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The Psychosocial Burden of LI-Fraumeni Syndrome Tumor Surveillance on Mutation and Non-Mutation Carriers Within Families

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THE PSYCHOSOCIAL BURDEN OF LI-FRAUMENI SYNDROME TUMOR
SURVEILLANCE ON MUTATION AND NON-MUTATION CARRIERS WITHIN
FAMILIES

by

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ABSTRACT

Individuals undergoing Li-Fraumeni syndrome (LFS) tumor surveillance are known to experience a significant psychosocial burden due to financial, emotional and logistical stresses. This study aims to increase understanding of the psychosocial impact of LFS tumor surveillance on both individuals with an LFS diagnosis and non-mutation carrier family members, expecting that both populations would experience similar burdens, to determine if there is an unmet need for support resources. We performed a mixed-methods study consisting of an online survey completed by 94 individuals with an LFS diagnosis and 29 non-mutation carrier family members and semi-structured phone interviews with 13 survey participant consisting of both mutation carriers (n = 9) and non-mutation carrier family members (n = 4). Regarding LFS-related support resources, only 20.7% of non-mutation carrier family member indicating utilizing online or in-person support groups and 51.7% reported desiring access to this resource, suggesting an unmet need in this population. When asked about top reasons for non-adherence to recommended LFS tumor surveillance, mutation carriers cited cost/insurance coverage and emotional/psychological reasons. Both groups had mean general anxiety (GAD-7) and cancer/tumor surveillance-related distress (IES-6) scores that were not statistically significantly different (GAD7: p = .704, IES-6: p = .288). A statistically significant moderate positive correlation was identified between IES-6 scores and the number of years the participant or their family member has been undergoing LFS tumor surveillance (p = .001). A factor that led to statistically significant decreases in both GAD-7 and IES-6

scores was higher satisfaction with the amount of LFS-related support resources utilized (GAD-7: p = .038, IES-6: p = .028). A factor that led to a statistically significant decrease in IES-6 scores was the perception that LFS tumor surveillance is effective (IES-6: p =.030). Several themes emerged from interviews, most notably related to attitudes toward support resources, coping styles, and communication with family and friends. This study identified factors associated with LFS tumor surveillance that may guide healthcare providers in better managing their patients and family members using available support resources and knowledge of perceived barriers and drawbacks to tumor surveillance.

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CHAPTER 1: LITERATURE REVIEW

1.1 Overview of Li-Fraumeni Syndrome

Li-Fraumeni syndrome (LFS), caused by mutations in the *TP53* gene, is a rare, highly penetrant, autosomal dominant hereditary condition that leads to a predisposition for many types of cancer (Li & Fraumeni, 1969; Malkin et al., 1990). The cancers most commonly associated with LFS include premenopausal breast cancer, brain cancer, adrenocortical tumors, leukemia, and sarcomas (Malkin et al., 1990). More recently, increased rates of other cancer types including colon, pancreatic, stomach, kidney, endometrial, ovarian, prostate, lung, and skin cancers have been reported (Ruijs et al., 2010). Not only do individuals with LFS frequently develop cancer at younger ages, often during childhood, they are also more likely to develop multiple primary cancers throughout their lifetime (Hwang et al., 2003; Hisada et al., 1998).

While cancer risk data varies, it is thought that the risk for cancer by age 31 is approximately 50% in females and 46% in males (Mai et al., 2016). The lifetime cancer risk for LFS is significantly higher in women (approximately 100%) than men (73%), primarily due to the increased risk for female breast cancer (Chompret et al., 2000). One study showed that individuals with LFS have a 57% risk to develop a second primary cancer and a 38% risk to develop a third primary cancer (Hisada et al., 1998). Initially thought to be a rare hereditary cancer predisposition syndrome, it is now thought that the prevalence of LFS may be anywhere from 1 in 5,000 to 1 in 20,000 individuals due to many individuals demonstrating less penetrant phenotypes (Gonzalez et al., 2009; Lalloo

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et al., 2003). Thus, these cancer risk estimates likely vary between individuals or different *TP53* variants.

The *TP53* gene is a tumor suppressor gene located on chromosome 17. The TP53 protein is an important transcription factor involved in regulating cell cycle arrest, apoptosis, senescence, DNA repair, and changes in metabolism. Cells that incur DNA damage and lack normal function of the TP53 protein can continue to survive and proliferate, leading to a variety of malignancies (Rivlin et al., 2011). There are currently nearly 500 different germline mutations in the *TP53* gene classified as pathogenic and causative of LFS with the majority being missense and frameshift variants (National Center for Biotechnology Information-ClinVar). An estimated 7-20% of pathogenic *TP53* mutations are *de novo* (Gonzalez et al., 2009).

