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The Decision-Making Process for Individuals at Risk for Hereditary Diffuse Gastric Cancer

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THE DECISION-MAKING PROCESS FOR INDIVIDUALS AT RISK FOR HEREDITARY DIFFUSE GASTRIC CANCER

by

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Abstract

Hereditary diffuse gastric cancer (HDGC) is caused by mutations in the CDH1 gene. Individuals who carry mutations in the CDH1 gene have as high as an 80% lifetime risk for gastric cancer. To reduce the high lifetime risk of gastric cancer, CDH1 mutation carriers are recommended to undergo a prophylactic total gastrectomy (TG). Individuals within this at-risk population face a difficult task of deciding whether to have genetic testing for the CDH1 mutation and to have a prophylactic TG. Currently, there is little research that examines the factors influencing decision-making for this population and their specific informational and support needs. We conducted semi-structured telephone interviews on 26 individuals at different points of this decision-making process. Participants were recruited from the No Stomach for Cancer online support group and other social media websites. To be included in the study, the participants had to be 18 years or older, have a family history of hereditary diffuse gastric cancer, and have not had clinical symptoms of HDGC. A family history of HDGC was defined as having one or more first or second degree relatives who 1) had diffuse gastric cancer and/or 2) tested positive for a CDH1 mutation. Eleven participants had already undergone a TG, nine were identified as CDH1 mutation carriers but were currently evaluating their prophylactic options, and six had a family history of CDH1 but had not yet pursued genetic testing. The interviews were analyzed using grounded theory to determine themes. These interviews illuminated that the four main factors influencing decision-making were the avoidance of cancer, family, the inadequacies of endoscopic

surveillance, and viewing a post-TG family member's experience. Additionally, many participants were frustrated with the lack of awareness for the condition and were concerned they had to become their own advocate for their healthcare. The results of this study can provide insight to genetic counselors and other medical professionals of how to help facilitate this decision-making process and how to provide appropriate psychosocial support for this population.

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Chapter 1: Background

Gastric cancer is the fifth most common type of cancer worldwide. Unfortunately, since most gastric cancer cases are detected at late stages, it is the third most common cause for cancer related deaths (van der Post et al., 2015). There are two main forms of gastric cancer. The first, intestinal-type, typically originates from the glands of the stomach and is initiated primarily by environmental factors (Hebbard et al., 2009). The second, diffuse gastric cancer, is characterized by a distinctive tumor pathology where the tumor cells are poorly-differentiated and can easily invade neighboring tissue (Onitilo, Aryal, & Engel, 2013). Diffuse gastric cancer is more typically caused by hereditary factors. In general, hereditary forms encompass approximately 1-3% of all gastric cancer cases (Hebbard et al., 2009).

Hereditary diffuse gastric cancer (HDGC) is caused by mutations in the CDH1 gene. This gene, located on chromosome 16, encodes for the E-cadherin protein that is responsible for intracellular adhesion properties (Onitilo et al., 2013). Mutations in the CDH1 gene confer a lifetime risk of gastric cancer of 70% for men and 56% for women (Hansford et al., 2015). However, some studies report that the lifetime risk for gastric cancer may be as high as 80% (Fitzgerald et al., 2010; Pharoah, Guilford, & Caldas, 2001; Syngal et al., 2015). For female mutation carriers, there is also a 42% risk of developing lobular breast cancer (Hansford et al., 2015). CDH1 mutations also increase a carrier's lifetime risk of colon cancer.

The hereditary nature of HDGC provides a unique opportunity for presymptomatic identification of potentially affected individuals. If a genetic mutation has not yet been identified in a family, the criteria for genetic testing for a CDH1 mutation is based purely on a personal and family history of cancer. The National Comprehensive Cancer Network (NCCN) criteria for genetic testing are as follows: 1) Two or more gastric cancer cases, with one being classified as diffuse type below age 50 2) three or more diffuse gastric cancer cases in first or second-degree relatives regardless of age 3) one case of diffuse gastric cancer in an individual below the age of 40 without a family history 4) a personal or family history of diffuse gastric cancer or lobular breast cancer, with one diagnosed before age 50 (NCCN, 2016). Once a mutation has been identified in a family, other relatives have the opportunity to also pursue genetic testing. This process allows potentially at risk individuals to discover their genetic status before displaying any symptoms of cancer and provides the time to pursue prophylactic options to reduce cancer risks.

Management

In order to reduce the high lifetime risk of gastric cancer, individuals harboring a CDH1 mutation are recommended to undergo a risk reduction total gastrectomy (TG) between the ages of 18 and 40 years (NCCN, 2016). The most common total gastrectomy procedure is referred to as Roux-en-Y reconstruction. This procedure involves removing the stomach tissue and reconnecting the end of the esophagus to the jejunum of the small intestine (Pandalai, Lauwers, Chung, Patel, & Yoon, 2011). A review by Seevaratnam et al. (2012) concluded that, of the 72 patients who tested positive for a CDH1 mutation and underwent a prophylactic total gastrectomy, 63, or 87.0%, of the individuals had a final

positive histopathology report. These results indicate that a majority of currently asymptomatic CDH1 positive individuals may actually already have cancerous foci present. Although a total gastrectomy is the current recommended management strategy to reduce gastric cancer risk, patients may feel overwhelmed by the thought of the surgery. Since this surgery is a radical procedure that results in lifelong diet and lifestyle modifications, many individuals at risk for diffuse gastric cancer may opt for surveillance techniques, either temporarily or permanently, in lieu of a total gastrectomy.

Surveillance includes upper endoscopies, traditionally done using a white-light procedure, with multiple random biopsies every six to-12 months. Typically, diffuse cancer, also referred to as signet-ring cell carcinoma, initiates below the surface epithelium and basic white-light endoscopy is unable to detect its presence (Hebbard et al., 2009). Unfortunately, these endoscopies may falsely reassure patients of the absence of gastric cancer (Lim et al., 2014). A study by Hebbard et al. (2009) examined endoscopy biopsies before surgery and the pathology of the gastric tissue post-gastrectomy. Out of the 23 patients they studied, 22, or 96%, had microscopic foci of diffuse/signet-ring cell carcinoma in the post-gastrectomy pathology. However, only 2 of these patients had detected these foci during preoperation esophagogastroduodenoscopy. In another study, only 2 out of 12 patients had signet ring cell adenocarcinoma detected preoperatively (Chen et al., 2011). In both studies, a majority of patients possessed diffuse cancer cells that were not detected with traditional endoscopy procedures. Therefore, due to the limitations of endoscopy surveillance, prophylactic total gastrectomy remains the primary recommendation for management. The reasons

individuals may choose a surveillance approach temporarily include child-bearing and family responsibilities, financial concerns, and fear of the TG (Lim et al., 2014).

Symptoms following Gastrectomy

Patients considering a total gastrectomy need to realize there are many physical and nutritional consequences resulting from the procedure. Weight loss is seen in nearly all patients immediately following gastrectomy with individuals typically losing more than 10% of their original body weight (Liedman, 1999; Worster et al., 2014). Dumping syndrome is another common side effect experienced after gastrectomy. The altered anatomy causes ingested food to pass too quickly into the small intestine. Early dumping syndrome, typically occurring 30 minutes after a meal, is caused by excessive hormones being secreted in response to this event. The resulting symptoms include palpitations, diarrhea, abdominal cramps, and nausea. Late dumping syndrome, typically occurring two to three hours after a meal, resembles hypoglycemia with symptoms including faintness, hunger, dizziness, and cold sweats (Mine et al., 2010; van der Post et al., 2015). Other associated comorbidities include lactose intolerance, malabsorption, steatorrhea, bloating, diarrhea, and iron and vitamin B12 deficiencies. To reduce some of these symptoms and nutritional needs, patients are advised to eat smaller, more frequent meals throughout the day. Additionally, supplementation of calcium, vitamin D, iron, and vitamin B12 is also recommended (Pandalai et al., 2011). The majority of patients' symptoms typically resolve within the 12 months following surgery; however, some physical and mental health issues may remain (Worster et al., 2014). Patients may benefit from meeting with a nutritionist pre- and post-surgery to discuss these nutritional topics.

Additionally, mental health professionals and other support systems may be useful to help cope with some of the lasting emotional consequences.

A study by Hallowell, Lawton et al. (2016) examined many of the psychosocial issues that are experienced when undergoing a prophylactic total gastrectomy. Specifically regarding the physical impacts, their participants reported significant appetite and dietary changes. Many reported some of the GI side effects, like dumping syndrome, and fatigue interfered with work and social lives. The psychological impacts comprised feelings of negative body image following surgery and the fact that participant's self-identity was threatened because they were unable to do some of the things that they enjoyed prior to surgery. Despite these life-altering changes, all of the participants reported a relief of anxiety that they had significantly decreased their lifetime risk of stomach cancer which in the end offset the negative side-effects. Therefore, because of the lifestyle changes, the authors stressed the importance of counseling patients prior to surgery about these changes, and highlighted the role that genetic counselors and other medical professionals have in assisting the patients through the recovery process.

