

Understanding of Management Guidelines in Patients with Lynch Syndrome

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Abstract

Lynch syndrome is an autosomal dominant hereditary cancer syndrome with relatively high prevalence. It is estimated that more than one million Americans have Lynch syndrome, and more than 95% have not been identified. Identification of these individuals is important so that measures can be taken for prevention or early detection of associated cancers. No existing studies assess how well individuals with Lynch syndrome understand these guidelines; some prior studies have assessed adherence to colonoscopies, the recommendation with the most evidence, with mixed results. The purpose of this study was to survey adults with a diagnosis of Lynch syndrome, to assess their understanding of and adherence to management guidelines and to learn about their experiences with healthcare providers and any barriers to following guidelines. A survey was distributed through two Lynch syndrome advocacy groups, Lynch Syndrome International and AliveAndKickn, via Facebook, Twitter, and email listservs. The survey had 312 responses; 278 of those responses met eligibility criteria and were analyzed. Most participants had above average education and household income. More than 70% of respondents indicated they had a colonoscopy in the past 12 months, and more than 95% understood they should have colonoscopies at least every two years. This survey provides a starting point for research surrounding education and understanding of medical management guidelines for individuals with Lynch syndrome. While the results indicate a high understanding of and adherence to management guidelines, the non-representative demographics may limit the generalizability of the study findings. Future studies

should aim to assess a more representative sample of individuals with Lynch syndrome, and consider how best to educate and increase access to genetic counseling and education for newly diagnosed individuals. The identification of more individuals with Lynch syndrome is an important public health genetics goal in order to increase surveillance in this group and decrease morbidity and mortality associated with cancer; attempts to achieve this goal should include a plan to educate and increase access to care for those with a new diagnosis.

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Preface

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1.0 Introduction

Lynch syndrome is an adult-onset hereditary cancer syndrome estimated to affect at least 1 in 300 individuals (Pearlman et al., 2017). It has an autosomal dominant inheritance pattern and is caused by a mutation in one of five genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*, *EPCAM*); these genes, aside from *EPCAM*, are part of the mismatch repair (MMR) pathway (Berg et al., 2009). Individuals with Lynch syndrome have risks for specific cancers that are higher than the general population; the two highest risks are for colorectal and for women, endometrial cancer. They are also more likely to have cancer at a younger age (under 50) (National Comprehensive Cancer Network, 2019). Lynch syndrome accounts for 3-5% of all colorectal cancers (Win et al., 2017). While it is estimated that more than one million Americans have Lynch syndrome, the vast majority of them have not been diagnosed (Rahm et al., 2018). It is important to identify affected individuals because the additional, recommended preventative care decreases morbidity and mortality (Berg et al., 2009). Several groups have created medical management guidelines based on evidence demonstrating the effectiveness of increased screening to prevent cancers or identify them at an early, more treatable stage (Berg et al., 2009; Hegde et al., 2014; National Comprehensive Cancer Network, 2019; Weissman et al., 2012). The most agreed upon recommendation is for individuals with Lynch syndrome to have frequent colonoscopies (every 1-2 years) starting at a younger age (20-25 years old) than is recommended for the general population. Colonoscopies are especially effective because polyps can be removed before they become cancerous; this is a rare opportunity to routinely prevent cancer, as opposed to detecting early-stage cancer or having a prophylactic surgery (National Comprehensive Cancer Network, 2019). The ability to decrease morbidity and mortality and the relatively high prevalence of Lynch

syndrome make both the identification and education of these patients important public health issues.

Some existing studies have explored the experiences of individuals with a diagnosis of Lynch syndrome. These include surveys of adults and their intentions to disclose their diagnosis to their children (K. I. Aktan-Collan et al., 2011), opinions on cancer screening (Hunter et al., 2017), satisfaction with healthcare providers for colorectal cancer survivors of individuals with Lynch syndrome compared to those with sporadic cancer (Burton-Chase et al., 2017), and quality of life for colon cancer survivors with Lynch syndrome with different types of surgery (Haanstra et al., 2012). These studies found that most individuals shared their diagnosis with their adult children (K. I. Aktan-Collan et al., 2011), survivors of colorectal cancer are happy with tumor screening when they understand the utility (Hunter et al., 2017), colon cancer survivors with Lynch syndrome are less satisfied with their healthcare providers than their counterparts without Lynch syndrome but both groups trust their providers equally (Burton-Chase et al., 2017), and individuals with Lynch syndrome who had a subtotal colectomy had similar quality of life to those with a partial colectomy (Haanstra et al., 2012). Another study surveyed individuals from families with Lynch syndrome who had tested positive or negative, to assess their psychosocial response to genetic testing, understanding of cancer screening recommendations, and perceived cancer risk. This study found that most individuals who test positive adapt to their diagnosis and undergo necessary screening long-term (Esplen et al., 2015). No existing surveys have focused on understanding of medical management recommendations for adults with Lynch syndrome.

The goal of this project was to develop a survey for adults (age 18 and older) with a diagnosis of Lynch syndrome, to assess their understanding of and adherence to medical management guidelines, experiences with cancer and cancer prevention, and experiences with

genetic counselors and other providers. While identification of individuals with Lynch syndrome is an important first step towards decreasing morbidity and mortality from related cancers, making these diagnoses is only helpful if patients understand their diagnosis, share it with their doctors, and understand and follow the recommended management guidelines. This survey is a small step towards the long-term goal of empowering people to work with their providers to ensure patients understand medical management guidelines, to ultimately decrease morbidity and mortality from cancer as well as healthcare costs associated with cancer treatment.

The second part of this project (Chapter 5), the creation of a toolkit for the general public with information about hereditary cancer with a focus on Lynch syndrome, is in collaboration with the Pennsylvania Cancer Coalition (PCC) Cancer Genetics/Genomics work group. The goal of this project is to identify resources that already exist and may be useful for individuals with a diagnosis of Lynch syndrome, or who are concerned about the possibility of a hereditary cancer syndrome. This toolkit provides a list of reliable resources in one place, so that members of the general public do not need to search for these resources on their own. This portion of the project has a strong public health focus; it aims to help educate the general public on an important public health genetics issue and to advance the genetics goals included in the Pennsylvania Cancer Control Plan.

1.1 Specific Aims

The following are the three specific aims of this project:

1. Develop an online survey in Qualtrics targeted to individuals with a diagnosis of Lynch syndrome, using published surveys as models.

2. Utilize this survey, which will be distributed through partnerships with Lynch syndrome-related advocacy groups via listservs and social media, to assess the following:
 - a. How well patients with Lynch syndrome can identify established clinical management guidelines, focusing on colonoscopies
 - b. How well patients with Lynch syndrome adhere to clinical management guidelines, and whether knowledge correlates with adherence
 - c. Whether or not patients with Lynch syndrome who have had genetic counseling differ in their knowledge of and adherence to guidelines from patients with Lynch syndrome who have not had genetic counseling
 - d. Barriers faced by individuals with Lynch syndrome that prevent them from following management guidelines
3. Utilize the survey results to consider how genetic counselors and other health professionals might better care for patients with Lynch syndrome and other hereditary cancer syndromes.

2.0 Literature Review

Lynch syndrome is a hereditary cancer syndrome associated with an increased risk of several cancers at younger ages, with the highest associated cancer risks being colorectal and endometrial cancers (Lynch, Snyder, Shaw, Heinen, & Hitchins, 2015). Originally termed hereditary non-polyposis colorectal cancer (HNPCC), the syndrome was renamed to avoid the misleading implications that it is only associated with colorectal cancer and that individuals with this syndrome do not have polyps (Lynch et al., 2015). A recent study found that as many as 1 in 279 individuals in the population have Lynch syndrome (Win et al., 2017) but prevalence estimates can be as low as 1 in 440 (Chen et al., 2006). This implies that at least one million Americans are affected. It is the most common hereditary predisposition to colorectal cancer (Lynch et al., 2015), accounting for 3-5% of all colorectal cancers (Win et al., 2017).

Lynch syndrome is an autosomal dominant condition, caused by a single germline mutation in one of four mismatch repair (MMR) genes: *MLH1*, *MSH2*, *MSH6*, and *PMS2*. Deletions at the 3' end of *EPCAM*, a gene upstream of *MSH2*, can also cause Lynch syndrome by interfering with *MSH2* expression (Lynch et al., 2015). When functioning properly, MMR proteins work alone and together as heterodimers to identify single-nucleotide mismatch errors in DNA replication, as well as small insertions and deletions (Guerrette, Wilson, Gradia, & Fishel, 1998). Cells missing one or more MMR proteins develop what is referred to as a “mutator phenotype,” or a higher than normal mutation rate. Since individuals with Lynch syndrome have one defective MMR gene in each of their cells, their entire genomes are affected (Martin-Lopez & Fishel, 2013). Patients with Lynch syndrome have one copy of the wild type allele, which is sufficient for mismatch repair; tumors form when the functioning copy is lost, and there is no backup copy to fix the errors

(Hemminki et al., 1994). This concept explains the increased risk in many hereditary cancer syndromes, and is known as Knudson's "two-hit hypothesis" (Knudson, 1985).

Lynch syndrome is associated with a lifetime risk of colorectal cancer as high as 75% (Giardiello et al., 2014). The cancer risks differ depending on the gene in which the mutation is located; mutations in *MLH1* and *MSH2* have the highest risks and *MSH6* and *PMS2* risks are lower. Cancer risks associated with *EPCAM* are thought to be similar to *MSH2* risks (National Comprehensive Cancer Network, 2019). Colorectal cancer is one of the most common cancer types in the general population, with roughly 135,000 diagnoses and 50,000 deaths in the United States each year (Siegel, Miller, & Jemal, 2017). Women with Lynch syndrome have a lifetime risk for endometrial cancer as high as 60% (Weissman et al., 2011). Lynch syndrome is thought to be responsible for approximately 3% of all colorectal cancer and 1.8% of all endometrial cancer (Biller, Syngal, & Yurgelun, 2019). Individuals with Lynch syndrome also have increased risks for other cancers, including ovarian, gastric, pancreatic, bladder, biliary tract, urothelial, small bowel, prostate, and brain/CNS. Risks for these cancers are higher than for the general population, but lower than the increased risks for CRC and endometrial cancers associated with Lynch syndrome (National Comprehensive Cancer Network, 2019). There is some evidence to suggest that women with Lynch syndrome have an increased risk for breast cancer, but conflicting studies make this a debated issue (Win, Lindor, & Jenkins, 2013).

2.1 Review of Management Guidelines

While medical management recommendations for individuals with Lynch syndrome were published as early as the 1990's (Lynch, 1996), it was not until the mid-2000's that evidence

suggested healthcare management such as colonoscopies and preventative surgeries may decrease morbidity and mortality from Lynch syndrome-related cancers (Lynch et al., 2015). Today, there are management guidelines suggested by several working groups, which rely on studies showing that certain medical interventions improve patient outcomes either by preventing cancer or identifying and treating it early (Berg et al., 2009; Giardiello et al., 2014; National Comprehensive Cancer Network, 2019).

Initially, preventative colectomy (removal of the colon) before cancer development was discussed as an option for individuals with Lynch syndrome, in the context of receiving genetic counseling and discussing all possible options with a surgeon (Lynch, 1996). This option was important because it was known that polyps turned to cancer more quickly in individuals with Lynch syndrome (Lynch, 1996). In 2000, a randomized controlled study that followed asymptomatic individuals from families with Lynch syndrome for 15 years demonstrated that colonoscopies were effective in preventing CRC, likely because polyps were removed before turning cancerous. Patients in this trial had colonoscopies every three years, and this study did not determine the optimal time interval for colonoscopies in affected individuals (Jarvinen et al., 2000). By 2006, several studies had found that frequent colonoscopies decreased both cancer incidence and mortality for individuals with Lynch syndrome (de Vos tot Nederveen Cappel et al., 2002; Dove-Edwin, Sasieni, Adams, & Thomas, 2005) and a literature review found evidence in favor of colonoscopies every one to two years starting starting at age 20 to 25 (or age 30 for *MSH6* mutation carriers) (Lindor et al., 2006). This evidence suggests that frequent colonoscopies are an important preventative measure for individuals with Lynch syndrome.

Gynecological surveillance for endometrial cancer for women with Lynch syndrome has also been evaluated. A 2002 study followed 292 women for up to 13 years depending on when

patients registered; 171 of them had a genetic diagnosis of Lynch syndrome, and the rest were from families with a history indicative of Lynch syndrome. The women were screened annually or every other year with transvaginal ultrasound (which was recommended at the time by the International Collaborative Group on HNPCC), but the two cases of endometrial cancer found during the study were identified based on symptoms, not on routine screening (Dove-Edwin et al., 2002). A similar but smaller study in 2003 followed 41 women with genetic mutations for Lynch syndrome or whose families met Amsterdam criteria for 10 years and performed annual transvaginal ultrasounds. Similarly, no cancers were detected via ultrasound and the one endometrial cancer in the study was found when the patient presented with symptoms (Rijcken, Mourits, Kleibeuker, Hollema, & van der Zee, 2003). These studies suggest the importance of patient education for women with Lynch syndrome regarding the symptoms of endometrial cancer. A 2007 study following 175 women with genetic diagnosis of Lynch syndrome similarly found transvaginal ultrasound did not detect asymptomatic cancers, but that endometrial biopsy was better at detecting early cancers (Renkonen-Sinisalo et al., 2007). Endometrial biopsy, however, is a more invasive procedure than ultrasound (Rijcken et al., 2003). Women with Lynch syndrome often have positive outcomes following endometrial cancer diagnosis, because symptoms manifest early when the cancer is still treatable (Renkonen-Sinisalo et al., 2007). These studies have not proven that screening is effective for decreasing morbidity and mortality associated with endometrial cancer for women with Lynch syndrome. The current NCCN recommendations for endometrial cancer are to consider biopsy every 1-2 years as a screening tool; screening via transvaginal ultrasound can also be considered in women who have reached menopause. Prophylactic hysterectomy can also be considered; the timing of this surgery depends on personal

factors such as reproductive decisions, family history of endometrial cancer, and which gene has the mutation (National Comprehensive Cancer Network, 2019).

Women with Lynch syndrome also have an increased risk of ovarian cancer, with a lifetime risk of up to 38% depending on the gene (National Comprehensive Cancer Network, 2019). While research regarding ovarian cancer surveillance and Lynch syndrome is limited (Helder-Woolderink et al., 2016), screening for ovarian cancer has been studied in women with HBOC (hereditary breast and ovarian cancer). While ovarian cancer may be detected via screening, the cancer is often late stage and may not improve outcomes (Andrews & Mutch, 2017). Studies of high-risk women, including those with hereditary cancer syndromes and family histories of ovarian cancer, have found that screening methods such as transvaginal ultrasound and CA-125 blood levels are not useful for early detection and do not decrease mortality due to ovarian cancer (Gerritzen et al., 2009; Olivier, Lubsen-Brandtsma, Verhoef, & van Beurden, 2006; Stirling et al., 2005). Results of these screenings tests are even more difficult to interpret in women who have not yet reached menopause (Stirling et al., 2005). Because screening detects some cancers, it may be used in some cases. Unlike the recommendation for yearly colonoscopies, the routine use of ovarian cancer screening for women with Lynch syndrome remains controversial (Andrews & Mutch, 2017). One method to decrease mortality from ovarian cancer in high-risk women is to have a prophylactic BSO (bilateral salpingo-oophorectomy); this can be done at the same time as a hysterectomy to minimize the number of surgeries. There are associated risks; one study found that 1.6 percent of these surgeries in women with Lynch syndrome had complications such as bleeding and infection (Schmeler et al., 2006). The current NCCN recommendation for ovarian cancer prevention in women with Lynch syndrome is patient education of symptoms associated with ovarian cancer (such as bloating and abdominal pain) and consideration of prophylactic BSO.

As with hysterectomy, timing of BSO is individualized and factors such as reproductive decisions and family history should be considered (National Comprehensive Cancer Network, 2019). The guidelines note that data do not support the utility of screening for ovarian cancer, but that transvaginal ultrasound and CA-125 blood levels “may be considered at the clinician’s discretion” (National Comprehensive Cancer Network, 2019, pp. LS-3). NCCN guidelines also note that preliminary evidence shows use of oral contraceptives can be useful in preventing gynecological cancers, and this option can be discussed with individual healthcare providers (National Comprehensive Cancer Network, 2019).

The NCCN guidelines provide the most detail for colorectal, endometrial, and ovarian cancers, but also include recommendations for and mention of other Lynch syndrome-associated cancers. Screening for gastric and small bowel cancers can be considered, especially for individuals with a family history of these cancers or who are of Asian ancestry; upper endoscopy can be performed every 3-5 years starting at age 40, or earlier and/or more frequently at the clinician’s discretion. There is insufficient evidence to definitively recommend screening for urothelial cancers, but individuals with *MSH2* mutations, especially males, and those with a family history of these cancers can consider a urinalysis every year starting at age 30-35. A yearly physical and neurological exam starting at age 25-30 is a screening option for central nervous system cancers, such as brain tumors (National Comprehensive Cancer Network, 2019). Although individuals with Lynch syndrome are known to have an increased risk for pancreatic cancer, there is insufficient evidence to recommend screening. Those with Lynch syndrome and a history of a first-degree relative with pancreatic cancer should be considered for surveillance (MRI and/or ultrasound via endoscopy), preferably at a center familiar with this type of screening (Syngal et al., 2015). Men with Lynch syndrome are at an increased risk for prostate cancer, though there are

no evidence-based recommendations for this group; NCCN recommends that men be screened for prostate cancer as outlined in their Prostate Cancer guidelines. Finally, there is debate about whether or not women with Lynch syndrome have an increased risk for breast cancer; the current recommendation is for women to be screened based on guidelines for the general population, or based on family history if family members have had breast cancer (National Comprehensive Cancer Network, 2019).

2.2 Adherence to Management Guidelines

While it is important for individuals with hereditary cancer syndromes to understand the medical management guidelines for their condition, it is equally important for them to adhere to the guidelines. Lack of adherence to guidelines decreases their ability to prevent cancer. Studies in the United States have conflicting conclusions about whether or not adherence to management guidelines for colonoscopies is satisfactory for individuals at high risk for CRC. One study followed 242 participants with *MLH1* and *MSH2* mutations from 57 families, and found that 97.1% of participants complied with having colonoscopies. This study defined compliance as having colonoscopies at least every three years (Jarvinen et al., 2009). Another study followed 98 individuals from 11 families with identified Lynch syndrome mutations; participants in this study were at a 25% chance to carry the familial mutation, and had never been diagnosed with CRC or had a colectomy. Participants had genetic testing during the study, and 22 of them tested positive for Lynch syndrome. Of the 22 individuals who tested positive, 73% reported having a colonoscopy within one year after learning of their genetic diagnosis, as opposed to 36% who reported having a colonoscopy before genetic testing. The authors concluded that genetic diagnosis

of Lynch syndrome increased motivation for CRC screening in individuals from families with Lynch syndrome (Halbert et al., 2004).

A survey of 270 individuals with a personal history or family history of CRC whose families met the Bethesda criteria found that adherence to colonoscopy screening recommendations could be improved. One hundred eighty-one of these individuals had either tested positive for a Lynch syndrome mutation and thus had a molecularly confirmed diagnosis or met Amsterdam I or II criteria but had not undergone genetic testing. The latter group was considered equally at risk for Lynch syndrome cancers as those who tested positive for the purposes of this study. One hundred thirty-two of these individuals (73%) had undergone a colonoscopy at least every two years and therefore adhered to the management guidelines. Individuals who had already been diagnosed with CRC or had relatives with CRC, especially at younger ages, were more likely to adhere to guidelines. Other factors, including socioeconomic status, having health insurance, and having higher levels of education were positively associated with higher adherence to guidelines. The study concluded that adherence to guidelines could be improved amongst those at high risk for CRC in the United States (Stoffel et al., 2010), especially because adherence rates for similar individuals in countries such as Finland are closer to 100% (Pylvanainen, Kairaluoma, & Mecklin, 2006). Another study of 165 individuals without a personal history of CRC who are from families that meet Amsterdam II criteria found that only 21.8% were aware that colonoscopies should be performed every 1-2 years, and 58% of participants had a colonoscopy during the two years in which the study took place. This study concluded that knowledge of and adherence to CRC screening in these families is poor and there is much room for improvement (Patel et al., 2016).

These studies of individuals at high risk for CRC have conflicting conclusions regarding adherence to screening recommendations; each study also has a slightly different population (individuals with a diagnosis of Lynch syndrome, individuals from families that meet Amsterdam II criteria, etc.) as well as a different definition of “adherence” and the suggested colonoscopy interval. The conclusion about whether or not adherence is satisfactory based on the percentage who have adhered is also somewhat subjective. These studies suggest that more could be done to educate individuals with CRC about their risks and appropriate screening methods.