1.2 Diagnosis of Li-Fraumeni Syndrome

In 1988, criteria for a clinical diagnosis of LFS was proposed by Drs. Frederick Pei Li and Joseph F. Fraumeni, Jr. Classic LFS criteria requires that the proband have all the following:

- A sarcoma diagnosed before age 45 years
- A first-degree relative with any cancer before age 45 years
- A first- or second-degree relative with any cancer before age 45 years or a sarcoma at any age (Li et al., 1988).

Approximately 70% of individuals who meet the clinical criteria for classic LFS have a detectable pathogenic *TP53* mutation (Peng et al., 2017).

In 2001, the Chompret criteria (most recently revised in 2015) was created to help medical providers identify individuals at the highest risk for carrying a pathogenic *TP53*

mutation (Bougeard et al., 2015). National Comprehensive Cancer Network (NCCN) guidelines recommend that anyone meeting the Chompret criteria should be offered germline genetic testing for LFS. The current Chompret criteria requires that the proband have the following (National Comprehensive Cancer Network, 2019):

- A tumor belonging to the LFS tumor spectrum (e.g. soft tissue sarcoma, osteosarcoma, brain tumor, pre-menopausal breast cancer, adrenocortical carcinoma, leukemia, lung bronchoalveolar cancer) before age 46 years AND at least one first- or second-degree relative with a LFS tumor (except breast cancer if the proband has breast cancer) before age 56 years or with multiple tumors; OR

- Multiple tumors (except multiple breast tumors), two of which belong to the LFS tumor spectrum and the first of which occurred before age 46 years; OR

- An adrenocortical carcinoma, choroid plexus tumor, or rhabdomyosarcoma of embryonal anaplastic subtype, at any age of onset, irrespective of family history; OR

- Breast cancer before age 31.

Gonzalez et al. (2009) demonstrated a sensitivity and specificity of the classic LFS and Chompret criteria together to be 95% and 52% respectively.

With the increased utilization of multigene panel testing and somatic tumor tissue testing, however, more individuals with pathogenic germline *TP53* mutations are being identified who do not meet the LFS clinical criteria. This suggests that LFS may have a wider phenotypic range than what had initially been thought. Rana et al. (2018) demonstrated that individuals diagnosed with LFS through a multigene panel were

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significantly older at their first cancer diagnosis and less likely to meet the LFS clinical criteria than those diagnosed with LFS through single-gene testing.

1.3 Li-Fraumeni Syndrome Management and Surveillance

In 2011, the first comprehensive clinical surveillance for people with LFS, often called the Toronto Protocol, was proposed (Villani et al., 2011). The goal of this comprehensive surveillance, involving both biochemical and imaging modalities such as whole-body MRI (WBMRI) and brain MRI, is to improve patient survival through early cancer detection and prevention. A recommendation for individuals with LFS is to avoid therapeutic radiation unless the benefits outweigh the risks due to increased sensitivity to radiation-induced cancers.

In the same study, the researchers investigated the effectiveness and feasibility of the proposed Toronto Protocol. Thirty-three individuals with confirmed *TP53* mutations participated, 18 of whom underwent surveillance. With the utilization of the proposed Toronto Protocol, 10 asymptomatic tumors (both small high-grade and low-grade or premalignant) were identified in 7 out of the 18 patients undergoing surveillance (39%). In the non-surveillance group, 12 high-grade, high-stage tumors developed in 10 patients. The three-year survival rate was 100% among those undergoing surveillance compared to 21% among the non-surveillance group (Villani et al., 2011). In 2016, this study was expanded with longer follow-up and a larger sample size. Eighty-nine confirmed *TP53* carriers participated, 59 of whom underwent surveillance. Forty asymptomatic tumors were detected in 19 (32%) of those 59 patients. Among the 49 patients who initially declined surveillance, 61 symptomatic tumors developed in 43 (88%) patients. The 5-year survival rate among those undergoing surveillance (88.8%) was statistically

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significantly higher than the 5-year survival rate among the non-surveillance group (59.6%) (Villani et al., 2016). The authors from both the 2011 and 2016 studies concluded that comprehensive tumor surveillance is feasible and should be incorporated into the routine management of LFS patients as it is associated with increased long-term survival due to earlier detection of cancers and tumors.

