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Assessment of Patient Satisfaction with the Provision of Fertility Information in Women with Lynch Syndrome

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Dedication

To my parents, Robert and Gina Hickey, and my grandmother, Barbara Hickey.

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First and foremost, I would like to thank my parents for their unwavering support and constant encouragement. Throughout my life, you have challenged me to reach my full potential. There are not enough ways that I can express my appreciation of all that you have done for me. Thank you for providing the support on which I built myself.

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Abstract

Lynch Syndrome (LS), one of the most common hereditary cancer syndromes, is primarily known for its substantially increased risks for colorectal cancer. The incidence of gynecologic cancers (endometrial and ovarian cancers) equals or exceeds the incidence of colorectal cancers in female patients with LS. The prevention and treatment methods for these cancers can drastically affect fertility and reproduction. Previous studies with cancer patients have revealed challenges in acquiring information related to these topics; thus far, no research has assessed whether there is an informational gap regarding fertility information for women in the LS population. The purpose of this study was to identify the amount of information received related to fertility and reproduction, assess patient satisfaction, and characterize current practices of this information delivery within our target patient population.

Data was collected from 154 women with LS. Likert scales were used to quantify the amount of information provided about major themes pertaining to fertility in LS: effects of cancer treatment, risk-reducing surgeries, fertility preservation and family planning. Overall, participants were more satisfied when they received more information about certain topics within these themes. There was a distinct lack of individualization in patient care, and lack of uniformity regarding the provision of this information among healthcare providers. Participant opinions indicate that genetic counselors may be an untapped resource in the provision of fertility and reproduction information to this population.

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Chapter 1. Background

1.1 Lynch Syndrome

A hereditary cancer syndrome is characterized by the inheritance of a genetic variant that predisposes its carrier to the development of cancers. Distinguishing features of hereditary cancer syndromes include an early onset of cancers, the occurrence of multiple primaries in a single individual, and several generations of affected individuals within a family. These syndromes account for 5-10% of all cancer diagnoses, and contribute to significant morbidity and mortality rates in the populations affected (Nagy, 2004). In order to reduce the clinical consequences, it is important to identify carriers through appropriate screening programs and genetic testing (Robson, 2003). Confirmation of a positive genetic diagnosis will detect at-risk individuals, justify increased surveillance, aid in medical management, and help in the decision-making concerning family planning and prophylactic interventions (Giardiello, 2014).

Lynch Syndrome (LS) is one of the most common hereditary cancer syndromes, with an estimated population prevalence of 1 in 400 (Nagy, 2004). It is characterized by a predisposition to a spectrum of cancers, but primarily known for its substantially increased risks for colorectal and endometrial cancer. The history of this syndrome began in the early 1900s when Dr. Aldred Warthin, a renowned pathologist, observed a pattern of gastrointestinal and uterine cancers occurring frequently in a large family [“Family G”] (Warthin, 1913). The medical records and family pedigrees in his study provided some of the first evidence of the heritable nature of cancer susceptibility, a concept that at

the time was still under scrutiny. In the 1960s, Dr. Henry T. Lynch encountered two families ["Family N" and "Family M"] that featured an extensive, multi-generational history of early onset colorectal cancer, among other cancers; this cancer burden was similar to the family described by Warthin (Lynch, 1966). After studying the collective data from the three families, Lynch proposed that the presence of a syndromic disorder was responsible for the cancer manifestation observed (Sehgal, 2014) and coined the name 'Cancer Family Syndrome' in 1971. Due to the increased risk for colorectal cancer, the condition was renamed Hereditary Nonpolyposis Colorectal Cancer (HNPCC) in 1984, which differentiated it from the other major inherited colorectal cancer syndrome, Familial Adenomatous Polyposis. However, HNPCC was deemed a misnomer, as there is a wide variety of extracolonic cancers associated with this syndrome, and was subsequently renamed Lynch Syndrome (Cohen, 2014).

LS is an autosomal dominant condition that increases lifetime risks for colonic and extracolonic cancers; the proposed risk values depend on the genetic variant inherited in a family, and the sex and age of the affected individual (Tiwari, 2016). LS accounts for 2-4% of all colorectal cancers (CRC) (Barrow, 2013), and affected individuals have as high as a 75% lifetime risk of developing CRC. The median age of diagnosis is between 44-61 years of age, with approximately 50% of all CRC tumors occurring below the age of 50. This age of onset is 20-25 years earlier than the onset in sporadic cases of CRC, which is typically at age 70 (Cohen, 2014). The progression of these CRC tumors exhibit an accelerated carcinogenesis: small adenomas will develop into carcinomas within 2-3 years in LS patients, versus the 8-10 years in the general population. Other features of

CRC in LS include the presence of synchronous and metasynchronous tumors, and an increased incidence of tumors in the proximal colon (Lynch, 2009).

While CRC is a major clinical consequence in LS, affected individuals also have substantial risks for extracolonic tumors. Female carriers of LS have a 15-61% risk for developing endometrial cancer, which is much higher than the 1.7% risk of the general population (Cohen, 2014; ACOG Practice Bulletin, 2014). The large risk range is due to the fact that different genes confer differing risk values. Endometrial cancer in LS also has an earlier age of onset at approximately 47-62 years, younger than the general population's typical age of onset at 70 (Cohen, 2014). LS accounts for 2% of all new ovarian cancer diagnoses (Malander, 2006). The incidence of ovarian cancer in the general population is 1.4%, but females with LS are at an increased risk for ovarian cancer (approximately 6.7-12%), manifesting between the ages of 41-51 years (Cohen, 2014). Both male and female carriers have a 0.7-13% risk of developing gastric cancer, which follows the trend of early onset. The lifetime risk for cancer of the urinary tract (including the bladder, renal pelvis and ureter) ranges from 1.9-11.2%, again depending on the genotype (Barrow, 2013). Individuals with LS are also at an elevated risk for cancers of the hepatobiliary tract, small bowel, pancreas and CNS tumors. Furthermore, there are variants of LS that are associated with specific cancer manifestations. Muir-Torre syndrome was originally identified as a separate and distinct condition, but genetic testing has proven its place on the LS spectrum. Muir-Torre syndrome is characterized by a 9% risk for sebaceous neoplasms in addition to the other cancer risks in LS (South, 2008). The Turcot variant of LS features CNS tumors, particularly glioblastomas, in additional to the elevated risk for other LS-associated cancers (Cohen, 2014).

LS is caused by a germline mutation in one of the genes involved in the DNA mismatch repair (MMR) pathway: *MLH1*, *MSH2*, *MSH6*, *PMS2,* or *EPCAM*. The function of the MMR proteins is to proofread the DNA for the presence of base-pair mismatches or small insertions or deletions introduced by replication error, and repair the mistakes. A compromised MMR system will result in the accumulation of somatic mutations, eventually leading to carcinogenesis (Cohen, 2014). In particular, defective MMR will cause variations within the microsatellites of the DNA. Microsatellites are short repetitive sequences within the genome; microsatellite instability (MSI) is a hallmark of LS tumors and is frequently used for patient evaluation (Umar, 2004). It is estimated that 80-90% of all LS cases are caused by deleterious mutation in *MLH1* and *MSH2*, and the remaining 10-20% of cases are due to *MSH6* and *PMS2* mutations (Giardiello, 2014). Approximately 3% of cases are caused by mutations in the *EPCAM* gene. Although EPCAM is not an MMR protein, certain mutations of *EPCAM* can lead to epigenetic silencing of the *MSH2*, resulting in a LS phenotype (Kempers, 2011).

Genotype-phenotype correlations have been elucidated in LS. Individuals with *MLH1* and *MSH2* mutations have the highest incidence risks and the widest array of possible cancer manifestations. Mutations in *MSH2* also has the highest risk for ovarian cancer, approximately 8-12% lifetime risk (Chen, 2007; Bonadona, 2011). Carriers of the *MSH6* mutation have the highest risk for endometrial cancer, at 16-61% lifetime risk (ACOG Practice Bulletin, 2014). The cancer risks for the *PMS2* mutation carriers fall at the lower end of the previously listed ranges, at 15% (Cohen, 2014). Due to the close interaction between *EPCAM* and *MSH2*, individuals with an *EPCAM* mutation have similar CRC risks as *MSH2*, but a reduced risk for endometrial cancer (Kempers, 2011).

For healthcare providers, it is important to note that LS features differing rates of penetrance depending on the genotype, and variable expressivity of cancers between family members with the same mutation (Cohen, 2014).

Genetic testing for LS is recommended for individuals who meet specific clinical and pathological guidelines. The original Amsterdam Criteria stipulated that in order to qualify for a clinical diagnosis of LS, an individual would need to have at least three family members affected with CRC, two successive generations of affected individuals, and at least one diagnosis of CRC before the age of 50 (Vasen, 1991). However, this criterion did not account for the extracolonic manifestations of LS and was later revised to require a family history of "LS-associated cancers" instead of just CRC (Vasen, 1999). The Revised Bethesda Guidelines were developed to identify patients at risk for LS who did not meet the Amsterdam Criteria, and included a MSI evaluation and immunohistochemical staining (IHC) the individual's CRC or endometrial tumor. If a biopsy was found to have a high load of MSI, it would raise suspicion for the presence of a germline MMR mutation. An IHC assay screens for the present or absence of MMR proteins in the tumor biopsies, which can indicate the presence of a germline mutation (Umar, 2004).

Identification of individuals at-risk for LS through these screening modalities and subsequent cascade testing is extremely important, as screening and preventative measures can be taken to improve overall morbidity and mortality. At-risk individuals are referred to genetic counseling for education about the medical, psychological, and familial implications of the disorder, the commencement of genetic testing, and the disclosure of the results (Vig, 2012). Once a diagnosis of LS is confirmed, there are

detailed management protocols that can be implemented. The National Comprehensive Cancer Network (NCCN) guidelines recommend increased surveillance for CRC through annual colonoscopies. The commencement age for the colonoscopy does not differ by the culprit gene: *MLH1*, *MSH2*, *MSH6*, *PMS2* and *EPCAM* mutation carriers should begin at 20-25 years. Colonoscopies should begin 2-5 years prior to the earliest diagnosed CRC in the family, and be repeated every 2-3 years. Screening for endometrial and ovarian cancer can include annual endometrial sampling, serum CA-125 assays and transvaginal ultrasound; however, there is no clear evidence supporting this screening, as the available modalities do not have sufficient sensitivity or specificity. A prophylactic total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) is recommended as a risk-reducing option after the completion of childbearing. There is no evidence supporting screening for gastric and small bowel cancers, but select individual or families may consider an esophagogastroduodenoscopy every 3-5 years beginning at 30-35 years. An annual urinalysis beginning at 30-35 years will screen for cancers of the urinary tract. A neurologic examination for CNS tumors can begin at 25-30 years. There are no screening recommendations for cancers of the hepatobiliary tract and pancreas. Finally, patients of reproductive age should be advised about options for prenatal diagnosis of LS and assisted reproductive technologies (ART), as well as the risk for Constitutional Mismatch Repair Deficiency syndrome (CMMRD) in offspring (NCCN, Version 2.2016).

1.2 Implications of Lynch Syndrome on Fertility

A diagnosis of LS can have significant implications on an individual's fertility and reproductive options. Individuals with LS are at a substantially increased risk for developing early onset colorectal cancers. Treatment for CRC can include chemotherapy, radiation therapy and surgical resection of the tumor. Different chemotherapeutic agents will have different levels of gonadotoxicity. For example, adjuvant therapy with fluorouracil (5-FU) will have little effect on fertility, but treatment with oxaliplatin may cause irreversible premature ovarian failure (POF). Radiation therapy is commonly used to treat rectal cancers, often given neoadjuvantly. The ovaries are extremely sensitive to radiation, and the conventional cumulative dose of radiation will cause POF in most women (Zbuk, 2009). Pelvic radiation can have obstetrical and neonatal consequences, most notably increased rates of miscarriage, preterm labor, placental abnormalities and low birthweight. These adverse outcomes are due to myometrial fibrosis, uterine vasculature damage and endometrial injury (Wo, 2009). There may be inherent risks for infertility associated with surgery for CRC. Postoperative adhesion formation in the pelvis can alter the normal anatomic relationship between the uterine tubes and ovaries, resulting in difficulties to conceive (Olsen, 2012).

A study conducted by Stupart et al. (2015) assessed the fertility rates of unaffected MMR mutations carriers and affected carriers with a CRC diagnosis. For the purposes of this study, "total fertility rates" was defined as the average number of children a hypothetical cohort of affected women would have if they had children at the population age-specific rate during their entire life. Total fertility for women with a CRC diagnosis decreased by almost 40% in comparison to the unaffected group. While this

appears to be a large reduction, the authors noted that the decision to have children is influenced by many psychosocial factors. Nevertheless, cancer-related mortality and morbidity, and effects of surgery and therapy can all be expected to play a role in the decrease of fertility observed in women with CRC. It is also important to note that, while fertility concerns may be incorporated as deciding factors, the exact management of CRC should be tailored to each patient's presentation, with the pros and cons of the chosen treatments weighed accordingly (Zbuk, 2009).

The incidence of gynecologic cancers equals or exceeds the incidence of colorectal cancers in female patients with LS (Mills, 2014). LS is responsible for a high proportion of endometrial cancer cases diagnosed below the age of 45, approximately 9-12% (Dorais, 2011). In the treatment of gynecologic malignancies in young adults, the interventions to spare fertility are concentrated on less radical surgery or a lower dose of drug therapy to spare the reproductive organs as much as possible for subsequent fertility (Lee, 2006). The standard treatment for endometrial cancer is a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) with a retroperitoneal lymphadenectomy (Dorais, 2011). Young women can pursue fertility-sparing options, which entail a dilation and curettage of the lesion followed by non-gonadotoxic chemotherapy or hormone management. The conservative approach to cancer treatment is only available for low-grade tumors that are confined to the endometrium; any patient who chooses this option must be informed of the risk of an undiagnosed synchronous or metasynchronous endometrial tumor, and the increased risk for relapse (Bovicelli, 2012; Hahn 2009). Alternately, immediate hysterectomy with ovarian conservation is another option for patients who wish to attempt pregnancy using a gestational carrier. However,

the rate of concurrent ovarian cancer in patients with premenopausal women with endometrial cancer is approximately 11-29% (Evans-Metcalf, 1998). This is likely exacerbated in women with Lynch Syndrome, whose baseline risk of ovarian cancer increased above the general population. The type of treatment will depend on the type of ovarian cancer, but the main treatment is surgery with debulking, with or without chemotherapy. The feasibility of fertility sparing surgery as a treatment for ovarian cancer is still hotly debated; this is especially due to the fact that ovarian cancer is the most lethal gynecologic malignancy and the majority of women present in advanced stages (Ditto, 2014; Raja, 2012).