2.3 Lynch Syndrome-Related Guidelines

Historically, guidelines known as the Amsterdam Criteria and Bethesda Guidelines have been used to evaluate patients to determine if they were at risk for having Lynch syndrome (Lynch et al., 2015). The Amsterdam Criteria were first developed by the International Collaborative Group on Hereditary Non-Polyposis Colorectal Cancer (ICG-HNPCC) in 1991. The group created clinical criteria used to diagnose families with Lynch syndrome (referred to at the time as HNPCC) (Vasen, Mecklin, Khan, & Lynch, 1991). The criteria were revised by the group in 1999 (Vasen, Watson, Mecklin, & Lynch, 1999). Both versions are listed in Table 1. The 1991 criteria, referred to later as “classic Amsterdam criteria,” (Vasen et al., 1999) focused on colorectal cancer only. The updated Amsterdam criteria in 1999 were broadened to include other Lynch-related cancers (CRC, endometrial, small bowel, ureter, and renal pelvis). The criteria were the same, with “HNPCC-related cancers” substituted for CRC (Vasen et al., 1999). Both versions of the criteria are outlined in Table 1. In their updated report, the group stated concerns that a substantial number of families with Lynch syndrome did not meet the original Amsterdam Criteria because non-

colorectal cancers were not included. This was a problem for both researchers, who wanted to investigate affected families, and the families themselves, who may be falsely reassured that their cancers were not hereditary (Vasen et al., 1999).

Table 1 Amsterdam Criteria

Original Criteria (Vasen et al., 1991)	Updated Criteria (Vasen et al., 1999)
There should be at least 3 relatives with CRC; one should be a first-degree relative of the other 2	There should be at least 3 relatives with an HNPCC-associated cancer (CRC, cancer of the endometrium, small bowel, ureter, or renal pelvis); one should be a first-degree relative of the other 2
At least 2 successive generations should be affected	At least 2 successive generations should be affected
At least 1 CRC should be diagnosed before age 50	At least 1 should be diagnosed before age 50
Familial adenomatous polyposis should be excluded	Familial adenomatous polyposis should be excluded in the CRC case(s) if any
Tumors should be verified by pathological examination	Tumors should be verified by pathological examination

(adapted from Vasen et al., 1999, p.1454, 1555)

The other clinical guidelines designed for Lynch syndrome are known as the Bethesda Criteria. The Bethesda Criteria were first developed in 1997 by the National Cancer Institute, as a collaboration during an international Lynch syndrome meeting (Rodriguez-Bigas et al., 1997). Whereas the Amsterdam Criteria allowed for clinical diagnosis based on family history, the Bethesda Criteria were created to determine who should receive MSI testing based on colorectal tumor characteristics in addition to family history. If a tumor was MSI-H, that person would then be referred for genetic counseling and germline testing (Rodriguez-Bigas et al., 1997). Another goal was to develop a different set of criteria that might detect affected families who did not meet the classic Amsterdam Criteria, which were the only criteria for HNPCC at the time (Rodriguez-Bigas et al., 1997). Eight criteria were developed (Table 2), and individuals who met any of them were considered to qualify for MSI tumor testing (Rodriguez-Bigas et al., 1997). The Bethesda

Criteria were revised in 2004; the group recognized that broader criteria would do a better job of finding individuals with Lynch syndrome, although performing MSI testing for every tumor was considered too costly (Umar et al., 2004). The newer criteria were simplified and broadened, to allow for cases such as having a second-degree relative with a Lynch-related cancer; language was also clarified for a broader audience, including primary care physicians. The group also created recommendations for germline testing in patients who met the Bethesda Criteria; ideally, the tumor would first be tested using MSI or IHC and those who tested positive could then have germline testing for the Lynch syndrome gene(s) indicated by the screening (Umar et al., 2004). Both versions are shown in Table 2.

Table 2 Bethesda Criteria

Original Criteria (adapted from (Rodriguez-Bigas et al., 1997, p. 1761))	Updated Criteria (adapted from (Umar et al., 2004, p. 15))
Guidelines for testing of colorectal tumors for microsatellite instability:	Tumors from individuals should be tested for MSI in the following situations:
1. Individuals with cancer in families that meet the Amsterdam Criteria	1. Colorectal cancer diagnosed in a patient who is less than 50 years of age
2. Individuals with two HNPCC-related cancers, including synchronous and metachronous colorectal cancers or associated extracolonic cancers (endometrial, ovarian, gastric, hepatobiliary, or small-bowel cancer or transitional cell carcinoma of the renal pelvis or ureter)	2. Presence of synchronous, metachronous colorectal, or other HNPCC-associated tumors (colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain tumors; sebaceous gland adenomas and keratoacanthomas; and carcinoma of the small bowel), regardless of age
3. Individuals with colorectal cancer and a first-degree relative with colorectal cancer and/or HNPCC-related extracolonic cancer and/or a colorectal adenoma; one of the cancers diagnosed at age <45 y, and the adenoma diagnosed at age <40 y	3. Colorectal cancer with MSI-H histology diagnosed in a patient who is less than 60 years of age
4. Individuals with colorectal cancer or endometrial cancer diagnosed at age <45y	4. Colorectal cancer diagnosed in one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under 50 years of age
5. Individuals with right-sided colorectal cancer with an undifferentiated pattern (solid/cribriform) on histopathology diagnosed at age <45 y	5. Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age
6. Individuals with signet-ring-cell-type colorectal cancer diagnosed at age <45 y	
7. Individuals with adenomas diagnosed at age <40 y	

Guidelines since the Amsterdam and Bethesda Criteria have outlined recommendations for issues such as who should be tested for Lynch syndrome and how individuals who test positive should be managed. In 2009, the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group reviewed existing studies related to diagnosis and testing of individuals with Lynch syndrome and published testing guidelines. The guidelines had five main goals: to specify the definition of Lynch syndrome and who has a diagnosis, evaluate family history beyond Amsterdam and Bethesda criteria, report on the utility of screening and diagnostic tests, clarify estimates for lifetime cancer risks in those with Lynch syndrome, and evaluate the costs and benefits of four different screening and testing strategies to identify families with Lynch syndrome (Palomaki, McClain, Melillo, Hampel, & Thibodeau, 2009). The group determined that the condition should be referred to only as “Lynch syndrome” (as opposed to “HNPCC”) and that an individual officially has Lynch syndrome if a germline pathogenic variant is found in one of the related genes. Whereas HNPCC had been defined by different criteria such as family history or tumor features, the availability of genetic testing allowed for a genetic definition of Lynch syndrome with greater sensitivity (Palomaki et al., 2009). The document outlined other evidence related to Lynch syndrome, including sensitivity and specificity of screening methods such as IHC, MSI, and *BRAF* mutation testing, medical management and lifetime cancer risks for individuals who test positive, and cost effectiveness of population tumor screening for new cases of CRC. Universal tumor screening for all colorectal cancers was recommended by this group. It was also determined that preventative colectomy is not recommended; the risks and benefits of colonoscopies as a screening tool were outlined, with evidence demonstrating that frequent colonoscopies are likely effective in CRC prevention for those with Lynch syndrome. Four strategies for tumor screening using various detection methods were outlined; although there was

not enough evidence for the group to make a recommendation, the costs and benefits of each approach are summarized as a guideline for groups making such decisions (Palomaki et al., 2009). While knowledge of some of the specifics in the EGAPP document have changed over the past decade, (lifetime cancer risks, evidence supporting or refuting medical management strategies, cost of genetic testing, etc.) this paper contains foundational principles and ideas that are still widely used.

Another important set of recent guidelines are the NCCN (National Comprehensive Cancer Network) guidelines. NCCN is a group of more than 1,300 clinicians from 28 member institutions that frequently review the recent literature and evidence for different kinds of cancer, including prevalence, how cancers are treated, and prognosis. Recommendations for each cancer type are summarized in a document that is updated frequently to reflect the most up-to-date literature (National Comprehensive Cancer Network, n.d.-a). Information is also provided for certain population groups, such as young adults, and supportive care, such as cancer-related fatigue. Guidelines are also provided for screening and prevention of common cancers including breast, colorectal, and cervical cancers. This section includes two “Genetic/Familial High-Risk Assessment” guidelines; one for colorectal cancer and the other for breast, ovarian, and pancreatic cancers (National Comprehensive Cancer Network, n.d.-b). The colorectal cancer document covers hereditary cancer syndromes that are associated with an increased risk of colorectal cancer, including Lynch syndrome. The guidelines are updated often to incorporate the most up-to-date evidence; three different versions were published in 2019 alone (National Comprehensive Cancer Network, 2019).

The latest NCCN guidelines for Lynch syndrome include a flowchart outlining who should receive genetic testing, detailed medical management guidelines for individuals with Lynch

syndrome, explanations and descriptions of tumor screening methods (IHC and MSI), and lifetime cancer risks for each Lynch syndrome gene. The medical management guidelines are helpful not just because they summarize evidence-based recommendations (such as colonoscopies every 1-2 years), but also because they outline the Lynch syndrome-related cancers that do not have evidence-based screening recommendations. Although individuals with Lynch syndrome are at increased risk for gastric, urothelial, and pancreatic cancers, there are no studies demonstrating a clear benefit from prophylactic surgeries or screening techniques. Other potential medical management, such as taking aspirin to reduce the risk of CRC and transvaginal ultrasounds to screen for endometrial cancer, are listed as strategies that can be considered although the evidence supporting them is not clear enough to recommend specific guidelines (National Comprehensive Cancer Network, 2019). While medical management of individuals with Lynch syndrome is ultimately decided by patients and their individual doctors, NCCN guidelines provide the evidence needed for clinicians to make recommendations based on their patients' personal and family circumstances. Detailed notes at the end of the NCCN document provide references for stated facts and further explanation, so that providers can read the primary literature themselves (National Comprehensive Cancer Network, 2019).

Other professional groups with published guidelines for Lynch syndrome are NSGC (National Society of Genetic Counselors), ACMG (American College of Medical Genetics), and ACG (American College of Gastroenterology) (Hegde et al., 2014; Syngal et al., 2015; Weissman et al., 2012). In 2012, NSGC published Lynch syndrome guidelines in collaboration with CGA-IGC (the Collaborative Group of the Americas on Inherited Colorectal Cancer). This paper provides an overview of MSI and IHC as Lynch syndrome screening techniques that can be used before germline testing, including how they compare with the historical Amsterdam and Bethesda

criteria, sensitivity and specificity in identifying individuals with Lynch syndrome, and technical details of the tests (Weissman et al., 2012). The paper recommends that MSI and IHC tumor testing should be used on CRC and endometrial cancers as “the first-line testing strategy for any patient being evaluated for [Lynch syndrome],” and that if tumor sample is unavailable for the proband, a relative’s tumor should be tested if possible (Weissman et al., 2012, p. 489). Germline genetic testing as a first-line test should be considered when no tumor sample in the family is available for testing. (Weissman et al., 2012). The NSGC has now retired these guidelines, and a committee is currently working on new guidelines for Lynch syndrome (National Society of Genetic Counselors, 2019).

ACG published medical management guidelines for several hereditary GI (gastrointestinal) cancer syndromes, including Lynch syndrome, in 2015. This paper recommended universal tumor screening (IHC or MSI) for all new CRC diagnoses; individuals with tumor features suggestive of Lynch syndrome should be evaluated by a genetics provider. Similar to the NCCN guidelines, this paper recommends colonoscopies at least every two years starting at age 20-25, with consideration of yearly colonoscopies. Yearly endometrial biopsy and transvaginal ultrasound should be offered to women with Lynch syndrome to screen for endometrial and ovarian cancers starting at age 30-35; removal of uterus and ovaries should be offered to women at age 40-45 to prevent these cancers. An esophagogastroduodenoscopy procedure with gastric biopsy can also be offered every 3-5 years starting at age 30-35; available data does not strongly support this screening method but it should be considered for individuals with a family history of gastric or duodenal cancers. This paper does not recommend further screening for other cancers (such as prostate and breast) beyond screening recommended for the general population, unless an individual has a family history of one of these cancers. Finally, although some studies suggest a daily dose of aspirin decreases the

risk of CRC for individuals with Lynch syndrome, this paper states there is not enough data to recommend it as a preventative measure (Syngal et al., 2015).

In 2015, the NSGC and ACMG published a joint paper with guidelines for patient referral due to concern for a hereditary cancer syndrome. While not specific to Lynch syndrome, the guidelines include situations where Lynch syndrome may be a differential diagnosis. For example, Lynch syndrome should be considered in an individual with CRC diagnosed under the age of 50, a proband with CRC at any age and a first degree relative with CRC or endometrial cancer at any age, or when a proband has a sebaceous adenoma or carcinoma and another Lynch syndrome cancer in the family. This paper also lists 10 tumor types associated with Lynch syndrome, including colorectal or endometrial adenocarcinoma, gastric cancer, and ovarian cancer. Tumor features seen in Lynch syndrome, including MSI and loss of one or more MMR proteins, are also outlined, along with limitations of the Amsterdam and Bethesda criteria. The paper reviews 27 other hereditary cancer syndromes in a similar manner, so that a provider knows the type of family history questions to ask and develop a set of differential diagnoses (Hampel et al., 2015). An addendum to these guidelines published in 2019 states that although the original paper remains accurate and helpful, knowledge of these hereditary cancer syndromes continues to change and grow. When reviewing a patient or family history, it is important to recognize that some patients may need a referral even if they do not strictly meet the criteria outlined in the guidelines (Bashford et al., 2019).

2.4 Identification of Individuals with Lynch Syndrome

While the prevalence of Lynch syndrome suggests at least one million Americans are affected, it is estimated that only two percent have been diagnosed (Rahm et al., 2018). This presents a public health issue; there is evidence that cancer screening can decrease morbidity and mortality from Lynch syndrome-related cancers (Berg et al., 2009), but individuals with Lynch syndrome cannot undergo increased surveillance unless they are aware of their diagnosis. As increased attention is placed on the identification of individuals with Lynch syndrome through public health genetics and other initiatives as described in this section, it is equally important to ensure that diagnosed individuals understand, have access to, and are compliant with screening recommendations. The purpose of this project is to assess compliance and understanding in those who already have a diagnosis.

Tumors caused by Lynch syndrome often have features that indicate that the person may have Lynch syndrome; these features allow a unique opportunity to screen individuals with cancers such as CRC and endometrial cancer for Lynch syndrome. Programs developed to screen all individuals diagnosed with colon and/or endometrial cancers via tumor testing are known as universal screening programs (Rahm et al., 2018). Universal screening is cost-effective and has been recommended rather than relying on the use of clinical criteria to identify more individuals with Lynch syndrome; the tumor is tested first for features that indicate a higher chance of Lynch syndrome (Centers for Disease Control and Prevention, 2014a; Palomaki et al., 2009). Those whose tumors test positive are then offered germline testing, which is often diagnostic for Lynch syndrome (Weissman et al., 2011). Although some individuals who do not have Lynch syndrome will be referred for genetic testing, money is saved by decreasing the number of germline tests to those most likely to have Lynch syndrome based on their tumor features (Weissman et al., 2011).

Universal screening has been found to be a cost-effective tool for identifying individuals with Lynch syndrome (Mvundura, Grosse, Hampel, & Palomaki, 2010); however, 10-15% of Lynch syndrome cancers will not be identified using tumor screening methods (Giardiello et al., 2014).

Because Lynch syndrome is relatively common and tumors can be prevented or identified early for those who are found to have a mutation, identifying individuals with Lynch syndrome, especially those who have not yet had cancer, is an important public health issue (Hampel et al., 2008). Research on large cohorts of CRC patients in the general population from the Ohio State University has demonstrated that universal screening is an effective way to identify individuals with Lynch syndrome (Hampel et al., 2008; Moreira et al., 2012). One study combined a previous cohort of 1,066 individuals with CRC whose tumors had MSI screening and subsequent germline testing and IHC for Lynch syndrome genes if MSI was positive (Hampel et al., 2005), with a new cohort of 500 patients with CRC whose tumors had MSI testing. Of these 500 tumors, 483 also had IHC testing for Lynch syndrome genes (17 did not have IHC because there was not enough tumor sample for the test). Those who had positive IHC or MSI results had germline genetic testing for Lynch syndrome (Hampel et al., 2008). Although participants who did not test positive on tumor screening did not have germline mutation testing, the study concluded that MSI and IHC had similar sensitivity to each other and that limiting germline testing to those who test positive could be a reasonable, cost-saving approach. This is especially true if cascade screening of family members is feasible, since testing for a known familial mutation is simple, cheaper than full gene sequencing, and informative (Hampel et al., 2008). Another study combined cohorts from multiple studies to examine 10,206 unrelated participants with CRC who had tumor analysis and/or germline testing for Lynch syndrome. Most participants had tumor screening (IHC or MSI) first and germline testing only if indicated, though less than 2% of the cohort had germline testing

without tumor analysis. The study concluded that universal tumor screening of all new CRC cases followed by germline testing for those whose tumors indicate possible Lynch syndrome is a highly sensitive, cost-effective approach. Although starting with germline testing would be the most sensitive test, it is considered too expensive to be a first-line test for all CRC diagnoses (Moreira et al., 2012). These studies demonstrate that identification of individuals with Lynch syndrome can feasibly be approached from a public health perspective with the goal of cancer prevention for those at increased risk.

There are also barriers to this approach; universal screening identifies the best candidates for germline genetic testing, and individuals who test positive must be willing and able to return to the clinic for a genetic counseling appointment. One study at Ohio State University performed IHC tumor testing for all new CRC cases at their institution for two years (270 cases). Those who tested positive on IHC were called and/or mailed a letter by a genetic counselor and encouraged to make an appointment with genetics. Thirty-four patients had results indicating they should see genetics; only 18 of these participants scheduled an appointment, and half of them (nine) later canceled. The other nine showed up to their appointments; seven of them chose to do further testing, resulting in two diagnoses of Lynch syndrome. Because 2.8% of CRC is caused by Lynch syndrome, this study should include 7.6 individuals with the condition. The study concluded that based on this number, only 26.3% of those with Lynch syndrome were identified by tumor screening. Barriers included that not all patients could be reached, some were uninterested in genetic counseling, and others had since passed away or were unavailable for other reasons, including incarceration (South et al., 2009). Although universal screening is effective at identifying individuals for further Lynch syndrome testing, an effective program requires considering the best ways to provide services to patients in a way that improves health for them and their families

(South et al., 2009). This study demonstrates that even if universal tumor screening is an effective way to make a diagnosis of Lynch syndrome, it will not be a successful public health initiative if patients do not pursue genetic counseling as recommended. While identification of individuals with Lynch syndrome is a barrier, we also need to ensure that once individuals are diagnosed they receive the proper medical care. This study will assess understanding of and adherence to management guidelines for individuals who already have a diagnosis of Lynch syndrome.

The CDC's (Centers for Disease Control and Prevention) OPHG (Office of Public Health Genomics) designates Lynch syndrome as a "Tier 1" condition; this means there is evidence proving that early diagnosis of Lynch syndrome allows for surveillance and pre-symptomatic treatment that can improve outcomes. The other two Tier 1 conditions are HBOC and FH (familial hypercholesterolemia). All three conditions are relatively prevalent in the population and highly underdiagnosed. The OPHG provides toolkits for each of these conditions with evidence-based recommendations on a population level (Centers for Disease Control and Prevention, 2014b). For Lynch syndrome, these recommendations include maintaining a rigorous cancer registry, offering germline genetic testing to individuals with personal and/or family histories suggestive of Lynch syndrome, and cascade screening for relatives of those who test positive for Lynch syndrome (Centers for Disease Control and Prevention, 2014a). The OPHG's designation of Lynch syndrome as a Tier 1 condition indicates that Lynch syndrome is a relevant public health concern, and that identifying and diagnosing those at risk can reduce morbidity and mortality from cancers caused by Lynch syndrome. This also demonstrates that for those with a diagnosis, understanding and following the evidence-based guidelines is important for prevention and early identification of cancer.

The two features of Lynch syndrome-associated cancers that can be used for universal screening are loss of expression of one or more MMR proteins, and MSI (microsatellite instability) (Biller et al., 2019). Presence of these features is not diagnostic of Lynch syndrome, but serves as an initial screening tool that determines which individuals with Lynch-related cancers should undergo germline genetic testing (Rahm et al., 2018).

Given that the large majority of Americans with Lynch syndrome have not been identified (Rahm et al., 2018), universal tumor screening of CRC and endometrial tumors has been proposed as a way to identify those who are undiagnosed (Palomaki et al., 2009). However, identification is only useful for cancer prevention if those with a diagnosis understand their risks and follow recommended guidelines for screening. It is important to discuss the ways in which we might identify these individuals, in the context of how well those who have already been diagnosed understand and adhere to cancer screening and prevention. One of two common tumor screening tests for Lynch syndrome is immunohistochemistry staining, known as “IHC.” IHC checks tumors for the presence or absence of the four MMR proteins associated with Lynch syndrome: *MLH1*, *MSH2*, *MSH6*, and *PMS2*. If expression of one or more of these proteins is missing, this indicates the tumor may have been caused by an underlying germline mutation in one of these genes. Germline genetic testing can also be targeted to one or two Lynch syndrome genes, based on the pattern of loss of expression (Weissman et al., 2011). Some sporadic tumors will have a positive IHC test, but 83% of Lynch syndrome tumors will test positive. However, the positive predictive value, as calculated from the published sensitivity and specificity, is approximately 34% (Palomaki et al., 2009). IHC testing also has the benefit of indicating which genes should be chosen for germline testing, which decreases the cost of genetic testing (Vasen et al., 2007).