To more quantitatively assess the resulting quality of life following a prophylactic total gastrectomy, Muir, Aronson, Esplen, Pollett, and Swallow (2016) utilized a longitudinal study to assess 18 individuals on topics such as their health-related quality of life, body image, psychological distress, regret, and decisional conflict. Their results showed that their patients displayed little to no regret, low decisional conflict, and a fairly stable view of body image. Their patients exhibited some mild changes in mental health scores following surgery, but did not exhibit severe symptoms of depression and anxiety. Their health-related quality of life decreased significantly following surgery, but returned

to baseline at 12 months. These results agree with the findings by Worster et al. (2014) that the majority of symptoms resolve at 12 months. Interestingly, the researchers noted that the health-related quality of life dipped again at 24 months; however, the severity of symptoms at this time point remained mild comparatively (Muir, Aronson, Esplen, Pollett, & Swallow, 2016).

Psychosocial concerns with cancer genetics decision making

A study by Underhill and Crotser (2014) interviewed women at risk for hereditary breast and ovarian cancer and assessed the decision-making process regarding prophylactic options for this population. The first theme that arose was planning for risk reduction and detection. This theme encompassed women's thoughts about weighing personal and family values, such as childbearing, against the risk of cancer; the differences between definitively knowing cancer risks, through means such as genetic testing, compared to actually acting upon that information; and finally, allowing enough time to fully process the information before making a decision. The next theme, interpreting complex information and making decisions, highlighted the complexity of decision making. They emphasized that one large decision may actually involve many smaller decisions and some women may need to rely more heavily than others on support systems to tackle the multitude of decisions. The final theme, experiencing consequences of risk related health decisions, comprised anticipating the outcomes of their decisions and the potential side effects that may result. To summarize all their findings, the authors concluded that most women in the decision-making process needed time to actively find a balance between their personal cancer risks and their personal values (Underhill & Crotser, 2013). Although this study was completed using patients at risk for hereditary

breast and ovarian cancer, the same principles are likely to translate to those at risk for hereditary diffuse gastric cancer. Utilizing this previous research, the proposed study will compare the responses and discover the similarities and possibly uncover any areas that may be unique to the HDGC population that require additional attention.

Peters, Laham, Pachter, and Winship (2014) summarized some of the current research regarding affective forecasting, or the process of predicting how one will feel in response to a future event. Two major themes arose from the review: impact bias and immune neglect. Impact bias refers to the trend that individuals typically overestimate the impact of a future event on their quality of life—especially negative events. Immune neglect refers to the phenomenon that individuals struggle with anticipating their level of adaptability to an event; often, these individuals are more resilient than they are consciously aware. In order to reduce the negative perceptions and to encourage views of resiliency, genetic professionals are recommended to expose patients to examples of a future event. These examples may include introducing the patient to a support group or to others who went through the event previously. The exposure provides concrete examples of how others responded to an event and hopefully encourages the patient to feel more informed and in control of the situation (Peters, Laham, Pachter, & Winship, 2014). The current study will illuminate some of the personal experiences of individuals within the HDGC population. Hopefully, future patients will reflect on the responses and encourage them to anticipate more positive outcomes and reinforce their abilities to cope with future events.

Many patients, especially those with a family history of stomach cancer or total gastrectomies, may face less decisional conflict regarding having the TG procedure.

Many of these individuals feel that the only remaining decision is when to actually have the prophylactic surgery completed (Lynch et al., 2008). These individuals may have experience firsthand with either the devastation of having gastric cancer, and consequently wanting to avoid that themselves, or rather the relative normalcy of life without having a stomach. On the contrary, those with little to no experience with the condition may be fearful of life without a stomach and may not be able to comprehend what their life will potentially be like. Several online support groups like 'No Stomach for Cancer' and the 'DeGregorio Family Foundation for Stomach and Esophageal Cancer Research' provide information and support for patients affected by HDGC. The 'No Stomach for Cancer' website includes informational documents detailing the process of gastrectomy and many of the post-surgical concerns for patients. While these are excellent resources to reference, there are potentially many affected individuals who are not in contact or even aware of these organizations. Therefore, these individuals may feel isolated and uninformed regarding the process ahead. This study will attempt to identify these shortcomings and inform future patients and medical professionals of ways to better facilitate the decision-making process.

An article published by Hallowell, Badger et al. (2016) investigated the major factors that influence decision making for a prophylactic total gastrectomy. They concluded that the major factors were the magnitude of associated cancer risks, the objective confirmation of cancer risks through a positive CDH1 mutation result or positive biopsy result on endoscopy, the burden of seeing affected family members, uncertainty of whether or not they would eventually develop cancer, perceptions of life following gastrectomy, and their view regarding endoscopy surveillance. Outside of the

article by Hallowell et al. there are few studies that examine the specific factors that influence decision making for a prophylactic total gastrectomy. Our current study will elaborate on their findings for factors influencing decision making. Additionally, our study is unique because we interviewed individuals who have yet to pursue CDH1 genetic testing; therefore, we obtained a new perspective of this population's thoughts regarding both pursuing testing and surgery. Every individual approaches decisions differently and will consequently require different levels of informational and social support during their decision-making process. By examining individuals at different time points of this process we will highlight support and informational needs that can be addressed by medical professionals at every stage.

Taking into consideration all the psychosocial concerns of this population, it is evident that many factors are involved in the decision-making process for genetic testing and prophylactic surgical options. This study aims to learn about these individuals' experiences in their own voices and hopes to identify factors that were viewed as helpful or deterred their decision-making process.

Chapter 2: Manuscript

The Decision-Making Process for Individuals at Risk for Hereditary Diffuse Gastric Cancer

2.1 Abstract

Hereditary diffuse gastric cancer (HDGC) is caused by mutations in the CDH1 gene. Individuals who carry mutations in the CDH1 gene have as high as an 80% lifetime risk for gastric cancer. To reduce the high lifetime risk of gastric cancer, CDH1 mutation carriers are recommended to undergo a prophylactic total gastrectomy (TG). Individuals within this at-risk population face a difficult task of deciding whether to have genetic testing for the CDH1 mutation and to have a prophylactic TG. Currently, there is little research that examines the factors influencing decision-making for this population and their specific informational and support needs. We conducted semi-structured telephone interviews on 26 individuals at different points of this decision-making process. Participants were recruited from the No Stomach for Cancer online support group and other social media websites. To be included in the study, the participants had to be 18 years or older, have a family history of hereditary diffuse gastric cancer, and have not had clinical symptoms of HDGC. A family history of HDGC was defined as having one or more first or second degree relatives who 1) had diffuse gastric cancer and/or 2) tested positive for a CDH1 mutation. Eleven participants had already undergone a TG, nine were identified as CDH1 mutation carriers but were currently evaluating their prophylactic options, and six had a family history of CDH1 but had not yet pursued genetic testing. The interviews were analyzed using grounded theory to determine themes. These interviews illuminated that the four main factors influencing decision-making were the avoidance of cancer, family, the inadequacies of endoscopic surveillance, and viewing a post-TG family member's experience. Additionally, many participants were frustrated with the lack of awareness for the condition and were

concerned they had to become their own advocate for their healthcare. The results of this study can provide insight to genetic counselors and other medical professionals of how to help facilitate this decision-making process and how to provide appropriate psychosocial support for this population.

2.2 Introduction

Hereditary diffuse gastric cancer (HDGC) is caused by mutations in the CDH1 gene which encodes for the E-cadherin protein that is responsible for intracellular adhesion properties (Onitilo et al., 2013). Mutations in the CDH1 gene confer a lifetime risk of gastric cancer of 70% for men and 56% for women (Hansford et al., 2015). However, some studies report that the lifetime risk for gastric cancer may be as high as 80% (Fitzgerald et al., 2010; Pharoah, Guilford, & Caldas, 2001; Syngal et al., 2015). For female mutation carriers, there is also a 42% risk of developing lobular breast cancer (Hansford et al., 2015). CDH1 mutations also increase a carrier's lifetime risk of colon cancer. The hereditary nature of HDGC provides a unique opportunity for presymptomatic identification of potentially affected individuals. Once a mutation has been identified in a family, other relatives have the opportunity to also pursue genetic testing. This process allows potentially at risk individuals to discover their genetic status before displaying any symptoms of cancer and provides the time to pursue prophylactic options to reduce cancer risks.