While endometrial surveillance may be effective, the value of surveillance for ovarian cancer is still under debate (Helder-Woolderink, 2016). The sensitivity and specificity of CA-125 screening is known to be poor, and ultrasound detection has many limitations, including the variation in result interpretation (Rauh-Hain, 2011). The most effective means of reducing cancer mortality is through risk-reducing surgery (RRS). Women with Lynch Syndrome are recommended to consider a total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) upon the completion of childbirth (NCCN, Version 2.2016; Chapman, 2015). However, the temporal pressure to pursue RSS has been shown to be a cause of anxiety in women of reproductive age. A study by Donnelly et al. (2013) assessed reproductive decision-making in young women who were carriers of a *BRCA1/*2 mutation; these mutations will predispose individuals to increased risk for breast and ovarian cancer. That study found that these perceived pressures caused distress in the patients and complicated social relationships. In addition, a major disadvantage of a TAH-BSO is the early onset of menopause, which can have an

increased risk of cardiovascular disease, loss of bone density, vaginal dryness, mood disturbances, and reduced libido (Chapman, 2015).

The field of fertility preservation is rapidly expanding to include multiple experimental and non-experimental options for female patients. Gonadal shielding during radiation or ovarian transposition (oophoropexy) away from the radiation field can be executed to reduce the amount of radiation damage to the ovaries. This technique, however, does not protect the uterus from radiation damage. Embryo and oocyte cryopreservation are established fertility preservation methods. These techniques require ovarian stimulation and harvesting, which can delay therapy, and involve expensive costs based on insurance coverage (Lee, 2006). Ovarian tissue cryopreservation is an experimental option that does not require ovarian stimulation, but does involve a laparoscopic procedure; it is a potential option for patients who need to urgently undergo aggressive therapy (ASRM, 2014). Fertility preservation options each come with risks, advantages and disadvantages. Interdisciplinary cooperation between surgeons, oncologists, gynecologists, reproductive endocrinologists and other healthcare providers is necessary for at-risk patients so that individualized options can be offered in advance of or concurrently with surgery or adjunctive treatment (Spanos, 2008). Some individuals may be concerned about the familial transmission of LS; due to the genetic nature of the condition, patients have a 50% chance of passing on their MMR mutation to their offspring. Prenatal diagnosis can be offered to expectant couples to determine the mutation status of a pregnancy. Preimplantation genetic diagnosis (PGD), offered in conjugation with an *in vitro* fertilization (IVF) cycle, allows for the identification of embryos lacking the familial mutation to be selected for implantation (Simpson, 2016).

1.3 Informational Exchange between Healthcare Providers and Patients

Providing patients and their families with adequate information concerning treatment and care is an ongoing challenge in most healthcare organizations. Kullberg et al. (2015) sought to evaluate patients' opinions on information provision in oncology wards. This study used patient satisfaction to measure the quality of care as perceived by the patients. Researchers concluded that there are deficits in the information exchange between hospitalized cancer patients and healthcare staff, and that adequate information is a prerequisite for patient participation in their own care. The issue of insufficient information exchange can therefore affect many areas of a patient's care. Finney Rutten et al. (2016) found that individuals affected with cancer report challenges acquiring information for decision-making throughout their care. This study found that information seeking among cancer patients has increased from 66.8% in 2003 to 80.8% in 2013, and is likely to continue increasing. Another important finding was that the most frequently listed first sources of information were healthcare providers and the Internet. Deficits in information exchange may be due to providers not rising to meet the increased information needs of their patients. It has been previously observed that communication difficulties exist in regards to fertility in cancer. In a recent study, participants reported that oncology care and fertility care were provided independently of each other, leading to fragmentation in both care and information provision (Goossens, 2015).

The American Society of Clinical Oncology (ASCO) states that oncologists are responsible to inform patients about the possible risks for impaired fertility associated with their cancer treatment and refer interested patients to reproductive specialists (Lee, 2006). However, Partridge et al. (2004) surveyed male and female cancer survivors of

reproductive age, and discovered that a least half have no memory of a discussion of fertility at the commencement of their treatment. In the participants that did recall an infertility discussion, most were dissatisfied with the quality and amount of information provided. Another study by Strong et al. (2007) echoes a similar sentiment. This study sought to quantify the incidence of fertility counseling in women of reproductive age prior to treatment for colorectal cancer. Based on medical records, less than 20% of women of reproductive age had documentation of counseling for post-treatment fertility. An ASCO special article hypothesized reasons why oncologists may not disclose fertility information: physicians are likely to prioritize discussions about immediate complications of a cancer diagnosis instead of discussing the potential for infertility (Lee, 2006). If oncologists are not disclosing this information, it creates a knowledge gap for patients. In some centers, a nurse specialist is able to fill this gap. Kelvin et al. (2016) compared satisfaction with the amount of fertility-related information received between reproductive-aged patients who did and did not receive counseling from a fertility clinical nurse specialist. The study found that patients benefited from additional in-depth counseling and education about fertility-related information. While the above evidence listed is not specific to Lynch Syndrome, it is applicable to the care of patients with LS due to their risk for early onset cancers that can influence their fertility. Oncologists and other healthcare providers may be providing fertility-based information to LS patients affected with cancer, but are likely not even in contact with presymptomatic carriers.

Genetic counseling is a recommended platform for the discussion of the cancer risk and management options for patients diagnosed with a hereditary cancer syndrome. The genetic counselor is equipped to comprehensively review the clinical consequences

of Lynch Syndrome with both at-risk patients and newly diagnosed cancer patients. Few other healthcare providers are involved with the discussion of risks for presymptomatic carriers as well as those affected with an LS cancer. Presymptomatic carriers are a population that can take advantage of increased surveillance, RRS and family planning. Genetic counselors are also involved with conversations related to reproductive concerns for this population, including the risk of transmission to offspring and the option of PGD (Biesecker, 2001). Previous research has revealed that cancer genetic counselors consider discussions of fertility preservation to be a part of their role (Volk, 2012). Goetsch et al. (2016) found that reproductive endocrinologists utilize genetic counselors for the care of individuals with an inherited cancer syndrome in regards to fertility preservation and PGD. Therefore, genetic counselors have a role in the fertility-related care of individuals with an inherited cancer syndrome, and may be the best resource to bridge the knowledge gap in regard to fertility for patients with LS.

1.4 Fertility-Related Informational Needs in Hereditary Cancer Syndromes

Another common hereditary cancer syndrome is the Hereditary Breast and Ovarian Cancer Syndrome (HBOC), a condition that is caused by mutations in the *BRCA1* and *BRCA2* genes. Mutation carriers have greater than an 80% lifetime risk for breast cancer and 40% risk for ovarian cancer by age 70 (Metcalfe, 2000). There have been several studies that have evaluated fertility-related information concerns in the *BRCA1/2* mutation carrier population. Quinn et al. (2010) assessed the informational needs of *BRCA* mutation carriers regarding issues of infertility and fertility options. Participants in this study expressed a strong desire for assistance with decision-making

and a need for better presentation of available fertility options. Another study by Kim et al. (2015) evaluated patient knowledge of the clinical impact of a BSO and views of fertility consultations in this patient population. It was noted that patients would benefit from additional emphasis on fertility in all of their appointments with healthcare providers, including genetic counseling. Studies in HBOC maybe generalizable to other hereditary cancer syndromes, including LS. It may be a trend in hereditary cancer syndromes that carriers need more accessible information regarding their fertility. However, because there are different cancer risks between individuals with HBOC and LS, there are different fertility concerns between these two populations. A practice guideline released by the National Society of Genetic Counselors (NSGC) states that the genetic counselor should include a provision of extensive client resources, including information concerning fertility and reproductive choices, when counseling an individual with a *BRCA1/2* mutation (Berliner, 2012). There has not been a similar guideline released in regards to LS.

In comparison to the extensive amount of data collected on the informational needs of *BRCA1/2* carriers, very few studies have investigated the needs of patients with LS. It can be expected that a deficit of information also exists in LS, but there is little research available on this topic. Using data collected from support groups for LS, a study by Corines et al (2016) advocated that increased knowledge empowers patients with LS to take a proactive role in their own health management. A previous study by Bannon et al. (2014) examined the educational and information needs of individuals with LS, but this assessment did not explore the informational needs related to fertility and reproduction. Therefore, it is important to establish the exact informational needs of this

population in order for adequate information provision. Of note, a study by Burton-Chase et al. (2017) found that LS CRC survivors reported lower levels of satisfaction with their healthcare providers than sporadic CRC survivors, particularly in regard to communication. This noted lack of satisfaction may exist broadly for individuals with LS.

Current studies regarding fertility and reproduction in patients with LS have only examined the attitudes towards reproductive decision-making for childbearing, prenatal genetic testing and assisted reproductive technologies (ART). Dewanwala et al. (2011) compared patient attitudes towards childbearing and prenatal testing before and after genetic testing for LS. This study's findings suggest that individuals with LS are interested in prenatal testing and PGD, and would consider having children earlier to allow for earlier RRS. Duffour et al. (2015) reported distress among MMR mutation carriers in regards to reproductive-decisions making, and increased interest in ART a year after genetic testing. These two studies prove that women with Lynch Syndrome are interested in the topics of fertility and reproduction, but they do not identify how and when these topics are being presented to patients. Thus far, there have not been any studies conducted that assess the need for information pertaining to the fertility implications of Lynch Syndrome in the reproductive-aged patient population.

Chapter 2. Assessment of Patient Satisfaction with the Provision of Fertility Information in Women with Lynch Syndrome

2.1 Abstract

Lynch Syndrome (LS), one of the most common hereditary cancer syndromes, is primarily known for its substantially increased risks for colorectal cancer. The incidence of gynecologic cancers (endometrial and ovarian cancers) equals or exceeds the incidence of colorectal cancers in female patients with LS. The prevention and treatment methods for these cancers can drastically affect fertility and reproduction. Previous studies with cancer patients have revealed challenges in acquiring information related to these topics; thus far, no research has assessed whether there is an informational gap regarding fertility information for women in the LS population. The purpose of this study was to identify the amount of information received related to fertility and reproduction, assess patient satisfaction, and characterize current practices of this information delivery within our target patient population.

Data was collected from 154 women with LS. Likert scales were used to quantify the amount of information provided about major themes pertaining to fertility in LS: effects of cancer treatment, risk-reducing surgeries, fertility preservation and family planning. Overall, participants were more satisfied when they received more information about certain topics within these themes. There was a distinct lack of individualization in patient care, and lack of uniformity regarding the provision of this information among healthcare providers. Participant opinions indicate that genetic counselors may be an

untapped resource in the provision of fertility and reproduction information to this population.

2.2 Introduction

Lynch Syndrome (LS) is one of the most common hereditary cancer syndromes, with an estimated population prevalence of 1 in 400 (Nagy, 2004). LS accounts for 2-4% of all colorectal (CRC) cancers (Barrow, 2013) and affected individuals have as high as a 75% lifetime risk of developing CRC (Cohen, 2014). The median age of diagnosis is between 44-61 years of age, with approximately 50% of all CRC tumors occurring below the age of 50. Female carriers of LS have a 15-61% risk for developing endometrial cancer, which is much higher than the 1.7% risk of the general population (Cohen, 2014; ACOG Practice Bulletin, 2014). The incidence of ovarian cancer in the general population is 1.4%, but females with LS are at an increased risk for ovarian cancer (approximately 6.7-12%). Similar to CRC, both the endometrial and ovarian cancers in LS manifest at earlier ages than the general population. Additional cancers associated with Lynch Syndrome include the risk for gastric, urinary tract, hepatobiliary, pancreatic and CNS.

The risk values for the colonic and extracolonic cancers depend on the genetic variant inherited in a family, and the sex and age of the affected individual (Tiwari, 2016). LS is caused by a germline mutation in one of the genes involved in the DNA mismatch repair (MMR) pathway: *MLH1*, *MSH2*, *MSH6*, *PMS2,* or *EPCAM* (Lynch, 2015). Individuals with *MLH1* and *MSH2* mutations have the highest incidence risks and the widest array of possible cancer manifestations. Mutations in *MSH2* also has the

highest risk for ovarian cancer, approximately 8-12% lifetime risk (Chen, 2007; Bonadona, 2011). Carriers of *MSH6* mutations have the highest risk for endometrial cancer, at 16-61% lifetime risk (ACOG Practice Bulletin, 2014). The cancer risks for the *PMS2* mutation carriers fall at the lower end of the previously listed ranges, at 15% (Cohen, 2014). Due to the close interaction between *EPCAM* and *MSH2*, individuals with an *EPCAM* mutation have similar CRC risks as *MSH2*, but a reduced risk for endometrial cancer (Kempers, 2011). For healthcare providers, it is important to note that LS features differing rates of penetrance depending on which gene is mutated, and variable expressivity of cancers between family members with the same mutation (Cohen, 2014).

A diagnosis of Lynch Syndrome can have significant implications on a woman's fertility and reproductive options, particularly due to the incidence and early onset of CRC, endometrial and ovarian cancers. Treatment for CRC can include chemotherapy, radiation therapy and surgical resection of the tumor, all of which can disrupt the fertility of a patient (Zbuk, 2009; Wo, 2009; Olsen, 2012). There are inherent risks for infertility associated with surgery for CRC, as postoperative adhesion formation in the pelvis can alter the normal anatomic relationship between the uterine tubes and ovaries, resulting in difficulties to conceive (Olsen, 2012). A study conducted by Stupart et al. (2015) assessed the fertility rates of unaffected MMR mutations carriers and affected carriers with a CRC diagnosis: total fertility for women with a CRC diagnosis decreased by almost 40% in comparison to the unaffected group. While there are many factors that influence the decision to have children, the effects of surgery and therapy for CRC are likely strong modifiers.

The incidence of gynecologic cancers equals or exceeds the incidence of colorectal cancers in female patients with LS (Mills, 2014). In the treatment of endometrial malignancies in young women, the interventions to spare fertility are concentrated on less radical surgery or a lower dose of drug therapy to spare the reproductive organs as much as possible for subsequent fertility (Lee, 2006). Fertility sparing options may be available for ovarian cancer, but its feasibility is still debated as ovarian cancer is the most lethal gynecologic malignancy and the majority of women present in advanced stages (Ditto, 2014; Raja, 2012).

While endometrial surveillance may be effective, the value of surveillance for ovarian cancer is still disputed (Helder-Woolderink, 2016). The most effective means of reducing gynecologic cancer mortality is through risk-reducing surgery (RRS), and women with LS are recommended to consider a total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO) upon the completion of childbirth (NCCN, Version 2.2016). Choosing a TAH-BSO does come an array of disadvantages, including the early onset of menopause (Chapman, 2015). Donnelly et al (2013) studied reproductive decision-making in young patients with another hereditary cancer syndrome, Hereditary Breast and Ovarian Cancer (HBOC), and found that the temporal pressures to pursue RSS cause an increase in distress and social complications for the patient, particularly in women who have not yet completed childbearing.

The field of fertility preservation can provide options for women in the LS population; these options can offered in advance of or concurrently with surgery or adjunctive treatment (Spanos, 2008). These options include gonadal shielding during radiation, ovarian transposition, embryo cryopreservation, etc. (Lee, 2006; ASRM, 2014).

Women with LS also have options for reproductive decision-making. Prenatal diagnosis can be offered to expectant couples to determine the mutation status of a pregnancy. Preimplantation genetic diagnosis (PGD), offered in conjugation with an *in vitro* fertilization (IVF) cycle, allows for the identification of embryos lacking the familial mutation to be selected for implantation (Simpson, 2016).