The other commonly used technique for Lynch syndrome tumor screening takes advantage of a hallmark feature of tumors caused by Lynch syndrome called microsatellite instability. There are places throughout the human genome, known as microsatellites, that contain the same nucleotides (usually one or two) repeated several times (Yurgelun & Hampel, 2018). Many tumors caused by Lynch syndrome have microsatellite instability, which is the tendency to find changes at microsatellites (Duval & Hamelin, 2002). Universal screening takes advantage of this tumor property by testing tumor samples; MSI regions of the tumor are examined and compared with those same DNA regions in that individual's non-cancerous cells. If enough changes are found by comparison, the tumor is labeled "MSI-high," or "MSI-H" and that patient is appropriate for referral for genetic counseling and testing (Yurgelun & Hampel, 2018). Having an MSI-H tumor does not guarantee the individual has Lynch syndrome; 15% of sporadic tumors will test MSI-H (Jin et al., 2013). Although most MSI-H tumors are sporadic, 20-25% are caused by Lynch syndrome. When used to identify individuals with Lynch syndrome, MSI has 93% sensitivity. This makes it an effective and cost-effective method to identify candidates for more costly germline testing (C. R. Boland & Goel, 2010).

Tumors that test positive for IHC or MSI can be further tested for other sporadic causes of the tumor, eliminating Lynch syndrome as a likely possibility. Sporadic CRC and endometrial tumors can be caused by promoter hypermethylation of *MLH1*, causing loss of *MLH1* expression in the tumor (Kane et al., 1997). These tumors can also test MSI-H, and in CRC are likely to be caused by mutations in the *BRAF* gene which cause *MLH1* promoter hypermethylation (Deng et al., 2004). Individuals whose tumors have *BRAF* mutations rarely have Lynch syndrome. Therefore, colorectal tumors with IHC testing that demonstrates loss of *MLH1* expression and are found to have a *BRAF* mutation do not need germline testing for Lynch syndrome, because the

BRAF mutation indicates a sporadic cause of the tumor (Jin et al., 2013). *BRAF* mutation testing can be added on to testing of colorectal tumors with these specific IHC results (missing expression of MLH1 and PMS2) to further reduce the number of patients who receive germline testing (Jin et al., 2013). It is also possible to find biallelic somatic mutations in the tumor without identification of a germline mutation in the individual; this is another sporadic cause of cancer which can appear to be caused by Lynch syndrome based on IHC testing. These patients may be diagnosed with “Lynch-like syndrome” (Carethers & Stoffel, 2015).

Tumor DNA can also be sequenced to help determine the likelihood that a patient has Lynch syndrome. A study of 465 CRC tumors (419 from the general population and 46 from individuals known to have Lynch syndrome) found that tumor sequencing had higher sensitivity than other tumor screening methods. Between both groups, a total of 58 individuals had Lynch syndrome; tumor sequencing correctly identified all of these participants. MSI and IHC with *BRAF* testing would have failed to identify five and six individuals from the general and known Lynch syndrome groups, respectively (Hampel et al., 2018). A recent position statement from the CGA-IGC recommends a simultaneous gene panel for both germline and tumor for individuals whose initial tumor screening indicates possible Lynch syndrome. This method helps more efficiently determine whether the patient is likely to have Lynch syndrome (especially in cases where a germline mutation cannot be found) or if the tumor is sporadic; the results are important for management of the individual and their family members. However, factors such as family history, the patient’s health insurance, and other patient and tumor characteristics (including patient preference), may influence a provider’s decision to start with one of the two tests (Heald et al., 2020). These newer papers indicate a shift away from traditional tumor screening for CRC (MSI, IHC) towards genetic sequencing of the tumor itself.

2.5 Reactions to Diagnosis

With the availability of genetic testing to diagnose individuals with Lynch syndrome, genetics professionals were unsure how patients would react to positive test results and the knowledge of an increased cancer risk, especially for previvors (individuals who test positive but have never had a cancer diagnosis). A study of members of 36 families with Lynch syndrome in Finland in the 1990s found that 75% of 381 participants chose to pursue genetic testing (K. Aktan-Collan et al., 2000). This was significantly different from the 43% of 208 individuals from Lynch syndrome families in the United States, offered testing around the same time (Lerman et al., 1999). The study in Finland also followed up with participants who chose to be tested; one year later, 86% of those who tested positive and 96% of those who tested negative were “extremely satisfied” with their decision to undergo testing (K. Aktan-Collan et al., 2000). A follow-up study in Finland found that one year after testing, anxiety levels remained unchanged for those who tested positive and negative. The most anxious time was the actual results disclosure; although it was suggested participants bring a friend or family member with them to the disclosure, only 30% followed this advice (K. Aktan-Collan, Haukkala, Mecklin, Uutela, & Kaariainen, 2001). A seven-year follow-up of these individuals found that those who had undergone testing for Lynch syndrome still did not experience significant psychological distress, and most were still content with their decision to take the test (K. Aktan-Collan et al., 2013).

Research on Lynch syndrome and similar hereditary cancer syndromes, such as HBOC, has also demonstrated that most individuals who test positive are not significantly harmed by learning their carrier status. One review paper about predictive genetic testing that included Lynch syndrome and FAP (familial adenomatous polyposis), in addition to Huntington’s disease and spinocerebellar ataxia found that genetic testing generally decreased anxiety for participants,

regardless of whether they tested positive or negative (Broadstock, Michie, & Marteau, 2000). It has also been found that there may be psychological benefits to predictive genetic testing for individuals at risk for Lynch syndrome and FAP. There may be less anxiety associated with these disorders than for HBOC, due to the clear-cut effectiveness of colonoscopies in cancer prevention (Meiser, 2005). In general, it has been found that genetic testing for hereditary cancer syndromes is not psychologically harmful over time to those who test positive or negative, and has clear benefits given the opportunity to screen more frequently and reduce cancer risks (Heshka, Palleschi, Howley, Wilson, & Wells, 2008).

2.6 Surveys of Individuals with Lynch Syndrome

While no existing studies have specifically examined understanding of medical management guidelines for individuals with Lynch syndrome, there have been other surveys of patients with Lynch syndrome (K. I. Aktan-Collan et al., 2011; Esplen et al., 2015; Hunter et al., 2017; Katz et al., 2016). One prior survey explored how patients responded and adjusted after genetic testing for Lynch syndrome. One hundred fifty-five individuals from families with Lynch syndrome took the surveys; participants who tested both positive and negative and received genetic counseling were recruited (Esplen et al., 2015). Participants were given several surveys, and evaluated for knowledge of CRC screening, personal cancer risk, and knowledge of hereditary colon cancer. The surveys also measured psychosocial factors, including quality of life, coping style, depression, anxiety, and distress (Esplen et al., 2015). Most participants adjusted well to their test results. Those who tested positive had more knowledge of hereditary cancer syndromes

and more accurate perceived colon cancer risk; some who tested negative continued with colonoscopy screening, which was an unexpected finding (Esplen et al., 2015).

Other surveys examined how and if individuals with Lynch syndrome share medical information with their relatives (K. I. Aktan-Collan et al., 2011; Hunter et al., 2017). A survey in Finland used the Likert scale to ask 248 parents with Lynch syndrome how they felt about sharing this information with their children and how difficult it was to discuss different topics with their children, such as a high lifetime risk of cancer and the parent's related emotions (K. I. Aktan-Collan et al., 2011). Most individuals with adult children had discussed the diagnosis of Lynch syndrome with their children, and most of those children chose to be tested (K. I. Aktan-Collan et al., 2011). Another survey examined interest in Lynch syndrome screening for patients recently diagnosed with CRC; most participants were interested in screening and intended to share results with their relatives. Most of those who already had a Lynch syndrome diagnosis had shared the news with at least one first-degree relative (Hunter et al., 2017). These studies imply that for the most part, people with Lynch syndrome or who are good candidates for Lynch syndrome testing feel the information would be useful for both themselves and their family members.

Adherence to Lynch syndrome guidelines was examined in patients with Lynch-like syndrome (LLS; individuals whose tumors have MSI but do not have a pathogenic variant in a Lynch syndrome gene). Thirty-four individuals who were 18 or older, had a diagnosis of CRC with abnormal tumor screening results, and a negative germline test for MMR mutations were included in the study. The survey showed that these patients were anxious about the possibility of having cancer again; 76% believed they should have a colonoscopy every 1-2 years, and fear of cancer recurrence was associated with believing colonoscopies should be done more often, though it was not correlated with adherence to recommendations (Katz et al., 2016). Some participants

(22%) thought their tumor testing results meant they tested positive for Lynch syndrome, and 74% felt they had an increased risk to have Lynch syndrome based on their tumor testing and/or germline test. Despite many participants thinking they were at increased risk for Lynch syndrome, most did not recommend genetic counseling for their relatives and did not connect their perceived increased cancer risk with the results of tumor testing (Katz et al., 2016).

2.7 Physician Knowledge of Lynch Syndrome

Surveys of primary care providers (PCPs) have found that many lack knowledge needed to identify and treat individuals with hereditary cancer syndromes; this is a problem, since primary care doctors have some of the best opportunities to take a family history and refer for genetics evaluation (Hamilton et al., 2017). A survey for individuals with Lynch syndrome, examining how to improve patient care in order to achieve the best outcomes, showed that patients wanted more information from their doctors about current research surrounding Lynch syndrome, as well as technical details about topics such as bowel prep and how a colonoscopy procedure works (Hennink et al., 2013).

It has been shown that many PCPs believe in the importance of genetic testing and the information it provides, but that there are barriers to gaining the knowledge necessary to help their patients appropriately. The limited time PCPs have with each patient and constant changes in the world of genetics are likely important factors (Mikat-Stevens, Larson, & Tarini, 2015). With recent advances in the use of genetic testing for precision medicine, it is increasingly important that PCPs are able to address these issues with their patients. However, focus groups with 51 family physicians, nurse practitioners, and other providers found that PCPs do not feel confident in their

knowledge of hereditary conditions and genetic testing and could use more support from and better relationships with genetics clinicians (Carroll et al., 2016). Another study surveyed 361 family practitioners (FPs) in Ontario to learn how they already use genomic medicine in their practices and what kind of education or outreach might be helpful to them on this topic. This study also found that FPs do not feel confident in their abilities to complete tasks such as interpreting genetic testing results and taking appropriate family histories. Only 32.9% of participants correctly answered a multiple choice question about Lynch syndrome; the question aimed to see whether FPs knew that a family history of endometrial cancer could increase suspicion for Lynch syndrome. The study concludes that there should be more effort to educate PCPs on genetic conditions, skills such as taking a family history, and provide easy access to informative resources (Carroll et al., 2019).

While most of this research on physician knowledge does not specifically address knowledge of Lynch syndrome, these studies indicate that PCPs are generally unprepared to address hereditary cancer syndromes and other genetic conditions. Given that Lynch syndrome is relatively common and highly underdiagnosed in the United States, PCPs could play an integral role in identifying, providing care for, and reviewing guidelines with patients who are diagnosed or at risk. Ensuring that physicians, in addition to patients, understand Lynch syndrome guidelines, is important because patients need providers with knowledge of the guidelines to help ensure they are undergoing appropriate preventative care.

The current literature indicates that Lynch syndrome is a relatively common hereditary cancer syndrome, for which diagnosis is beneficial. There is strong evidence demonstrating that frequent colonoscopies starting at a younger age than the general population are effective in colorectal cancer prevention. The vast majority of Americans with Lynch syndrome have not been

diagnosed, and therefore are unaware they should pursue potentially life-saving preventative care. Management for other increased cancer risks is also available, though strong evidence is lacking and decisions are often specific to individuals and their healthcare providers. This study aims to determine how well individuals with a diagnosis of Lynch syndrome understand and adhere to colonoscopy guidelines, and assess potential barriers faced by this population. There are proven public health methods that can be used to identify individuals with Lynch syndrome on a population level, and the results of this study may prove useful when helping newly diagnosed individuals manage their healthcare.

3.0 Manuscript

3.1 Background

Lynch syndrome is a relatively common hereditary cancer syndrome with autosomal dominant inheritance (Lynch et al., 2015). The prevalence is estimated to be as high as 1 in 279 (Win et al., 2017), with lower estimates around 1 in 440 (Chen et al., 2006). Lynch syndrome is typically an adult-onset condition, and is associated with several cancers (Lynch et al., 2015). The highest risks are for colorectal cancer (as high as 75%) and endometrial cancer (for women; as high as 60%), but there is an increased risk of other cancers, including ovarian, stomach, pancreatic, urinary tract, small bowel, sebaceous skin, and brain cancers (Weissman et al., 2011). Lynch syndrome is caused by a single mutation in one of five genes: *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*. These genes are part of the mismatch repair (MMR) pathway, with the exception of *EPCAM* which is located upstream of *MSH2*. Deletion in a specific area of *EPCAM* can eliminate *MSH2* expression, causing the Lynch syndrome phenotype (Lynch et al., 2015).

It is estimated that at least one million Americans have Lynch syndrome, but that the vast majority have not been diagnosed (Rahm et al., 2018). Individuals at risk for Lynch syndrome are often referred for genetic counseling or testing based on personal and/or family history factors. Personal factors include Lynch syndrome-related tumors (such as colorectal or endometrial cancers) with tumor features indicative of Lynch syndrome (absent expression of one or more MMR proteins, or relatively high microsatellite instability) (Weissman et al., 2011; Yurgelun & Hampel, 2018). Family history factors that have been identified as suspicious for Lynch syndrome include Lynch syndrome-related cancers under the age of 50, multiple family members with Lynch

syndrome-related cancers, and cancer in multiple consecutive generations (Vasen et al., 1999). Because Lynch syndrome is relatively common and there are medical recommendations for reducing morbidity and mortality, the identification of these individuals is an important public health genetics issue (Hampel et al., 2008).

Although today's Lynch syndrome guidelines include information about who should be considered for genetic testing, the larger focus is medical management of individuals with a diagnosis of Lynch syndrome. In 2009, the EGAPP Working Group published management guidelines based on available evidence regarding effectiveness of cancer prevention strategies (Palomaki et al., 2009). Highlights of this document include the recommendation of frequent colonoscopies starting at an earlier age than the general population and recommendation against preventative colectomy; detailed analysis of tumor screening methods, including sensitivity, specificity, and cost-effectiveness; and the recommendation that the syndrome be termed "Lynch syndrome" instead of HNPCC (hereditary non-polyposis colorectal cancer), the historical name (Palomaki et al., 2009).

Another important set of medical management guidelines are the NCCN "Genetic/Familial High-Risk Assessment" guidelines for colorectal cancer. These guidelines are usually updated more than once a year and summarize the latest evidence for Lynch syndrome and other hereditary cancer syndromes associated with CRC. The guidelines include a summary of tumor screening and who should receive it, a table of cancers associated with Lynch syndrome along with lifetime percentage risks for each gene, and evidence-based recommendations for decreasing cancer morbidity and mortality (National Comprehensive Cancer Network, 2019). The recommendation with the most evidence is to have colonoscopies every one to two years, starting at age 20-25. Other medical management is listed for consideration; preventative care such as having a

prophylactic hysterectomy and bilateral salpingo-oophrectomy (for women), upper endoscopy, and taking aspirin to reduce the risk of CRC are listed as options that may be helpful although there is insufficient evidence to prove their utility. These treatments are meant to be discussed with the patient's providers to determine whether extra screening/surgery may be of benefit to the individual patient. The end of the document contains detailed notes with references, making the primary literature accessible for providers (National Comprehensive Cancer Network, 2019).

Medical management specifically for individuals with Lynch syndrome has been discussed in the literature since the 1990s when preventative colectomy was considered as the primary recommendation for preventing colorectal cancer (Lynch, 1996). In the mid-2000s, several studies showed that early and frequent colonoscopies are effective enough for cancer prevention that prophylactic removal of the colon is unnecessary (de Vos tot Nederveen Cappel et al., 2002; Dove-Edwin et al., 2005; Jarvinen et al., 2000). Gynecological surveillance for women with Lynch syndrome has also been debated; transvaginal ultrasound and endometrial biopsy have both been considered as means of detecting endometrial cancer early. This screening has not been proven effective in the early detection of uterine cancer, so women can consider one or both of the screening methods every 1-2 years, and may eventually have a prophylactic hysterectomy (Dove-Edwin et al., 2002; Renkonen-Sinisalo et al., 2007; Rijcken et al., 2003). Endometrial cancer typically causes noticeable symptoms for women, and patients often have good outcomes if they act early (Renkonen-Sinisalo et al., 2007). NCCN guidelines recommend that women with Lynch syndrome receive education about these symptoms (National Comprehensive Cancer Network, 2019). Surveillance for ovarian cancer has also been studied, mostly in the context of hereditary breast and ovarian cancer (Helder-Woolderink et al., 2016). Ovarian cancer is often not identified until late stage, and has a high mortality rate (Andrews & Mutch, 2017). Screening for ovarian

cancer via transvaginal ultrasound or CA-125 blood levels can be considered, but the most effective way to decrease the risk of mortality from ovarian cancer in high-risk women is to have a prophylactic BSO (Schmeler et al., 2006). There is also some evidence that oral contraceptives can help prevent gynecological cancers in high-risk women; patients can discuss this option with their providers (National Comprehensive Cancer Network, 2019).

Adherence to management guidelines for individuals with Lynch syndrome has also been studied; this is an important topic because medical management guidelines cannot decrease cancer burden if individuals with hereditary cancer syndromes do not adhere to them. Studies in the United States examining adherence to colonoscopy recommendations of individuals with Lynch syndrome have conflicting results. One study found a high compliance of 97.1%, but defined compliance as having a colonoscopy at least once every three years (Jarvinen et al., 2009). It has also been found that individuals known to be at risk for Lynch syndrome based on diagnosed family members are more compliant with colonoscopies after undergoing a genetic test and receiving a positive result (Halbert et al., 2004). While the results of these studies are promising, another study found only 73% compliance with colonoscopies, defined as having a colonoscopy at least once every two years (Stoffel et al., 2010). Several studies have concluded that there is room for improvement (Patel et al., 2016; Stoffel et al., 2010), citing other countries such as Finland with close to 100% compliance with colonoscopies (Pylvanainen et al., 2006). This study will assess adherence to colonoscopy guidelines by asking individuals with Lynch syndrome how recently their last colonoscopy was, and how often they typically have colonoscopies.

No existing studies have surveyed individuals with Lynch syndrome to assess understanding of medical management guidelines, though other surveys have been done. Surveys of individuals with Lynch syndrome have shown that most adjust well to their genetic testing

results (K. Aktan-Collan et al., 2001; K. Aktan-Collan et al., 2013; K. Aktan-Collan et al., 2000), most individuals with Lynch syndrome who have adult children have shared this information with them (K. I. Aktan-Collan et al., 2011), and most individuals with a diagnosis have disclosed to at least one first-degree relative (Hunter et al., 2017).

Physician knowledge of Lynch syndrome and cancer genetics has also been assessed, which can be important to both the identification and appropriate management of individuals with Lynch syndrome. Surveys of primary care providers have found that many lack the knowledge needed to treat patients with hereditary cancer syndromes (Hamilton et al., 2017), and that while PCPs feel genetic testing is important, they experience barriers to learning more about genetics such as limited time with patients and the rapidly changing field of genetics (Mikat-Stevens et al., 2015). Individuals with Lynch syndrome have also indicated that they would like more information from their doctors about their genetic condition (Hennink et al., 2013). Focus groups and surveys with PCPs, family practitioners (FPs), and other non-genetics providers have shown that they do not feel confident in their abilities to apply family history and genetics concepts in their practices (Carroll et al., 2019; Carroll et al., 2016).

The purpose of this study is to assess understanding of and adherence to medical management guidelines from adults with a diagnosis of Lynch syndrome, and to understand their experiences with screening, surgeries, genetic counselors, and other providers. Management guidelines are only useful if affected patients have the understanding and ability to follow them. Adherence and barriers will also be assessed; some individuals may understand the guidelines but choose not to or are unable to follow them. This study also aims to understand more about patient experience with genetic counseling, and the involvement of other healthcare providers in patient care. Ultimately, the overarching goal of this study is to gain more information about individuals

with Lynch syndrome and their experiences, and use their responses to help genetic counselors and other healthcare providers better care for patients with Lynch syndrome and other hereditary cancer syndromes.

3.2 Methods

3.2.1 Study Participants

This study was designed for adults, ages 18 and older, who have been diagnosed with Lynch syndrome. The focus of the study was to assess how well individuals with Lynch syndrome understand and adhere to medical management guidelines, so the survey was aimed at participants with either a genetic or clinical diagnosis. The consensus in the genetic counseling community is not to offer testing for at-risk individuals until age 18, unless family history indicates there may be an increased risk and/or screening suggested during childhood (Riley et al., 2012). We excluded these individuals from participation in the survey because by nature of their age of diagnosis, they are part of an unusual subgroup.

This survey was distributed through two nonprofit organizations dedicated to Lynch syndrome. Lynch Syndrome International is a group run by individuals, families, and medical providers in the Lynch syndrome community whose goal is to provide support and education for individuals with Lynch syndrome and increase awareness of Lynch syndrome worldwide. AliveAndKickn was founded by a cancer survivor with Lynch syndrome and his wife; their mission is to gather data to help researchers and to support the Lynch syndrome community. Both groups posted a link to the survey on their Facebook pages, and AliveAndKickn also included the

survey link in an email to their listserv. A response rate cannot be calculated for this survey, because the total number of individuals who saw or received the survey is unknown. Lynch Syndrome International's Facebook page has 10,227 followers (Facebook, 2010) and AliveAndKickn has 2,906 Facebook followers (Facebook, 2011); however, it is unknown how many of these followers saw the posts and how many would have been eligible for the survey. The survey was posted on Facebook twice by these groups: towards the beginning of March 2020 and towards the end of March 2020. The survey's opening statement (Appendix B) also encouraged participants to share the survey with family members with Lynch syndrome; it is unknown how many individuals received the survey from others and what their response rate was. The survey was anonymous and did not track any identifying information from participants. The survey was closed on April 6, 2020.