In order to reduce the high lifetime risk of gastric cancer, individuals harboring a CDH1 mutation are recommended to undergo a risk reduction total gastrectomy (TG) between the ages of 18 and 40 years (NCCN, 2016). Patients considering a total gastrectomy need to weigh the physical and nutritional consequences resulting from the procedure. Weight loss is seen in nearly all patients immediately following gastrectomy

with individuals typically losing more than 10% of their original body weight (Liedman, 1999; Worster et al., 2014). Dumping syndrome is another common side effect experienced after gastrectomy resulting in palpitations, diarrhea, abdominal cramps, nausea, faintness, hunger, dizziness, and cold sweats (Mine et al., 2010; van der Post et al., 2015). Other associated comorbidities include lactose intolerance, malabsorption, steatorrhea, bloating, diarrhea, and iron and vitamin B12 deficiencies. To reduce some of these symptoms and nutritional needs, patients are advised to eat smaller, more frequent meals throughout the day. Additionally, supplementation of calcium, vitamin D, iron, and vitamin B12 is also recommended (Pandalai et al., 2011).

Since this surgery results in lifelong diet and lifestyle modifications, many individuals at risk for diffuse gastric cancer may opt for surveillance techniques, either temporarily or permanently, in lieu of a total gastrectomy. Surveillance for patients with CDH1 mutations includes upper endoscopies with random biopsies every 6-12 months. Typically, diffuse cancer, also referred to as signet-ring cell carcinoma, initiates below the surface epithelium of the gastric tissue and basic endoscopy procedures are unable to detect its presence (Hebbard et al., 2009). Unfortunately, these endoscopies may falsely reassure patients of the absence of gastric cancer (Lim et al., 2014). A study by Hebbard et al. (2009) examined endoscopy biopsies before surgery and the pathology of the gastric tissue post-gastrectomy. Out of the 23 patients they studied, 22, or 96%, had microscopic foci of diffuse/signet-ring cell carcinoma in the post-gastrectomy pathology. However, only 2 of these patients had detected these foci during preoperative esophagogastroduodenoscopy. Therefore, due to the limitations of endoscopy surveillance, a prophylactic total gastrectomy remains the primary recommendation for

management. The reasons individuals may choose a surveillance approach temporarily include child-bearing and family responsibilities, financial concerns, and fear of the total gastrectomy (Lim et al., 2014).

Individuals at risk for HDGC face a daunting task of deciding whether or not to have genetic testing for the CDH1 mutation. Although genetic testing is informative for clinical management, it is possible that many patients may struggle emotionally with the definitive nature of a positive test result. An even more daunting decision may be to decide whether or not to undergo a prophylactic total gastrectomy to reduce the high lifetime risk of gastric cancer. Many patients, especially those with a family history of stomach cancer or total gastrectomies, may face less decisional conflict regarding having the TG procedure as they may have firsthand experience with either the devastation of having gastric cancer, and consequently wanting to avoid that themselves, or rather the relative normalcy of life without having a stomach (Lynch et al., 2008).

An article published by Hallowell, Badger et al. (2016) investigated the major factors that influence decision making for a prophylactic total gastrectomy. Their participants included both individuals who have gone through a gastrectomy and individuals with confirmed CDH1 mutations but had yet to undergo the surgery. From these interviews, they concluded that the major factors were the magnitude of associated cancer risks, the objective confirmation of cancer risks through a positive CDH1 mutation result or positive biopsy result on endoscopy, the burden of seeing affected family members, uncertainty of whether or not they would eventually develop cancer, perceptions of life following gastrectomy, and their view regarding endoscopy surveillance (Hallowell, Badger et al., 2016). Outside of that article, there are few studies

that examine the specific factors that influence decision-making for a prophylactic total gastrectomy at different stages of the process.

The overall purpose of this study is to gain insight into how individuals at risk for HDGC make decisions regarding pursuing genetic testing and prophylactic total gastrectomies. This study should help to illuminate factors that influence this decision and potential resources or support systems that are helpful to patients who are faced with this decision-making process. We anticipate that individuals with more family members impacted by HDGC will be more likely to pursue genetic testing and prophylactic surgical options. Additionally, this information will help inform genetic counselors and other medical professionals how they can better facilitate these decisions with their patients. The expectation is that these findings will be beneficial to future individuals at risk for HDGC, and that these individuals will feel more prepared, will be empowered, and will have a better concept of the life that results after their decision-making process.

2.3 Materials and Methods

Participants were recruited from the No Stomach for Cancer online support group and other social media websites, such as Facebook. To be included in the study, the participants had to be 18 years or older, have a family history of hereditary diffuse gastric cancer, and have not had clinical symptoms of HDGC. A family history of HDGC was defined as having one or more first or second degree relative who 1) had diffuse gastric cancer and/or 2) tested positive for a CDH1 mutation. Interested participants were invited to contact the research coordinator to schedule a telephone interview.

The semi-structured interviews were conducted over the phone by a single researcher. On average, the interviews lasted 68.5 minutes (range 39-99 minutes). The

interview topics involved questions regarding their family history, their motivations/hesitancies towards testing and surgery, where the participant obtained information, and areas where the medical system can better support the participant's needs. The telephone interviews were recorded and transcribed verbatim. Using grounded theory, the transcriptions were analyzed and compared to one another to determine common themes. A theme was considered once three or more participants shared a similar response. These qualitative responses presented the data in the language of the participants, without aiming to present the data in more theoretical ways. The first and second author separately coded the data in order to reduce bias. Themes were discussed until the authors reached an agreement. This study received approval from the University of South Carolina Institutional Review Board (IRB).

2.4 Results

2.4.1 Demographics. Twenty-seven individuals were interviewed. One interview was excluded due to the individual being unable to answer the questions independently. Of the 26 interviews included for analysis, six (23.1%) participants were categorized as pre-testing/pre-surgery since they had not pursued genetic testing but had a confirmed family member with a CDH1 mutation, nine (34.6%) were categorized as post-testing/pre-surgery since they had confirmed CDH1 mutations and were in the process of deciding whether to pursue a gastrectomy, and 11 (42.3%) participants were categorized as post-testing/post-surgery since they had previously undergone a prophylactic total gastrectomy. The 27 individuals represented 17 distinct families. Several participants were enrolled into the study using snowball sampling by being referred by a family member.

The participants' demographic information is detailed in Table 2.1. There were 23 female participants (88.5%) and 3 male participants (11.5%) who had an average age of 36.9 years (range 18-71y). The pre-testing/pre-surgery participants were all single and did not have children. Of the post-testing/pre-surgery group, 77.8% had children and of the post-testing/post-surgery group, 81.8% had children.

As seen in Table 2.2, all of the participants had at least one relative diagnosed with stomach cancer in either a first, second, or third-degree relative, but only 21 witnessed their family member have cancer. Sixteen of the 26 participants (61.5%) had a family member who had a prophylactic total gastrectomy.

Figure 2.1 examined how the number of post-TG family members influenced decisions about TG. The results show that the pre-TG participants (n=16) who reported that they would not pursue a TG had fewer family members post-TG. Four out of the five (80%) participants refusing a TG had zero post-TG family members. In contrast, all the participants with two or more post-TG family members reported they would eventually have the surgery. While we noted anecdotally that participants with more post-TG family members were more likely to pursue a TG, our results were not statistically significant ($p= 0.146$).

Additionally, there were no statistically significant differences between the three groupings based on age or the number of relatives affected by HDGC. The lack of statistical significance was likely due to the small sample size.

2.4.2 Major factors influencing decision-making.

2.4.2.1 Avoidance of cancer. All of the participants recognized that a CDH1 mutation increased their lifetime risk of developing stomach cancer and therefore used the risk as a

motivator to consider pursuing genetic testing and surgery. However, for some, watching a family member suffer from cancer heightened their personal awareness of that risk even further. Twenty-one participants reported that they had watched a close family member diagnosed with stomach cancer and the majority commented that exposure was a factor that encouraged them to pursue both genetic testing and surgery.

> I know she was in a lot of pain, and it was pretty brutal…when you see it that up close and upfront and how much they are suffering and how much pain they are in…you really see how severe the cancer can be on a person, how brutal it can be for someone, how painful it is. So it changes your mindset. (participant #1)

Looking from the opposite perspective, while all the participants had at least one relative diagnosed with stomach cancer in the family, five participants never saw a relative actually struggle with the disease. As a result, many could not justify the need for such a significant surgery since the cancer risk was intangible.