Interdisciplinary cooperation between healthcare providers is necessary to offer individualized options to at-risk patients, but providing patients with adequate information concerning treatment and care is an ongoing challenge. Finney Rutten et al. (2016) found that individuals affected with cancer report challenges acquiring information for decision-making throughout their care. These communication difficulties certainly exist in regard to fertility and cancer. In a recent study, participants reported that oncology care and fertility care were provided independently of each other, leading to fragmentation in both care and information provision (Goossens, 2015). Kelvin et al. (2016) compared satisfaction with the amount of fertility-related information received between reproductive-aged patients who did and did not receive additional counseling about fertility options. The study found that patients benefited from additional in-depth counseling and education about fertility-related information.

The American Society of Clinical Oncology (ASCO) states that oncologists are responsible to inform patients about the possible risks for impaired fertility associated with their cancer treatment and refer interested patients to reproductive specialists (Lee, 2006). However, Partridge et al. (2004) surveyed male and female cancer survivors of reproductive age, and discovered that a least half have no memory of a discussion of fertility at the commencement of their treatment. In the participants that did recall an

infertility discussion, most were dissatisfied with the quality and amount of information provided. Another study by Strong et al. (2007) sought to quantify the incidence of fertility counseling in women of reproductive age prior to treatment for colorectal cancer. Based on medical records, less than 20% of women of reproductive age had documentation of counseling for post-treatment fertility. An ASCO special article hypothesized reasons why oncologists may not disclose fertility information: physicians are likely to prioritize discussions about immediate complications of a cancer diagnosis instead of discussing the potential for infertility (Lee, 2006). This hypothesis may be true of other providers as well, such as gynecologists, reproductive endocrinologists, etc. If healthcare providers are not disclosing this information, it creates an informational disparity for patients.

Genetic counselors may be the best resource to bridge the knowledge gap in regard to fertility for patients with LS. While oncologists and other healthcare providers may be providing fertility-based information to LS patients affected with cancer, these providers are likely not in contact with presymptomatic carriers, another group that would benefit greatly by a discussion of the fertility risks in LS. Genetic counseling is a recommended platform for the discussion of the cancer risk and management options for patients diagnosed with a hereditary cancer syndrome, including presymptomatic carriers and diagnosed cancer patients. They are equipped to manage conversations related to reproductive concerns for this population, including the risk of transmission to offspring and the option of preimplantation genetic diagnosis (PGD) (Biesecker, 2001). Previous research has revealed that cancer genetic counselors consider discussions of fertility preservation to be a part of their role (Volk, 2012). Goetsch et al. (2016) found that

reproductive endocrinologists utilize genetic counselors for the care of individuals with an inherited cancer syndrome in regards to fertility preservation and PGD. Increased emphasis by genetic counselors on topics related to fertility may benefits patients. However, there is a lot unknown about the current practices in fertility information provision; characterization of current practices is necessary in order to consider the implementation new techniques.

The available research regarding informational needs about fertility and reproduction in LS is limited. However, there have been several studies that have evaluated the fertility-related information concerns of individuals in the HBOC population. Quinn et al. (2010) found a strong desire for assistance with decision-making and a need for better presentation of available fertility options. Another study by Kim et al. (2015) evaluated patient knowledge of the clinical impact of a prophylactic BSO and views of fertility consultations in the HBOC population. It was noted that patients would benefit from additional emphasis on fertility in all of their appointments with healthcare providers, including genetic counseling. These studies indicate that, overall, there needs to be a more focused provision of fertility information to mutation carriers in HBOC. It can be expected this fertility-related information deficit also exists for patients with LS. Current studies regarding fertility and reproduction in patients with LS have only examined the attitudes towards reproductive decision-making for childbearing, prenatal genetic testing and assisted reproductive technologies (Dewanwala, 2011; Duffour, 2015). The available research indicates that women with LS are interested in the topics of fertility and reproduction, but thus far, no research has assessed the information gap regarding fertility and reproduction information for this patient population. This study

sought to evaluate the current practices of information delivery by identifying the amount of information received on specific topics related to fertility and reproduction, assess patient satisfaction of the disclosure of this information, and identify ways to establish a more comprehensive care regimen for women with LS.

2.3 Materials and Methods

Study Population

This research study collected quantitative and qualitative data from women with LS. From this population, both presymptomatic women and women affected with cancer were invited to participate. However, individuals were required to meet specific eligibility criteria in order to proceed with the questionnaire. The eligibility criteria ensured that only the opinions of the targeted patient population would be captured by the study. Participants must have been diagnosed with LS at a reproductive age, which for the purposes of this study is defined as between the ages of 18-45. Participants were also required to have a known pathogenic mutation in an MMR gene; pathogenic mutations are clinically actionable, and would therefore warrant the initiation of an appropriate management protocol. Additionally, there was specific exclusionary criteria: participants with a recent diagnosis who have not returned for a follow-up appointment with their healthcare provider were excluded from this study, as their initial appointment may not have covered all of the relevant information to pertaining to their diagnosis with LS. Males were also excluded from participating in the questionnaire, as the fertility concerns for LS differ between men and women. Eligibility and ineligibility were determined by a series of questions at the beginning of the survey; participants who were determined to be

ineligible were skipped out of the questionnaire using the branch logic function of the survey programming software provided by SurveyMonkey.com.

Survey Distribution

Participants were recruited by an invitational flyer (Appendixes A and B) to take the online survey. The principle investigator contacted different online support organizations for individuals with cancer via e-mail to request participation. The e-mail request explained the purpose of the research study and asked for assistance in distributing the invitation and link for the online survey to its members. The invitation was distributed through the following organizations: the Hereditary Colon Cancer Foundation, I Have Lynch Syndrome, Inc., Lynch Syndrome International, and the Oncofertility Consortium. The participating organizations circulated the invitations through e-mailing lists, websites, Facebook pages, Twitter, and other mediums of communication. The survey link was issued between September and October 2016, and was available for completion through December 15, 2016.

Instrumentation

For this research study, an original online survey was developed through SurveyMonkey.com. The principle investigator constructed the questionnaire (Appendix C), which was comprised of both quantitative and qualitative questions, following a mixed methods research model. Quantitative questions were used to measure categorical information about the participants, while the qualitative questions were used to provide deeper insight into the participants' experience in regard to fertility and LS. The questionnaire consisted of a series of multiple choice, Likert scale, and free response questions designed to assess the participant's overall satisfaction with the fertility-related

information given to them by their healthcare provider(s) upon or after their diagnosis of LS. Within the questionnaire, definitions were provided for some of the terminology used in order to promote participant comprehension. The consent agreement was provided on the first page of the questionnaire (Appendix D); in order to move forward in the questionnaire, participants needed to indicate their consent.

Standard demographic information obtained related to the participant's current age, gender, level of education, relationship status, country and region of residency, and ethnicity. The survey also included questions specific to LS in order to further categorize the participants: age at diagnosis, relationship status at the time of diagnosis, familial MMR gene, and whether or not the participant was affected with cancer at the time of their diagnosis. The demographic and categorical data provided variables for correlation studies during the statistical analysis.

The rest of the questionnaire was divided into four sections, which each focused on a different aspect of fertility concerns in LS: effects of cancer treatment, prophylactic surgery, fertility preservation, and family planning. All four sections had a similar composition of questions. Each section had a Likert scale, which aimed at assessing the amount information provided about specific topics related to the section heading. Other questions in the sections evaluated additional features of information provision, such as the timing of the information provision and the healthcare provider involved. The final question in each section assessed the participant's overall satisfaction with the information provided for the topics; this part of the questionnaire format was adapted from a previous study by Kelvin et al. (2016). For this question, participants could select whether they were "satisfied," "not satisfied," or "not interested" in the topics covered by

that section. Participants also had the option of providing additional comments at the end of every section. The last series of questions in the survey focused on the utility of genetic counseling for fertility-related information provision for women with LS.

Data Analysis

Statistical analysis for the quantitative data was conducted using Statistical Package for the Social Sciences 24.0 (SPSS). While the four main sections of the questionnaire were analyzed independently of each other, the same analyses were conducted for each section. The primary assessment focused on how the amount of information provided about specific topics modified the satisfaction of the participants; this analysis was conducted via one-way ANOVA. The amount of information provided was quantified by calculating the average response to each item in the Likert scale questions; the response of each item was coded 1 ("I received no information about this topic") through 5 ("I received a lot of information about this topic").

A series of additional one-way ANOVAs were conducted to assess for association between the amount of information provided and other modifying variables. The variables were dichotomous to allow for comparisons: individuals affected with cancer vs. presymptomatic carriers, individuals who had completed childbearing vs. those that had not completed childbearing, and a comparison between the gene implicated in the family. Chi-Square for association tests were conducted to assess overall satisfaction between difference groups of participants. Pearson's correlation and descriptive statistics were used to evaluate the rest of the data, including demographic information, and information collected about healthcare providers, and topics discussed by genetic counselors.

Responses to the open-ended questions were analyzed through inductive analysis, and organized based on common themes. The themes were coded by the principle investigator and reviewed by all authors. Participants' responses to these questions were brief and covered a limited range of topics; however, they offered valuable insight into the personal experience of the participants.

In order to maximize the amount of data collected in this study, partially completed surveys were included in the data analysis. Participants needed to have completed at least two out of the four sections to be included in the analysis

2.4 Results

Eligibility

Of the 274 individuals that began the questionnaire, 172 met the eligibility criteria. Ineligible participants included men (N=2), minors (N=2), individuals diagnosed with LS after the age of 45 (N=62), individuals without a known pathogenic variant in an MMR gene (or *EPCAM*) (N=14), and individuals who did not return to their healthcare provider after their diagnosis (N=9). Of the 172 participants who met the eligibility criteria, 18 individuals did not complete at least two of the four major sections within the questionnaire. This resulted in a total of 154 participants who were both within our target population and had completed at least half of the questionnaire.

Demographics

The demographic information for the participants in this study is depicted in Table 2.1. The majority of women who participated in this study were between the ages of 36-45 (40.2%), Caucasian (95.4%), married (72.0%), college-educated (43.8%), and

living in the United States (85.4%). Almost half (46.1%) were diagnosed with LS between the ages of 26-35. Participants were asked to report which gene was responsible for their LS: *MLH1* was reported by 28.6%, *MSH2* by 44.8%, *MSH6* by 13.6%, *PMS2* by 11.7%, and *EPCAM* by 1.3%.

Most of the participants (61.7%, N=95) were presymptomatic at the time of their diagnosis with LS, indicating that they had pursued predictive genetic testing (referred to in this study as "presymptomatic carriers"). The remaining 38.3% (N=59) were diagnosed with cancer before they were found to have LS (Table 2.2). Participants were asked to report which cancer(s) they were diagnosed with: 58.8% reported colorectal cancer, 19.1% reported endometrial cancer, 8.8% reported ovarian cancer, and 13.2% selected "Other." Those that selected "Other" reported a variety of cancers, including breast, thyroid, and sebaceous carcinoma. Of note, many individuals reported multiple cancers at early ages of onset, which is not unexpected within this patient population.

Participants were asked to report their status in family planning at the time of their diagnosis with LS. Individuals who had completed their family prior to their diagnosis accounts for 48.7% (N=75). The remaining 51.3% (N=79) had not yet completed their family (Table 2.2).

Cancer Risks and Effects of Cancer Treatment

This section of the questionnaire collected data on the amount of information provided to the participants about cancers risks and the effects of cancer treatment on fertility. Skip logic was used to identify participants who have spoken with their healthcare provider about the potential impacts of cancer treatment on fertility. Only 34.4% (N=53) of participants completed the corresponding section of the questionnaire.

A one-way ANOVA was conducted to determine if the satisfaction status of the participants was altered depending on the amount of information provided about a given topic relating to cancer risks in LS and the effects of cancer treatment on fertility (Table 2.3). There was a trend towards statistical significance ($p \leq .05$) for one topic ("The risk for cancer will differ based on your gene") [$F(2, 50)=3.010$, $p=.058$]: individuals who received more information about this topic reported satisfaction with their experience.

A one-way ANOVA was conducted to identify whether or not there is a difference in the amount of information provided about the topics in this section to individuals that were affected with cancer at the time of their diagnosis with LS and presymptomatic carriers with LS (Table 2.4). Statistically significant differences were observed for one topic: "The risk for cancer will differ based on your gene" [$F(1, 52)=4.828$, $p=.032$]. Additionally, a trend toward statistical significance was noted for "The effects of radiation on your reproductive organs" [$F(1, 51)=3.513$, $p=.067$]. For these two topics, presymptomatic carriers received more information than individuals affected with cancer.

A one-way ANOVA was conducted to establish whether there was a difference in the amount of information provided between individuals who had completed their family and those who had not completed their family at the time of their diagnosis with LS (Table 2.5). There were no statistically significant findings observed.

A one-way ANOVA was conducted to examine whether or not there was a difference in LS. There were no statistically significant findings observed.

In order to identify the healthcare providers involved in the provision of this information, participants were provided a list of healthcare providers and asked to select

the provider(s) who discussed with them information about cancer risk and the effects of cancer treatment (Figure 2.1). The majority of participants selected oncologist (33.0%, N=29), and the second most frequently selected provider was genetic counselor (24.0%, N=21). Only 2.0% of participants (N=5) reported that no healthcare provider discussed the information with them. Next, the participants were asked to select the healthcare provider was most effective at discussing this information: 43.0% of individuals selected oncologist and 26% selected genetic counselor.

Pearson's correlation was run to assess the relationship between the timing of the information and participant satisfaction. There was a statistically significant negative correlation (r^2=-.386, p=.004) between these variables: individuals who received information about these topics greater than 6 months after their diagnosis with LS were less satisfied.

Finally, participants were asked to share any comments they had about this section of the survey. Many participants reported that the treatment of their cancer took precedence over every other concern (N=8). One participant stated:

> "I was more overwhelmed with my cancer diagnosis and cancer treatment. (Treatment) was a priority, but more information (about the effects) would have been nice."

Others participants revealed that they would have preferred a more focused discussion about the effects on cancer treatment on fertility (N=5):

> "I would have preferred to have had more of a conversation about my options with a specialist in fertility. I also would have liked follow up appointment/s post-treatment to assess if my fertility had been effected."

Risk-Reducing Surgery

This section of the questionnaire collected data on the amount of information provided to the participants about the risk-reducing surgical options for women with LS. Skip logic was used to identify participants who have spoken with their healthcare provider about risk-reducing surgeries. The majority of participants, 85.7% (N=132), completed this part of the questionnaire. More than half (51.5%, N=68) reported that they had some type of prophylactic surgery at the time of this questionnaire, and 58.8% (N=40) of those participants were presymptomatic carriers.

A one-way ANOVA was conducted to determine if the satisfaction status of the participants was altered depending on the amount of information provided about a given topic relating to risk-reducing surgery options (Table 2.6). Statistically significant differences were observed for five of six topics: "The timing of a risk-reducing hysterectomy" [$F(2, 128)=6.875$, $p=.001$], "The timing of a risk-reducing oophorectomy" [$F(2,128)=9.617$, $p=.000$], "My family history should be considered when planning for a risk-reducing surgery" [$F(2,127)=5.247$, $p=.006$], "The side effects of a risk-reducing oophorectomy before menopause" [$F(2,128)$, $p=.000$], and "The option of a risk-reducing hysterectomy with ovarian preservation" [$F(2,128)=7.160$, $p=.001$]. For these topics, individuals who received more information about this topic reported satisfaction with their experience.