3.2.2 Survey Design and Development

This survey and project were approved by the Institutional Review Board at the University of Pittsburgh as an exempt study on December 19, 2019. The survey was developed in Qualtrics; it has 44 questions, including sections addressing Lynch syndrome diagnosis, experience with genetic testing and genetic counseling (if applicable), experience with cancer screening and surgeries related to Lynch syndrome cancers, understanding of and adherence to medical management guidelines, and demographics. The first few questions ask if the participant has taken the survey before, whether they have a diagnosis of Lynch syndrome, and how old they are, to ensure they are eligible to take the survey. These were the only three questions that required responses; all other questions were optional and participants could return to prior questions or exit the survey at any point. If a response to an eligibility question made the participant ineligible, skip

logic was in place to end the survey. Skip logic was also used throughout this survey. A copy of the survey questions is included in Appendix B.

3.2.3 Data Analysis

Data were collected and analyzed in Qualtrics (Qualtrics, 2019). Responses were filtered in Qualtrics to remove responses that did not meet inclusion criteria described above; respondents who did not answer all of the questions related to inclusion criteria were also excluded from analysis. Included data were downloaded to a CSV format and cleaned in the spreadsheet. Additional recoded variables were added to the CSV file as needed, in order to group some responses together for statistical analysis. Many respondents skipped at least one of the questions; missing responses were not included in the analysis for the skipped question (aside from the demographics questions listed in Table 3), but these participants' responses were included for the questions they did answer. Analysis included descriptive statistics using Qualtrics and statistical analysis in Stata/SE 15.1 using the CSV file with cleaned data (StataCorp, 2017). Stata was used for Fisher's exact test and chi-squared test of independence. A small qualitative analysis was done using Qualtrics, for the final question, "Please include any additional comments and/or feedback about the survey." These responses were sorted into themes using Qualtrics software.

A chi-squared test of independence was used to evaluate whether adherence to colonoscopies is significantly different between age groups. Age was based on the question "How old are you?" and recoded into two groups: under age 50, and age 50 or older. Adherence was assessed using the question, "How often do you usually have colonoscopies?" Responses were recoded, so that those who selected "more than once a year," "every year," or "every two years" were considered to adhere and those who selected a longer interval were considered not to adhere.

Participants who selected “other” wrote in an explanation; based on their written response, they were categorized as adhering, not adhering, or were excluded from analysis because it was unclear whether or not they adhere. Respondents who indicated in the “other” section that they no longer need colonoscopies due to a surgery were also excluded from this statistical test.

A Fisher’s exact test of independence was used to evaluate this same adherence question, for only participants who indicated they live in the United States. A chi-squared test could not be performed because the expected value of one of the cells was less than 5. Participants who answered “I do not live in the United States” in response to the question “How would you describe the area of the United States in which you live?” were excluded from this analysis; participants who did not respond to this question were also excluded. Those who selected “Other” had the opportunity to write in responses; participants who listed another country (Canada, the UK, etc.) were excluded from this analysis. Those who wrote in a location in the United States (Colorado, Texas, etc.) were included in this analysis. For this question, all “other” responses were re-coded as there were no ambiguous responses.

To determine whether individuals who have had a visit with a genetic counselor have a better understanding of management guidelines than those who have not seen a genetic counselor, a Fisher’s exact test of independence was done. A chi-squared test could not be performed because the expected value of one of the cells was less than 5. Participants who answered the question, “Have you ever had a visit with a genetic counselor?” were included in this analysis. Responses to the question, “What is your understanding of how often it is recommended that you have a colonoscopy?” were recoded as correct or incorrect. Those who selected “Every year” or “Every 1-2 years” were recoded as correctly understanding management guidelines; those who selected a longer interval were recoded as having an incorrect understanding.

3.3 Results

This survey received 312 responses. 278 were eligible to be included based on their responses to the required eligibility questions. Most of the ineligible responses started the survey but only answered the first or second question.

3.3.1 Participants Demographics

Participant demographics are summarized in Table 3. Respondents ranged in age from 18-19 to 70-79. The largest age categories were 40-49 with 25.9% of participants (n=72), and 50-59 with 26.3% of participants (n=73). Most participants were female (89.6%, n = 249). The vast majority of participants (90.6%) selected “White” as their ethnicity (n=252), although some of these respondents selected other ethnicities as well. Sixteen participants (5.8%) selected an ethnicity other than white. Participants were a relatively high-income group; the most common response to annual household income (35.6%) was “greater than \$100,000” (n = 99). Most participants were college graduates; 29.5% indicated that they completed a bachelor’s degree (n = 82), 19.4% have a master’s degree (n = 54), and 6.1% (n = 16) have a degree beyond master’s. The majority of participants live in the continental United States; 31 participants (11.2%) do not live in the United States. More than half of participants are employed full time (55.0%, n = 153). The majority of participants are covered by private insurance (77.0%, n = 214), and only 9 participants (3.2%) indicated they are uninsured.

Table 3 Participant Demographics

Demographic	Number Respondents (%)
Gender	
Male	28 (10.1%)
Female	249 (89.6%)
Other	0 (0.0%)
Prefer not to answer/Unanswered	1 (0.4%)
Current Age	
18-19	2 (0.7%)
20-24	5 (1.8%)
25-29	10 (3.6%)
30-39	55 (19.8%)
40-49	72 (25.9%)
50-59	73 (26.3%)
60-69	51 (18.3%)
70-79	10 (3.6%)
80 or older	0 (0%)
Ethnicity	
White	252 (90.6%)
Black or African-American	1 (0.4%)
Hispanic or Latino	6 (2.2%)
American Indian or Alaska Native	4 (0.7%)
Asian	3 (1.1%)
Native Hawaiian or Pacific Islander	0 (0.0%)
Other	2 (0.7%)
Prefer not to answer/Unanswered	18 (6.5%)
Approximate Annual Household Income	
Less than \$20,000	5 (1.8%)
\$20,000 - \$40,000	18 (6.5%)
\$40,000 - \$60,000	26 (9.4%)
\$60,000 - \$80,000	35 (12.6%)
\$80,000 - \$100,000	39 (14.0%)
More than \$100,000	99 (35.6%)
Prefer not to answer/Unanswered	56 (20.1%)
Highest Level of Education	
Some high school	2 (0.7%)
High school graduate	55 (19.8%)
Associate's degree	42 (15.1%)
Bachelor's degree	82 (29.5%)
Master's degree	54 (19.4%)
Beyond master's degree	16 (5.8%)
Prefer not to answer/Unanswered	27 (9.7%)
Employment Status	
Employed full-time	153 (55.0%)
Employed part-time	36 (12.9%)
Currently not employed	21 (7.6%)
Student	4 (1.4%)
Not working due to disability	9 (3.2%)

Table 3 Continued

Other	38 (13.7%)
Unanswered	17 (6.1%)
Health Insurance	
Medicare	33 (11.9%)
Medicaid	1 (0.4%)
Private insurance	214 (77.0%)
Marketplace	10 (3.6%)
Does not currently have health insurance	9 (3.2%)
Unanswered	24 (8.6%)
Area of the United States	
Northeast	59 (21.2%)
Midwest	52 (18.7%)
Southeast	48 (17.3%)
Northwest	25 (9.0%)
Southwest	36 (12.9%)
Non-contiguous US	1 (0.4%)
Does not live in the US	31 (11.2%)
Other	8 (2.9%)
Unanswered	18 (6.5%)

3.3.2 Lynch syndrome diagnosis and genetic testing experience

Age of diagnosis of Lynch syndrome ranged from under 18 to 70-79 years old; the majority of participants were 30-39 (28.4%, n = 78), 40-49 (27.6%, n = 65), or 50-59 (23.6%, n = 65). About half of participants (50.9%, n = 140) were the first person in their family to be diagnosed with Lynch syndrome. Slightly less than half of respondents (47.1%, n = 128) had a diagnosis of cancer before their Lynch syndrome diagnosis.

When asked what type of provider ordered their genetic testing, genetic counselor was the most common response (37.6%, n = 103), followed by oncologist (27.7%, n = 76). Of the 13.4% (n = 36) of participants who selected “other,” common responses included surgeon and gastroenterologist. Two participants said their family members ordered the test for them, two said physicians of family members ordered their test (child’s pediatrician and daughter’s oncologist), and two participants ordered the test themselves (one mentioned Color, a genetic testing lab with doctors who can approve testing requested by patients). Two participants said they were tested

through research. Notably, 3 respondents (1.1%) said they have not had genetic testing for Lynch syndrome.

When asked if they had ever had a visit with a genetic counselor (GC), 91.1% (n = 246) said yes and 8.9% (n = 24) said no. The majority of those who had seen a genetic counselor (62.6%, n = 157) indicated that they saw the GC both before and after having their genetic test; 22.3% (n = 56) saw a GC only after their test results came back, and 12.8% (n = 32) saw a GC only before having a genetic test.

3.3.3 Experience with cancer screening and surgeries

Participants were asked questions about their experiences with cancer screening and surgeries related to Lynch syndrome-associated cancers. When asked when they had their last colonoscopy (Table 4), more than two-thirds of respondents (73.0%, n = 197) said it was in the last 12 months; the next most common response was 1-2 years ago (17.4%, n = 47), and only 9.6% (n = 26) said it had been more than 2 years. Those who selected “more than 5 years ago were asked to specify;” of these 14 respondents, six indicated that they have had a colectomy and six said they have never had a colonoscopy (because they are too young, it is not covered by their insurance, or for unspecified reasons). Participants were also asked how often they usually have colonoscopies (Table 4), to gauge whether their answer to the prior question was indicative of their normal pattern. In keeping with the prior question, the most common response was every year (64.8%, n = 175) followed by every 2 years (19.6%, n = 53). Twenty-nine participants (10.7%) selected “other” and were asked to specify; responses included recent diagnosis or recently had their first colonoscopy, have never had a colonoscopy, and no longer needed due to removal of colon. A chi-

squared test of independence found that adherence to colonoscopy recommendations does not significantly differ between individuals under age 50 vs 50 and older (p=0.065).

Table 4 Frequency of Colonoscopies

Question	Respondents (%)
When was your last colonoscopy?	
In the past 12 months	197 (73.0%)
1-2 years ago	47 (17.4%)
2-3 years ago	7 (2.6%)
3-4 years ago	2 (0.7%)
4-5 years ago	3 (1.1%)
More than 5 years ago	14 (5.2%)
How often do you usually have colonoscopies?	
More than once a year	5 (1.9%)
Every year	175 (64.8%)
Every 2 years	53 (19.6%)
Every 3 years	4 (1.5%)
Every 4 years	0 (0.0%)
Every 5 years	4 (1.5%)
Other	29 (10.7%)

Table 5 shows frequency of colonoscopies, including only the subset of individuals who indicated they live in the United States. The majority of participants (72.3%, n = 162) had their last colonoscopy in the past 12 months, followed by 17.9% (n = 40) who had their last colonoscopy 1-2 years ago. Two-thirds of United States participants indicated they usually have colonoscopies every year (66.2%, n = 149); the next most common response was every 2 years (18.7%, n = 42). For both questions, percentage of respondents for each answer were similar between the whole cohort (Table 4) and those who indicated they live in the United States (Table 5). A Fisher's exact

test comparing those under 50 with those 50 or older in the United States did not show a statistically significant difference for adherence ($p=0.2001$, $OR = 0.377$, $95\% CI = [0.0615, 1.716]$).

Table 5 Frequency of Colonoscopies (United States only)

Question	Respondents (%)
When was your last colonoscopy?	
In the past 12 months	162 (72.3%)
1-2 years ago	40 (17.9%)
2-3 years ago	7 (3.1%)
3-4 years ago	2 (0.9%)
4-5 years ago	1 (0.5%)
More than 5 years ago	12 (5.4%)
Total Responses	224
How often do you usually have colonoscopies?	
More than once a year	4 (1.8%)
Every year	149 (66.2%)
Every 2 years	42 (18.7%)
Every 3 years	3 (1.3%)
Every 4 years	0 (0.0%)
Every 5 years	3 (1.3%)
Other	24 (10.7%)
Total Responses	225

Participants were also asked which barriers (if any) they have experienced that interfere with having a colonoscopy. More than two-thirds of respondents (67.9%, $n = 184$) indicated that they have not encountered any barriers to having colonoscopies. The most common barrier was that colonoscopies are too expensive (11.8%, $n = 32$). Thirty-one participants (11.4%) selected “other;” several respondents indicated that their doctor did not believe they needed the extra

screening, would not do a colonoscopy more than every two years, or that insurance would not cover the screening. Other responses included risk factors, such as an underlying condition or pregnancy, and bad experiences with prior procedures or procedure prep. Participants were then asked what they think might be some general barriers to having colonoscopies, based on their own experiences and those of family members. Respondents had the option to select more than one option. The most frequent option was dislike of colonoscopies (prep and procedure) (30.3%, n = 147) followed by cost (25.0%, n = 121), fear of cancer diagnosis (20.2%, n = 98), and inability to take a day off from work (11.6%, n = 56). Less common selections were unsure whether colonoscopies will reduce cancer risk (3.1%, n = 15) and unable to travel to colonoscopy center (2.1%, n = 10). Thirty-eight participants (7.8%) wrote in barriers under “Other;” these included fear, difficulty finding a driver to take the patient home after the procedure, insurance refusal to pay for younger individuals, increasing wait times to schedule the procedure, and doctors not understanding that someone with Lynch syndrome needs colonoscopies at a younger age.

Next, participants were asked about their experiences with surgeries related to Lynch syndrome cancers. Approximately one-third of respondents (32.6%, n = 85) indicated that they have had part or all of their colon removed. Most of these participants had only part of their colon removed (64.6%, n = 62). Fifteen participants had their entire colon removed (15.6%), 10 participants had the entire colon and rectum removed (10.4%), and one participant had only their rectum removed (1.0%). These respondents were asked about the reason for their colorectal surgeries, to understand how many of the surgeries were cancer-related. Most indicated they had surgery because of a cancer diagnosis (71.8%, n = 74); four participants (3.9%) had prophylactic surgery to prevent cancer, and nine (8.7%) had polyps that required surgery. Options unrelated to Lynch syndrome were inflammatory bowel disease (1.0%, n = 1) and diverticulitis (1.0%, n = 1).

Nine participants (8.7%) selected “other;” their responses included a mass or growth, diagnosis of other cancers (endometrial, ovarian), and the combination of family history of colon cancer and other issues (ex: diverticulitis).

Participants who did not select “Male” as their gender earlier in the survey were directed via skip logic to questions about their uterus and ovaries. This question allowed participants to select more than one option, as it pertained to multiple organs. The responses are summarized in Table 6. More than two-thirds of these respondents indicated that they have had both their uterus and ovaries removed (68.4%, n = 167). Thirty-six respondents (14.8%) indicated that they plan to have both their uterus and one or more ovaries removed in the future. Eleven participants (4.5%) indicated they have already had at least one of these organs removed (uterus and/or one or more ovaries) and plan to have the remaining organs removed in the future; this group therefore requires more than one surgery. Some participants are not included in this table because their responses were illogical; for instance, one person indicated they already had their uterus and both ovaries removed, and also that they were planning to have their uterus and one or more ovaries removed.

Table 6 Female Respondents’ Uterine and Ovarian Surgeries

Response(s)	Participants (%)
Uterus AND both ovaries removed	167 (68.4%)
Uterus AND one ovary removed	1 (0.4%)
Uterus removed	14 (5.7%)
Both ovaries removed	3 (1.2%)
One ovary removed	1 (0.4%)
Planning to have uterus AND one or more ovaries removed in the future	36 (14.8%)
Planning to have uterus removed in the future	4 (1.6%)
Planning to have one or more ovaries removed in the future	2 (0.8%)
Uterus AND one ovary removed; planning to have ovary removed in the future	4 (1.6%)
Uterus removed AND planning to have one or more ovaries removed in the future	3 (1.2%)
Have not had these surgeries and do not plan to have them	3 (1.2%)
Total Responses	244

Table 7 shows responses from a subset of participants who indicated they are female, age 40 or older, and have never had a cancer diagnosis. Women in this group are old enough to have had prophylactic surgery or made a definitive decision, and any surgeries would not be due to cancer diagnosis. The majority of this group have had their uterus and ovaries removed (73.3%, n = 33). Six participants (13.3%) are planning to do both surgeries; all other participants have had at least one surgery. No participants in this group indicated that they have not had either surgery and are not planning to have them. One participant was excluded from analysis due to an illogical response (indicated she had her uterus removed in the past and that she was planning to have it removed in the future).

Table 7 Uterine and Ovarian Surgeries in Older Female Respondents Without Cancer

Response(s)	Participants (%)
Uterus AND both ovaries removed	33 (73.3%)
Uterus removed	3 (6.7%)
Both ovaries removed	1 (2.2%)
Planning to have uterus AND one or more ovaries removed in the future	6 (13.3%)
Uterus AND one ovary removed; planning to have ovary removed in the future	1 (2.2%)
Uterus removed AND planning to have one or more ovaries removed in the future	1 (2.2%)
Have not had these surgeries and do not plan to have them	0 (0.0%)
Total responses	45

Of those who have had their uterus removed, more than half (54.1%, n = 100) had prophylactic surgery to prevent cancer and 23.8% (n = 44) had the surgery because they were diagnosed with uterine cancer. Eight participants (4.3%) had the surgery because they had ovarian cancer, 13 participants (7.0%) had the surgery when diagnosed with another cancer, and 20

participants (10.8%) had the surgery for reasons unrelated to cancer such as fibroids or endometriosis. More than half (62.4%, n = 116) had the surgery after their diagnosis of Lynch syndrome.

Of participants who had one or more ovaries removed, more than half had prophylactic surgery to prevent cancer (56.8%, n = 100). One-fifth of respondents had the surgery because they were diagnosed with uterine cancer (21.6%, n = 38) and 7.4% (n = 13) had a diagnosis of ovarian cancer. Sixteen respondents (9.1%) had the surgery because they were diagnosed with a cancer other than uterine or ovarian, and 2.1% (n = 9) were for reasons unrelated to cancer, such as cysts. More than half of respondents (65.3%, n = 115) had this surgery after being diagnosed with Lynch syndrome.

3.3.4 Medical management guidelines

The next part of the survey asked questions related to the medical management guidelines for colonoscopies to understand if or how participants have learned about the guidelines and how well they understand the guidelines. When asked their understanding of how often they should have a colonoscopy, the majority of participants selected once a year (65.9%, n = 174). The next most common response was every 1-2 years (31.1%, n = 82), followed by every 2-3 years (3.0%, n = 8). No participants selected the intervals longer than every 2-3 years. When asked if they have ever been given conflicting information about how often they should have colonoscopies, the majority answered no (72.9%, n = 194).

Comparison between respondents whose understanding of how often they should have a colonoscopy was “every year” or “every 1-2 years” and those who selected a longer interval

showed there was no statistical difference between those who have and have not had a visit with a genetic counselor (p=0.5299, OR = 0.6725, 95% CI = [0.0803, 31.6642]).

Respondents were asked which providers they have discussed Lynch syndrome medical management guidelines with; the most common response was genetic counselor (72.3%, n = 193), followed by gastroenterologist (64.8%, n = 173), oncologist (47.6%, n = 127), and primary care doctor (37.5%, n = 100). Only six participants (2.3%) indicated they had not discussed medical management guidelines with any healthcare providers. Thirteen participants (4.9%) discussed these guidelines with other providers; write-in responses included gynecologic oncologist (two respondents wrote that it was unclear whether this provider should be counted as oncologist or gynecologist), dermatologist, and urologist. This information is summarized in Table 8.

Table 8 Providers Who Discussed Medical Management Guidelines with Respondents

Provider	Number of Respondents
Genetic counselor	193 (72.3%)
Cancer genetics doctor	48 (18.0%)
Primary care doctor	100 (37.5%)
Gynecologist	95 (35.6%)
Gastroenterologist	173 (64.8%)
Oncologist	127 (47.6%)
Surgeon	66 (24.7%)
Other	13 (4.9%)
None	6 (2.3%)
Total Responses	267

Participants were also asked who they have discussed medical management guidelines with besides healthcare providers. Of all options selected, the most frequent were other family members (who do not have Lynch syndrome) (30.7%, n = 209) and family members with Lynch syndrome

(30.6%, n = 208). One-quarter of responses were friends (25.4%, n = 173) and 11.6% (n = 79) were other individuals with Lynch syndrome. Eleven responses (1.6%) were “Other”; write-in responses included others who have had Lynch syndrome-related cancers, employer, spouse, and Facebook. Three responses discussed talking with the general public, such as talking with medical students and colleagues, writing for the media, and writing a book.

More than two-thirds of respondents (70.6%, n = 185) stated they are involved in at least one online or in-person support group related to Lynch syndrome. These respondents were asked to select all groups with which they participate; the most common response was Facebook (73.3%, n = 173); one-fifth of responses (21.6%, n = 51) indicated an advocacy group (ex: Lynch Syndrome International). Only three participants (1.3% of responses) said they belong to an in-person support group. Five respondents (2.1%) wrote in another social media platform; these included Instagram and Colontown.