In 2017, the Toronto Protocol was revised by an international multi-disciplinary working group of experts focused on developing surveillance guidelines for pediatric cancer predisposition syndromes, including LFS (Kratz et al., 2017). NCCN has also published LFS surveillance recommendations that closely resemble those of the Toronto Protocol that focus primarily on adult management without specifically addressing recommendations for children (National Comprehensive Cancer Network, 2019). The revised Toronto Protocol includes surveillance recommendations for adrenocortical carcinoma (ACC), brain tumors, soft tissue and bone sarcomas, breast cancer, gastrointestinal (GI) cancer, and melanoma (Kratz et al., 2017). This protocol recommends:

- Children (Starting at diagnosis to age 18)
    - Complete physical exam every 3-4 months
    - ACC: Ultrasound of the abdomen and pelvis every 3-4 months
    - Brain tumor: Annual brain MRI
    - Soft tissue and bone sarcoma: Annual WBMRI
- Adults
    - Complete physical exam every 6 months
    - Women: breast cancer

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- Breast awareness starting at age 18 years

- Clinical breast examinations twice a year starting at age 20 years

- Annual breast MRI between the ages of 20 and 75 years (ideally alternating with WBMRI every 6 months)

- Consideration of a risk-reducing bilateral mastectomy

o Brain tumor: Annual brain MRI

o Soft tissue and bone sarcoma:

- Annual WBMRI

- Annual ultrasound of the abdomen and pelvis

o Gastrointestinal cancer: Upper endoscopy and colonoscopy every 2–5 years starting at age 25 years

o Melanoma: Annual dermatologic examinations

In 2018, Bojadzieva et al. investigated the diagnostic performance of WBMRI and brain MRI in patients participating in the Li-Fraumeni Syndrome Education and Early Detection (LEAD) screening program at MD Anderson in Houston, TX. Of the 63 LFS patients seen during the study period (April 1, 2013 and October 1, 2016), 53 patients underwent a WBMRI and 35 patients underwent a brain MRI. The WBMRI detected primary tumors in six patients (11.3%), tumor recurrence in one patient (1.9%), and cancer metastases in one patient (1.9%). The brain MRI detected primary low-grade brain tumors in three patients (8.6%) and missed three tumors that were subsequently diagnosed in between surveillance intervals. The authors concluded that the detection rate of cancers and tumors through the use of WBMRI and brain MRI warrant implementing those imaging studies into the clinical management of individuals with LFS.

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Saya et al. (2017) investigated the cancer detection rate with WBMRI in 44 *TP53* mutation carriers in the United Kingdom, where the only current screening recommendation at the time was an annual breast MRI. WBMRI identified a cancer in 6 (13.6%) of *TP53* mutation carriers during the study. The authors concluded that the cancer detection rate with WBMRI warranted adding it to the national guidelines for the management of adult *TP53* mutation carriers. In addition to its efficacy, Tak et al. (2019) that pre-symptomatic tumor surveillance for individuals with LFS had a 98% probability of being the most cost-effective option for early cancer detection for these patients when compared to a non-surveillance strategy.

1.4 Psychosocial Concerns Associated with Comprehensive Tumor Surveillance for Hereditary Cancer Syndromes

There have been several studies that have investigated the impact of tumor surveillance on individuals affected with various hereditary cancer syndromes. Gopie et al. (2012) performed a meta-analysis that investigated the psychosocial burden of surveillance for individuals with hereditary cancer syndromes such as LFS, familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome (PJS), hereditary breast and ovarian cancer syndrome (HBOC), and Lynch syndrome. They identified 32 different studies and found that surveillance for most hereditary cancers was associated with positive psychosocial outcomes. However, surveillance for hereditary cancer syndromes where individuals are at a higher risk for multiple tumors in multiple organ systems, such as LFS, PJS, Von Hippel Lindau syndrome (VHL), FAP, and Multiple Endocrine Neoplasia (MEN) syndrome type 1 was found to be associated with higher levels of distress and a lower quality of life. Poorer psychological outcomes were associated with a

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personal history of cancer, female gender, having a family history of cancer in first degree relatives, negative illness perception, and coping style.