A one-way ANOVA was conducted to identify whether or not there is a difference in the amount of information provided about the topics in this section to individuals that were affected with cancer at the time of their diagnosis with LS and presymptomatic carriers with LS (Table 2.7). Statistically significant differences were

observed for two topics: “The option of a risk-reducing hysterectomy with ovarian preservation” [F(1, 130)=4.828, p=0.32], and “The use of birth control to reduce my cancer risk” [F(1, 130)=4.183, p=.043]. For these two topics, presymptomatic carriers received more information than individuals affected with cancer.

A one-way ANOVA was conducted to establish whether there was a difference in the amount of information provided between individuals who had completed their family and those who had not competed their family (Table 2.8). Statistically significant findings were observed for two of the six topics: “The side effects of a risk-reducing oophorectomy before menopause” [F(1, 130)=5.861, p=.017], and “The use of birth control to reduce my cancer risk [F(1, 130)=9.473, p=.003]. For these topics, individuals who had completed their families received more information than individuals who had not completed their family.

A one-way ANOVA was conducted to examine whether or not there was a difference in the amount of information provided to the participant based on the gene that caused their LS. There were no statistically significant findings observed.

Participants were provided a list of healthcare providers and asked to select the provider(s) who discussed with them information about risk reducing surgeries (Figure 2.2). The majority of participants selected gynecologist (35.0%, N=77), and the second most frequently selected provider was genetic counselor (33.0%, N=73). Only 1% of participants (N=3) reported that no healthcare provider discussed the information with them. Next, the participants were asked to select the healthcare provider was most effective at discussing this information: 41.0% of individuals selected gynecologist, while 37% selected genetic counselor.

Pearson's correlation was run to assess the relationship between the timing of the information provision about risk-reducing surgeries and participant satisfaction. There were no statistically significant findings.

Participants were asked to share any comments they had about this section of the survey. One theme that emerged is that, prior to having a risk-reducing surgery, there was very little discussion about post-surgery quality of life (N=11). Many individuals reported that they felt that the symptoms of surgical menopause had not been adequately communicated to them.

> "I did not feel like I had enough information on menopause (or) hormone replacement options instead (of surgery)."

Another theme was the pressure to pursue surgery (N=8). One participant shared:

> "I guess I was made to feel that I didn't have much of a choice if I wanted to avoid cancer. It was presented along the lines that there was no "reason to keep those organs" since I was finished having children. I was made to feel that I was lucky to have not been diagnosed with cancer so far, so (I should) have everything removed immediately."

Another participant said:

> "I did not have cancer but consulted with a gynecologic oncologist. I could tell she was unhappy with my decision to keep one ovary."

Fertility Preservation

This section of the questionnaire collected data on the amount of information provided to the participants about fertility preservation techniques. This section did not

use the Skip Logic function used in the previous sections. Almost all of the participants (97.4%, N=150) completed this section.

A one-way ANOVA was conducted to determine if the satisfaction status of the participants was altered depending on the amount of information provided about a given topic relating to fertility preservation (Table 2.9). Statistically significant differences were observed for all four topics: "The option to shield or move the ovaries during radiation therapy" [$F(2, 140)=7.200$, $p=.001$], "Embryo or egg cryopreservation (freezing)" [$F(2,140)=34.887$, $p=.000$], "Ovarian tissue cryopreservation (freezing)" [$F(2,140)=14.606$, $p=.000$], and "Ovarian stimulation will delay cancer treatment" [$F(2,140)=13.134$, $p=.000$]. For these topics, individuals who received more information about this topic reported satisfaction with their experience.

A one-way ANOVA was conducted to identify whether or not there is a difference in the amount of information provided about the topics in this section to individuals that were affected with cancer at the time of their diagnosis with LS and presymptomatic carriers with LS (Table 2.10). There were no statistically significant findings observed in this analysis.

A one-way ANOVA was conducted to establish whether there was a difference in the amount of information provided between individuals who had completed their family and those who had not completed their family at the time of their diagnosis with LS (Table 2.11). Statistically significant findings were observed for all four topics: "The option to shield or move the ovaries during radiation therapy" [$F(1, 148)=4.375$, $p=.038$], "Embryo or egg cryopreservation (freezing)" [$F(1, 148)=18.915$, $p=.000$], "Ovarian tissue cryopreservation (freezing)" [$F(1, 148)=18.126$, $p=.000$], and "Ovarian stimulation

will delay cancer treatment" [F(1, 148)=8.017, p=.005]. For these topics, individuals who had not completed their families received more information than those that had completed their families.

A one-way ANOVA was conducted to examine whether or not there was a difference in the amount of information provided to the participant based on the gene that caused their LS. There were no statistically significant findings observed.

In order to identify the healthcare providers involved in the provision of this information, participants were provided a list of healthcare providers and asked to select the provider(s) who discussed with them information about fertility preservation (Figure 2.3). The most frequently selected healthcare provider was gynecologist (13.0%, N=21), and the second was oncologist (9.0%, N=14). However, 63.0% of participants (N=102) reported that no healthcare provider discussed the information with them. Next, the participants were asked to select the healthcare provider was most effective at discussing this information: there was no strong consensus, with 31.0% selecting oncologist, and 27.0% selecting gynecologist.

Pearson's correlation was run to assess the relationship between the timing of the information provision about fertility preservation and participant satisfaction. There were no statistically significant findings.

The final question of this section was an open-ended question, requesting participants to share any additional comments. Some participants reported that their healthcare providers appeared to make assumptions about their interest in this type of information (N=5). As one participant described:

> "My doctor was more apt to write off any preservation because I have two children rather than being interested if we wanted anymore."

Another subset of participants revealed that, due to the lack of information they received from their healthcare providers, they had to research these topics themselves (N=7). One participant acknowledged the inequality of the situation, saying:

> "I was satisfied because I was a self advocate and did my own research. I met another young woman who went through treatment a few months before me at the same place, and she did not receive the information I did (because she didn't initiate conversation). This is a huge problem; young women need to be told their options."

Family Planning

This section of the questionnaire collected data on the amount of information provided to the participants about family planning options. This section did not have a Skip Logic function. Again, almost all of the participants (90.3%, N=139) completed this section.

A one-way ANOVA was conducted to determine if the satisfaction status of the participants was altered depending on the amount of information provided about a given topic relating to family planning (Table 2.12). Statistically significant differences were observed for all six topics: "The chance that your children will have Lynch Syndrome" [$F(2, 130)=10.619$, $p=.001$], "The use of an in vitro fertilization (IVF) cycle" [$F(2,130)=15.178$, $p=.000$], "Prenatal diagnosis for Lynch Syndrome" [$F(2,129)=10.284$, $p=.000$], "Preimplantation genetic diagnosis (PGD) for Lynch Syndrome" [$F(2,129)=8.471$, $p=.000$], "Adoption" [$F(2,129)=9.762$, $p=.000$], and "Surrogacy"

[F(2,129)=9.688, p=.000]. For these topics, individuals who received more information about this topic reported satisfaction with their experience.

A one-way ANOVA was conducted to identify whether or not there is a difference in the amount of information provided about the topics in this section to individuals that were affected with cancer at the time of their diagnosis with LS and presymptomatic carriers with LS (Table 2.13). There was a trend towards statistical significance for one topic: "The chance that your children will have Lynch Syndrome" [F(1, 137)=3.496, p=.064]. For this topic, presymptomatic carriers received more information than individuals affected with cancer.

A one-way ANOVA was conducted to establish whether there was a difference in the amount of information provided between individuals who had completed their family and those who had not completed their family at the time of their diagnosis with LS (Table 2.14). Statistically significant findings were observed for all six topics: "The chance that your children will have Lynch Syndrome" [F(1, 137)=15.145, p=.000], "The use of an in vitro fertilization (IVF) cycle" [F(1, 137)=36.238, p=.000], "Prenatal diagnosis for Lynch Syndrome" [F(1, 136)=18.022, p=.000], "Preimplantation genetic diagnosis (PGD) for Lynch Syndrome" [F(1, 136)=18.487, p-.000], "Adoption" [F(1, 136)=21.716, p=.000], and "Surrogacy" [F(1, 136)=19.557, p=.000]. For these topics, individuals who had not completed their families received more information than those that had completed their families.

A one-way ANOVA was conducted to examine whether or not there was a difference in the amount of information provided to the participant based on the gene that caused their LS. One statistically significant finding was observed: individuals who

reported having a mutation in the *EPCAM* gene received less information about these topics than individuals with mutations in *MSH1*, *MLH2*, *MSH6* and *PMS2* [F(4, 134)=2.77, p=.030].

In order to identify the healthcare providers involved in the provision of this information, participants were provided a list of healthcare providers and asked to select the provider(s) who discussed with them information about fertility preservation (Figure 2.4). The most frequently selected healthcare provider was genetic counselor (29.0%, N=47), and the second was gynecologist (9.0%, N=32). Approximately one third (32.0%, N=51) of participants reported that no healthcare provider discussed the information with them. Next, the participants were asked to select the healthcare provider was most effective at discussing this information: 51% selected genetic counselor.

Pearson's correlation was run to assess the relationship between the timing of the information provision about family planning and participant satisfaction. There were no statistically significant findings.

Finally, participants were asked to share any additional comments they had about this section of the questionnaire. The major theme that emerged from this section is the temporal pressure felt by the participants (N=7). One participant shared:

> "My doctor basically told me if I want anymore children I needed to do it (as soon as possible) then consider hysterectomy. That was all I was told."

Overall Satisfaction

A chi-square test for association was conducted for overall reported satisfaction between individuals who were affected with cancer at the time of their diagnosis and presymptomatic carriers. No statistically significant findings were observed. However,

there was a trend toward statistical significance for the section about risk-reducing surgery options [χ^2=4.852, p=.088]: individuals affected with cancer were overall more satisfied then presymptomatic carriers with the information they received about these topics.

A chi-square test for association was conducted for overall reported satisfaction between individuals who had completed their families and individuals who had not completed their families. There were statistically significant findings for three of the four sections: individuals who had completed their family were more satisfied with the information they received about cancer risks and the effects of cancer treatment on fertility [χ^2=15.998, p=.000], fertility preservation [χ^2=20.612, p=.000], and family planning [χ^2=22.615, p=.000]. Additionally, a trend toward statistical significant was observed for the other section: individuals who had completed their families were more satisfied with the information they received about risk-reducing surgery options [χ^2=5.570, p=.062].

Genetic Counseling

The final section of the questionnaire focused on genetic counseling for LS, and was completed by 133 individuals. The majority (81.9%, N=109) reported that they had met with a certified or licensed genetic counselor. Participants were asked to select which topic(s) were introduced to them by their genetic counselor from a list: cancer risk for LS, effects of cancer treatment on fertility, risk-reducing surgeries for LS, fertility preservation options, and family planning options. The most frequently selected topic was cancer risks for LS (reported by 108 participants), followed by risk-reducing surgeries for LS (N=89).

Next, participants were asked to select which topics they would have wanted their genetic counselor to provide more information about regarding their LS diagnosis. The majority of individuals again selected cancer risks for LS and risk-reducing surgeries for LS. There was, however, an increase in the amount of participants who selected the other options (Figure 2.5).

Additional Comments

At the end of the questionnaire, participants were asked to share their final comments about their experience with the topics covered by this research study. From these comments, some important themes emerged. The first was the need for more a more balanced conversation about the effects of cancer treatment on fertility and the aftermath of a risk-reducing surgery (N=6). As one participant illustrated:

> "Be more honest … It was all sunshine and "you're making the best choice; you want to be around for your family." I felt very betrayed after surgery when I had to deal with terrible hot flashes, bladder leakage, skin changes."

Another theme was the psychological stress that comes with a lack of information about their options with LS (N=10):

> "There (were) no answers. Depression is the only definite outcome in Lynch (syndrome)."

2.5 Discussion

This study explored the informational needs of women with LS. The focus of this study was to assess patient satisfaction with the disclosure of information pertaining to fertility and reproduction to women with LS, and to measure the amount of information

provided about these topics to this patient population. Additionally, this research allows us to evaluate the current practices of information delivery by identifying the healthcare provider involved in patient education, timing in relation to diagnosis, and the topics of this discussion. Analysis of these results can allow us to identify areas for improvement in the care and management of women with LS.

Overall, participants were more satisfied with their experience when they received more information. In the section of the questionnaire about cancer risk and the effects of cancer treatment on fertility, we found statistical significance between the amount of information provided and satisfaction for only one topic ("The risk for cancer will differ based on your gene"). For the remaining four topics, the amount of information provided did not affect satisfaction rates. This indicates that "The risk for cancer will differ based on your gene" is an important topic to discuss with patients. In the sections about risk-reducing surgery, fertility preservation and family planning, increased information was associated with increased satisfaction for almost all of the covered topics, which suggests that this information is important to patients, and therefore should be covered in detail by a healthcare provider. Patient satisfaction is an extremely important part of healthcare, and satisfaction is a proven measure of healthcare quality and success (Prakash, 2010). Additionally, satisfaction has been positively correlated with adherence to screening and treatment (Bredart, 2010). These findings prove that tangible changes in the amount of information provided to a patient can alter their satisfaction and improve their healthcare experience.

The Likert scales in this study were utilized to compare the amount of information provided to different categories of participants, and assess the relationship between

participant satisfaction and information provision. These measures also revealed that, overall, participants did not receive a lot of information on these topics. Participants were able to select a number 1 through 5 to designate the amount of information they received on a specific topic, with 1 equating to "I received no information about this topic" and 5 equating to "I received a lot of information about this topic." The calculated average of the amount of information provided about the topics was 2.10. It is clear that participants did not receive a lot of information about topics relating to fertility and reproduction. This may indicate that the average patient is not aware of the plethora of options, resources, and support available to them.

One initiative of this study was to identify whether there was a difference in the amount of information provided to individuals who were affected with cancer at the time of their Lynch syndrome diagnosis, and individuals who were presymptomatic at the time of their diagnosis. For some topics in the sections about cancer risks and the effects of cancer treatment, risk-reducing surgery, and family planning, we observed that presymptomatic carriers received more information about certain topics than individuals affected with cancer. The differences in information provision between these groups may be due to the status of the patient at the time of their diagnosis: individuals with cancer may have more pressing matters to discuss than fertility and reproductive information. Nonetheless, these differences begs the question of whether or not there *should* be a difference in the amount of information provided between these two subsets of the patient population; as there are no available guidelines that direct providers to differentiate the information they provided between these two subsets of patients, we should not have observed this difference. For example, individuals who are affected with cancer have the

same chance of transmitting LS to their current and future children; therefore, this information is also essential for their overall care.

To further study the differences in the experience of individuals affected with cancer and presymptomatic carriers, their overall satisfaction levels were compared across the four sections. There was a trend towards statistical significance for the risk-reducing surgery section. Overall, individuals who were affected with cancer were more satisfied than the presymptomatic carriers. This may indicate an increased need for healthcare providers to emphasize the risk-reducing surgery options during their discussions with that category of patients.