> …but just to go do [a TG] preventively when I don't have any first-hand experiences… do these people have first-hand experience seeing close family members die of stomach cancer? I have not… Now, like I said, if I had all of these family members around me dying at a young age: oh, that's enough evidence for me, yes, thank you very much I will go get that done. Where I am right now I don't feel that I am informed enough to make a decision like that. (participant #7)

Figure 2.2 examined how the number of family members affected by HDGC influenced decisions about TG. The results show that the pre-TG participants (n=16) who reported that they would not pursue a TG had fewer family members affected by HDGC. All three

participants who had three or more affected family members reported that they will eventually pursue a TG.

Twenty participants recognized the value of pre-symptomatic genetic testing and surgical options due to the intimidating cancer risks. They reported feeling motivated to pursue these options in order to regain control of their life and take steps to reduce their cancer risk.

> Because when you hear things like 'genetic mutation' you feel like all of the control has been taken away from you and it was really encouraging to realize that we have choices, we have options, and that we have…there is legitimately a full and thriving life on the other side. (participant #15)

2.4.2.2 Family. Family was another sentiment that encouraged the participants to want to pursue genetic testing and surgery. Ten participants reported they used family as a motivator to pursue testing and 14 reported family as a motivator to have the TG. In general, they felt driven to find out their genetic status and to reduce their cancer risks so they could be around for their children and spouses. One participant whose mother passed away from stomach cancer stated her motivations to be around for her daughter:

> My main focus was wanting to be here for [my daughter]. So anyway that I can possibly be here, because, like, my mom missed graduations, she missed weddings, she missed having babies, and that stuff all stinks. And it stinks to not have your mom there for those things and so she was my main drive, she was my main motivation. (participant #12)

Familial motivations for testing were more slanted toward information gathering. Eight participants recognized the importance of learning their genetic status in order to be able to provide that information to their family.

> I knew that this information would certainly put me more in control of my life and future decisions. And, you know, knowing for my child, for my daughter. That there would or wouldn't be a possibility that she would have this gene too. (participant #8)

On top of just providing the genetic information, some felt motivated to go through the surgery to be a role model for relatives that may test positive in the future. When asked what her motivations were for pursuing a TG, one woman responded:

> Probably my family, my kids. I wanted to, you know, knowing that they are going to have to be tested someday. I want to show them an example that you can face this and do it in an empowering way and a positive way and that [it] will be okay. (participant #11)

In general, the participants recognized that their personal situation had impacts on their family members whether it is purely for information's sake or to be around to be a part of their lives.

2.4.2.3 Endoscopy surveillance inadequacies. While endoscopy is the recommended screening option for patients who have not yet pursued a total gastrectomy, 10 of the 26 (38.5%) participants recognized that it is not a great tool for surveillance. For many, this fact was another motivating factor to undergo the TG:

> So when I went in and they said okay, these are your three options: A. you can do nothing, B. you can do endoscopies every six months and we can cross our fingers

> and hope that we find something but generally by the time that we find something it's too late, or C. you can have a complete gastrectomy. I felt like for me, there was no question that of course I was going to have a complete gastrectomy. (participant #12)

Yet, despite the inadequacies of endoscopy as a screening tool, six participants still valued its use to help make decisions regarding surgery. Three individuals had cancer cells identified on an endoscopy and commented that they then had no choice but to proceed with the surgery. However, they were glad to have validation that they were making the right decision.

> I was navigating through both options equally, heavily, and I just didn't know what to do. So in a way I was glad they found the cells in there because it made the choice easier for me. If they hadn't found anything, I would still be very confused. (participant #4)

Three individuals who were resistant to pursuing a TG at the time of the interview remarked that a positive endoscopy result would ultimately make the decision for them to move forward:

> My son and daughter and I have all made the decision that if any of us have a signet cell [on an endoscopy scan], we are having a complete gastrectomy. (participant #9)

2.4.2.4 Viewing post-TG relatives' experiences. The final major factor influencing the participants' decisions was whether they had seen a family member go through a TG. Sixteen participants had seen a family member have a prophylactic total gastrectomy (five pre-testing/pre-surgery; three post-testing/pre-surgery; and eight post-testing/post-

surgery). All 16 (100%) of these participants reported that they used their family member as a resource while making these decisions. For many, it was encouraging to view how post-TG family members have a fairly normal lifestyle following surgery.

> When I look at the seven people that have had their stomachs removed, it's really not negatively affecting them right now. Yeah, they have no stomach, but…other than them eating more frequently and smaller meals, that's really the only difference in their life. You know, I don't think that going through the surgery is really going to, you know, complicate your life too much. (participant #23)

From the opposite perspective, eleven participants reported seeing a family member experience a complication during their recovery period. Of those 11, five expressed that it made them uneasy when considering whether they wanted the TG or not.

> My dad and my aunts had good times and had bad times obviously in the recovery, I think everyone does but… it's just hard seeing it secondhand, like seeing someone else go through it and then knowing like that might have to be me someday kind of thing. I know it is inevitable if it is something I have to deal with but… I don't know, it's a little bit nerve-racking. (participant #22)

However, 14 participants had seen multiple family members have the surgery and tried to incorporate both the good and bad experiences into making their decisions and into planning how they would make their own recovery better.

> My cousin was just a mess, and then her sister had hers and she was not so good either a couple times, and then their other sister had hers, and she did great…so they were the only three I had to go by, those three, and they were all so different, all three of them were so different. So yeah, I was freaked out about that a little

bit and I just kept saying: well this is what I am going to do, I am learning from them, I am learning what to do and what not to do. (participant #16)

Despite having to weigh the positive and negative aspects of their family member's situations, many still realized it would be a much more difficult decision if they didn't have that background knowledge of their family member's experience.

> I think it would be a lot different if I was the first one to test positive and people were telling me to go get my stomach removed, I think it would be a lot different if I hadn't known people that had gone through it and, you know, are living their lives normally now. (participant #3)

2.4.3 Other elements of decisions. In addition to the major factors influencing the uptake of genetic testing and prophylactic TG, other more minor elements emerged in the interviews.

2.4.3.1 Timing of decisions. Table 2.3 details the ages and the time-spans between the participants' decisions. The post-testing/pre-surgery participants had a median age of 47 years at the time of their testing compared to the post-testing/post-surgery participants whose median age was 30 years. For the post-testing/post-surgery participants, it took an average of 19.4 months between discovering their CDH1 mutation status and having the TG. For the post-testing/pre-surgery participants, there was an average of 15.7 months between finding out their CDH1 mutation result and the timing of their interview.

Of the 15 individuals who have yet to undergo a TG, 5 (33.3%) commented that they were utilizing their family history to plan timing of testing and potential surgeries. Many recognized that the ages of stomach cancer diagnoses were older than their current ages; therefore, they perceived that they had time to delay before making a decision.

> Because even though maybe statistically it happened in the 20s or 30s or whatever, the two instances in my family have been in the 50s, it feels that [we have] more time to make that decision. (participant #5)

Looking from a different perspective, one woman from the post-testing/post-surgery grouping reported that prior to her surgery she struggled with her need for a TG since she was already past the average age of cancer onset:

> You've got to make a decision and I am thinking they say it erupts at the age of 20 to 40, and then I am thinking: okay, I am 55, I don't even think I've got this, but I've still got to do this? (participant #19)

2.4.3.2 How much does my family history apply? Five participants in the study had their CDH1 mutation detected through a breast cancer risk gene panel. They all had the testing for their personal or family history of breast cancer and the majority were not counseled that they were being tested for cancer risks outside of breast cancer. As a result, their positive CDH1 mutation results came as a surprise.

> I was in such disbelief, like I could not understand like, I had like no, no, nobody in my family with gastric cancer. It was just like a horrible nightmare. (participant #4)

Some wondered whether there are still things to be learned about the associated cancer risks with CDH1 mutations. Now that more individuals are being picked up incidentally through breast cancer gene panels, many questioned if the reported cancer risks are not as accurate as previously believed.

> When we first learned about this, we learned that there are only 100 families on the planet that had the gene, CDH1. Well, I'll bet you that is a heck of a lot

> different now because they hadn't been testing any families except those who had lost people to gastric cancer… but now that there are so many people who were being tested for genes, and they find that so many people having the CDH1 [mutation] who don't have stomach cancer, I think that is going to alter the percentages. (participant #9)

The discrepancy between the appearance of a typical CDH1 family history and the participants' family histories presented a conflict in whether the cancer statistics still applied to them. However, the situation also presented a sense of hope that their family was less likely to be affected.

> There must be more families out there like us who do test positive for the CDH1 [gene] and don't end up struggling with hereditary diffuse gastric cancer. (participant #9)

With both examples, the participants were clearly looking back at their family history to assess their personal risks for the timing and the likelihood of the onset of cancer. Especially for those who did not fit within the mold of a typical CDH1 family, many participants had to weigh several of these influential factors into their decision-making process which may have altered the difficulty of these decisions.