3.3.5 Cancer Diagnoses

Participants were asked which types of cancer they had been diagnosed with (Table 9); this question included the option to select more than one response. The most common response was “I have never been diagnosed with cancer” (36.1%, n = 100). The most common cancers were colorectal (27.4%, n = 76), endometrial/uterine (20.5% of females, n = 51), and other (18.4%, n = 51). Written in responses for “other” included some cancers associated with Lynch syndrome, and others that are not known to be related. Of the 252 participants who responded to this question, 52 (20.6%) have been diagnosed with two or more cancers, 100 (39.7%) have had one cancer diagnosis, and 100 (39.7%) have never had a cancer diagnosis.

Table 9 Respondents' Past Cancer Diagnoses

	Female	Male	Total
Bladder	1 (0.4%)	1 (3.9%)	2 (0.8%)
Brain	0 (0.0%)	0 (0.0%)	0 (0.0%)
Breast	18 (8.0%)	0 (0.0%)	18 (7.1%)
Colorectal	63 (27.9%)	13 (50.0%)	76 (30.2%)
Endometrial/Uterine	51 (22.6%)	0 (0.0%)	51 (20.2%)
Gastric	2 (0.9%)	1 (3.8%)	3 (1.2%)
Ovarian	12 (5.3%)	0 (0.0%)	12 (4.8%)
Pancreatic	2 (0.9%)	0 (0.0%)	2 (0.8%)
Prostate	1 (0.4%)	0 (0.0%)	1 (0.4%)
Small bowel	4 (1.8%)	0 (0.0%)	4 (1.6%)
Other	48 (21.2%)	3 (11.5%)	51 (20.2%)
Never diagnosed with cancer	89 (39.4%)	11 (42.3%)	100 (39.7%)
Total Participants	226	26	252

3.3.6 Participant Comments

At the end of the survey, participants were given the open-ended question, “Please include any additional comments and/or feedback about the survey below;” 50 participants (18.0%) submitted a comment. A qualitative analysis was done for these responses to identify themes. The most common theme was comments about personal medical history (38.0%, n = 19); these included details about participants’ cancer history, diagnosis with Lynch syndrome, or surgeries. Participants shared details such as how their cancers were identified, age at identification of pre-cancerous polyps, and what prompted their providers to recommend genetic testing. One participant shared that they have another GI medical condition which may explain some of their answers. A related theme was family history (26.0%, n = 13), which had some overlap with personal history. Respondents shared details such as the types of cancers found in their families

and knowledge of cancer in the family for multiple generations. Some participants shared details of their family histories that were suspicious for Lynch syndrome; these were often first-degree relatives diagnosed with cancer at a young age.

Nine of these responses (18.0%) commented on barriers faced by individuals with Lynch syndrome. Some had suggestions, such as “Better prep procedures would help get people to do colonoscopies” and “We need better research and training of medical doctors.” Two participants mentioned difficulties having colonoscopies at a younger age than the general population; one described being told on the day of her procedure by a nurse that she was too young and another had a family member whose insurance does not pay for colonoscopies under age 50 despite a diagnosis of Lynch syndrome. One participant said that their children have not been tested “for fear that health insurance will deny them coverage in the future as they possibly change jobs.”

Another common theme was gratitude for conducting this survey (16.0%, n=8). These participants were grateful to have someone conducting research on Lynch syndrome. Responses included “I hope this helps in making people more aware of Lynch Syndrome,” “Any studies that can help train medical professionals in how to guide Lynch Syndrome patients are so appreciated,” and “I love that someone does this! Lynch needs to be understood by professionals and people.” One participant also indicated gratitude for their diagnosis, stating that, “Lynch Syndrome saved my life.”

Five participants (10.0%) commented on the questions asked in this survey, including that it was “Unclear if non-US Lynch carriers can participate in this survey” and that the question about having one’s uterus and ovaries removed did not include an “unsure” option for individuals who are young and have not yet decided. Four participants (8.0%) shared that they do not live in the United States (two in Canada and two in Europe). Three responses (6.0%) mentioned how a

diagnosis of Lynch syndrome has affected their relationship with other family members. For instance, “I have family members who refuse to talk to me / get tested because they do not want lynch syndrome in their medical charts.” Three other responses (6.0%) were related to their medical providers; one participant wrote they were told by their gynecologist that they did not need screening such as colonoscopies and “Never saw him again after that.” Another said, “Biggest barrier facing Lynchies is lack of knowledge by medical ‘professionals.’”

3.4 Discussion

The responses to this survey are generally reassuring; the majority of participants understood recommendations for how often to have colonoscopies and most showed good adherence to these guidelines. Ninety percent of participants indicated they have had a colonoscopy in the last two years and 85% said they usually have colonoscopies every year or every 1-2 years; this indicates very good adherence to medical management recommendations in the survey respondents. Several respondents who have not had a colonoscopy for more than five years wrote that they had a surgery (such as a colectomy) rendering the procedure unnecessary, or that they were too young to have the procedure (which could be adherence or could indicate an inaccurate understanding, depending on the age of the participant). Statistical analysis did not reveal a significant difference in adherence between those under age 50 and those age 50 and older; this indicates that younger individuals are adhering as well as those who are old enough to receive colonoscopies without a diagnosis of Lynch syndrome. These results showing good adherence are similar to another study which found that 97% of individuals with Lynch syndrome had a colonoscopy in the last three years (Jarvinen et al., 2009). However, other studies in the United

States have found only 73% (Stoffel et al., 2010) or 58% (Patel et al., 2016) of individuals with Lynch syndrome had a colonoscopy in the past two years; there is conflicting evidence on this topic. The demographics of this study (high income, high education level, large percentage with private insurance) may be associated with a high colonoscopy compliance rate. While Jarvinen et al. did not report demographics aside from gender (2009), the demographics of the other two studies included a majority of participants with more than \$50,000 annual income, more than half were college graduates, and more than 95% had health insurance (Patel et al., 2016; Stoffel et al., 2010). Therefore, demographics of these studies have trends similar to ours. Still, our findings support moving forward with public health initiatives such as universal tumor screening, in attempts to identify as many individuals with Lynch syndrome as possible. Even if this group is not representative of the Lynch syndrome population, these findings indicate that understanding of and adherence to medical management guidelines is an attainable goal.

Two-thirds of participants indicated they have not encountered any barriers to having colonoscopies. Colonoscopies are also recommended for the general population, but starting at a later age and less frequently than for individuals with Lynch syndrome (Benard, Barkun, Martel, & von Renteln, 2018). In the general population, it has been found that individuals with lower income, lower education, and who are from minority backgrounds have lower compliance with colonoscopies. Studies have also shown that these individuals face more barriers to having colonoscopies, such as cost and insurance coverage, low health literacy, and lack of understanding of the risks and benefits of the procedure (Kiviniemi, Klasko-Foster, Erwin, & Jandorf, 2018). The respondents to this study may have been less likely to experience disparities in the social determinants of health, which may be why such a high percentage have not encountered barriers. However, it is important to note that because this study did not include many participants from

minority and lower income populations, we cannot conclude that members of these groups with Lynch syndrome would not understand and/or adhere to management guidelines.

Of the participants who responded to the questions about female gynecological cancers, more than two-thirds stated they have had their uterus and both ovaries removed. More than half of participants who had their uterus and one or more ovaries removed had the surgery in order to prevent cancer. The group of females aged 40 and older who have never had a cancer diagnosis all had at least one surgery or stated they were planning to have surgery. Current NCCN guidelines state that screening for endometrial and ovarian cancers with methods such as endometrial biopsy, transvaginal ultrasound, and CA-125 blood levels can be considered although evidence has not proven their clinical utility for cancer detection. Prophylactic removal of the uterus and ovaries after childbearing are listed as options to consider (National Comprehensive Cancer Network, 2019); many women in the study chose this option. Members of the older group without cancer were much more likely to have had their surgery for preventative reasons and may more accurately demonstrate these decisions of women with Lynch syndrome. Participants in their teens, 20's, and 30's may not have decided or considered whether they will have these surgeries; even if they have made a decision, their current responses may not reflect what they end up doing in the future.

When asked their understanding of how often they should have colonoscopies, nearly two-thirds of participants selected once a year. Current NCCN guidelines suggest a colonoscopy every 1-2 years, with the caveat that individuals considered higher risk due to factors such as gender, age, and gene mutation may need them closer to once a year (National Comprehensive Cancer Network, 2019). Participants are likely told by their providers how often to have colonoscopies; the understanding of these individuals that they should have colonoscopies every year may reflect providers erring on the side of caution by choosing the shorter time interval. Some of these

participants likely also have some of the risk factors mentioned above which necessitate having more frequent colonoscopies.

The demographics of respondents in this study are not representative of the Lynch syndrome population. While Lynch syndrome equally affects all genders, races/ethnicities, and socioeconomic status groups (Hegde et al., 2014), this group is almost 90% female, more than 90% white, and more than one-third are from households with greater than \$100,000 annual income. The difference in our study population may be related to the identification of individuals with Lynch syndrome. It is estimated that only two percent of individuals who have Lynch syndrome in the United States have been identified (Rahm et al., 2018). Studies have shown that women with more education and higher incomes are more aware of hereditary causes of breast cancer (MacNew, Rudolph, Brower, Beck, & Meister, 2010) and that racial and ethnic minorities have lower awareness of cancer genetic testing (Mai et al., 2014). Black women have been shown to use cancer genetics services less than white women, despite having a higher mortality rate from breast cancer (Nikolaidis et al., 2019). Given the small percentage of Americans with Lynch syndrome who have a diagnosis, the demographics of the respondents could be explained, in part, by a disparity in those individuals who are referred to or accessing services that lead to a diagnosis. The demographics of this survey and literature about who receives genetic services reiterate the importance of public health genetics efforts aimed at identifying more individuals with Lynch syndrome, especially those who may be less likely to be identified clinically, have some knowledge of genetics, or seek out genetics services on their own.

Additionally, it may be that individuals in the reported demographics are more likely to be aware of and join supports groups and their social media pages. Thus, the method of advertising (through social media and email listservs of advocacy groups) may have reached these individuals

more easily. It is unclear why many more women responded to this survey than men, though perhaps they are more likely to have a diagnosis, more likely to follow the social media pages of these organizations, and/or more willing to participate in health research. These organizations may not be as appealing to individuals from groups not represented in this survey, and members of these groups may have more urgent priorities than responding to a survey. Due to the skewed demographics, these results may not be applicable to all individuals with a diagnosis of Lynch syndrome, or they may indicate differences between those who have been diagnosed and those who have not yet been identified.

It is also important to note that underserved populations may be less likely to participate in studies due to mistrust of the healthcare system. Research has shown that African-American and Latino individuals are more likely to think healthcare workers are being dishonest with them or withholding information, and believe that they may be treated differently in the healthcare system and in health research than members of other groups (Smirnoff et al., 2018). These concerns are rooted in past medical mistreatment of minority groups. As a result, members of these groups are less likely to participate in healthcare-related research (Hughes, Varma, Pettigrew, & Albert, 2017; Martinez, Cummings, Karriker-Jaffe, & Chartier, 2017). Discussions with members of these groups have elicited suggestions for increasing participation in research, including exploring the community's thoughts on the research topic and ways it might be useful or relevant to that group (Martinez et al., 2017), and including members of the community in carrying out the study and/or recruitment and providing monetary compensation to participants (Hughes et al., 2017). These barriers and potential strategies should be considered in future research, as it will be important to reach out to individuals with Lynch syndrome in underrepresented groups.

The most common response to the question asking which type of provider ordered the individual's genetic test was genetic counselor; the vast majority of participants (91.1%) indicated they have had a visit with a genetic counselor. This number is strikingly high, as prior studies have indicated that many individuals at risk for hereditary cancer syndromes are never referred for genetic counseling (Ahn & Port, 2017; Hoskins, 2018). This cohort therefore had unusually high access to genetic counselors. This cohort also had excellent adherence to and understanding of management guidelines, with 86.3% stating they have a colonoscopy at least every two years and 97% understanding they should have a colonoscopy at least every two years. These results may indicate that genetic counselors are important in helping individuals with Lynch syndrome understand medical management guidelines. Currently, there are too few genetic counselors in the United States to meet patient demand (Hoskovec et al., 2018); research has shown that non-genetics providers do not have the knowledge or resources necessary to properly treat individuals with hereditary cancer syndromes (Carroll et al., 2016; Hamilton et al., 2017). Strong efforts should be made to increase access for genetic counseling to more individuals with hereditary cancer syndromes and/or strong family histories of cancer, to help ensure a good understanding of recommended medical management. Education of other health care providers is equally important, given that not all individuals have easy access to genetic counselors. Additionally, patients typically interact more often with providers such as primary care doctors, even if they have seen a genetic counselor in the past.

Almost all participants (97%) listed at least one healthcare provider with whom they have discussed medical management guidelines for Lynch syndrome. The most common response was genetic counselor, which was not surprising since most respondents indicated they have had a visit with a genetic counselor. Although genetic counselors are a limited resource (Hoskovec et al.,

2018), it appears that for this cohort, individuals were aware of and able to access genetic counseling services. Only about one-third of participants indicated they had discussed guidelines with a primary care doctor or gynecologist. It has been shown that internists have a limited understanding of genetic testing and hereditary conditions (Klitzman et al., 2013) and that half of gynecologists are uncomfortable with screening guidelines for Lynch syndrome (two-thirds are uncomfortable with CRC screening guidelines) (Frey et al., 2014). Providers such as PCPs and gynecologists see patients regularly for wellness exams, and ideally they would have the knowledge to discuss management guidelines with their hereditary cancer patients. The lack of these discussions with patients may be due to their discomfort with the information. It has also been shown that in general, providers are interested in training to learn more about genetics (Klitzman et al., 2013); this is important to keep in mind as public health genetics initiatives are considered. Those with expertise in genetics should consider helping colleagues who are not genetics experts learn more so they can better assess and treat their patients.

More than two-thirds of participants stated they are part of a support group, and Facebook was the most common type of support group selected. Literature about health and online support groups has found these groups can provide emotional support for individuals with health conditions such as lung cancer (Taylor & Pagliari, 2019) and parents of children with cancer (Gage-Bouchard, LaValley, Mollica, & Beaupin, 2017). Less than 2% of respondents in a support group in this study indicated they belong to an in-person support group. This survey was distributed over social media, including on Facebook, so those who found and answered the survey are probably more likely to be a member of an online support group than the general Lynch syndrome population. The high rates of participation in support groups along with the high adherence to medical management guidelines suggest that perhaps being part of a support group

increases adherence. Support groups are a unique opportunity to interact with others with the same genetic condition, and this shift towards online support groups allows for connection around the world. Future public health genetics efforts should consider encouraging individuals with Lynch syndrome and other hereditary cancer syndromes to join support groups. This could be achieved by education of providers, who can share the information with patients when they are diagnosed with Lynch syndrome. Although most of these respondents had seen a genetic counselor, most also discussed their diagnosis with other providers. For this reason, providers seen more regularly for wellness exams should be educated about support groups and other resources for their patients.

Around 60% of respondents to this survey have had a cancer diagnosis; 47.1% of respondents were diagnosed with cancer before receiving their Lynch syndrome diagnosis. The two most common cancers were colorectal and uterine/endometrial; these are the two cancers with the highest risks associated with Lynch syndrome (National Comprehensive Cancer Network, 2019). All other Lynch syndrome cancers listed in the survey were selected by at least one participant, except brain cancer. Of note, the only participant who indicated a diagnosis of prostate cancer also selected female gender; prostate cancer only affects males as the prostate is a male organ (National Comprehensive Cancer Network, 2019). This participant likely incorrectly selected their gender or cancer type, although another possibility is that this person is biologically male but has transitioned or now identifies as female.

3.4.1 Limitations

This study has several limitations. As previously mentioned, the demographics are not representative of the population of individuals affected with Lynch syndrome. Respondents to this survey are almost entirely white and have above average education and household income. This

cohort may be more representative of individuals who know they have a diagnosis of Lynch syndrome; it is difficult to know, but perhaps those with more education and monetary resources are more likely to receive a proper diagnosis. Regardless, the results of this survey cannot be generalized to all individuals with Lynch syndrome. For example, a truly representative group would likely have a much higher percentage of individuals who have experienced at least one barrier when having a colonoscopy. This survey does, however, provide a starting point which can be used to start thinking about how to educate and increase access to necessary healthcare for individuals with Lynch syndrome and other hereditary cancer syndromes. As public health efforts to identify more individuals with Lynch syndrome are implemented, this study suggests that informing individuals of online support groups and ensuring access to genetic counselors or providers with an understanding of current management guidelines may be important to increase adherence to these guidelines.

The demographics and responses in this study may also have been skewed by how the survey was distributed. Individuals who are made aware of and active in the Lynch syndrome organizations we partnered with, specifically those motivated to follow them on social media, were likely more easily reached by this survey. There may also have been some bias from those who decided to take the survey. Responses to the open-ended question at the end of the survey indicated that many participants were grateful to see someone studying Lynch syndrome and were therefore motivated to take this survey to contribute to the literature surrounding their genetic diagnosis. Participants were encouraged to send this survey to family members or others they know with Lynch syndrome, so it is possible some members of the same families or friend groups with similar experiences were over-represented.

Another limitation is that the responses to this survey were self-reported and we cannot verify their accuracy. For instance, one participant selected female as their gender and also reported having a diagnosis of prostate cancer; this was likely an error. It is possible that some respondents believe they have a diagnosis of Lynch syndrome, misremember the age when they received their diagnosis, or are confused about the exact type of cancer they were diagnosed with. It is also possible that participants understand the guidelines and adjusted their answers about colonoscopies based on this knowledge; this could be an example of social desirability bias. Looking through medical records would have been the best way to verify responses, but was not within the scope of this study design.

3.4.2 Future Directions

This survey was a preliminary study to assess how well individuals with Lynch syndrome understand the medical management guidelines, their experiences with genetic counselors and other healthcare providers, and how well they adhere to recommendations for colorectal cancer prevention. Because the demographics of participants were not representative, it would be ideal to obtain survey responses from a wider audience. One caveat is that most individuals with Lynch syndrome have not been diagnosed and would therefore not respond to this type of survey; perhaps a different study could aim to understand whether this survey is representative of individuals who have a diagnosis. Are white, wealthier, more educated Americans more likely to have already been diagnosed with Lynch syndrome, or is the group more diverse than this study implies? This possibility emphasizes the importance of public health approaches that aim to overcome social determinants of health. One way to reach minority populations with Lynch syndrome could be to identify an individual with a diagnosis who is willing to talk with others of the same race, ethnicity,

or other identifying factor. This approach could be used to increase trust in that population and encourage participation in studies that will ultimately be useful to those individuals. Another possible approach is to conduct focus groups with members of minority groups who have Lynch syndrome, and use their input to develop a strategy for reaching a more diverse cohort.

Assessment of how well individuals with Lynch syndrome understand and adhere to medical management guidelines is important if we are to identify more individuals with Lynch syndrome in the future. Tools such as universal tumor screening and cascade testing can help increase diagnoses, but having a diagnosis is only helpful if proper preventative care is available to and understood by patients. With the shortage of genetic counselors and limited knowledge of other healthcare providers, making new diagnoses has the potential to overwhelm the current genetic counseling infrastructure. A public health plan should be made to identify more individuals with Lynch syndrome, with an infrastructure to support education about Lynch syndrome. The results of this survey are just one small step towards that ultimate goal.

3.5 Conclusions

The goal of this study was to survey adults with a diagnosis of Lynch syndrome, to assess their understanding of medical management guidelines, how well they adhere to these guidelines, their experiences with providers including genetic counselors, and barriers they have faced in understanding or following the guidelines. Many respondents had an accurate understanding of how often they should have colonoscopies, and many had not faced barriers to having these procedures. The demographics of respondents were not representative; most were white and had

above average income and education level. For this reason, these results are a starting point but are not generalizable to all individuals with Lynch syndrome.

Assessment of understanding of management guidelines is important if we are to improve diagnosis of Lynch syndrome. The vast majority of Americans with Lynch syndrome are unaware they have an increased cancer risk; public health efforts should be made to identify and educate these individuals. There must be a plan in place so that education and identification of these individuals does not overwhelm our healthcare system and the limited number of genetic counselors. This study provides a starting point for future studies to consider the best ways to educate this population and increase their access to necessary medical care in order to save lives and decrease the burden of cancer on our healthcare system.

4.0 Research Significance to Genetic Counseling and Public Health

This survey assesses the experiences of individuals who have been diagnosed with Lynch syndrome, with the goal of addressing needs specific to this group. Although respondents to this survey were largely of specific demographic groups (mostly white, above average education level and income, mostly insured), these results can be used as a starting point for further assessment and research. Most of these participants understood how often to have colonoscopies, and most of them had met with a genetic counselor. These results can be discussed in the context of implications for genetic counseling and the 10 essential services of public health.