Another initiative of this study was to evaluate the differences in the amount of information provided to individuals who had completed their families at the time of their diagnosis with Lynch syndrome, and those who had not completed their families. While there were no differences noted in the section about cancer risk and the effects of cancer treatment on fertility, there were statistical findings observed in the other three sections. For the risk-reducing surgery section, we found that individuals who had completed their families received more information about these topics than the other group. It is not unexpected that individuals who have completed their family are receiving more information on risk-reducing surgeries, as the NCCN guidelines (NCCN, 2.2016) recommends that all women consider a TAH-BSO after completion of childbearing. It may be that women who are past childbearing are in a life stage where they are ready for such information; however, more research is needed to investigate this difference. In the sections about fertility preservation and family planning, individuals who had not completed their families received more information about these topics than those that had

finished their families. This is a positive finding, as family planning topics are more applicable to individuals who have not completed their families. These results show that the discussion of family planning seems to be targeted to the appropriate individuals.

We compared the overall satisfaction rates over the four sections of this questionnaire between individuals who had completed their families and those that had not. Overall, individuals who had completed their families were more satisfied with their experience than individuals who had not completed their families. Combined with the prior results, this indicates that although individuals who have not completed their families are receiving more information about these topics, they are not satisfied with their experience. This study has identified areas of dissatisfaction, though more research is needed to determine why patients are dissatisfied. Possible explanations may be that the quality of information is insufficient. Another explanation may be that the information is not being individualized to the patient. One participant noted that the doctor did not discuss information about fertility preservation because she already had children; healthcare providers may be generalizing their discussion and not taking the individual concerns of their patients into account.

Our participants' reported gene frequencies did not match up to the expected percentages. Many studies quote the percentages listed by Lynch and de la Chappelle (2003), who stated that *MLH1* and *MSH2* account for 90% of reported variants, and *MSH6* accounts for the majority of the remaining cases. In our study, *MLH1* and *MSH2* variants comprised only 73.4% (28.6% and 44.8%, respectively). *MSH6* was reported by 13.6% of participants, *PMS2* by 11.7%, and *EPCAM* by 1.3%. Interestingly, there was essentially no statistically significant difference in the amount of information provided to

participants based on their reported gene. Our one significant finding, that individuals with *EPCAM* mutation received less information about family planning options, is not generalizable, as there were only two participants with *EPCAM* mutation in our study.

There are different cancer risks at different ages depending on the gene that is causing LS. For example, individuals with an *MSH2* mutation have the highest risk for ovarian cancers (Bonadona, 2011); one would assume that these participants should be receiving a lot of information on fertility and reproduction. The current NCCN guidelines do not differentiate screening or RSS recommendations based on the patient's genotype; our results show that healthcare providers are following those guidelines, as all of our participants were receiving similar amounts of information, regardless of genotype. However, with clear differences reported on the cancer risks per gene and with this study reporting a need for individualization based on the patient, it may be time for professional societies to re-evaluate their recommendations for the care and management of individuals with LS. Indeed, other studies have echoed our findings. Bonadona et al. (2011) noted that while TAH-BSO should be considered for women with *MLH1* or *MSH2*, the role of gynecological surgery for *MSH6* carriers is debatable. Cohen et al. (2014) suggested that it is important to incorporate gene- and age-specific data to provide the most comprehensive care of patients with LS. Thus far, gene-specific guidelines have not been released from any professional organizations.

The timing of information provision can often play a critical role in a patient's healthcare experience. In our study, we found a negative correlation between timing and satisfaction for the section about cancer risks and the effects of cancer treatment on fertility: individuals who received this information greater than six months after their

diagnosis were less satisfied. This is a reasonable finding, as cancer treatment is often enacted swiftly, and receiving information about these topics a long period of time after a diagnosis could limit the options available to a patient. For the other three sections, there were no significant findings about the relationship between timing and information provision. This suggests that it may not be necessary to discuss certain topics during the initial diagnosis, but that some topics may be presented in the several months following a patient's diagnosis with LS.

In this study, we requested that participants report the healthcare provider who was involved with the provision of information regarding the topics in the four sections. An oncologist, a gynecologist and a genetic counselor were the providers that were most often selected, which indicates that these three providers are most often involved in this information provision; therefore, those providers should be aware of their responsibility in this matter, and ensure that they are discussing this information to their patients, or referring the patients to another provider that can manage this role.

Notably, in the fertility preservation section, a large percentage (63.0%) of participants indicated that no healthcare provider discussed those topics with them. This is a *major* issue, as a lack of discussion about these topics creates an informational gap for patients. In regard to fertility preservation, ASCO stated that oncologists are responsible to discuss possible risks of impaired fertility and refer interested patients to reproductive specialists (Lee, 2006); ACOG does not have specific recommendations about these topics in regard to LS (ACOG Practice Bulletin, 2014). Since these two providers were most often selected as the source of discussions about fertility preservation by our participants, these providers should either be equipped for discussion

of these topics, or equipped to make an appropriate referral. Research by Volk et al. (2012) revealed that cancer genetic counselors consider discussions of fertility preservation to be a part of their role. Therefore, a referral to a genetic counselor may be an appropriate avenue to eliminate this informational gap.

Additionally, we found that 32.0% of participants reported that no healthcare provider discussed with them topics relating to family planning. The current NCCN guidelines recommend that patients be informed about inheritance risk, prenatal diagnosis and ART options (NCCN, 2.2016). ASCO and ACOG do not have any guidelines regarding the discussion of family planning in patients with LS (Lee, 2006; ACOG Practice Bulletin, 2014). However, inheritance risk and others topics in this section are often featured in genetic counseling sessions for hereditary cancer syndromes. Again, this finding provides support to the expanded use of genetic counselors in the care of these patients.

Participants were also able to select the provider whom they thought was most effective at discussing this information. In three of the four sections (cancer risk and effects of cancer treatment, risk-reducing surgery options, and family planning), a substantial percentage of participants selected genetic counselor. Again, this implies that there is a need for expansion of the genetic counselor's role in regard to the provision of this information. As previously stated, genetic counselors may take on the responsibility to make sure the above topics are effectively communicated to their patients (Goetsch, 2016; Volk, 2012; Biesecker, 2011). Increased emphasis by genetic counselors on topics related to fertility and reproduction may provide benefit to patients. Additionally, genetic counselors are trained in resource awareness, and would be able to bridge an

informational gap for a patient by identifying options for a patient to access this information.

To further study the genetic counseling appointments for our participants, we asked which topics pertaining to fertility and reproductive information were discussed by their genetic counselor. Individuals could select topics from a list that represented the main subjects covered in this questionnaire. The most frequently selected subjects were "cancer risk for Lynch syndrome" and "risk-reducing surgeries for Lynch syndrome." However, when asked which topics participants *would* have wanted their genetic counselor to discuss, many individuals selected the other available topics ("effects of cancer treatment on fertility", "fertility preservation options", and "family planning options") in addition to those two topics. These findings may indicate an increased patient interest in an expansion of the topics covered by a genetic counselor in regard to fertility and reproductive information, which is a sentiment echoed in the previous paragraph.

The qualitative aspects of this study allowed for a more in depth understanding of the participants' experience. First, many participants voiced the need for more a focused fertility consultation. This may be accomplished through a referral to a fertility specialist, or from appropriate delivery of this information from the healthcare provider involved with the patient's care. Additionally, participants felt pressured to pursue risk-reducing surgeries, and this pressure appeared be exacerbated by a lack of information about these surgeries and the potential side effects. Some participants reported completing their own research on these topics because healthcare providers did not readily discuss those topics with them. A number of participants who had chosen to pursue a risk-reducing surgery

stated that they were not adequately warned about the onset of menopause. And finally, lack of information or answers about one's future with LS can cause significant psychological stress, which can negatively impact many aspects of one's life. Many of these reported issues can be ameliorated by increased information provision and targeting this provision to the appropriate patients.

Limitations

There are some limitations to consider when evaluating this study. First, there was a clear lack of diversity within our study participants. The majority of participants were married, educated Caucasians who fit into a narrow sociodemographic band, which reduces our ability to generalize this study's results to all women with LS. Second, participants were asked to recall the content of discussions that had occurred, in some cases, many years ago. The responses in retrospective studies such as ours may not be entirely accurate due to the chance for inaccurate recall. The topics selected for inclusion in this study did not encompass *all* of the available topics about fertility and reproduction in LS; for example, participants were not asked about the information they received about the chance for CMMRD in their offspring. Since the NCCN guidelines recommend discussion of the chance for CMMRD in patients with LS, future research on this subject should include information about that topic. Another limitation is that our participant population was acquired through online support groups, which can introduce a sampling bias. While this is a limitation, it also adds an interesting layer to our results as individuals who participate in support groups are generally "information-seekers". Our study shows that these information-seekers are not getting a lot of information from their healthcare providers about fertility and reproductive concerns in LS. Finally, for our

ANOVA analyses, we did not meet the assumption of homogeneity of variance, indicating that there may be better modes of analyses that could be applied to our dataset.

Research Recommendations

This study has revealed new data about the informational needs regarding fertility and reproductive information for women with LS, and provides a number of opportunities for future research. Conducting a qualitative study on this subject matter would allow for a more in-depth understanding of the participants' experience, and also provide information about the quality of the discussion on these topics, rather than just the quantity of information provided. Our study focused on the patient's perspective of their healthcare experience; it would be interesting to conduct this study using oncologists, gynecologists and genetic counselors as a participant population. Research into how the healthcare providers present this information, the extent of detail they include, the types of referrals they make, and the types of patients they target will reveal the healthcare providers' perspective, and may also identify flaws in current practice. Finally, the development of specific education tools for the distribution of information relating to fertility and reproduction for women with LS may help to eliminate the informational gap in knowledge for this patient population.

2.6 Conclusions

This study sought to provide insight to the needs of women with LS in respect to information about fertility and reproduction. By surveying this patient population, we were able to evaluate the current practices of this information delivery and identify areas for improvement. Our results establish that this type of information is important to

women with LS, and its appropriate provision can contribute to a patient's overall satisfaction with their healthcare experience. However, patients are not receiving a large amount of information regarding the topics covered in this study, which can lead to a decreased in patient awareness of the options, resources, and support available to them. This lack of comprehensive information provision can also increase their perceived psychosocial stress.

Our results also reveal two seemingly conflicting recommendations: the need for uniformity and the need for individualization. It is essential that we create a more uniform strategy for the provision of this information to this patient population. Guidelines should be created identifying the extent of and type of information that should be provided, and the healthcare providers that should be involved with this process. However, it is also crucial that this information be individualized to fit the patient's specific needs. In particular, the information provided must to be tailored to the patient's age, current status in regard to cancer burden and family planning, and, most importantly, their genotype.

Finally, this research implies a need for expansion of the genetic counselor's role in the provision of fertility and reproductive information for women with LS. Participants identified genetic counselors as the most effective healthcare provider to discuss these topics, and genetic counselors are well equipped to manage the discussion, counseling and referral process associated with this subject matter. Increased emphasis by genetic counselors on topics related to fertility and reproduction may present a way to eliminate the knowledge gap for women with LS. Overall, this study has contributed to our

understanding of the perspectives of women with LS, and has provided strategies to promote more comprehensive care of this patient population.

Table 2.1 Participant Demographic Information

Individual Participant	N	(%)	*Individual Participant*	N	(%)
Current Age	N=154		**Country of Origin**[1]	N=123	
18-25 years	6	(3.9)	Australia	6	(4.9)
26-35 years	58	(37.7)	Canada	5	(4.1)
36-45 years	62	(40.2)	New Zealand	1	(0.8)
>46 years	28	(18.2)	Norway	1	(0.8)
			Sweden	1	(0.8)
Age at LS Diagnosis	N=154		United Kingdom	4	(3.2)
<18 years	2	(1.3)	United States	105	(85.4)
18-25 years	20	(13.0)			
26-35 years	71	(46.1)	**Region of the United States**	N=105	
36-45 years	61	(39.6)	Northeast[2]	27	(25.7)
			Southeast[3]	16	(15.2)
Gene	N=154		Midwest[4]	28	(26.7)
MLH1	44	(28.6)	Southwest[5]	11	(10.5)
MSH2	69	(44.8)	Rocky Mountain[6]	6	(5.7)
MSH6	21	(13.6)	Pacific[7]	17	(16.2)
PMS2	18	(11.7)			
EPCAM	2	(1.3)	**Ethnicity**	N=132	
			American Indian/Native	3	(2.3)
Highest Education	N=130		Asian/Pacific Islander	0	(0)
Some High School	0	(0)	Black/African Am.	0	(0)
High School/GED	8	(6.2)	Hispanic or Latino	3	(2.3)
Some College	22	(16.9)	White/Caucasian	126	(95.4)
Associate's Degree	9	(6.9)			
Bachelor's Degree	57	(43.8)	**Relationship Status**	N=154	
Some Graduate School	7	(5.4)	Married	111	(72.0)
Graduate Degree	27	(20.8)	Widowed	0	(0)
			Divorced	6	(4.0)
			Separated	1	(0.6)
			In a Domestic Partnership	4	(2.6)
			In a Relationship	23	(15.0)
			Single, Never Married	9	(5.8)

[1]Participants were able to choose from a pre-populated list of 154 countries
[2]Includes ME, VT, NH, MA, CT, NY, RI, PA, NJ
[3]Includes DE, MD, DC, VA, WV, NC, SC, KY, TN, FL, GA, AL, MS, AR, LA
[4]Includes OH, IN, IL, MI, WI, MN, IA, MO, ND, SD, NE, KS
[5]Includes OK, TX, NM, AZ
[6]Includes CO, UT, WY, MT, ID, NV
[7]Includes WA, OR, CA, HI, AK

Table 2.2 Additional Participant Characteristics

Individual Participant	N	(%)
Which best describes your health status at the time of your diagnosis with LS?	N=154	
I was diagnosed with cancer, then discovered I have LS.	59	(38.3)
I had genetic testing and discovered I have LS.	95	(61.7)
Which best describes your family status at the time of your diagnosis with LS?	N=154	
I had completed my family/ I was not interested in having children.	75	(48.7)
I had not completed my family.	79	(51.3)

Table 2.3 Amount of Information Provided and Participant Satisfaction: Cancer Risks and the Effects of Cancer Treatment

Cancer Risks and Effects of Cancer Treatment	Not Satisfied			Satisfied			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The risk for cancer will differ based on your gene.	17	2.53	1.77	29	2.41	1.80	(2, 50)	3.10	0.058
The risk for cancer will differ based on your age.	17	2.53	1.77	29	3.31	1.87	(2, 49)	0.95	0.393
The effects of chemotherapy on your reproductive organs.	17	2.00	1.80	29	2.76	1.97	(2, 49)	0.85	0.433
The effects of radiation on your reproductive organs	17	1.65	1.90	29	2.03	2.17	(2, 49)	0.29	0.753
The effects of surgery for CRC on your ability to conceive a pregnancy.	17	1.53	1.46	28	2.36	2.04	(2, 49)	1.60	0.212

Table 2.4 Information Provision between Individuals Affected with Cancer vs. Presymptomatic Carriers: Cancer Risks and the Effects of Cancer Treatment

Cancer Risks and Effects of Cancer Treatment	Affected with Cancer			Presym. Carrier			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The risk for cancer will differ based on your gene.	35	2.54	1.93	19	3.68	1.60	(1, 52)	4.83	0.032
The risk for cancer will differ based on your age.	34	2.76	1.89	19	3.63	1.74	(1, 51)	2.71	0.106
The effects of chemotherapy on your reproductive organs.	34	2.47	2.08	19	2.42	1.57	(1, 51)	0.01	0.928
The effects of radiation on your reproductive organs	34	1.47	2.11	19	2.53	1.68	(1, 51)	3.51	0.067
The effects of surgery for CRC on your ability to conceive a pregnancy.	34	1.76	1.83	19	2.26	1.85	(1. 51)	0.89	0.348

