed Name: _____Date _____
(day/month/year)

Signature: _____ Role in the study:_____

Appendix J: Interview Guide

Hello, May I speak with ___? This is Natasha Osawa from the University of Manitoba. How are you doing today? *Establish rapport*

Is now still an okay time for you to do the interview?

I need to review the consent form with you before beginning. You should have received it by email/mail, are you able to have it in front of you as we go through it?

[Read Interview Consent Form]

[Begin interview after receiving verbal consent]

Thank you again for agreeing to participate in this interview. I will be asking you a range of questions. Please feel free to let me know if you would prefer to not answer a question, or if you would like to take a break at any time. We will be speaking together for about an hour today.

1. When we last spoke, you said you received your genetic test results for Lynch syndrome about _____ ago.
    - What was that experience like for you? Can you describe your feelings when you got your test results, and if those feelings have changed over time?
    - What motivated you to attend genetic counselling and get genetic testing for Lynch syndrome?
    - Was there anything that made you hesitate?
    - Were you the first in the family to have genetic testing for LS?
    - Which of your close relatives (parents, siblings, kids) know about LS in the family?
        - Which of your more distant relatives (aunts, uncles, cousins, grandparents) know about LS in the family?
2. Did you choose to tell your relatives about Lynch syndrome? (Which relatives?)
    - YES
        - How long did you wait to tell your relatives after getting your genetic test results back?
        - Were there some relatives you chose to inform and others you chose not to tell? Tell me more about those decisions.
        - Can you describe the way you told your relatives? (Was it in person, by phone?)
        - What factors helped you discuss with these relatives? (Facilitators: being emotionally or physically close, feeling knowledgeable about LS, cancer prevention options)
        - Did you face any challenges when talking about LS with your relatives? (Barriers: distance, family dynamics, lack of knowledge, age of relatives, cultural taboos) How did you overcome these challenges?

    - Did receiving the LSFP help you tell any relatives who you had not told previously?
- NO / NOT ALL
    - Can you tell me more about your reasons for not telling these relatives about Lynch syndrome? (Feeling emotionally or physically unable, Physical distance, no contact info available, Family dynamics, Lack of knowledge, Age of relatives, Cultural norms / taboos, Gender roles)
    - Did receiving the Lynch Syndrome Family Package make you reconsider telling those relatives?
- Were you provided anything to share with your relatives from your genetic counsellor, such as a family letter?
    - Yes → did you use it?
        - How does it compare to the Lynch Syndrome Family Package?
    - No → having seen the Lynch Syndrome Family Package now, do you think that would have been helpful back then?

3. What was your overall impression of the Lynch Syndrome Family Package?

    Emotions
    - How did you feel reading the package?
    - We wonder if some people might feel that this package is an invasion of their privacy. Did you ever feel that sharing this letter was an invasion of your privacy? What was that like for you?
    - Some people might feel overwhelmed / worried after reading this package. Did you ever feel that way? What was that like for you?
    - How do you think your relatives would respond to receiving this package?

    Information
    - Overall, what was your opinion of the information content of the package?
    - Did you know this information about Lynch syndrome already? How did you learn this?
    - Was there information missing that you think we should add?
    - Were there any parts of the package that were confusing or unclear?
    - Was there any information that seemed unnecessary?

    Actions
    - When considering what you should do after reading the package, what did you feel your options were?
    - What did you decide to do next?
4. Did you share the package with any relatives yet? What factors influenced this decision?
    - Would you share this package with your relatives?
    - Would you consider sending this package to a relative you are not close to?
    - Do you think the self-referral form would be easy for your relatives to use?
    - How did they respond? Any positive or negative comments?

5. Of all the communication options that you have available – mailing a paper letter, making a phone call, sending email, website link, video – is there one mode of communication that you think you would be best for sharing information with your relatives?
    - Would you take the same approach with all relatives, or how might this vary for you?
        - And what is driving that variation? In other words, if you wouldn't use the same approach with all relatives, what determines which approach you would use?
    - Did you look for more information about Lynch syndrome after reading the package?
        - If so, where did you look? Did you feel there was adequate information available?

6. Did you face any challenges in arranging to see a genetic counsellor, attending your appointments, or receiving results? (getting a referral, long wait time)
    - The Self-referral form was designed to make it easier for people to access genetic counselling. Did you use any similar tools to help make your appointment? Can you suggest any other tools that we could use to make things easier for people?
7. Do you have any relatives who know about their risk for Lynch syndrome but have not seen a genetic counsellor?
    - Have you talked about LS with these relatives? How do you feel about their decision not to get genetic counselling or testing?
8. The current approach requires people with LS to talk to their relatives, with no direct involvement from healthcare providers. Who do you feel should be responsible for sharing this information and why?
9. Please describe your (and your family's) experience with accessing genetic testing in Manitoba.
    - Are there other barriers in Manitoba you or your relatives faced? (Insurance concerns, anxiety, wait for results) For example, People in other countries have said that the cost of genetic testing makes it difficult for some people to access it, but it is covered by provincial funding here in Manitoba.
        - If relatives are untested, what are their reasons for not having genetic testing?
    - Were there systems in place that made it easy for you to get genetic testing?
10. Overall, do you think the healthcare system is doing enough for families with Lynch syndrome? Can you recommend any improvements?
11. Is there anything else that you would like to add that would be helpful for us to know?

<u>Examples of Affirmations:</u>
- "Thank you for sharing your experience. That sounds like it was a ___ experience for you"
- "Mhm, right, ok, yes, etc" *show active listening*

<u>Examples of Probes:</u>
- "Tell me more about that"
- "Can you give me an example of that"
- If still being vague after a few probes, move on (don't jeopardize rapport)

Examples of Wrap-Up:
- Wait for lull in conversation then interject
- Summarize and bring back to main point of what they're saying
- "Thanks for sharing that, just being mindful of time, the next question I wanted to ask you is"
- "Thanks for sharing that, I'm still looking forward to hearing your experience for the next question and would like to move on for the sake of time"

[Interview concludes]

Thank you very much for participating in this interview. We will mail you a $25 Amazon gift card as appreciation for your time. What mailing address/email is best for us to use?

If you have any additional questions about this research study or how the information you provided is being used, please feel free to contact me by phone or email, my contact information is on the consent form. Thank you again for your time.