2.4.4 Difficulty of decisions. Of the 20 participants who already had genetic testing, 17 (85%) reported that having genetic testing was an easy decision to make. Of the six participants in the pre-testing group who were currently deciding about genetic testing, five reported that they will eventually have genetic testing, with four viewing it an easy decision.

Compared to genetic testing, the participants considered the decision about pursuing a prophylactic total gastrectomy to be much more difficult. Eighteen expressed that the decision to have a TG was difficult. Interestingly, 10 of the 18 (55.6%) knew logically that having the surgery was the correct decision but still felt overwhelmed by the weight of such a life-altering surgery. When one woman was asked whether the decision to have a TG was easy or difficult she responded:

> I can't say it was easy… I knew I had to have it done, so there is no doubt about that, I knew that I had to have it done…I mean, I struggled with just the fear and not knowing what to expect. (participant #20**)**

Eight participants felt differently and said that the TG was an easy decision for them, with three calling the decision a "no-brainer".

> It was kind of a no-brainer, if you can live without a stomach why wouldn't you? Instead of giving yourself an 83% chance of stomach cancer, especially this kind, and then a 4% chance of survival if you get it? I feel like with those odds, it's a no-brainer. For me it was anyway. (participant #12)

When assessing the post-testing/pre-surgery group's thoughts about whether they wanted to pursue a TG, six of the nine (66.7%) said that they would eventually have the surgery. Reasons for delaying surgery consisted of allowing time to emotionally prepare, insurance complications, and scheduling around other life events. The remaining three felt that they currently didn't have enough evidence to proceed with surgery.

For the pre-testing participants, 3 of the 6 (50%) said they would have a TG if their test result came back positive. Two said that if they received a positive test result

they would have to assess their feelings and their current life situation before making a decision. One participant explicitly stated he would not pursue a TG.

Interestingly, an unprompted theme that emerged was that many of the participants had different views about their post-TG pathology which ultimately impacted their satisfaction with their decision. Four participants acknowledged that they hoped that the post-TG pathology would reveal that they already had cancer cells growing in their stomach. They felt like the presence of these cells provided validation that they made the right decision in undergoing a TG prophylactically. One woman explained why she was pleased to have a positive pathology:

> "Because, you know, here you are healthy and then having to make a huge decision, I almost wanted it to come back something because that would just reassure me that I did the right decision. Again, so… thank God. It was there." (participant #18)

After discovering that their post-TG pathology was clear, two participants struggled because they lacked that validation that cancer cells had begun growing. They questioned if they actually would have ever developed cancer in their lifetime and whether the sacrifice of having the surgery was unbeneficial.

> The fact that my pathology was clear made me kind of wonder if I needed to do it, and that's kind of been a struggle… that has made the recovery a little bit harder too because I didn't have that 'oh, okay I made the right decision, I know I was going to get cancer', or 'cancer was there so I was going to die if I didn't have the surgery'. Not having that was kind of a hard one to swallow. (participant #13)

Clearly, the decisions to pursue genetic testing and a prophylactic TG are layered with many considerations with not all individuals sharing the same opinion on their ease.

2.4.5 Information sources and additional needs. The sources of information and topics in need of additional information likely also contributed to how the participants viewed these decisions. The participants gathered information about genetic testing and surgery from a variety of sources. Twenty-two of the 26 (84.6%) participants reported that they used the internet as a resource for researching information about genetic testing and surgery. More specifically, 18 out of those 22 (81.8%) directly stated that they used the No Stomach for Cancer support group website.

Seventeen individuals (65.4%) reported that they utilized family members to obtain information. Of note, all six of the pre-testing/pre-surgery grouping reported that their family members were their only means of obtaining information. One woman who had not yet pursued genetic testing commented:

> So I didn't do a lot of research, but my mom did, obviously did a ton of research and so I had her to kind of explain things to me so she kind of did the research and then translated it over to me. (participant #17)

When asked, the pre-testing/pre-surgery individuals felt comfortable that they had enough information at this time. If a question ever came up in the future, they reported that they would rely on a family member as the primary resource to acquire the respective answer. However, several expressed that once they get to the point of wanting to pursue testing, they may do more research independently.

Through various means, all but one of the participants had been exposed to an individual without a stomach. Twenty out of the 25 (80.0%) read blog posts created by

individuals who had previously undergone a TG, 16 of the 25 (64%) had post-TG family members, and 12 of the 25 (48%) actually spoke to individuals post-TG who were not biologically related to them. Many utilized a combination of the three. Participants who had family members post-TG tried to learn from their family members' experiences and adapt it in order to make a smoother transition for themselves.

> I've gotten a bunch of tips from them, too. Which helps, you know? They've all said, "Okay, do this and not this. Do this and not that. This works for me, but it doesn't work for them." So I know that whenever I do have my surgery, I've got five immediate family members that I can say, hey, did y'all deal with this? Is this normal? Did you go through this? How do I make it better? (participant #8)

While it is helpful to use the experience from their families, others recognized the value of speaking to someone who was not biologically related to them in order to obtain a different perspective. One young adult woman who had post-TG family members described how helpful it was to hear a stranger speak about pregnancy post-TG:

> My whole family had already been through that part of their lives before they had the surgery, so for me to be able to hear her talk, you know, she had kids perfectly normal and the experience was as normal as it could be for her which is really reassuring for me. So it's good to have people I can hear speak that I don't share genes with. (participant #22)

For more professional resources, 16 individuals received information from a genetic counselor. The topics covered by genetic counselors primarily consisted of explaining genetic risks, the process of genetic testing, and, in the presence of a positive result, that a TG was the recommended preventative management. Sixteen individuals received

information from other medical professionals including gastroenterologists, nurse practitioners, oncologists, and surgeons. Their surgeons provided the specific details of the procedure of the surgery and in general terms what life looked like post-TG.

Six of the 11 (54.5%) participants of the post-testing/post-surgery grouping and four out of the nine (44.4%) post-testing/pre-surgery grouping expressed that they wished their doctors would have provided more specific information about life after surgery. The majority recognized they would have a lengthy recovery period following surgery, would lose a significant amount of weight, and would require changes to their diet, but few fully understood what their future day-to-day life may be like. In addition to more specific details regarding resulting quality of life, seven participants specifically requested that more emphasis should be put on creating a nutritional plan prior to surgery.

> Literally all the dietitian did was hand me a little piece of paper with like 10 bullet points about like how I should eat after surgery and I was just like, this is absolutely ridiculous, like nobody gave me any information really on what I should be eating which was the main…that was like the whole thing in my life that changed the most…there was no one in that role really just telling me how the eating would change, like maybe helping me strategize that sort of thing. (participant #17)

2.4.6 Advocate for self. Due to the lack of knowledge surrounding the CDH1 gene and the variation in treatment for post-TG patients, many participants expressed frustration with having to be an advocate for themselves.

One of the most frustrating aspects of this decision-making process was the unfamiliarity with the CDH1 gene. Fifteen of the 20 (75.0%) participants who were either

post-testing/post-surgery or post-testing/pre-surgery encountered a medical professional who had never heard about the CDH1 gene. For many, it was disconcerting to be treated by a doctor unfamiliar with their diagnosis.

> I had done all the reading online and had done all the research and I kept talking to medical professionals [who] had read fewer articles than I had. (participant #5)

Some experienced physicians who provided treatment or recommendations that were in conflict with the guidelines for CDH1 patients. One woman described how her endoscopy scan wasn't performed with the correct protocol due to the physician's unfamiliarity:

> Well, the protocol they can read online if you're going to do this is that you need to do 30 random biopsies…because [the doctor] doesn't have experience with the CDH1 gene mutation, [he] did like three or four biopsies. You know, the protocol is 30, he does three…It was just sort of like the one I did…was a total waste because it wasn't, you know, it wasn't done in the way it was supposed to be done. (participant #5)

In response, many participants felt like they had to become their own expert in order to verify they were receiving the proper treatment. However some recognized the limitations in this:

> I am not an expert on everything, I have become as much of an expert as I can, but there is still a lot that I do not know and so when I am having to be my own advocate and handle so much of this, if there is something that I don't know about, I don't know to ask about it. (participant #6)

Frustrated by the lack of knowledge from their local physicians, many participants traveled to large hospital systems that had experience with other CDH1 patients and consequently had better knowledge of how to treat their patients.