This study demonstrated that these participants are discussing Lynch syndrome and management guidelines with a wide variety of providers beyond just genetic counselors. Studies have shown that non-genetics providers have limited knowledge about hereditary cancer syndromes and other genetic conditions (Carroll et al., 2019; Carroll et al., 2016; Hamilton et al., 2017). Primary care providers in particular have some of the best opportunities to identify individuals at risk for hereditary cancer syndromes based on personal and family histories, and help with medical management of those at high risk for cancer (Hamilton et al., 2017). These studies and the responses to this survey suggest that education of non-genetics providers about hereditary cancer is a worthwhile pursuit. This kind of large-scale education would be a public health approach to improving identification of and care for those at increased cancer risk, whether they have a genetic diagnosis or not. This kind of education could be accomplished through initiatives such as trainings at conferences or online, and continuing education credits could be an incentive to participate.

The participants in this study seemed to be well-educated about medical management guidelines and successful at adhering to them. More than 70% of respondents said they had discussed Lynch syndrome medical management guidelines with a genetic counselor (and more than 90% had seen a genetic counselor), and more than 90% of participants understood that they should have a colonoscopy at least every two years. These results indicate that genetic counselors and other providers (such as gastroenterologists) are successful in reviewing medical management guidelines with their patients, at least within this highly educated cohort. Genetic counselors should note that 65% of respondents indicated that they should have colonoscopies once a year. Although NCCN guidelines state that patients should have colonoscopies every 1-2 years (National Comprehensive Cancer Network, 2019), the results of this survey imply that providers (presumably including genetic counselors) are telling their patients to have colonoscopies once a year. This is something for GCs to be aware of as they counsel their patients about the medical management recommendations. Inclusion of risk factors such as age and gender can also be discussed, since NCCN guidelines recommend shorter intervals between colonoscopies for those with more risk factors (National Comprehensive Cancer Network, 2019). These risk factors may be part of the reason that many participants have been told by their providers they should undergo colonoscopies once a year.

This survey is also relevant to public health. The Core Public Health Steering Committee developed the 10 essential services of public health, which describe the functions that the field of public health aims to accomplish (Centers for Disease Control and Prevention, 2020b). This survey addresses the essential services, “Inform, educate, and empower people about health issues” and “Research for new insights and innovative solutions to health problems”(Centers for Disease Control and Prevention, 2020b, para. 4).

While this survey itself does not inform or educate individuals about Lynch syndrome and associated medical management guidelines, it does assess how well individuals with this diagnosis have been informed and educated. When a patient is given a hereditary cancer syndrome diagnosis, it is the responsibility of their provider to explain the medical recommendations to decrease morbidity and mortality from cancer, or to refer to a provider with expertise (such as a genetic counselor). While these management guidelines were created to decrease the burden of cancer, they are only useful if individuals with the diagnosis are properly educated and have access to care. If more Americans are to be successfully diagnosed with Lynch syndrome in the future, a major part of that process is education at diagnosis. One purpose of this survey was to assess whether changes need to be made to that education process. While the results of this study imply that the current education process is effective, this only applies to this specific subset of individuals. Although more than 60% of these participants have never encountered barriers to having colonoscopies, research shows that there are many barriers to having colonoscopies for members of the general public, of racial or ethnic minorities, and/or lower socioeconomic status (Kiviniemi et al., 2018). While this survey has indicated that participants are well-informed and educated about their genetic condition, this may not be the case for all individuals who have a diagnosis of Lynch syndrome or will receive one in the future. Public health genetics efforts should strive to improve education for those with hereditary cancer syndromes, especially as more individuals receive a diagnosis.

This survey also addresses the public health function of “Research for new insights and innovative solutions to health problems (Centers for Disease Control and Prevention, 2020b, para. 4).” A goal of this survey was to assess whether new solutions are needed to address the health of individuals with Lynch syndrome. Half of these participants were the first person in their family

to be diagnosed with Lynch syndrome. If cascade testing worked effectively, that percentage should be lower because for each proband there would likely be multiple others in the family with a diagnosis. More than 45% of participants also had a cancer diagnosis before they were diagnosed with Lynch syndrome; a public health goal should be to find ways to identify more individuals before they have cancer, so that future cancers are prevented or detected early. The survey also asked about barriers to having colonoscopies; this knowledge can help increase access to this important cancer-preventing procedure. Some participants wrote in barriers that had not been identified in the literature, such as the need to have another person attend the procedure with the patient. The responses to some of these survey questions provide a starting point for considering new ways to increase access to necessary healthcare for these patients.

This project provides information about diagnosis and the ordering of genetic testing that genetic counselors can use to better understand the experiences of some of their patients. The survey also helps consider the best ways to increase access to care for this population, which will become more important as more undiagnosed individuals are hopefully identified. Ultimately, because this sample is not truly representative of the Lynch syndrome population, the results cannot be generalized. However, this study provides a starting point for considering some of these issues and how best to direct future research.

5.0 Public Health Essay

Lynch syndrome is an autosomal dominant hereditary cancer syndrome estimated to affect at least one million Americans (Win et al., 2017); the majority of these individuals have not yet been identified (Rahm et al., 2018). Affected individuals have up to a 75% lifetime risk of developing colorectal cancer, the cancer type most strongly associated with Lynch syndrome (Giardiello et al., 2014). Colorectal cancer can be prevented or identified early with regular colonoscopies that include removal of pre-cancerous polyps (Lindor et al., 2006). Other cancers associated with Lynch syndrome may be prevented or identified early with the use of prophylactic surgery and cancer screening. The identification of individuals with Lynch syndrome is an important public health issue because cancer screening decreases morbidity and mortality associated with cancer, which in turn decreases the cancer burden on our medical system (Berg et al., 2009). The purpose of this chapter is to create a toolkit for the general public on the topic of hereditary cancer with a focus on Lynch syndrome as part of the efforts of the Pennsylvania Cancer Coalition Genetics/Genomics Work Group in response to genetics/genomics goals included in the Pennsylvania Cancer Control Plan. While there are many available resources on this topic, they do not all contain reliable information. Resources also differ by intended audience (physicians, patients, etc.) and are found on a variety of websites and other media, such as books. This toolkit provides a list of resources with accurate information related to Lynch syndrome and hereditary cancer that may be useful to members of the general public.

5.1 Background

5.1.1 Cancer Control Plans

The purpose of a Comprehensive Cancer Control Plan (CCC) is to assess cancer prevalence in a specific community (such as a state) and identify ways to outline strategies to help decrease the cancer burden in that community. In the United States, each state has their own CCC, and they are typically updated every five years (Centers for Disease Control and Prevention, 2019b). The CDC runs the National Comprehensive Cancer Control Program, which provides resources and guidance to individual states as they develop their plans (Centers for Disease Control and Prevention, 2018). The movement towards creating these plans in the United States originated in the early 1990s (Given, Hohman, Kostelecky, & Vinson, 2018). The definition of a CCC includes three elements: “collaboration among diverse multi-sector stakeholders to reduce duplication of effort and maximize existing resources, use of data to drive priority actions and use of research results to identify evidence-based interventions to implement those priorities, [and] development and implementation of a written strategic plan that is reflective of the community’s cultural context and health system to guide efforts” (Given et al., 2018, p. 2).

Development and implementation of CCC’s has also been considered internationally. In 2006, the CDC worked with the American Cancer Society (ACS), National Cancer Institute (NCI), and Union for International Cancer Control (UICC) to develop training sessions called forums, to be conducted internationally. These groups hosted annual forums from 2006-2008, and in 2013 the project was revisited and there have been several forums since then (Given et al., 2018). In 2012, the NCI spearheaded an effort to help communities around the world create their own CCC’s and created the International Cancer Control Partnership (ICCP) to carry this out. The ICCP has a

website with resources for groups creating a CCC (Given et al., 2018). As of 2015, 87% of countries had a CCC, up from only 48% in 2000. Unfortunately, 25% of these plans are not carried out (Romero et al., 2018). While cancer has become more recognized as a public health burden over the past 20 years, there is still plenty of progress to be made not only in creating CCC's, but to ensure these plans are practical and can be implemented.

In the United States, the development and implementation of CCC's since the mid-1990's have demonstrated success. One key to success has been collaboration between agencies on a state and federal level and with other relevant stakeholders. Resources and ideas have been combined to achieve progress in a way that would not have been possible individually (Hayes, Hohman, Vinson, & Pratt-Chapman, 2018). Although each plan is specific to its community's population, common factors for success have been identified. These include a diverse membership representative of the population, communication campaigns designed to reach the general public (phone calls, print media, etc.), and careful consideration of the audience and the cultural context that shapes their behavior and risk factors (Hayes et al., 2018).

As the understanding of genetics and genomics and how they relate to cancer has evolved, states have been adding genetics and genomics goals to their CCCs. A 2005 study of 30 states found that 18/30 CCC plans included goals related to genomics. Sixteen of these states were interviewed, and nine of them had started implementing these goals. Themes related to these goals included education of the public, education of providers, and discussion of family history (Irwin, Zuiker, Rakhra-Burris, & Millikan, 2005). A similar study assessed the 50 CCCs for all states in 2010, to see what had changed since the 2005 study; CCCs were searched for terms related to genetics/genomics, and a survey was sent to state CCC coordinators. This study found that 47/50 states included at least one related term; 43 included "family history" and 40 mentioned "gene" or

“genetics.” Thirty-two of these states listed a specific goal related to genetics/genomics; themes included education of the public and providers, collaboration with other groups or organizations, and research. The study concluded that more states included genetics/genomics in their CCCs in 2010 than in 2005, although the impact of these additions is unclear (Laufman, Duquette, & Trepanier, 2012). A more recent study found that 36/51 (71%) states have a goal or objective in their CCC related to genetics/genomics; 19 of these states have goals or objectives related specifically to Lynch syndrome or hereditary colon cancer, and 10-11 others refer more broadly to hereditary or familial cancer (Green et al., 2019). At the time the Green et al. (2019) paper was published, Pennsylvania was one of the 15 states that did not include any goals or objectives related to genetics/genomics in their CCC.

5.1.2 Health Literacy

Health literacy is “the degree to which an individual has the capacity to obtain, communicate, process, and understand basic health information and services to make appropriate health decisions” (Centers for Disease Control and Prevention, 2019d, para. 2). Individuals with high health literacy have the skills to use information related to their personal health in order to make appropriate decisions for their own health care; numeracy skills are also an important component of health literacy (Nutbeam, McGill, & Premkumar, 2018). Health literacy skills allow individuals to have more autonomy and control over their own healthcare and related decision-making (Nutbeam, 2008). A 2003 study found that only 12% of adults in the United States have “proficient” health literacy; the rest have “intermediate,” “basic,” or “below basic” health literacy. Racial minorities and individuals living in poverty had lower health literacy skills on average (Kutner, Greenberg, Jin, & Paulsen, 2006). These relatively low health literacy levels of the

average American and demographic factors that can affect health literacy are important to keep in mind when recommending health resources for the general public.

Studies have shown that genetic concepts are especially difficult for the public to understand. Interviews with members of the general public show a profound misunderstanding of basic genetics concepts, including that genes may be located in a certain part of the body only such as the brain or the heart, and that “genetics” is related to acquired traits and/or education. In order to understand more complex genetics concepts, such as inheritance patterns, misunderstandings of basic concepts would first need to be corrected (Lanie et al., 2004). There has been very little research on understanding of numbers as they relate to genetic information, but it is known that numeracy skills affect decision-making and are important in the context of genetics and genetic counseling (Lea, Kaphingst, Bowen, Lipkus, & Hadley, 2011). These findings are important to consider in the context of individuals with or at risk for Lynch syndrome. Numeracy is important for concepts such as the lifetime risk of different cancers and the chances of passing on a condition to one’s children. Basic genetics concepts are also important for understanding the inheritance pattern, and for understanding who in the family is at risk and that whether the mutation is passed on to each child is random.

The CDC has a tool, the “Clear Communication Index,” which can be used to assess how easily members of the general public (or other intended audience) may understand a document meant to communicate information. The Index asks a series of questions about the document, and provides a number scoring how readable and understandable the product is. It can be used by individuals who are assessing documents already created, or aid with the creation of new documents. This tool emphasizes concepts such as knowing the intended audience and developing the product for them; using pictures, headings, and bullet points to avoid large chunks of text; and

emphasizing the takeaway message at the start of the document with visual support. Language should be simple enough for the audience to understand, and when larger words (such as complicated medical terms) are used they should be defined. Numbers should be used only when necessary (to avoid too much reliance on the public's numeracy skills), with consideration for the most digestible way to present them (ex: say "8 out of 10" instead of 81%). Simple visual designs can also be used to help convey complicated numbers such as percentages and fractions (Centers for Disease Control and Prevention, 2019a). When reading the material, the intended audience should be able to understand the information presented and know what to do with it, without having to do research on their own such as math calculations or looking up complicated words. The guidelines in the Clear Communication Index can be used as a framework to evaluate the usefulness of the items in this toolkit.

5.1.3 Pennsylvania Cancer Coalition Work Group

This project is being carried out as a part of the Pennsylvania Cancer Coalition (PCC) Cancer Genetics/Genomics Workgroup. The Pennsylvania State Department of Health houses a Department of Cancer Prevention Control and a cancer registry, which collects data on all new cancer cases in the state. Every five years, this department develops a cancer control plan for the state of Pennsylvania. The Pennsylvania Cancer Control, Research and Advisory Board (CAB) is an 11-member committee of experts appointed by the governor of PA to advise the PA Secretary of Health on cancer control, prevention, and research, and to approve the PA Cancer Control Plan. During planning of the 2019-2023 PA Cancer Control Plan, the PA Deputy Secretary for Health Promotion and Disease Prevention requested that genetics and genomics goals be included in this cycle, after learning that many states include these types of goals. The CAB did not have the

expertise to create goals specific to genetics and genomics, and created the Cancer Genetics/Genomics Committee to advise them (A. Durst, personal communication, April 13, 2020).

This ad hoc committee was tasked with advising the CAB on how to include goals specific to genetics and genomics in the 2019-2023 PA Cancer Control Plan (A. Durst, personal communication, April 13, 2020). The committee, which included professionals with experience in genetics, cancer, public health, insurance, and other specialties, developed a report that included goals in the following areas: data and surveillance; education of healthcare providers and the public; and policy, insurance and systemic change. Data and surveillance goals aim to track data and increase access to genetics services for underserved areas of PA. Education goals aim to continuously educate and update both providers and the general public; this included the formation of a work group to carry out these goals. Finally, policy goals include supporting a proposed amendment to the genetic counselor licensure laws in PA to allow genetic counselors to order tests independently and to increase funding to help carry out the goals of this report (PA CAB Cancer Genetics/Genomics Committee, 2019). This report was completed at several in-person meetings as well as remote work between those meetings (A. Durst, personal communication, April 13, 2020).

Once the report had been finalized and the goals developed for cancer genetics and genomics, the PCC work group was formed in order to carry out these goals. Anyone can apply to join the work group by completing a form online through the PCC website. Members could be seen as a “team of stakeholders” for cancer control in the state of Pennsylvania. The group includes professionals from the state whose work is related to genetics, cancer, and/or public health. This group is tasked with deciding how to carry out the genetics/genomics goals outlined by the Cancer

Genetics/Genomics Committee and then implementing programs to meet those goals. There are many issues to address related to cancer genetics and genomics; the group is prioritizing activities that will have the largest impact on PA citizens, while minimizing needed funding to carry out these tasks. The main current initiative from this group is the creation of online hereditary cancer toolkits, one for providers and another for patients/members of the general population. The toolkit for providers is currently being developed by members of the workgroup (A. Durst, personal communication, April 13, 2020).

As a student member of the PCC Cancer Genetics/Genomics Workgroup, I was tasked with completing the patient toolkit for Lynch syndrome. It includes resources such as websites, risk assessment tools, and podcasts that may be helpful for individuals with a diagnosis of Lynch syndrome or who are concerned about the possibility of a hereditary cancer in their families. While some of these resources are specifically about Lynch syndrome, others pertain more broadly to hereditary cancer syndromes. These resources will eventually be published as a patient toolkit on the Live Healthy PA website, along with other resources for patients added by the work group and the provider toolkit.

5.2 Methods

5.2.1 PCC work group

The author joined the PCC work group in March, 2020. The work group is led by co-chairs Andrea Durst, MS, DrPH, LCGC and Alanna Kulchak Rahm, MS, PhD, LGC, who are genetic counselors in Pennsylvania with public health experience. The work group holds meetings every

1-2 months, which alternate between in-person meetings in Harrisburg, PA and remote meetings through Skype. During the time period the author was involved with the work group (March – June 2020) all meetings took place over Skype due to the COVID-19 pandemic. Meetings are run by the co-chairs, and revolve around discussion of the work group’s initiatives (dividing up tasks, sharing progress made, etc.) The main focus of the work group during this time was the formation of a hereditary cancer tool kit for non-genetics healthcare providers. Updates on the patient toolkit were presented at each workgroup call, and feedback from the group was incorporated into future versions of the toolkit.

5.2.2 Identification of Resources

Resources that could be useful for individuals with Lynch syndrome or suspicion for a hereditary cancer syndrome were identified using prior knowledge and by searching the internet. The author had already used some of these resources while training in genetic counseling and public health genetics, including Lynch syndrome non-profits, the CDC website including the My Family Health Portrait tool, NSGC’s “Find a Genetic Counselor” tool, podcasts related to hereditary cancer, and NCCN guidelines. The PCC work group has begun their provider toolkit, and this list was referenced as some resources such as the CDC’s My Family Health Portrait could be useful for both providers and patients and are therefore included on both lists. The provider toolkit also contains categories, such as somatic tumor testing, that should be included in the patient toolkit but with links to different resources to address the patient audience. The National Coordinating Center for the Regional Genetics Networks website was also used to identify resources; the website provides a search tool to look for resources created by any of the seven regional genetics networks (National Coordinating Center for the Regional Genetics Networks,

n.d.n.d.). Resources were searched by topic (“cancer”) and by intended audience (“patients and/or families” and “public health”).

Resources were reviewed to assess whether they are relevant to Lynch syndrome and/or hereditary cancer, and whether the content was appropriate for the general public (using the CDC Clear Communication Index as a guide) or could be useful for a patient to discuss with their provider. Appropriate resources were included in this list.

5.3 Patient Toolkit for Lynch Syndrome

As part of this project, an annotated list of resources with descriptions and analyses was created for the workgroup’s reference. A resource list with shorter explanations of each of the included entries was also constructed for inclusion on the website. Included below is the patient toolkit, a collection of resources for the general public related to hereditary cancer with a focus on Lynch syndrome. This list will be used as the basis for the development of the online patient toolkit for Lynch syndrome.

Lynch Syndrome International: <https://lynchcancers.com/> (Lynch Syndrome International, 2019)

Sentence for website: Lynch Syndrome International is a nonprofit dedicated to Lynch syndrome; their website contains helpful information about Lynch syndrome, links to other resources, and ways to get involved in the Lynch syndrome community. You can also follow them on Facebook for regular updates and join their Facebook support group for individuals with Lynch syndrome.

Lynch Syndrome International (LSI) is a non-profit dedicated to Lynch syndrome. The group is founded and is run by individuals with a diagnosis of Lynch syndrome, their family members, and professionals (such as doctors and genetic counselors) with expertise in Lynch syndrome. Their website contains multiple informational resources, including the genes and types of cancer associated with Lynch syndrome, a brief explanation of autosomal dominant inheritance, details about surgeries such as hysterectomy, relevant preventative care, and names of resources that might be helpful for individuals with Lynch syndrome and/or cancer who need financial assistance. Some pages on their website contain links to other helpful websites, such as family history tools and journal articles about preventative care and GINA. LSI also has a Facebook page where articles and relevant news are shared, and a Facebook group for individuals with Lynch syndrome to post and talk with each other. Their website also has volunteer opportunities, including being paired with others in your area with Lynch syndrome. While the LSI website has abundant information, the many pages on different topics are not organized in a logical way and it can be difficult to know where to click to learn more about a certain topic. The CDC Clear Communication Index User Guide recommends that large amounts of information should be broken down to make it more readable; this can be achieved several ways, such as with bullet points, shorter sections with headings, or with images. Language should be simple and have a clear message (Centers for Disease Control and Prevention, 2019a). On LSI's website, the pages and fact sheets tend to be dense, written in long paragraph form, and could use editing for tone and extraneous writing. One page has a screenshot of the NCCN guidelines from 2016; this is a wonderful resource to share, but the guidelines have been updated several times since the screenshot was taken. Although LSI's website can be overwhelming, this would be a good resource

for answers to some basic questions and ways to be in contact with others in the Lynch syndrome community.

AliveAndKickn: <https://www.aliveandkickn.org/> (AliveAndKickn, 2018a)

Sentence for website: AliveAndKickn is a nonprofit dedicated to Lynch syndrome; their website contains helpful information about Lynch syndrome, the opportunity to join a patient registry, and links to other helpful resources. You can also follow them on Facebook and Twitter for regular updates.

AliveAndKickn is a non-profit dedicated to Lynch syndrome; it was founded by Dave Dubin, a cancer survivor with Lynch syndrome, and his wife. Their website includes basic information about Lynch syndrome, including the associated genes, percentage lifetime risks for different cancers, recommended screening, and links to other websites with further information such as NSGC's "Find a Genetic Counselor." AliveAndKickn has also developed a registry for individuals with Lynch syndrome, which patients can join on their website. Users can also apply for peer to peer support from another individual with Lynch syndrome, read the stories of individuals with Lynch syndrome, and download small infographics with information about Lynch syndrome from their social media toolkit. There are links to helpful resources such as the latest NCCN guidelines (although the user must create a free account for this link to be successful, which may be confusing) and a patient-friendly explanation of MSI tumor screening. The organization is also active on social media (Facebook, Twitter) and has a blog and podcast specific to Lynch syndrome.