Table 2.5 Information Provision between Individuals who have Completed their Family vs. Individuals who have not Completed their Family: Cancer Risks and Effects of Cancer Treatment

Cancer Risks and Effects of Cancer Treatment	Completed Family			Not Completed Family			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The risk for cancer will differ based on your gene.	33	2.64	1.98	21	3.43	1.66	(1, 52)	2.32	0.134
The risk for cancer will differ based on your age.	32	3.09	1.96	21	3.05	1.77	(1, 51)	0.01	0.931
The effects of chemotherapy on your reproductive organs.	32	2.19	1.84	21	2.86	1.96	(1, 51)	1.60	0.212
The effects of radiation on your reproductive organs.	32	1.53	1.95	21	2.33	2.06	(1, 51)	2.05	0.158
The effects of surgery for CRC on your ability to conceive a pregnancy.	32	1.75	1.81	21	2.24	1.87	(1, 51)	0.89	0.348

Table 2.6 Amount of Information Provided and Participant Satisfaction: Risk-Reducing Surgery

Risk-Reducing Surgery	Not Satisfied			Satisfied			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The timing of a risk-reducing hysterectomy.	60	3.42	1.39	67	3.98	1.49	(2, 128)	6.88	0.001
The timing of a risk-reducing oophorectomy.	60	2.80	1.63	67	3.85	1.64	(2, 128)	9.62	0.000
My family history should considered when planning for a risk-reducing surgery.	59	2.97	1.65	67	3.63	1.75	(2, 127)	5.25	0.006
The side effects of a risk-reducing oophorectomy before menopause.	60	2.10	1.31	67	3.64	1.60	(2, 128)	23.03	0.000
The option of a risk-reducing hysterectomy with ovarian preservation.	60	1.78	1.30	67	2.79	1.91	(2, 128)	7.16	0.001
The use of birth control to reduce my cancer risk.	60	1.90	1.64	67	1.93	2.00	(2, 128)	1.17	0.314

Table 2.7 Information Provision between Individuals Affected with Cancer vs. Presymptomatic Carriers: Risk-Reducing Surgery

Risk-Reducing Surgery	Affected with Cancer			Presym. Carrier			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The timing of a risk-reducing hysterectomy.	45	3.51	1.80	87	3.74	1.36	(1, 130)	0.64	0.424
The timing of a risk-reducing oophorectomy.	45	3.24	1.94	87	3.33	1.65	(1, 130)	0.08	0.783
My family history should considered when planning for a risk-reducing surgery.	45	2.98	2.09	86	3.42	1.54	(1, 129)	1.88	0.173
The side effects of a risk-reducing oophorectomy before menopause.	45	3.00	1.92	87	2.73	1.57	(1, 130)	0.78	0.378
The option of a risk-reducing hysterectomy with ovarian preservation.	45	1.69	1.95	87	2.61	1.53	(1, 130)	8.87	0.003
The use of birth control to reduce my cancer risk.	45	1.44	1.86	87	2.13	1.79	(1, 130)	4.18	0.043

Table 2.8 Information Provision between Individuals who have Completed their Family vs. Individuals who have not Completed their Family: Risk-Reducing Surgery

Risk-Reducing Surgery	Completed Family			Not Completed Family			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The timing of a risk-reducing hysterectomy.	72	3.79	1.64	60	3.50	1.37	(1, 130)	1.20	0.275
The timing of a risk-reducing oophorectomy.	72	3.62	1.83	60	2.93	1.59	(1, 130)	5.05	0.026
My family history should considered when planning for a risk-reducing surgery.	72	3.28	1.91	59	3.25	1.56	(1, 129)	0.01	0.939
The side effects of a risk-reducing oophorectomy before menopause.	72	3.14	1.72	60	2.43	1.60	(1, 130)	5.86	0.017
The option of a risk-reducing hysterectomy with ovarian preservation.	72	2.42	1.90	60	2.15	1.52	(1, 130)	0.77	0.381
The use of birth control to reduce my cancer risk.	72	1.46	1.76	60	2.42	1.81	(1, 130)	9.47	0.003

Table 2.9 Amount of Information Provided and Participant Satisfaction: Fertility Preservation

Fertility Preservation	Not Satisfied			Satisfied			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The option to shield or move the ovaries during radiation therapy.	65	0.92	1.08	27	1.07	1.75	(2, 140)	7.20	0.001
Embryo or egg cryopreservation.	65	1.22	1.33	27	2.81	2.09	(2, 140)	34.89	0.000
Ovarian tissue cryopreservation.	65	0.85	0.67	27	1.41	1.76	(2, 140)	14.60	0.000
Ovarian stimulation will delay cancer treatment.	65	0.92	0.95	27	1.60	2.10	(2, 140)	13.13	0.000

Table 2.10 Information Provision between Individuals Affected with Cancer vs. Presymptomatic Carriers: Fertility Preservation

Fertility Preservation	Affected with Cancer			Presym. Carrier			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The option to shield or move the ovaries during radiation therapy.	56	0.78	1.53	94	0.66	0.78	(1, 148)	0.44	0.507
Embryo or egg cryopreservation.	56	1.39	1.99	94	1.06	1.31	(1, 148)	1.49	0.224
Ovarian tissue cryopreservation.	56	0.70	1.19	94	0.76	0.86	(1, 148)	0.12	0.727
Ovarian stimulation will delay cancer treatment.	56	0.96	1.61	94	0.69	0.90	(1, 148)	1.77	0.185

Table 2.11 Information Provision between Individuals who have Completed their Family vs. Individuals who have not Completed their Family: Fertility Preservation

Fertility Preservation	Completed Family			Not Completed Family			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The option to shield or move the ovaries during radiation therapy.	85	0.54	1.07	65	0.92	1.15	(1, 148)	4.38	0.038
Embryo or egg cryopreservation.	85	0.72	1.23	65	1.80	1.81	(1, 148)	18.92	0.000
Ovarian tissue cryopreservation.	85	0.45	0.75	65	1.11	1.15	(1, 148)	18.13	0.000
Ovarian stimulation will delay cancer treatment.	85	0.55	1.05	65	1.11	1.35	(1, 148)	8.02	0.005

Table 2.12 Amount of Information Provided and Participant Satisfaction: Family Planning

Family Planning	Not Satisfied			Satisfied			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The chance that your children will have Lynch syndrome.	55	3.56	1.61	39	4.41	1.39	(2, 130)	10.62	0.000
The use of an in vitro fertilization (IVF) cycle.	55	1.71	1.54	39	2.43	2.10	(2, 130)	15.72	0.000
Prenatal diagnosis for Lynch syndrome.	55	1.69	1.54	38	2.03	1.92	(2, 129)	10.28	0.000
Preimplantation genetic diagnosis (PGD) for Lynch syndrome.	55	1.67	1.56	38	1.87	2.04	(2, 129)	8.47	0.000
Adoption.	55	1.33	1.35	38	1.37	1.48	(2, 129)	9.76	0.000
Surrogacy.	55	1.25	1.28	38	1.29	1.56	(2, 129)	9.68	0.000

Table 2.13 Information Provision between Individuals Affected with Cancer vs. Presymptomatic Carriers: Family Planning

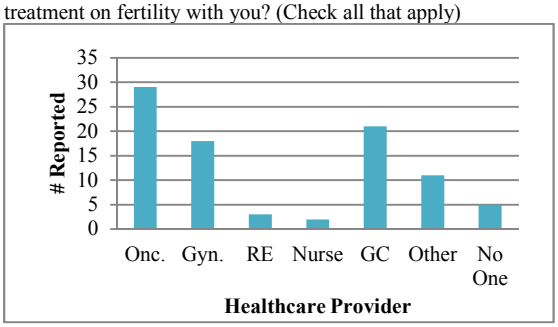
Family Planning	Affected with Cancer			Presym. Carrier			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The chance that your children will have Lynch syndrome.	53	3.11	2.07	86	3.72	1.72	(1, 137)	3.49	0.064
The use of an in vitro fertilization (IVF) cycle.	53	1.47	1.97	86	1.52	1.61	(1, 137)	0.03	0.866
Prenatal diagnosis for Lynch syndrome.	52	1.27	1.73	86	1.49	1.55	(1, 136)	0.59	0.442
Preimplantation genetic diagnosis (PGD) for Lynch syndrome.	52	1.21	1.68	86	1.43	1.65	(1, 136)	0.56	0.455
Adoption.	52	0.90	1.43	86	1.09	1.20	(1, 136)	0.69	0.407
Surrogacy.	52	1.06	1.65	86	0.89	0.97	(1, 136)	0.53	0.468

Table 2.14 Information Provision between Individuals who have Completed their Family vs. Individuals who have not Completed their Family: Family Planning

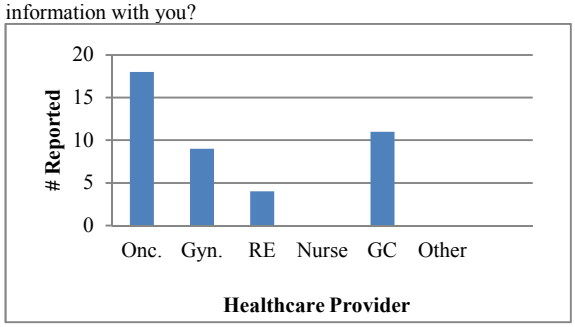
Family Planning	Completed Family			Not Completed Family			df	F	p-value
	N	Mean	SD	N	Mean	SD			
The chance that your children will have Lynch syndrome.	79	2.97	2.07	60	4.17	1.33	(1, 137)	15.14	0.000
The use of an in vitro fertilization (IVF) cycle.	79	0.81	1.33	60	2.42	1.82	(1, 137)	38.24	0.000
Prenatal diagnosis for Lynch syndrome.	78	0.92	1.44	60	2.03	1.63	(1, 136)	18.02	0.000
Preimplantation genetic diagnosis (PGD) for Lynch syndrome.	78	0.85	1.39	60	2.00	1.76	(1, 136)	18.49	0.000
Adoption.	78	0.60	0.98	60	1.57	1.44	(1, 136)	21.72	0.000
Surrogacy.	78	0.56	0.99	60	1.47	1.41	(1, 136)	19.56	0.000

Cancer Risks and Effects of Cancer Treatment[1]

Which healthcare provider discussed the effects of cancer treatment on fertility with you? (Check all that apply)



Which healthcare provider was most effective at discussing this information with you?

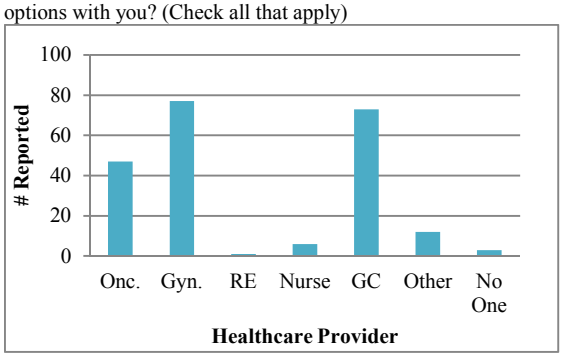


[1]The following abbreviations were used for this chart: Onc. (Oncologist), Gyn. (Gynecologist), RE (Reproductive Endocrinolgist), and GC (Genetic Counselor). Additionally, the selection of "No One" indicates that no healthcare provider discussed these topics with the participant.

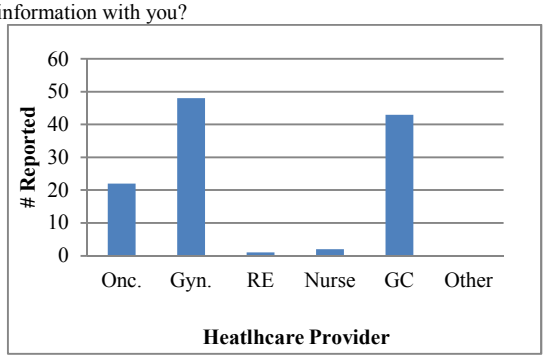
Figure 2.1 Healthcare Providers: Cancer Risks and Effects of Cancer Treatment

Risk-Reducing Surgery[1]

Which healthcare provider discussed risk-reducing surgery options with you? (Check all that apply)



Which healthcare provider was most effective at discussing this information with you?

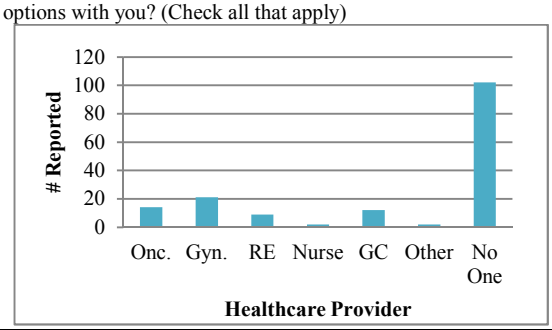


[1]The following abbreviations were used for this chart: Onc. (Oncologist), Gyn. (Gynecologist), RE (Reproductive Endocrinologist), and GC (Genetic Counselor). Additionally, the selection of "No One" indicates that no healthcare provider discussed these topics with the participant.

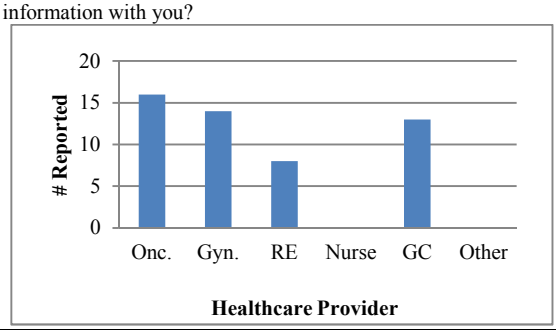
Figure 2.2 Healthcare Providers: Risk-Reducing Surgery

Fertility Preservation[1]

Which healthcare provider discussed fertility preservation options with you? (Check all that apply)

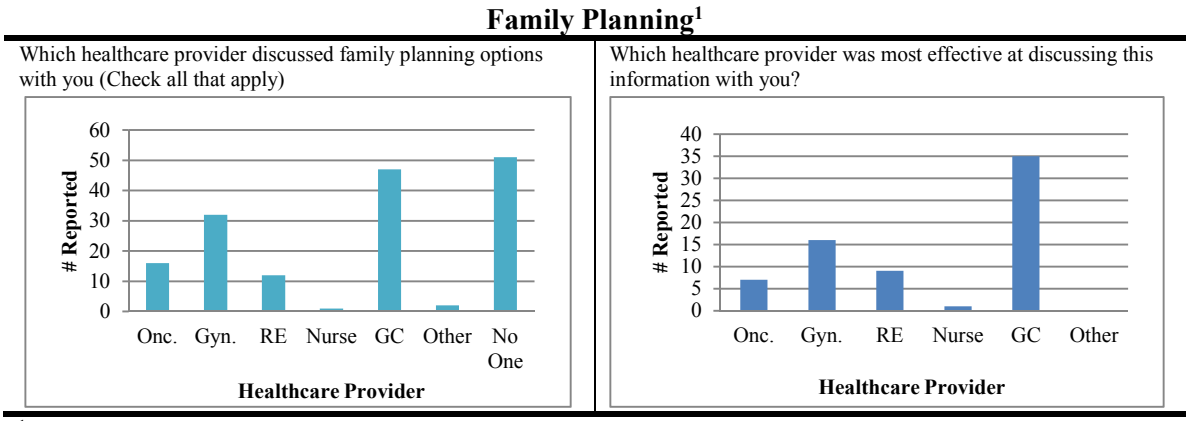


Which healthcare provider was most effective at discussing this information with you?