Table 2.1: Demographic Information for Participants

Demographics (n= 26)		(%)
Age		
Average	36.9y	
Range	18-71y	
Gender		
Female:Male	23:3	88.5:11.5%
Pre-testing/pre-surgery (n= 6)		
Marital Status		
Single	6	100%
Married	0	0%
Divorced	0	0%
Have Children	0	0%
Post-testing/pre-surgery (n= 9)		
Marital Status		
Single	2	22.2%
Married	4	44.4%
Divorced	3	33.3%
Have Children	7	77.8%
Months since CDH1 testing		
Average	15.7mo	
Range	0.5-48mo	
Post-testing/Post-surgery (n= 11)		
Marital Status		
Single	1	9.1%
Married	9	81.8%
Divorced	1	9.1%
Have Children	9	81.8%
Months since gastrectomy		
Average	24.6mo	
Range	0.5-90mo	

Table 2.2: Number of Family Members with Stomach Cancer and Post-TG

	Pre-test/ Pre-surgery (n=6)		**Post-test/ Pre-surgery (n=9)**		**Post-test/ Post-surgery (n=11)**	
Number of family members with stomach cancer (p=0.808)	n	%	n	%	n	%
0	0	0%	0	0%	0	0%
1-2	5	83.3%	7	77.8%	8	72.7%
3+	1	16.7%	2	22.2%	3	27.3%
Number of family members with prophylactic TG (p=0.146)	n	%	n	%	n	%
0	1	16.7%	6	66.7%	3	27.3%
1-2	3	50%	2	22.2%	4	36.4%
3+	2	33.3%	1	11.1%	4	36.4%

Table 2.3: Timing and Ages of Participants

Pre-test/pre-surgery	
Age at interview	
Average	26.3y
Median	19.5y
Range	18-58y
Years aware of family history	
Average	4.5y
Median	5y
Range	1-9y
Post-testing/pre-surgery	
Age at interview	
Average	42.7y
Median	47y
Range	24-71y
Age at testing	
Average	42.2y
Median	47y
Range	24-70y
Time between positive result and interview	
Average	15.7mo
Median	17mo
Range	0.5-48mo
Post-testing/post-surgery	
Age at interview	
Average	38y
Median	33y
Range	25-58y
Age at testing	
Average	34.5y
Median	30y
Range	16-56y
Time between positive result and surgery	
Average	19.4mo
Median	8mo
Range	2-84mo
Age at surgery	
Average	36.1y
Median	31y
Range	21-56y

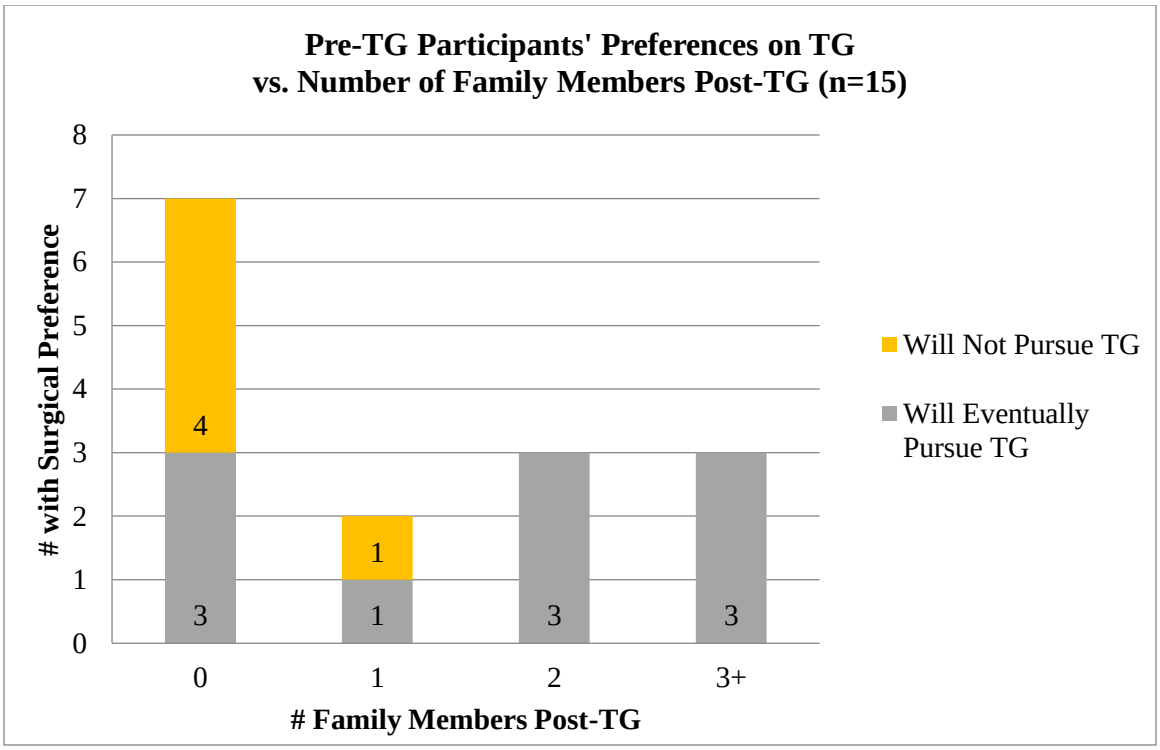

Figure 2.1: Pre-surgery participants reported whether or not they would eventually pursue a TG. Preferences were compared to the number of family members with a TG.

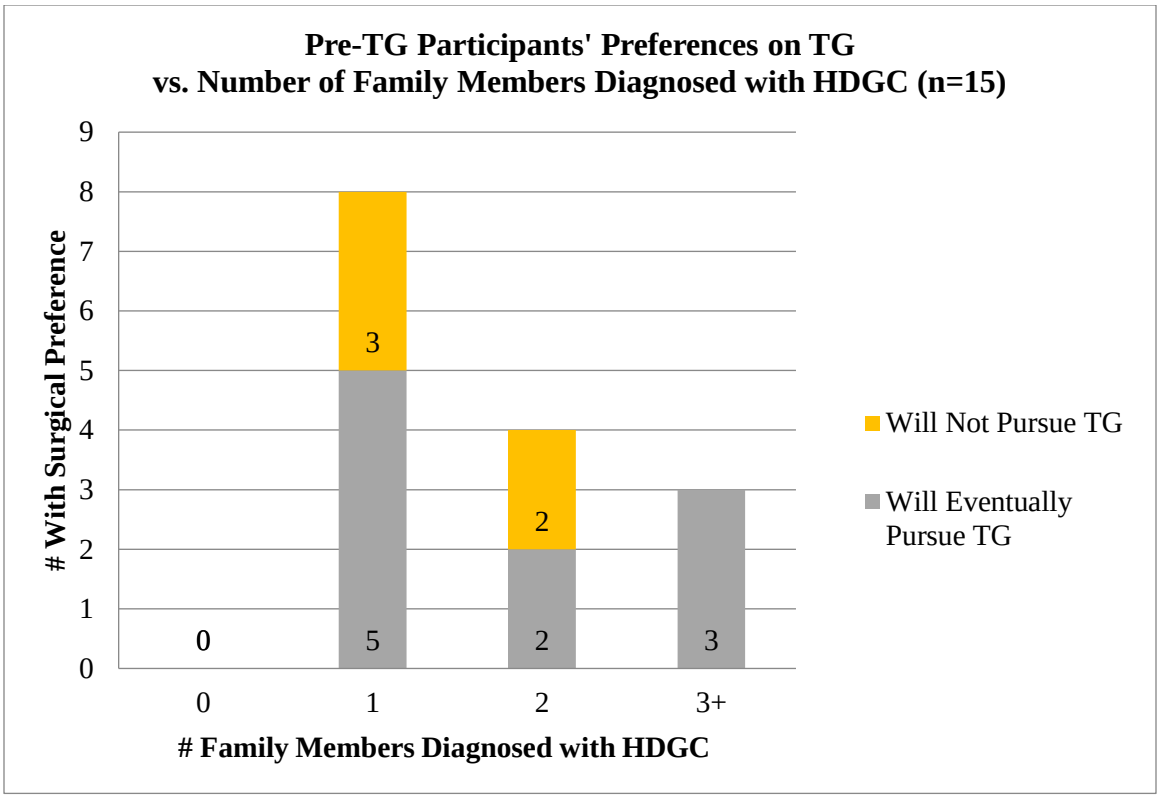

Figure 2.2: Pre-surgery participants reported whether or not they would eventually pursue a TG. Preferences were compared to the number of family members affected with HDGC. All of the participants had at least one family member affected by HDGC.

2.5 Discussion

This study investigated how individuals at risk for hereditary diffuse gastric cancer due to a positive CDH1 mutation or a family history of HDGC make decisions regarding pursuing genetic testing for the CDH1 gene and for a prophylactic total gastrectomy. Participants were captured at different points of this decision-making process to assess the factors influencing decision-making and their specific informational and psychosocial needs.