National Cancer Institute (NCI) patient resources: <https://www.cancer.gov/about-cancer/causes-prevention/genetics/directory> (National Cancer Institute, 2019b)

Sentence for website: These pages include basic explanations of cancer genetics: how genetic changes can be related to cancer, tumor genetic testing, and genetic testing for increased cancer risks that can run in families. This information could be useful if you have recently been diagnosed with cancer or suspect cancer might run in your family. These resources may be best used alongside a visit with your doctor.

NCI has several pages on topics related to hereditary cancer (under “Consumer Resources from NCI) that could be useful for individuals looking for more information about how genetics is related to cancer. Some of the language used is high-level, using phrases such as “DNA-damaging carcinogens;” other times, technical words such as “somatic” are briefly explained. The CDC Clear Communication Index recommends that information be written using words the audience (in this case, the general public) regularly uses (Centers for Disease Control and Prevention, 2019a). These pages do not fully meet that recommendation, but because some terms are defined audience members with relatively higher health literacy skills may find them useful. They include helpful background information regarding hereditary cancer syndromes, genetic testing, and genetic counseling.

“Genetics and Cancer:” This page reviews what genes are and explains that cancer is caused by somatic (acquired) mutations. There is a brief overview of hereditary cancer syndromes, brief descriptions of some of these syndromes, and examples of features in family history that might indicate hereditary cancer. The difference between germline and tumor testing is also explained, along with the type of information that can be gained from each (National Cancer Institute, 2017a).

“Tumor DNA Sequencing in Cancer Treatment:” This page reviews the details of tumor DNA testing. The information includes how the testing can be useful (for cancer treatment), how

the specimen is obtained, different types of testing, and what the results may or may not indicate for the patient. Limitations of the testing and cost are also addressed (National Cancer Institute, 2017b).

“Genetic Testing for Inherited Cancer Susceptibility Syndromes:” This page briefly introduces much of the background that would be covered in a cancer genetic counseling session. It includes concepts such as penetrance and expressivity, autosomal dominant inheritance, the three types of results that can be identified on a germline genetic test, features in a family and/or individual that increase suspicion for hereditary cancer, and how to decide which person in the family is ideal to test first. The role of a genetic counselor is also explained, as well as cost of testing, potential benefits and harms, and GINA and genetic discrimination (National Cancer Institute, 2019a).

Disease Info Search: <https://www.diseaseinfosearch.org/Lynch%20syndrome/3371>
(Disease InfoSearch, n.d.)

Sentence for website: This website explains the basics of Lynch syndrome, including how it runs in families and cancer types related to Lynch syndrome. It also includes links to other dependable websites where you can read more about topics related to Lynch syndrome.

The Lynch syndrome page on Disease Info Search’s website provides a brief overview of Lynch syndrome; basic information is provided, such as the 50% risk of passing on the condition to one’s children, the cancers associated with Lynch syndrome, and the fact that there is special medical management for this condition. Someone reading this page would take away the most basic facts about Lynch syndrome, without being overwhelmed by detail. A nice feature of this website is that it links to other resources for the given condition; users on the Lynch syndrome page can click the left side of the page to easily access related news articles, organizations (such

as Lynch Syndrome International and AliveAndKickn), clinical trials, and journal publications. The main page links Mayo Clinic and Genetic & Rare Diseases Information Center as “trusted medical sites.” These outside links go into further detail about Lynch syndrome and contain reliable information. This website is therefore a good place to find multiple types of resources related to Lynch syndrome.

CDC Hereditary Colon Cancer:

https://www.cdc.gov/genomics/disease/colorectal_cancer/index.htm (Centers for Disease Control and Prevention, 2019c)

Sentence for website: The CDC (Centers for Disease Control and Prevention) provides resources for the general public about different health conditions. This page provides basic facts about colon cancer that is hereditary (runs in families) and is a helpful overview of topics including how to understand the results of tumor genetic screening, the importance of family history, and how genetic counseling can be helpful.

The CDC’s page on hereditary colorectal cancer covers many important topics. The importance of family history is stressed in several places, which ideally helps reiterate that message for users. Basic facts, such as the number of CRC cases in the United States each year, are shared. The page about Lynch syndrome briefly explains the associated cancers and genes, with a basic explanation of inherited genes and how cancer occurs. There is a simple, understandable explanation of tumor screening along with tables for the possible results of IHC and MSI, and whether each result says the individual is likely or unlikely to have Lynch syndrome. There is a list of specific family history findings that could be concerning for Lynch syndrome, and a link to the Surgeon General’s Family Health History tool. The page on genetic counseling explains how counseling can be helpful and reasons a doctor might refer someone. The possible results of genetic

testing are explained, along with a brief explanation of what a result might mean for the patient and for their family, separated by those who have had a CRC diagnosis and those who have not. Medical management guidelines are explained, emphasizing that colonoscopies are recommended and other screening can be considered but that these screenings do not have strong evidence to support them. Finally, there are several stories of individuals with Lynch syndrome. While this website could easily be overwhelming to members of the general public, almost every pertinent topic is covered and the information is reliable. It could be a good place to direct a patient with questions on one topic, such as tumor screening or genetic testing.

NYMAC When to Refer to Genetics:

https://www.wadsworth.org/sites/default/files/WebDoc/Red%20Flag%20Final_Cancer4.30.pdf

(NYMAC Regional Genetics Network & New York State Department of Health, n.d.)

Sentence for website: This guide lists “red flags” in a family medical history that might suggest an increased risk of cancer. You and your doctor may review this guide and your family medical history together to decide whether a cancer genetics evaluation is appropriate for you or someone else in your family.

This document was created by the NYMAC Regional Genetics Network; it outlines situations where referral to cancer genetics should be considered. Although it was written for healthcare providers to reference when referring their patients, it could be helpful for members of the general public as well. The document includes a summary of red flags for hereditary cancer syndromes, including specific cancers that are concerning regardless of age (ex: ovarian), tumor characteristics (ex: colon or uterine cancers with abnormal MSI or IHC results), and early age of onset. Cancers associated with Lynch syndrome are listed, as well as cancers associated with HBOC. Links are included to NCCN guidelines, including the guidelines for hereditary colon

cancer. Resources for finding a genetics provider are also included. While this document includes wording that may be confusing for the general public (phrases such as “pathogenic variant” and “mismatch repair deficiency”), the non-medical language is simple and a patient could find this resource useful. For instance, an individual from the general public would likely understand that cancers at a younger age and multiple cancers in one person are signs of concern for hereditary cancer. This is also a resource that patients could share with their providers, for help assessing their potential need for a cancer genetics referral.

GINA & You Fact Sheet: http://ginahelp.org/GINA_you.pdf (Genetic Alliance, National Coalition for Health Professional Education in Genetics, & The Genetics & Public Policy Center, 2010)

Sentence for website: GINA is a law that prevents health insurance and employers from treating you unfairly based on a genetic diagnosis. This fact sheet is a brief overview of GINA, including situations where it does and does not apply.

This two-page fact sheet about GINA is a nice patient-friendly resource. Complicated terms such as “genetic information” and “genetic services” are defined, making it easier for the general public to understand. The CDC Clear Communication Index recommends simple language, with explanations for unfamiliar terms when the use of complicated language is unavoidable (Centers for Disease Control and Prevention, 2019a). This sheet is a condensed, more digestible summary of the information on the GINA Info website, which contains complicated details including higher-level language. It makes good use of bullet points and pictures, which are also recommended by the Clear Communication Index (Centers for Disease Control and Prevention, 2019a), and appears less intimidating than the full website. Definitions of terms are included in a small column on the side of the page for easy reference, although some of these definitions are written at a higher

literacy level than would be ideal for this type of resource. After setting the background for GINA and explaining what it is, there is an explanation of what GINA does not cover (current symptoms, other types of insurance, small employers, and the military). This information is equally important as explaining what GINA does cover, and it is emphasized appropriately. The most important takeaway messages are written in a different color and larger font; highlighting the most salient messages and use of visual cues including font are recommended by the CDC Clear Communication Index (Centers for Disease Control and Prevention, 2019a). This fact sheet is a good summary of the most important parts of GINA; patients who want to know more can follow the link to the GINA Info website for more detail and clarification.

CDC My Family Health Portrait: <https://phgkb.cdc.gov/FHH/html/index.html> (Centers for Disease Control and Prevention, 2020a)

Sentence for website: This website helps you draw out your family medical history by entering different family members, their medical conditions, and their ages. Family history is an important tool for considering your medical risks, including cancer. You can bring this history to your doctor for help directing your own medical care.

This tool from the CDC allows any person to create their own pedigree by entering personal and family information. The user starts by entering their own personal information (name, date of birth, assigned sex at birth, known health conditions, race and ethnicity, etc.), and can then add relatives and their information. Information about each of these relatives can then be manually entered (date of birth, health conditions, etc.) Cancers can be added for each family member; this includes the type of cancer and age of diagnosis. When looking at the pedigree, the user can select a condition to highlight (a type of cancer, or another condition such as high blood pressure). This is a useful tool for anyone in the general population to draw a pedigree for their family, even if

they have never heard of a pedigree and are unsure where to start. There are limitations for which relatives can be added; for instance, great-grandmothers or great-uncles are not options. This tool could be a great way to encourage members of the general public to start thinking about family history; viewing the list of conditions such as cancer and high blood pressure listed as options may help the user remember a condition in the family they would have otherwise forgotten. It may also prompt individuals to ask family members questions, such as age of diagnosis. The pedigree could also be printed and brought to one's doctor for help discussing relevant information in the family history.

Family Health History Toolkit:

<http://www.heartlandcollaborative.org/files/2014/07/HeartlandFamilyToolkit-9-28-07.pdf>

(Heartland Regional Genetics and Newborn Screening Collaborative, n.d.)

Sentence for website: Family history is an important tool to help decide the chances that a higher risk of cancer (or other medical conditions) runs in a family. This guide can help you think about how to talk with family members and record their medical history, which you can bring to your doctor or a genetic counselor to help plan your healthcare.

This toolkit was written by the Heartland Regional Genetics Network; it is a 24-page document written for the general public with information about the importance of family health history. It includes advice for when and how to start these conversations with family members. There are suggestions for how to approach family members (in a group vs. one-on-one) and the types of questions to ask related to health conditions (age of onset, age of death for those who have passed away, etc.). The toolkit includes a list of conditions that are important to know about if they run in one's family, such as cancer, diabetes, and pregnancy losses. The document includes suggestions for recording this information, and questions to ask one's doctor when sharing the

information. Red flags to look for, such as unusually early onset of conditions and multiple members of the family affected, are included. A list of questions to ask about each family member is included as a guide. Finally, there is information about genealogy resources, when someone should consider seeing a genetic counselor, and ideas for fun ways to review health history with one's family. The document contains links to helpful resources, such as NSGC and the CDC's family health history page. The document is written in friendly language for the general public; although it has a lot of text, it is broken into sections which make it easier to navigate and it includes plenty of bullet points and pictures to break up the text.

PREMM5: <https://premm.dfci.harvard.edu/> (Dana-Farber Cancer Institute, 2016)

Sentence for website: This tool asks questions about your family history of cancer to predict the chance that you have Lynch syndrome (in a percentage). You can do this on your own or with help from your doctor. It is fast to complete and may help your doctor decide whether genetic counseling or testing could be helpful for you.

PREMM5 is a Lynch syndrome risk model that provides the chances of having a Lynch syndrome mutation after questions about personal and family history are answered. While the intended audience is healthcare providers, this model is more accessible and easier to use than other cancer risk models (ex: CaGene, BRCAPro). The language is high level so it may not be appropriate for all patients. Some complicated terms are defined for a general audience, such as "endometrial," "first-degree relatives," and "second-degree relatives." Other terms are not defined, such as "sebaceous," "germline mutation," and "inherited cancer predisposition syndrome." As discussed in the CDC Clear Communication Index user guide, resources most friendly to the general public include definitions of all unfamiliar terms (Centers for Disease Control and Prevention, 2019a). The questions themselves are simple, if the person is familiar with the cancer

types (or at least knows if a given cancer type applies to someone in their family or not) and understands the provided definitions of first- and second-degree relatives. This tool could be discussed with a general provider or a nurse, who could explain the questions in terms the patient understands. It is quick enough to be used during a short check-up.

Patient Stories from Grey Genetics podcast: <https://www.greygenetics.com/podcast/>
(Grey Genetics, 2019)

Sentence for website: This podcast, hosted by a genetic counselor, includes interviews with individuals living with many different genetic conditions. There have been several episodes about Lynch syndrome and other hereditary cancer syndromes; you can look through the titles and descriptions to find these episodes and hear others' experiences with hereditary cancer.

While not specific to hereditary cancer, this podcast is run by a genetic counselor and consists of her interviews with patients. There have been at least two episodes interviewing an individual with Lynch syndrome. The titles and descriptions of each podcast make it clear who is being interviewed and which disease or topic is covered, so a patient looking to hear about Lynch syndrome could easily find those episodes. The interviews include many questions about the patient's experience with cancer (if applicable) or cancer in the family, referral for genetic counseling or testing, the process of diagnosis and how each of these things made the patient feel. There have been many episodes about hereditary cancer (including HBOC and Li-Fraumeni syndrome), and the themes and feelings discussed would likely speak to individuals with any hereditary cancer syndrome. The goal of this podcast is to share the patient perspective, and that comes through with the questions the host asks. It is hoped that listening to this podcast can help individuals with hereditary cancer and other genetic conditions feel less alone with their diagnoses.

AliveAndKickn Podcast: <https://www.aliveandkickn.org/podcast> (AliveAndKickn, 2018b)

Sentence for website: This podcast is hosted by Dave Dubin, who has Lynch syndrome and is a cancer survivor. He has conversations with other patients and doctors who belong to the Lynch syndrome community about their experiences.

Dave Dubin, the founder of Lynch syndrome non-profit AliveAndKickn, hosts a podcast where he talks with individuals with a connection to the Lynch syndrome community. Dave has Lynch syndrome himself and interviews people in his network, including physicians (such as GI doctors with hereditary cancer knowledge), other individuals with Lynch syndrome, and other cancer survivors. The podcasts are informative and the conversational style is entertaining; Lynch syndrome and related cancers are discussed from varying perspectives. The conversations with other patients are relatable, and the healthcare providers interviewed are friendly and present information in an accessible manner. Individuals with Lynch syndrome may enjoy this podcast as a space dedicated to discussing their hereditary cancer syndrome and related issues.

NSGC blog: Is Direct-to-Consumer Genetic Testing Right for You?:

<https://www.nsgc.org/p/bl/et/blogid=53&blogaid=577> (Estabrooks Hahn, 2016)

Sentence for website: If you are considering doing a Direct-to-Consumer genetic test (a genetic test that you can order yourself), this blog post explains some issues to consider. A genetic counselor explains some of the unexpected results that can be discovered with this type of test.

This blog post is written by a genetic counselor, and briefly explains in patient-friendly language what a direct-to-consumer test is and some things to consider before doing such a test. The possibility of learning unexpected information is emphasized, as well as the possibility that these results will be life-changing. Examples are provided, such as new information about disease

risk or unexpected familial relationships. This post is several years old, and mentions that the FDA has now regulated information that can be learned about disease risk. Since then, the FDA has allowed more health-related testing. For instance, Ancestry now offers testing for about a dozen Lynch syndrome variants (Ancestry, n.d.). This post does also mention that surprises such as new familial relationships can also be positive if they are well-received, which is an important point. The post does not discourage DTC testing, but rather explains some points to consider before testing. The post ends with a brief discussion of how genetic counselors can be helpful, along with a link to NSGC’s “Find a Genetic Counselor” tool.

Find a Genetic Counselor: <https://www.findageneticcounselor.com/> (National Society of Genetic Counselors, n.d.)

Sentence for website: A genetic counselor can evaluate your family medical history and help decide whether genetic testing may be appropriate for you. You can use this search tool to find a genetic counselor in your area. Search “in person” to find a genetic counselor in your area or “by phone” to find a genetic counselor who can talk with you over the phone or through video chat. Select “cancer” as the specialization if you are looking for a genetic counselor to evaluate your personal or family cancer history.

Genetic counselors are important resources for navigating the possibility or diagnosis of a hereditary cancer syndrome; a patient may be interested in seeing a genetic counselor, but may not know where to find one. This directory was created by the National Society of Genetic Counselors (NSGC), and has a list of current members of the organization, the type of counseling they do (ex: pediatrics, cancer, prenatal), and their location. If a patient wants to find a counselor in their area, they can search by state and/or postal code, within a certain radius. Search results can also be filtered by specialty; individuals with concern for hereditary cancer could choose “Cancer,” and

counselors in other specialties would be filtered from the results. Genetic counselors can also be searched by name, or by the institution they are affiliated with. This is a useful tool for a patient who knows they need to see a genetic counselor but is unsure where to find one. The link can easily be shared and is easy to remember. One downside is that the directory only includes genetic counselors who are members of NSGC and the genetic counselor has to update their personal information regularly. This means not all genetic counselors can be found in this database and some may have outdated information if they have changed jobs.

Find a Genetic Clinic: <https://clinics.acmg.net/> (American College of Medical Genetics and Genomics, 2020)

Sentence for website: This website allows you to search for a clinic that provides genetics services. Select “cancer risk” at the bottom of the page if you are looking for providers to evaluate your personal or family history of cancer. You can check the box “Show clinics with no physical locations” if you are interested in meeting with a genetics provider over the phone or through video chat instead of in person.

This is a relatively new database from ACMG that allows the general public to search for a genetics clinic. It has a broader list of locations than NSGC’s “Find a Genetic Counselor” and includes specialty clinics such as the Sickle Cell Program and Huntington’s Disease Society of America Center of Excellence. These types of clinics can be found even if they do not have a genetic counselor who is a member of NSGC, which broadens the results. Users can search by clinic type (such as “cancer”), city/location, or state. They can also select the specialty they are searching for; the list includes specialties such as Reproductive Genetics in addition to the broader Genetic Counseling. The search function includes locations that only provide services via telehealth, and users can select the “Show clinics with no physical locations” box to include these

clinics. When a user clicks on a clinic, a link to a website and/or phone number are provided if available. Some results found in this search engine seem unlikely to provide clinical genetics services, such as pharmacies. The ability to choose a specialty type is useful if the user knows what they are looking for, though big words such as “Cardiovascular” may be confusing for the general public. A few of the specialties have short descriptions which are helpful. This database has the potential to be very useful for members of the general public who know the type of services they are seeking.

What to expect when meeting with a genetic counselor:

<https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/what-expect-when-meeting-genetic-counselor> (American Society of Clinical Oncology, 2018)

Sentence for website: This page has information about the process of genetic counseling and how it can be useful for individuals or families with cancer. The page includes a list of things to bring with you to a genetic counseling appointment and what to expect during your visit.

This page on cancer.net explains the purpose of genetic counseling and what to expect from a visit with a cancer genetic counselor. It includes a list of the many roles of genetic counselors, beyond just offering and ordering genetic tests (risk assessment, emotional and psychological impacts of testing, privacy of genetic information, etc.) This page includes instructions on how to prepare for a session (which medical records to bring, gathering relevant family medical history, types of cancer and age of diagnosis) and clarifies that this information is helpful but not mandatory. There is also a suggestion to bring someone else with you to the appointment to help remember information and ask questions. The topics covered in a genetic counseling session are listed (family history, testing options, details about the test), as well as what to expect after the session (including that the GC should provide anticipatory guidance). A link is provided to the

NSGC website to help find a genetic counselor. This page is a thorough overview of the cancer genetic counseling process, and dispels some common myths about genetic counseling (ex: that the only purpose is to order a genetic test). While there are large blocks of text on this page that could be a lot of information for a patient to take in at once (especially if juggling multiple appointments related to cancer), all of the information is relevant and this could be a helpful resource for anticipatory guidance. The use of bullet points makes the information more digestible, as suggested by the CDC Clear Communication Index (Centers for Disease Control and Prevention, 2019a).

NCCN guidelines patient version (colon cancer):

<https://www.nccn.org/patients/guidelines/content/PDF/colon-patient.pdf>

(National Comprehensive Cancer Network, 2018)

Sentence for website: NCCN (National Comprehensive Cancer Network) publishes guidelines for patients with many types of cancer. This is a link to the colon cancer guide but you can visit their website to find guides for other cancer types. The guide includes explanations of the ways doctors might describe or test your tumor, an overview of treatment options, and other concepts related to colon cancer. You must create a free account in order to access these guides.

NCCN has a patient guide for colon cancer (as well as other cancer types). It is written in patient-friendly language and reviews many concepts related to a diagnosis of colon cancer. These include an explanation of GI tract anatomy and colon cancer, description of tumor testing and how it can be helpful, different kinds of treatments and common side effects, and an explanation of tumor staging and localized versus metastatic cancer. Patients with a diagnosis of colon cancer can look up concepts they have discussed with their doctor; the guide also encourages readers to keep reading and bringing questions to their provider to increase understanding of their diagnosis and

treatment plan. Lynch syndrome is briefly mentioned several times, usually in reference to the importance of family history and possibility of a hereditary cancer syndrome. This guide could be very useful for individuals with a diagnosis of colon cancer and their family members. The NCCN patient guideline page includes guidelines for other cancers such as rectal, uterine, ovarian, kidney, and stomach. Some cancers have translations of their guides into other languages.