[1]The following abbreviations were used for this chart: Onc. (Oncologist), Gyn. (Gynecologist), RE (Reproductive Endocrinologist), and GC (Genetic Counselor). Additionally, the selection of "No One" indicates that no healthcare provider discussed these topics with the participant.

Figure 2.3 Healthcare Providers: Fertility Preservation



[1]The following abbreviations were used for this chart: Onc. (Oncologist), Gyn. (Gynecologist), RE (Reproductive Endocrinologist), and GC (Genetic Counselor). Additionally, the selection of "No One" indicates that no healthcare provider discussed these topics with the participant.

Figure 2.4 Healthcare Providers: Family Planning

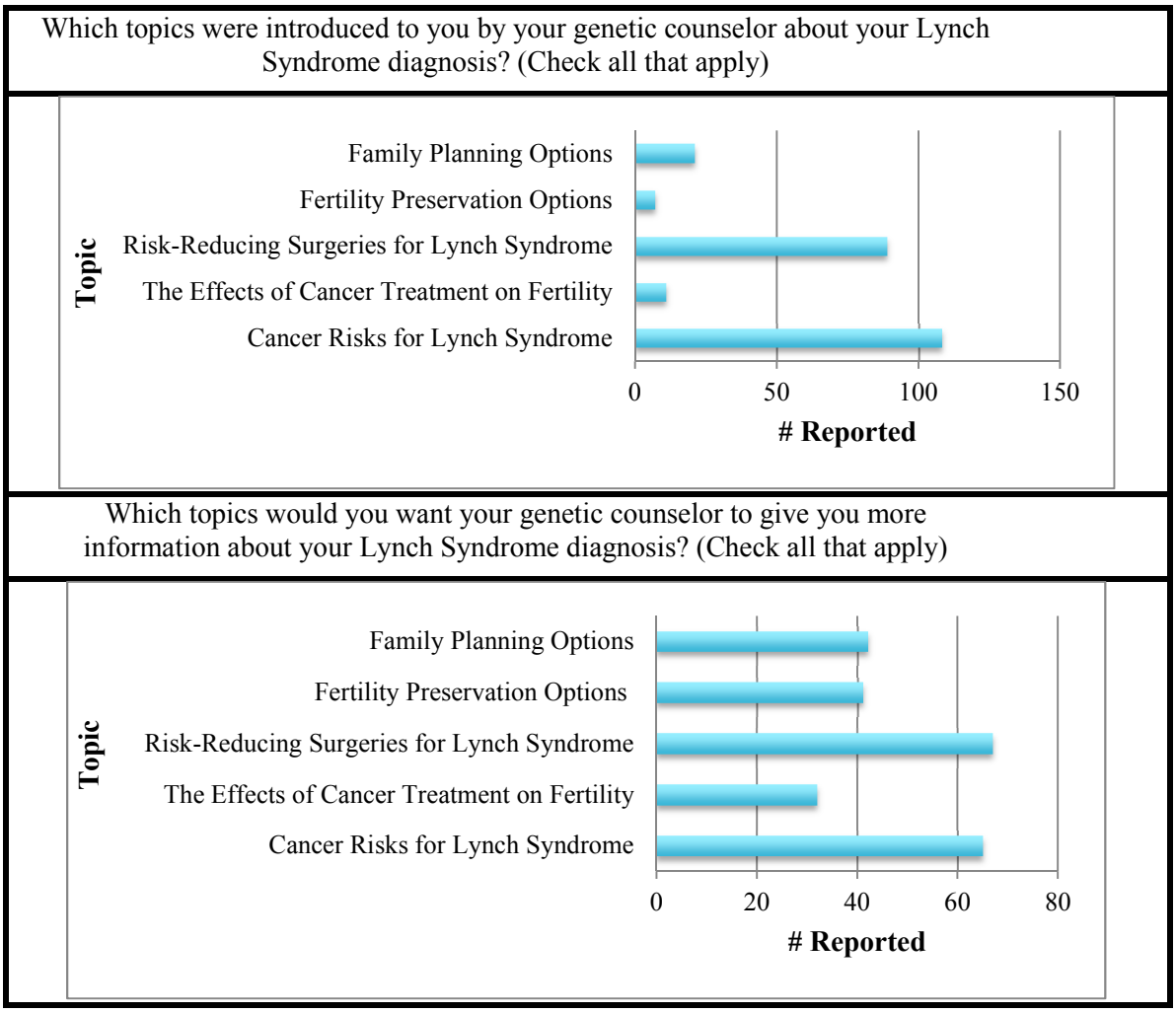


Figure 2.5 Genetic Counseling for LS

Chapter 3. Conclusions

This study sought to provide insight to the needs of women with LS in respect to information about fertility and reproduction. By surveying this patient population, we were able to evaluate the current practices of this information delivery and identify areas for improvement. Our results establish that this type of information is important to women with LS, and its appropriate provision can contribute to a patient's overall satisfaction with their healthcare experience. However, patients are not receiving a large amount of information regarding the topics covered in this study, which can lead to a decreased in patient awareness of the options, resources, and support available to them. This lack of comprehensive information provision can also increase their perceived psychosocial stress.

Our results also reveal two seemingly conflicting recommendations: the need for uniformity and the need for individualization. It is essential that we create a more uniform strategy for the provision of this information to this patient population. Guidelines should be created identifying the extent of and type of information that should be provided, and the healthcare providers that should be involved with this process. However, it is also crucial that this information be individualized to fit the patient's specific needs. In particular, the information provided must to be tailored to the patient's age, current status in regard to cancer burden and family planning, and, most importantly, their genotype.

Finally, this research implies a need for expansion of the genetic counselor's role in the provision of fertility and reproductive information for women with LS. Participants identified genetic counselors as the most effective healthcare provider to discuss these topics, and genetic counselors are well equipped to manage the discussion, counseling and referral process associated with this subject matter. Increased emphasis by genetic counselors on topics related to fertility and reproduction may present a way to eliminate the knowledge gap for women with LS. Overall, this study has contributed to our understanding of the perspectives of women with LS, and has provided strategies to promote more comprehensive care of this patient population.

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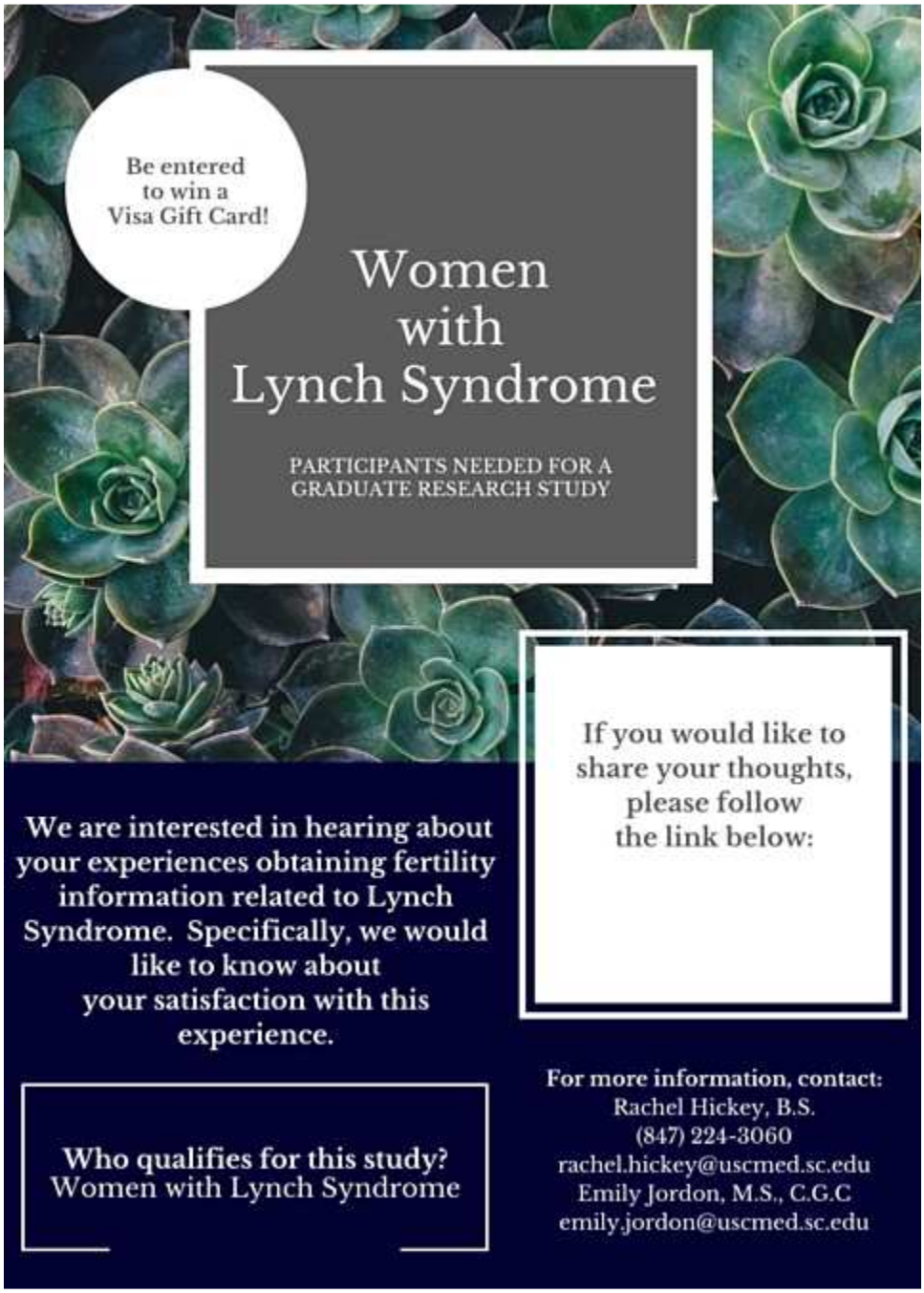
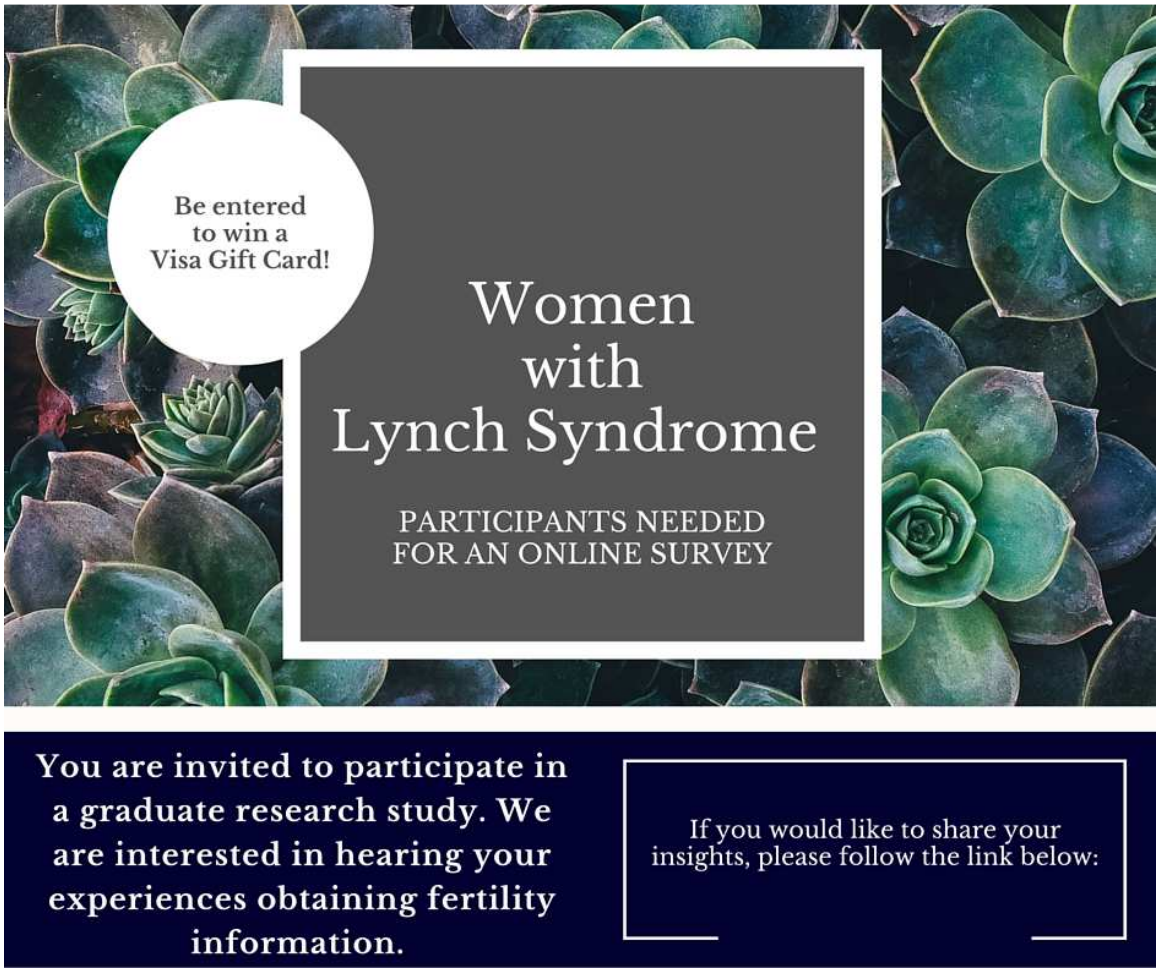
Appendix A. Invitational Flyer



Appendix B. Facebook Post



Appendix C. Survey Questionnaire

Important Definitions

Lynch Syndrome

Lynch Syndrome is an inherited condition that is characterized by an increased risk for early onset cancers, including colorectal, endometrial, ovarian and gastric cancers. The genes that cause Lynch Syndrome are *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*.

Fertility

Fertility is the ability to naturally conceive and carry a pregnancy.

Gender

1.) What is your gender?

- ☐ Male
- ☐ Female
- ☐ Other
- ☐ Prefer not to say

Age

2.) What is your current age?

- ☐ Below 18 years old
- ☐ 18-25 years old
- ☐ 26-35 years old
- ☐ 36-45 years old
- ☐ 46 years or older

3.) How old were you when you were diagnosed with Lynch Syndrome?

- ☐ Below 18 years old
- ☐ 18-25 years old
- ☐ 26-35 years old
- ☐ 36-45 years old
- ☐ 46 years or older

Participant Details

4.) Based on your genetic testing results, which gene was found to have a disease-causing change?

- ☐ MLH1
- ☐ MSH2
- ☐ MSH6
- ☐ PMS2
- ☐ EPCAM
- ☐ I do not recall
- ☐ I have a variant of unknown significance

5.) Did you return to a healthcare provider for a follow-up appointment after your diagnosis with Lynch Syndrome?