The four major factors influencing decision-making in this study were the avoidance of cancer, family, the inadequacies of endoscopy surveillance, and viewing a post-TG family member's experience. Similar results have been reported by Hallowell, Badger et al. (2016), who found that the major factors influencing TG decisions were the magnitude of associated cancer risks, the objective confirmation of cancer risks through a positive CDH1 mutation result or positive biopsy result on endoscopy, the burden of seeing affected family members, uncertainty of whether or not they would eventually develop cancer, perceptions of life following gastrectomy, and their views regarding endoscopy surveillance.

Generally, the factors influencing the decision to pursue genetic testing were primarily focused on the avoidance of cancer and family. Avoidance of cancer referred to the fact that the participants wanted to have the genetic information in order to make educated health decisions. Family influences were related to wanting that genetic information to have the ability to inform and be a role-model for other at-risk relatives.

While many regarded the decision to pursue genetic testing as straight-forward, the decision of pursuing a total gastrectomy was more complex. When considering a

decision for a TG, the four major influencing factors often overlapped with one another. Twenty-four participants had comments that fell within two or more different influencing factor themes. Sixteen participants reported three or more. One example of this overlapping complexity involves the integration of avoidance of cancer and familial influences. All of the participants recognized that a CDH1 mutation increased their lifetime risk for cancer and utilized that knowledge when making decisions regarding pursuing genetic testing and a TG. However, for some, that fact alone was not enough to undergo a TG. A few participants were single and didn't have any children and, because of their lack of dependents, they considered the surgery unnecessary. In contrast, others with spouses and children felt that it was their responsibility to pursue surgery to reduce their cancer risks—allowing them to continue to provide for their family. Another example of overlapping factors was that, in general, the participants viewed their risk of developing cancer as quite significant while the ability for endoscopy surveillance to accurately detect the development of cancer cells was quite low. The combination of the two factors ultimately influenced many participants to undergo the TG to guarantee their reduced risk and eliminate the uncertainty of when or whether they would even develop cancer. Collectively, these examples highlight the complexity and overlapping factors influencing decision-making for a TG.

When considering how many factors are present in this decision-making process, it is understandable that individuals may have varying degrees of comfort when choosing whether or not to pursue genetic testing or a prophylactic TG. Overall, 85.0% of the participants considered the choice to pursue genetic testing as an easy decision while 69.2% considered pursuing a TG as a difficult decision.

The post-testing/post-surgery participants waited an average of 19.4 months between learning their CDH1 mutation status before having a TG. Many reported reasons for delaying surgery included optimal timing for the extensive recovery period, insurance barriers, family planning, and fear of what life may be like after surgery. These results were similar to the findings of Lim et al. (2014) whose participants temporarily chose a surveillance approach in place of a TG for reasons of family responsibilities, child-bearing, financial concerns, and fear of the total gastrectomy. For the post-testing/pre-surgery participants, the average length of time aware of their CDH1 mutation status was 15.7 months; therefore, many have not reached the average threshold timing between testing and surgery. Underhill et al. (2013) observed that women's decisions regarding prophylactic bilateral mastectomies and oophorectomies required a balance between reducing their personal cancer risks and their own personal values. Perhaps for our study, that span of time between testing and TG was indicative of the time required for the participants to find their own personal balance before making a final decision.

What was interesting in our results was that of the participants who reported that the decision to have a gastrectomy was difficult, over half reported that they knew logically it was the correct decision and that they would eventually have the surgery. This finding was comparable to the results of Lynch et al. (2008) who found that once the participants were educated on the natural history of HDGC and the inadequate screening techniques, the question was no longer if they should get a TG but when they should get a TG. Although these patients perceive a TG as the correct option, barriers, such as fear of life after TG and insurance and financial concerns can prevent patients from following through with having the surgery. This situation creates an avenue where medical

professionals can provide psychosocial support to this population while patients make their surgical decisions. Additionally, as the time span between testing and surgery suggests, this psychosocial support may be required over the course of several years while patients take time to make their surgical decisions.

Another aspect of psychosocial support would be to acknowledge the mental health concerns that may be related to this decision-making process. Several post-gastrectomy participants reported experiencing depression in the extensive recovery period. Others who were pre-surgery acknowledged that undergoing a TG may trigger depression and subsequently delayed their decisions in order to safeguard their mental health. If signs of mental health concerns arise, medical professionals should refer their patients to meet with a mental health professional.

Medical professionals and support systems to these patients also need to understand that patients' views and needs will vary. Even faced with a similar situation, patients may have different reactions as they deal with the various aspects of this decision-making process. For example, some participants viewed the decision of having a TG as a "no-brainer" while others considered it a cumbersome decision. Another example was how some participants were relieved to hear their post-TG pathology was clear, which indicated they truly had the gastrectomy prior to any cancer development, while others struggled with a clear pathology because they felt like they underwent the surgery in vain. Because not all patients cope in the same way, it is important for medical professionals to approach these topics sensitively and validate whatever feelings emerge during this decision-making process.

Several participants had their CDH1 mutation detected on a breast cancer panel after pursuing genetic testing for their personal or family history of breast cancer. Understandably, these results came as a surprise because their family histories did not match that of a typical CDH1 family. As a result, many questioned whether their cancer risks differed from the reported cancer risks for CDH1 mutation carriers. One participant insightfully reflected on the fact that, historically, individuals were never tested for CDH1 mutations unless they had diffuse gastric cancer. Now in the age of pre-symptomatic panel testing for cancer predisposition, we are detecting individuals with CDH1 gene mutations who would not have fit the historical criteria for testing. This fact opens numerous questions of whether these mutations may exhibit genotype/phenotype correlations where families may have higher or lower cancer risks depending on their particular mutation. Another question that is raised is how should medical professionals counsel about these risks and how heavily should the counseling be based on the patient's family history. These questions are certainly not unique to CDH1 mutations and the increasing uptake of cancer gene panels may illuminate with time how to best address these concerns.

Another area of distress related to the fact that many participants didn't realize that panel testing could detect cancer risks outside of breast cancer. Again, this situation is not unique to this particular patient population and highlights the importance of providing patients with pre-test counseling in order to educate on what information the test can identify and on what information is outside of the scope of the test. Another element to add to pre-test counseling could involve genetic discrimination and the Genetic Information Nondiscrimination Act (GINA, 2008). While this policy has many

protections for patients, several of our participants regretted that they were not aware that they could be declined from receiving life or long-term care insurance in the presence of positive test results.

One frequent source of frustration for the participants was that they had to become their own advocates for their healthcare. Unfortunately, many participants felt like they had received more information about CDH1 mutations from their research online than they received from their medical professionals. Some said their local physicians had never even heard of the CDH1 gene or the idea of utilizing a total gastrectomy for cancer prevention. This unfamiliarity caused patients distress because these professionals could not provide guidelines for care regarding endoscopy surveillance, surgery, and post-surgery recovery. In the end, many felt like they actually had to educate their doctors about what care they should receive. However, many were not confident enough in their understanding of the guidelines to convey this information properly.

Another frustration arose from patients trying to utilize surveillance techniques. Many participants reported having an endoscopy in which the medical provider inadequately performed the procedure, despite being given the proper protocol for CDH1 patients. Instead of taking the recommended 30+ biopsies, many providers simply followed the protocol of an individual at normal population risk for stomach cancer. The participants were understandably frustrated by these incidents and were scared that they had received improper care.

Because of the discrepancies between what they were reading online and their experiences with medical professionals unfamiliar with the diagnosis, many felt

confused, overwhelmed, and scared they were not receiving appropriate care. In response, several of the participants chose to go to larger medical centers where many other CDH1 patients had received treatment. There, in general, the participants felt more comfortable that they were receiving the proper care. While a great resource, financial burdens and other logistical concerns can unfortunately be barriers for many patients to travel and receive this kind of specialized care.

Even at specialized centers, the participants felt like their medical professionals gave vague explanations of what life looked like after surgery and how to approach post-TG nutrition. Because of the lack of information, many participants wanted to hear directly from someone post-TG what their resulting quality of life might be like. The participants established contact with post-TG individuals through online support groups, through referrals of a medical professional to contact a past patient, or through a family member who had already gone through the surgery. This contact provided mixed feelings. Some participants felt a sense of hope when hearing about the experiences of those who had a positive outcome after surgery. Others were intimidated to hear about some of the complications resulting from the surgery and worried if they would have similar complications. Overall, most were thankful to have that exposure. Many realized life would be different post-TG and hoped that they could utilize the experiences of individuals who came before them in order to make an easier transition for themselves.