NCCN Guidelines – Genetic/Familial High-Risk Assessment: Colorectal:

https://www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf

(National Comprehensive Cancer Network, 2019)

Sentence for website: NCCN (National Comprehensive Cancer Network) publishes guidelines for Lynch syndrome, with management recommendations (such as how often one should have colonoscopies) based on research. They are updated several times a year to include the latest evidence. The guidelines are complicated and meant for healthcare providers, but you can bring these to your doctors to read so they can help decide the best way to manage your health. You must create a free account in order to access these guidelines.

These are the NCCN's guidelines for providers regarding hereditary colorectal cancer; they include known evidence and recommendations regarding Lynch syndrome and other hereditary cancer syndromes related to colorectal cancer. While these guidelines are highly technical and not written for the general public, patients can be aware of them and bring them to their providers. Primary care providers, gynecologists, and other providers may be unaware of these guidelines and can use them to help best treat their patients. These guidelines include official evidence-based recommendations, along with some medical management without sufficient evidence but can be considered for individual patients with help from their providers. Also included are ranges for lifetime cancer risks, provided separately for each of the four MMR genes associated with Lynch

syndrome. The guidelines also include information about interpretation of and recommendations for tumor testing using IHC or MSI, guidelines for taking a family history, and criteria for considering Lynch syndrome as a possible diagnosis. At the end of this document there is a more detailed discussion of the evidence with references, so that providers can look at the primary literature themselves.

***This Really Isn't About You* by Jean Hannah Edelstein** (Edelstein, 2018)

Sentence for website: This is a memoir written by a woman who was diagnosed with Lynch syndrome in her early 30s, after her father passed away from cancer. She writes about struggles common to many young adults (such as finding a partner and deciding when to have children) and how her diagnosis shaped this time in her life.

This book is a memoir written by a woman with Lynch syndrome. She tells the story of her father's death from cancer, her experience with genetic testing, and the ways her life was affected by this diagnosis. As a young woman in her early 30s, the author struggled with the knowledge that she would likely eventually die from cancer. She discusses how a diagnosis of a hereditary cancer syndrome is not the same as being "sick," but she also felt she was no longer "healthy." She writes about her relationship with her two siblings, who both tested negative for Lynch syndrome. The author felt pressure from her doctors to start a family as soon as possible so that she could have her uterus and ovaries removed to decrease her cancer risks. This led to pressure to find a partner, and her diagnosis affected her dating life. In short, this is the memoir of a young adult trying to figure out her life, in the context of her father's death and her personal diagnosis of Lynch syndrome.

AliveAndKickn blog: <https://www.aliveandkickn.org/news> (AliveAndKickn, 2020)

Sentence for website: This blog from the Lynch syndrome non-profit AliveAndKickn contains posts related to Lynch syndrome. Click on “Living with Lynch” to read posts written by individuals in the Lynch syndrome community. Click on “News” for posts related to new research, including studies seeking participants with Lynch syndrome.

AliveAndKickn has a blog with posts related to Lynch syndrome. All posts can be viewed in order, but they are also separated into sections which make it easier for users to find the type of post they are looking for. The “Living with Lynch” category has posts from various individuals with Lynch syndrome who write about their experiences. “News” has information about new studies related to Lynch syndrome, awareness events, and opportunities for patients such as research studies. The third category, “Programming Update,” has news about advocacy groups, their collaborative efforts, and goals they have accomplished. Viewing all posts at once can be overwhelming, especially since the layout allows the viewer to see the titles of many posts at once. The categories are a useful way for users to find the information they are looking for. Reading posts from others with Lynch syndrome could be helpful to individuals who feel alone with their diagnosis or want to learn how others are coping successfully. The news has some useful information, though it is not updated often enough to be a reliable source for the many Lynch syndrome-related developments that are happening.

***Cancer Family: The Search for the Cause of Hereditary Colorectal Cancer* by Richard Boland** (R. Boland, 2015)

Sentence for website: This book is written by a man whose family members passed away at young ages from colorectal cancer for generations. He writes about how his family history inspired him to become a doctor and researcher and find the genetic mutation that caused his family’s “curse.”

This book is written by a man whose family members had passed away at young ages from cancer (often colorectal cancer) for many generations. Members of the family felt cursed and considered themselves at high-risk, but had no explanation for why this was happening to them. This striking family history (including his father's young death from colorectal cancer) motivated the author to become a doctor and researcher. The book touches on the history of hereditary cancer syndromes, including that eugenicists believed individuals from this family should be sterilized; this resulted in family members attempting to keep their cancer history a secret. The author writes about his quest to identify the mutation that had affected his family members for generations.

5.4 Discussion

The purpose of this toolkit is for use by the general public; it will be most useful for individuals with Lynch syndrome or who are concerned about the possibility of a hereditary cancer syndrome in their family. A version of this toolkit will be posted on the Live Healthy PA website, where it is most likely to be viewed by residents of Pennsylvania. The website is universally accessible, so the toolkit may also be used by individuals outside Pennsylvania. The information in this toolkit is not specific to individuals in PA, so ideally it will be used by individuals in other parts of the United States and possibly the world. The toolkit is provided only in English, so it is not accessible to individuals who do not speak English.

This toolkit may also be used by providers, to share with their patients after a diagnosis of Lynch syndrome or discussion about hereditary cancer. Providers can also use these resources to guide discussions with their patients; reference to specific documents in this toolkit could help

supplement the conversation and allow the patient to review relevant materials as they process the information and form questions.

This toolkit will need to be updated regularly; the field of genetics is constantly changing, and resources can quickly become outdated. For instance, the NCCN guidelines for colorectal hereditary cancer syndromes had three versions in the year 2019 alone (National Comprehensive Cancer Network, 2019). The network of individuals involved with the PCC work group for genetics/genomics can work together to stay aware of updates to existing resources, or new resources that may be helpful for patients. However, as member of this group are volunteers with many other priorities and this project has limited funding (A. Durst, personal communication, April 13, 2020), other methods of updating the website should be discussed. The creation of this toolkit for a public health genetics student worked well, and perhaps in the future other students could review and update the toolkit as part of their practicum experiences. A thorough review of the toolkit at least once a year would be ideal, though it may not be feasible. Discussion with individuals with Lynch syndrome or other hereditary cancer syndromes could also prove quite useful, as patients know which resources have been most useful to them. Ideally, at least one patient advocate would be included in the process of reviewing and updating these resources.

This toolkit addresses the public health essential service to “inform, educate, and empower people about health issues,” (Centers for Disease Control and Prevention, 2020b, para. 4). Its goal is to help ensure that members of the general population in Pennsylvania (and hopefully other states) have access to reliable resources related to Lynch syndrome and related topics, such as the importance of family history and how to access a genetics healthcare provider. If this toolkit is updated regularly, individuals searching for this type of information will find helpful resources on this website. They will have information to help make their own decisions about screening and

preventative surgeries, and be able to share resources such as the NCCN guidelines with their providers who may not be familiar with Lynch syndrome. Research has shown that individuals with Lynch syndrome are unhappy with the information they receive from their providers related to their diagnosis (Hennink et al., 2013). The creation of patient toolkits such as this one is an important step towards empowering the general public to learn on their own and bring relevant information to their providers.

This toolkit also addresses the public health essential service to “link people to needed personal health services and assure the provision of health care when otherwise unavailable” (Centers for Disease Control and Prevention, 2020b, para. 4). The toolkit includes items for members of the general public to help find a genetic counselor or a genetics clinic, including via telehealth. Because there are too few genetic counselors to meet demand and some individuals may need to travel several hours to see a GC in person (Hoskovec et al., 2018), access to genetics services over the phone or through video chat is crucial on a public health level. These tools can also provide supplemental information, which is important given that many non-genetics providers feel unconfident in their abilities to provide correct, up-to-date information for patients with genetic conditions such as Lynch syndrome (Carroll et al., 2016). While this toolkit does not directly link members of the general public to healthcare providers, it gives them the tools to find an appropriate provider on their own and to conduct their own Lynch syndrome-related research.

5.5 Conclusions

The creation of this toolkit and the plan to publish it on the Live Healthy PA website are important steps towards providing reliable information about Lynch syndrome and related topics

(such as family history and genetic counseling) to the general public. As a common chronic disease in the United States, cancer places a high burden on the healthcare system. State cancer control plans are an important step towards decreasing that burden, as well as morbidity and mortality due to cancer. The inclusion of a genetics/genomics section in these control plans provides a plan to identify more of these cancers before they develop or at early stages. If members of the general public can be better educated about topics such as family history and have access to credible sources related to hereditary cancer, they can work with their providers and larger public health efforts to identify individuals at increased risk for cancer. Because Lynch syndrome is one of the most common hereditary cancer syndromes, individuals with this condition need to be both identified and receive proper medical management. This toolkit works towards that goal by educating the general public about Lynch syndrome and related topics.

Appendix A Internal Review Board Approval

University of Pittsburgh
Institutional Review Board

Human Research Protection Office
3500 Fifth Avenue, Suite 106
Pittsburgh, PA 15213
Tel (412) 383-1480
www.hrpo.pitt.edu

APPROVAL OF SUBMISSION (Exempt)

Date:	December 19, 2019
IRB:	STUDY19090320
PI:	Claire McDonald
Title:	Understanding of Management Guidelines in Patients with Lynch Syndrome
Funding:	None
Grant Title:	None

The Institutional Review Board reviewed and approved the above referenced study. The study may begin as outlined in the University of Pittsburgh approved application and documents.

Approval Documentation

Review type:	Initial Study
Approval Date:	12/19/2019
Exempt Category:	(2)(i) Tests, surveys, interviews, or observation (non-identifiable)

Determinations:	None
Approved Documents:	<ul style="list-style-type: none">• Survey, Category: Data Collection;• AliveAndKickn letter of support.pdf, Category: Other;• Exempt Application Form, Category: IRB Protocol;• Intro Script, Category: Recruitment Materials;• Lynch Syndrome International letter of support.pdf, Category: Other

As the Principal Investigator, you are responsible for the conduct of the research and to ensure accurate documentation, protocol compliance, reporting of possibly study-related adverse events and unanticipated problems involving risk to participants or others. The HRPO Reportable Events policy, Chapter 17, is available at <http://www.hrpo.pitt.edu/>.

Clinical research being conducted in an UPMC facility cannot begin until fiscal approval is received from the UPMC Office of Sponsored Programs and Research Support (OSPARS).

If you have any questions, please contact the University of Pittsburgh IRB Coordinator, [Dana DiVirgilio](#).

Please take a moment to complete our [Satisfaction Survey](#) as we appreciate your feedback.

Appendix B Survey

Appendix B.1 Qualtrics Introductory Text

My name is Claire McDonald, and I am currently a Genetic Counseling graduate student at the University of Pittsburgh. I am conducting this study in partial fulfillment of the requirements for my master's degree in Genetic Counseling.

I would like to invite you to participate in a research study for adults (ages 18 and older) with a diagnosis of Lynch syndrome. Its goal is to assess understanding of Lynch syndrome medical management guidelines. Your participation in this study is voluntary. If you choose to participate, please complete the following 10- to 15-minute survey. There are no anticipated risks in this study. There are no direct benefits to you for participating in this survey.

This is an anonymous survey; no identifying information will be collected at any point. Research records will be kept in an online secure database, and only researchers will have access to the records. You may skip any question that you feel uncomfortable answering and are free to stop taking the survey at any time. This study was approved as an exempt study by the University of Pittsburgh IRB, Study #19090320.

The results will be shared anonymously in aggregate (group) form in the final study. These results will be shared to help improve care for individuals with Lynch syndrome.

If you have any questions, you are encouraged to contact the researcher at cem139@pitt.edu, or her adviser, Andrea Durst, at adurst@pitt.edu.

Thank you very much for your participation!

Appendix B.2 Survey

<p>1. We have shared this survey through several organizations; have you taken this survey before?</p> <p>a. Yes b. No</p>
<p>We will start with some introductory questions.</p>
<p>2. Have you been diagnosed with Lynch syndrome?</p> <p>a. Yes b. No</p>
<p>3. What is your gender?</p> <p>a. Male b. Female c. Other d. Prefer not to answer</p>
<p>4. How old are you?</p> <p>a. Under 18 b. 18-19 c. 20-24 d. 25-29 e. 30-39 f. 40-49 g. 50-59 h. 60-69 i. 70-79 j. 80 or older</p>
<p>The following questions are about your Lynch syndrome diagnosis.</p>
<p>5. How old were you when you were diagnosed with Lynch syndrome?</p> <p>a. Under 18 b. 18-19 c. 20-24 d. 25-29 e. 30-39 f. 40-49 g. 50-59 h. 60-69 i. 70-79 j. 80 or older</p>
<p>6. Were you the first person in your family to be diagnosed with Lynch syndrome?</p> <p>a. Yes b. No</p>
<p>7. Were you diagnosed with Lynch syndrome after a personal cancer diagnosis?</p> <p>a. Yes b. No</p>

The following questions ask about your genetic testing experience.	
8. Who ordered the genetic test that diagnosed you with Lynch syndrome?	<ul style="list-style-type: none"> a. Genetic counselor b. Primary care doctor c. Oncologist (cancer doctor) d. Gynecologist e. I have not had genetic testing for Lynch syndrome f. Other (please specify)
9. Have you ever had a visit with a genetic counselor (a healthcare professional trained to talk with patients about the genetics of cancer, take a family medical history, and order and discuss genetic test results)?	<ul style="list-style-type: none"> a. Yes b. No
10. Did you see the genetic counselor before your genetic test, after your genetic test, or both?	<ul style="list-style-type: none"> a. Before my genetic test only b. After my genetic test only c. Both before and after my genetic test d. N/A
The following questions ask about your experience with cancer screening and surgeries related to Lynch syndrome cancers.	
11. When was your last colonoscopy?	<ul style="list-style-type: none"> a. In the past 12 months b. 1-2 years ago c. 2-3 years ago d. 3-4 years ago e. 4-5 years ago f. More than 5 years ago (Please specify)
12. How often do you usually have colonoscopies?	<ul style="list-style-type: none"> a. More than once a year b. Every year c. Every 2 years d. Every 3 years e. Every 4 years f. Every 5 years g. Other (please specify)

<p>13. What barriers have you experienced, if any, in having a colonoscopy? Select all that apply.</p> <ul style="list-style-type: none"> a. Colonoscopies are too expensive b. I feel I am too young to start colonoscopies c. My doctor says I am too young to start colonoscopies d. I have decided not to have colonoscopies for the foreseeable future e. I cannot take a day off from work for the procedure f. I am too busy to have a colonoscopy g. I was not told that I needed a colonoscopy h. I do not know where to go to get a colonoscopy i. There is no doctor in my area who performs colonoscopies j. Other (please specify) k. I have not experienced any barriers to having a colonoscopy
<p>14. Have you had part or all of your colon removed?</p> <ul style="list-style-type: none"> a. Yes b. No
<p>15. What kind of colorectal surgery did you have?</p> <ul style="list-style-type: none"> a. Removal of part of the colon b. Removal of rectum only c. Removal of the entire colon d. Removal of entire colon and rectum e. I'm not sure what kind of surgery I had f. N/A
<p>16. Please indicate the reason that you had a colorectal surgery</p> <ul style="list-style-type: none"> a. I was diagnosed with cancer b. I had surgery to prevent cancer c. I had one or more polyps that required surgery d. I have inflammatory bowel disease (Crohn's or ulcerative colitis) e. I had diverticulitis f. Other (please specify) g. N/A
<p>17. Have you had or do you plan to have any of the following surgeries? Check all that apply.</p> <ul style="list-style-type: none"> a. Uterus removed b. Only one ovary removed c. Both ovaries removed d. Planning to have uterus removed in the future e. Planning to have one or more ovaries removed in the future f. I have not had these surgeries and I do not plan to have them g. N/A

<p>18. If you have had your uterus removed, please indicate the reason that you had your uterus removed.</p> <ul style="list-style-type: none"> a. I was diagnosed with uterine cancer b. I was diagnosed with ovarian cancer c. I was diagnosed with another cancer d. I had it removed to prevent cancer e. I had medical problems unrelated to cancer (fibroids, endometriosis, abnormal bleeding, etc.) f. N/A
<p>19. Did you have your uterus removed before or after you were diagnosed with Lynch syndrome?</p> <ul style="list-style-type: none"> a. Before being diagnosed with Lynch syndrome b. After being diagnosed with Lynch syndrome c. N/A
<p>20. If you had your ovary or ovaries removed, please indicate the reason that you had this surgery.</p> <ul style="list-style-type: none"> a. I was diagnosed with uterine cancer b. I was diagnosed with ovarian cancer c. I was diagnosed with another cancer d. I had them removed to prevent cancer e. I had medical problems unrelated to cancer (ex: cysts) f. N/A
<p>21. Did you have your ovaries removed before or after you were diagnosed with Lynch syndrome?</p> <ul style="list-style-type: none"> a. Before being diagnosed with Lynch syndrome b. After being diagnosed with Lynch syndrome c. N/A
<p>22. Please select any cancers you have been diagnosed with.</p> <ul style="list-style-type: none"> a. Colorectal or colon b. Endometrial or uterine c. Ovarian d. Gastric or stomach e. Pancreatic f. Small bowel g. Brain h. Bladder i. Prostate j. Breast k. Other (please specify) l. I have never been diagnosed with cancer

The following questions assess your understanding of management guidelines and how you have learned about these guidelines.

23. What is your understanding of how often it is recommended that you have a colonoscopy?
- a. Every year
 - b. Every 1-2 years
 - c. Every 2-3 years
 - d. Every 3-4 years
 - e. Every 4-5 years
 - f. Every 5 years

24. Which providers have discussed the Lynch syndrome management guidelines with you? Check all that apply.
- a. Genetic counselor
 - b. Cancer genetics doctor
 - c. Primary care doctor
 - d. Gynecologist
 - e. Gastroenterologist (doctor specializing in the digestive system, including the colon and stomach)
 - f. Oncologist (doctor specializing in cancer)
 - g. Surgeon
 - h. None
 - i. Other (please specify)

25. Besides your providers, with whom have you discussed cancer screening? Check all that apply.
- a. Family members with Lynch syndrome
 - b. Other family members
 - c. Friends
 - d. Other individuals with Lynch syndrome
 - e. Other (please specify)

26. Have you been given conflicting information about how often you should have a colonoscopy?
- a. Yes
 - b. No

27. Are you a member of any online or in-person support groups related to Lynch syndrome?
- a. Yes
 - b. No

28. Which support groups are you involved in? Please select all that apply.
- a. Facebook
 - b. Other social media platform (please specify)
 - c. Local/in-person
 - d. Advocacy Organization (ex: Lynch Syndrome International)
 - e. Other (please specify)
 - f. N/A

<p>29. Based on your personal and family members' experiences, what do you think are some general barriers to having regular colonoscopies? Please select all that apply.</p> <ul style="list-style-type: none"> a. Cost b. Fear of cancer diagnosis c. Unable to travel to colonoscopy center d. Unsure whether colonoscopies will reduce cancer risk e. Dislike of colonoscopies (prep and procedure) f. Unable to take a day off from work g. Other (please specify)
<p>The following questions will cover basic demographic information.</p>
<p>30. What ethnicity or ethnicities do you identify with?</p> <ul style="list-style-type: none"> a. White b. Black or African-American c. Hispanic or Latino d. American Indian or Alaska Native e. Asian f. Native Hawaiian or Pacific Islander g. Other h. Prefer not to answer
<p>31. What is your approximate annual household income?</p> <ul style="list-style-type: none"> a. Less than \$20,000 b. \$20,000 - \$40,000 c. \$40,000 - \$60,000 d. \$60,000 - \$80,000 e. \$80,000 - \$100,000 f. More than \$100,000 g. Prefer not to answer
<p>32. What is your highest level of education?</p> <ul style="list-style-type: none"> a. Some high school b. High school graduate c. Associate's degree d. Bachelor's degree e. Master's degree f. Beyond master's degree (Ph.D., DrPH, MD, etc.) g. Prefer not to answer
<p>33. What is your employment status?</p> <ul style="list-style-type: none"> a. Employed full-time b. Employed part-time c. Currently not employed d. Student e. Not working due to disability f. Other (please specify)

<p>34. What kind of health insurance do you have (if any)? Please check all that apply.</p> <ul style="list-style-type: none"> a. Medicare b. Medicaid c. Private insurance (ex: through an employer) d. Marketplace (Affordable Care Act/Obamacare) e. I do not currently have health insurance
<p>35. How would you describe the area of the United States in which you live?</p> <ul style="list-style-type: none"> a. Northeast b. Midwest c. Southeast d. Northwest e. Southwest f. Non-contiguous US (Alaska, Hawaii) g. I do not live in the United States h. Other (please specify)
<p>36. Where did you learn about this survey? Please check all that apply.</p> <ul style="list-style-type: none"> a. Lynch Syndrome International b. AliveAndKickn c. Family member d. Friend e. Other (please specify)
<p>37. Please include any additional comments and/or feedback about the survey below.</p>
<p>Thank you very much for your participation!</p>

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