- ☐ Yes
- ☐ No

6.) Select the situation that best applies to you.

- ☐ I was diagnosed with cancer, and afterwards I was found to have Lynch Syndrome
- ☐ I pursued genetic testing and found that I have Lynch Syndrome
- ☐ Other (please specify)

7.) What cancer were you diagnosed with? (Check all that apply)

- ☐ Colon cancer
- ☐ Rectal cancer
- ☐ Endometrial cancer
- ☐ Ovarian cancer
- ☐ Gastric cancer
- ☐ Urinary Tract cancer
- ☐ Other cancer (please specify)

8.) Please list your age at the diagnosis of each cancer (Example: Colon, 26; Endometrial, 44)

9.) Which of the following best describes your current relationship status?

- ☐ Married
- ☐ Widowed
- ☐ Divorced
- ☐ Separated
- ☐ In a domestic partnership or civil union
- ☐ In a relationship
- ☐ Single, never married
- ☐ Other (please specify)

10.) Which of the following best describes your relationship status at the time of your diagnosis with Lynch Syndrome?

- ☐ Married
- ☐ Widowed

- ☐ Divorced
- ☐ Separated
- ☐ In a domestic partnership or civil union
- ☐ In a relationship
- ☐ Single, never married
- ☐ Other (please specify)

11.) Which of the following best describes your status at the time of your diagnosis with Lynch Syndrome?

- ☐ I was done with childbearing because I had completed my family
- ☐ I had not yet completed my family
- ☐ I had not yet started a family but planned to have children in the future
- ☐ I was not interested in having children
- ☐ Other (please specify)

Cancer and Cancer Treatment

12.) Did your provider discuss with you the impact of potential cancer treatment (such as chemotherapy) on fertility?

- ☐ Yes
- ☐ No

(page break)

13.) Which topics were discussed with you about the effects of cancer treatment on fertility? (1- I received no information on this topic, 5- I received a lot of information on this topic)

	1	2	3	4	5	Not Applicable
The risk of cancer will differ based on your gene.						
The risk of cancer will differ based on your age.						
The effects of chemotherapy on your reproductive organs.						
The effects of radiation on your						

reproductive organs.						
The effects of surgery for colorectal cancer on your ability to conceive a pregnancy.						

14.) Approximately how long after your diagnosis with Lynch Syndrome did you receive information about the effects of cancer treatment on fertility?

- ☐ I received this information when I received my diagnosis
- ☐ I received this information within a month after my diagnosis
- ☐ One month after my diagnosis
- ☐ Six months after my diagnosis
- ☐ One year after my diagnosis
- ☐ More than one year after my diagnosis
- ☐ I did not receive this information
- ☐ I do not recall
- ☐ Other (please specify)

(page break)

15.) Which healthcare provider discussed the effects of cancer treatment on fertility with you?

- ☐ Oncologist
- ☐ Gynecologist
- ☐ Reproductive Endocrinologist
- ☐ Nurse/Nurse Specialist
- ☐ Genetic Counselor
- ☐ No healthcare provider discussed this information with me
- ☐ Other (please specify)

16.) Which healthcare provider was most effective at discussing this information with you?

A drop down menu of the above options

17.) What informational resources were provided to you on these topics?

- ☐ A referral to a fertility specialist or reproductive endocrinologist
- ☐ An informational pamphlet or fact sheet
- ☐ A website
- ☐ A book
- ☐ A support group
- ☐ I was not provided any resources about this topic
- ☐ Other (please specify)

18.) Which resource was most helpful?

A drop box menu of the above options

19.) Were you satisfied with the amount of information you received about the effects of cancer treatment on your fertility?

- ☐ I was satisfied with the amount of information I received
- ☐ I was not satisfied because I did not receive enough information
- ☐ I was not satisfied because I did not receive any information
- ☐ I was not interested in receiving this type of information

20.) Please share any additional comments you have.

Risk-Reducing Surgery and Other Alternatives

21.) Did your provider discuss with you the impact of risk-reducing surgeries (such as a hysterectomy) on fertility?

- ☐ Yes
- ☐ No

Important Definitions

The following definitions will be helpful for the next section of this questionnaire:

Risk-Reducing Surgery

Surgery to reduce the risk of having cancer (also known as prophylactic surgery).

Hysterectomy

Surgery to remove the uterus

Oophorectomy

Surgery to remove one or both of the ovaries

Hysterectomy with Ovarian Preservation

Surgery to remove the uterus but keep, or preserve, one or both of the ovaries.

(page break)

22.) Have you had any of the following surgeries because of your diagnosis with Lynch Syndrome? (Check all that apply)

- ☐ Risk-Reducing Hysterectomy
- ☐ Risk-Reducing Oophorectomy
- ☐ No, I have not had a risk-reducing surgery
- ☐ Other (please specify)

(page break)

23.) Which topics were discussed with you about risk-reducing surgery for Lynch Syndrome? (1- I received no information on this topic, 5- I received a lot of information on this topic)

24.) Approximately how long after your diagnosis with Lynch Syndrome did you receive information about risk-reducing options?

- ☐ I received this information when I received my diagnosis
- ☐ I received this information within a month after my diagnosis
- ☐ One month after my diagnosis
- ☐ Six months after my diagnosis
- ☐ One year after my diagnosis
- ☐ More than one year after my diagnosis
- ☐ I did not receive this information
- ☐ I do not recall
- ☐ Other (please specify)

(page break)

25.) Which healthcare provider discussed information about risk-reducing options with you?

- ☐ Oncologist
- ☐ Gynecologist
- ☐ Reproductive Endocrinologist
- ☐ Nurse/Nurse Specialist
- ☐ Genetic Counselor
- ☐ No healthcare provider discussed this information with me
- ☐ Other (please specify)

26.) Which healthcare provider was most effective at discussing this information with you?

A drop down box of the above options

27.) What informational resources were provided to you on these topics?

- ☐ A referral to a fertility specialist or reproductive endocrinologist
- ☐ An informational pamphlet or fact sheet
- ☐ A website
- ☐ A book
- ☐ A support group
- ☐ I was not provided any resources about this topic
- ☐ Other (please specify)

28.) Which resource was most helpful?

A drop down box of the above options

29.) Were you satisfied with the amount of information you received about risk-reducing options for Lynch Syndrome?

- ☐ I was satisfied with the amount of information I received
- ☐ I was not satisfied because I did not receive enough information
- ☐ I was not satisfied because I did not receive any information
- ☐ I was not interested in receiving this type of information

30.) Please share any additional comments you have.

Fertility Preservation

The following definitions will be helpful for the next section of this questionnaire:

Risk-Reducing Surgery
Surgery to reduce the risk of having cancer (also known as prophylactic surgery).

Hysterectomy
Surgery to remove the uterus.

Oophorectomy
Surgery to remove one or both of the ovaries.

Hysterectomy with Ovarian Preservation
Surgery to remove the uterus but keep, or preserve, one or both of the ovaries.

31.) Which topics were discussed with you about fertility preservation options? (1- I received no information on this topic, 5- I received a lot of information on this topic)

	1	2	3	4	5	Not Applicable
The option to shield or move the ovaries during radiation therapy.						
Embryo or egg cryopreservation (freezing).						
Ovarian tissue cryopreservation (freezing).						
Ovarian stimulation will delay cancer treatment.						

32.) Approximately how long after your diagnosis with Lynch Syndrome did you receive information about fertility preservation?

- ☐ I received this information when I received my diagnosis
- ☐ I received this information within a month after my diagnosis
- ☐ One month after my diagnosis
- ☐ Six months after my diagnosis
- ☐ One year after my diagnosis
- ☐ More than one year after my diagnosis
- ☐ I did not receive this information
- ☐ I do not recall
- ☐ Other (please specify)

(page break)

33.) Which healthcare provider discussed information about fertility preservation options with you?

- ☐ Oncologist
- ☐ Gynecologist
- ☐ Reproductive Endocrinologist
- ☐ Nurse/Nurse Specialist
- ☐ Genetic Counselor
- ☐ No healthcare provider discussed this information with me
- ☐ Other (please specify)

34.) Which healthcare provider was most effective at discussing this information with you?

A drop down box of the above options

35.) What informational resources were provided to you on these topics?

- ☐ A referral to a fertility specialist or reproductive endocrinologist
- ☐ An informational pamphlet or fact sheet
- ☐ A website
- ☐ A book
- ☐ A support group
- ☐ I was not provided any resources about this topic
- ☐ Other (please specify)

36.) Which resource was most helpful?

A drop down menu of the above options

37.) Were you satisfied with the amount of information you received about fertility preservation?

- ☐ I was satisfied with the amount of information I received
- ☐ I was not satisfied because I did not receive enough information
- ☐ I was not satisfied because I did not receive any information
- ☐ I was not interested in receiving this type of information

38.) Please share any additional comments you have.

Family Planning

39.) Which topics were discussed with you about family planning options? (1- I received no information on this topic, 5- I received a lot of information on this topic)

	1	2	3.	4	5	Not Applicable
The chance that your children will have Lynch Syndrome.						
The use of an *in vitro* fertilization (IVF) cycle.						
Prenatal diagnosis of Lynch Syndrome.						
Preimplantation genetic diagnosis (PGD) for Lynch Syndrome.						
Adoption.						
Surrogacy						

40.) Approximately how long after your diagnosis with Lynch Syndrome did you receive information about family planning options?

- ☐ I received this information when I received my diagnosis
- ☐ I received this information within a month after my diagnosis
- ☐ One month after my diagnosis
- ☐ Six months after my diagnosis
- ☐ One year after my diagnosis
- ☐ More than one year after my diagnosis
- ☐ I did not receive this information
- ☐ I do not recall
- ☐ Other (please specify)

(page break)

41.) Which healthcare provider discussed this information with you?

- ☐ Oncologist
- ☐ Gynecologist
- ☐ Reproductive Endocrinologist
- ☐ Nurse/Nurse Specialist
- ☐ Genetic Counselor
- ☐ No healthcare provider discussed this information with me
- ☐ Other (please specify)

42.) Which healthcare provider was most effective at discussing this information with you?

A drop down menu of the above options

43.) What informational resources were provided to you on these topics?

- ☐ A referral to a fertility specialist or reproductive endocrinologist
- ☐ An informational pamphlet or fact sheet
- ☐ A website
- ☐ A book
- ☐ A support group
- ☐ I was not provided any resources about this topic
- ☐ Other (please specify)

44.) Which resource was most helpful?

A drop down menu of the above options

45.) Were you satisfied with the amount of information you received about family planning options?

- ☐ I was satisfied with the amount of information I received
- ☐ I was not satisfied because I did not receive enough information
- ☐ I was not satisfied because I did not receive any information
- ☐ I was not interested in receiving this type of information

46.) Please share any additional comments you have.

Genetic Counseling for Lynch Syndrome

47.) Have you previously met with a certified or licensed genetic counselor (CGC, LGC)?

- ☐ Yes
- ☐ No
- ☐ Not Sure

48.) Which topics were introduced to you by your genetic counselor about your Lynch Syndrome diagnosis? (Check all that apply)

- ☐ Cancer Risks for Lynch Syndrome
- ☐ The Effects of Cancer Treatment on Fertility

- ☐ Risk-Reducing Surgeries for Lynch Syndrome
- ☐ Fertility Preservation Options
- ☐ Family Planning Options

49.) Which topics would you want your genetic counselor to give you more information about your Lynch Syndrome diagnosis? (Check all that apply)

- ☐ Cancer Risks for Lynch Syndrome
- ☐ The Effects of Cancer Treatment on Fertility
- ☐ Risk-Reducing Surgeries for Lynch Syndrome
- ☐ Fertility Preservation Options
- ☐ Family Planning Options

50.) Please share any additional comments you have.

Additional Demographic Information

51.) What is the highest level of education that you have completed?

- ☐ Some High School
- ☐ High School or GED
- ☐ Some College
- ☐ Associate's Degree
- ☐ Bachelor's Degree
- ☐ Some Graduate School
- ☐ Graduate School (Master's, PhD, MD, JD, etc.)

52.) In what country do you currently reside in?

A drop down menu of countries is provided for this question.

53.) What is your ethnicity?

- ☐ American Indian or Alaskan Native
- ☐ Asian or Pacific Islander
- ☐ Black or African American
- ☐ Hispanic or Latino
- ☐ White/Caucasian
- ☐ Prefer not to answer
- ☐ Other (please specify)

54.) Which U.S. region do you currently reside in?

- ☐ Northeast (ME, VT, NH, MA, CT, NY, RI, PA, NJ)
- ☐ Southeast (DE, MD, DC, VA, WV, NC, SC, KY, TN, FL, GA, AL, MS, AR, LA)
- ☐ Midwest (OH, IN, IL, MI, WI, MN, IA, MO, ND, SD, NE, KS)
- ☐ Southwest (OK, TX, NM, AZ)
- ☐ Rocky Mountain (CO, UT, WY, MT, ID, NV)
- ☐ Pacific (WA, OR, CA, HI, AK)

Drawing Information

All participants are invited to enter a drawing for a $25 Visa gift card. If you are interested, please select "Yes." You will be guided to a page that requests your name and email contact. Your contact information will not be used for any other purposes beyond sending you the gift card if you have won.

55.) Are you interested in entering a drawing to win a $25 Visa gift card?

- ☐ Yes
- ☐ No

Please provide your name and email contact.

Name

Email Contact

Please follow the link below for access to the online survey:
https://www.surveymonkey.com/r/Preview/?sm=K8ch01rRedrDI7s8ioFRr_2BqnkVBgp5R1zjvZoRP4Bbo_3D

Appendix D. Participant Consent Agreement

We would like to invite women with Lynch Syndrome to participate in a study about the delivery of fertility information. The purpose of this study is to understand how information about fertility issues is presented to women with Lynch Syndrome. We will ask you about your satisfaction of your experience with this topic.

Your participation would be greatly appreciated, as your opinions will increase our understanding of the specific needs of women with Lynch Syndrome We believe that the results of this study will contribute to better presentation of fertility information to patients, the creation of more thorough practice guidelines, and increased consistency in the care of this patient population.

Your participation in the study is voluntary, and you can withdraw from the study at any time. Participating in the study involves the completion an online survey. The survey is anonymous, meaning that we will not collect any personal information that could identify you or connect you to your responses. However, if you are interested in being entered into a raffle for a $25 Visa gift card, you can include your name and contact information at the end of the survey. Your contact information will not be used for any other purposes beyond sending you the raffle prize if you have won. This survey should take approximately 15 minutes to complete. Questions in the survey will ask you about your satisfaction of the delivery and presentation of fertility-related information, the healthcare providers involved, the resources that you received, and demographic information about yourself.

This study is being conducted by Rachel Hickey, a genetic counseling student at the University of South Carolina Medical School for a Master's Thesis project. Emily Jordon, a genetic counselor at the University of South Carolina, is the faculty thesis advisor for this study. If you have any questions about this study, please contact us.

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For questions about your rights as a participant, you may contact the Office of Research Compliance at the University of South Carolina at (803) 777-7095.

By clicking the "Next" button below, you are indicating your consent to participate in

this study.

Thank you for sharing your insight.