Several participants suggested the idea of providing patients with a summary document that could be given to medical professionals who are unfamiliar with the CDH1 gene. Genetic counselors often provide summary letters to patients after consultations. Studies show that these letters are appreciated by the patients because they

promote higher levels of understanding of the information discussed (Cassini et al., 2011; Hallowell & Murton, 1998). Our study reinforces the idea that it may be helpful if medical professionals, like surgeons and gastroenterologists, provide documentation summarizing the guidelines for the patient's care. In turn, patients can share this information with medical professionals unfamiliar with the condition to create a smoother transition of care and minimize the need for patients to personally educate their providers. Additionally, these summary documents could be sent to potentially affected relatives as educational materials about the familial condition.

2.5.1 Strengths and limitations. To date, we are familiar with only one other study by Hallowell, Badger et al. (2016) that utilized qualitative interviews to assess the decision-making process for individuals at risk for HDGC. Our study is unique from theirs in that we were able to obtain several participants who had yet to undergo genetic testing in order to assess whether there were any unique information needs that this population required. Another strength of our study is that qualitative interviews present the ability to discover themes that may have emerged outside of the original scope of the interview question guideline leading to richer data collection. One limitation of our study was that our participants were gathered from online support groups who may be representative of those who are more willing to share about their experiences and have internet access. The only male participants belonged to the pre-testing grouping, therefore gender differences may be present in the other decision-making stages that we were unable to capture. Additionally, we did not obtain information about race or socioeconomic status and therefore could not assess whether there were differences based off of these demographic characteristics.

2.5.2 Practice implications.

1. Decision-making regarding a prophylactic-gastrectomy is complex. Many patients recognize having a TG is something they want in the future but are overwhelmed by the weight of actually having the surgery. Therefore, support from medical professions may be needed long-term.
2. Acknowledge that patients may view the same situation with completely opposite opinions. Be sensitive and validate whatever opinion the patient presents.
3. To allow for fully-informed decisions and to minimize unnecessary distress, medical professionals providing cancer genetic testing should provide pre-test counseling to highlight the major benefits and risks of the testing. This counseling should also include a discussion of the Genetic Information Nondiscrimination Act and how it relates to the patient's personal situation.
4. A need exists to establish better resources that medical professionals can use as educational tools that detail life post-gastrectomy and the resulting nutritional concerns. If the medical professional is unable to provide this information, they should refer to reputable support websites like No Stomach for Cancer.
5. To minimize burden on patients, create a summary document that patients can provide to their medical professionals who are unfamiliar with CDH1 which details specific care guidelines. Additionally, this summary document can be used as a tool to also inform potentially at risk relatives.

Chapter 3: Conclusions

In conclusion, this study examined how individuals at risk for hereditary diffuse gastric cancer made decisions regarding pursuing genetic testing and a prophylactic total gastrectomy. The major factors influencing decision making included the avoidance of cancer, family, the inadequacies of endoscopy surveillance, and viewing a post-TG family member's experience. Participants often experienced multiple factors at a time indicating the complexities of these decisions. Information about genetic testing and a TG was obtained from the internet, other family members, genetic counselors, and other medical professionals. Despite having these resources for information, participants felt like they were still missing information about life post-TG and the resulting nutritional concerns. Additionally, because many of their medical professionals were unfamiliar with the condition, participants were concerned that they had to be their own advocate for their healthcare. Overall, a need exists to raise awareness of the CDH1 gene and have protocols in place so this information is conveyed effectively to medical providers and patients. Finally, all medical professionals in contact with this population need to have an awareness of the complexity of these decisions and realize psychosocial support may be required over the course and even beyond the timing of this decision-making process.

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Appendix A: Interview Question Guide

Consent statement

You are agreeing to participate in a telephone interview as a part of a genetic counseling graduate school research project. This interview will last approximately 45 minutes to 1 hour. Your participation in this project is voluntary. You may withdraw from the study at any time. If at any time there is a question you are not comfortable answering, please let me know and we can proceed on to the next question.

With your consent, this conversation will be recorded and transcribed. All responses gathered from the interviews will be kept anonymous and confidential. If a quotation is used from this interview, all identifying information will be removed and you will be assigned an alternative name.

If you have any questions regarding this research, you may contact either myself or my faculty adviser, Victoria Vincent, MS, CGC. If you have any questions about your rights as a research participant, you may contact the Office of Research Compliance at the University of South Carolina at (803)777-7095.

Do you consent to this research study?

Demographic information

1. Age
2. Sex M F
3. Highest level of education
    a. High school diploma/GED, technical/vocational school, some college, associate's degree, bachelor's degree, master's degree, professional degree
4. Relationship status
    a. Single, committed relationship, married/domestic partnership, separated, widowed, divorced
5. Do you have any children?
    a. Age?

Interview Questions

6. Have you been diagnosed with HDGC?
    a. Was that based on symptoms, result of screening, post-gastrectomy pathology, or other?
    b. At what age did you get diagnosed?

7. Are there others in your family with HDGC or a CDH1 mutation before your diagnosis or are you the first to be diagnosed?
    a. If others, who?
    b. Do you have family members diagnosed with other types of cancer?
8. Did you opt to have genetic testing? Yes No
9. Have you had a gastrectomy? Yes No
10. What age did you recall first learning about the chance for you to have HDGC?
    a. How was the HDGC risk presented to you? (e.g. phone, email, in person)
11. What kind of information did you know before you had testing/surgery?
12. What was your understanding about your cancer risk prior to testing/surgery?
    a. How often did/do you worry about developing cancer?
    b. What types of cancers are you at risk for?
    c. For women, how do you perceive your lobular breast cancer risk compared to HDGC?
    d. How do you perceive your colon cancer risk compared to HDGC?
13. Genetic testing
    a. At what age did you get genetic testing?
    b. How long ago was the testing (what year)?
        i. Who provided that testing? (Physician/Genetic Counselor)
        ii. Timing between first learning about family history and testing
            1. What events sped up or slowed down decision to have testing?
    c. If no, are you planning on having testing?
        i. If yes, when do you anticipate that will be?
            1. What is the reasoning for that timing?
        ii. If no, what is the reasoning?
    d. What motivated you to have (or not have) genetic testing?
    e. Where did you get your information about genetic testing?
        i. Did you seek it out?
            1. Where did you look?
            2. Was it helpful?
            3. What was lacking?
        ii. Was it given to you?
            1. By whom?
            2. Was it helpful?
            3. What was lacking?
    f. Where did you find information that was most helpful? Least helpful?
        i. What information encouraged you to have genetic testing?
        ii. What information held you back?
    g. What additional information do you wish you had before genetic testing?
    h. Did you find the decision to have testing easy to make or difficult?
        i. What made it easy or hard?
    i. What were your expectations of the results of testing?

j. What was your reaction to your test results?
    i. Did your experience match your prior expectations?
k. How has testing changed your level of concern, worries, perspective?

14. Gastrectomy
    a. At what age did you have a gastrectomy?
        i. How long ago was the surgery? What year?
        ii. Timing between genetic testing and surgery
            1. What events sped up or slowed down decision to have gastrectomy?
    b. If no, are you planning on having a gastrectomy?
        i. If yes, have you thought about when it will be?
            1. What is the reasoning for that timing?
        ii. If no, what is the reasoning?
    c. What motivated you to have (or not have) a gastrectomy?
    d. Where did you get your information about the surgery?
        i. Did you seek it out?
            1. Where did you look?
            2. Was it helpful?
            3. What was lacking?
        ii. Was it given to you?
            1. By whom?
            2. Was it helpful?
            3. What was lacking?
    e. Where did you find information that was most helpful? Least helpful?
        i. What information encouraged you to have the surgery?
        ii. What information held you back?
    f. What additional information do you wish you had before surgery?
    g. Did you find the decision to have surgery easy to make or difficult?
        i. What made it easy or hard?
    h. What were your expectations of the results of the surgery?
    i. Did your experience match your prior expectations?
    j. How has the surgery changed your level of concern, worries, perspective?

15. Support systems
    a. Who provided support during the decision making process?
        i. E.g. family, support groups, medical professionals/genetic counselors?
    b. Who did you share your situation with?
        i. When did you share that information?
            1. Was there a reasoning for that timing?
        ii. Who was the most supportive?
            1. How were they supportive?
        iii. Who was the least supportive?
            1. How could they have been better?

        iv. How did you share that information? (e.g. meet in person, telephone, letter, email)
    c. Who did you choose not to tell? Why?
16. Experience with medical professionals (e.g. genetic counselor, primary care physician, gastroenterologist, surgeon)
    a. Positive experiences
    b. Negative experiences
        i. How could these negative experiences be made better?
    c. Finish this sentence: "I wish that my doctor knew…"
        i. Referring to gastroenterologist, surgeon, primary care physician, etc.
17. Looking back, is there anything you would have done differently?
18. Advice to someone who may be in your position one day
19. Do you have any family members who would be eligible or interested in this study?