1.4.1 LFS Mutation Carriers

Individuals undergoing comprehensive surveillance for LFS experience a particularly significant psychosocial impact including significant burden and stress related to tumor surveillance, such as logistical issues (e.g. insurance coverage, organization and navigation within hospital systems); feeling drained, exhausted; and negative emotions (e.g. anxiety, fear, and skepticism). These individuals also shared that they feel the tumor surveillance provides them with significant benefits, including peace of mind, early detection of cancers and tumors, having more knowledge, and a sense of control. Most of the individuals studied feel that, despite its burdens and drawbacks, the tumor surveillance is effective and they wish to continue participating in the screening (Jhaveri et al., 2015; Lammens et al., 2010; McBride et al., 2017; Ross et al., 2017).

McBride et al. (2017) demonstrated that patients with an LFS diagnosis experience a significant decrease in anxiety two weeks post-WBMRI when compared to baseline anxiety levels assessed prior to undergoing WBMRI. This decrease in anxiety immediately after WBMRI was not sustained, however. In addition, lack of social support, female gender and high perceived risk for developing cancer were associated with higher levels of distress and lower quality of life in individuals with LFS (Lammens et al., 2010).

1.4.2 Familial Impact of Tumor Surveillance

Several studies have investigated how tumor surveillance for hereditary cancer syndromes psychosocially impacts non-mutation carrier family members and close non-

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kin of those undergoing the surveillance. Lammens et al. (2011) demonstrated that 28%
of partners of individuals with an LFS or VHL diagnosis reported clinically relevant
levels of syndrome-related distress (n = 14), which was significantly correlated with their
affected partner's distress levels. Higher distress levels were also associated with younger
ages and less social support. Seventy-six percent of partners felt that professional
psychosocial support should be offered to them on a routine basis (n = 38).

Annual LFS tumor surveillance has led couples to experience feelings of
significant stress and worry about receiving abnormal results and ongoing information
about risk-reducing surgeries. (Young et al., 2018). In 2016, Peters et al. demonstrated
that non-mutation carriers in LFS families and their close non-kin experience reportedly
higher anxiety symptoms when compared to those with an LFS diagnosis. In a 2015
study by Kasparian et al., 15 individuals with VHL and 8 VHL caregivers reported
experiences such as anxiety related to the possibility and uncertainty of future tumor
development, difficulty in obtaining both satisfactory medical and psychosocial care,
feeling the burden of needing to undergo lifelong tumor surveillance, frustrations related
to finances, and stress related to taking on caregiver responsibilities. Previous literature
highlighted the use of protective buffering (behavior and communication to shield and
isolate others from negative psychosocial effects) by both LFS and VHL mutation
carriers and their non-mutation carrier family members. (Young et al., 2018).

1.5 Rationale of the Present Study

The majority of existing literature on the psychosocial burdens of comprehensive
LFS surveillance, as described above, focuses on individuals with a diagnosis of LFS.
Current literature on how LFS surveillance specifically impacts non-mutation carrier

family members focuses primarily on partners and spouses and does not address other non-mutation carrier relationships (e.g. parent-child). Non-mutation carrier family members are defined as a family member who does not carry a pathogenic *TP53* mutation and therefore does not have a diagnosis of LFS. While non-mutation carrier family members are not undergoing the comprehensive tumor surveillance themselves, many of these individuals are actively involved in the management of their family member's LFS surveillance as a caregiver and/or significant source of support (emotionally, financially, and logistically) for their family member(s) with LFS. Additionally, watching a loved one go through frequent cancer screenings and/or risk-reducing surgeries and worrying about a loved one's cancer risk may bring about negative emotional reactions. They may experience a significant burden and could potentially benefit from additional psychosocial or logistical support. Therefore, the rationale of this study is to expand knowledge and understanding of the psychosocial impact of LFS tumor surveillance on those with a diagnosis of LFS and their non-mutation carrier family members.

1.6 Purpose of the Present Study

This project is being conducted to explore how comprehensive Li-Fraumeni Syndrome (LFS) tumor surveillance psychosocially impacts both mutation carriers and non-mutation carrier family members. The aims of this study are as follows:

1. Identify challenges related to LFS tumor surveillance experienced by individuals affected with LFS and non-mutation carrier family members.

    a. *Hypothesis: Challenges for these populations include logistical challenges (for example, scheduling appointments, transportation to appointments, geographical location), financial burdens, surveillance burnout/fatigue,*

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and frequent worry/anxiety regarding test results and the possibility of a new cancer diagnosis.

2. Identify factors associated with tumor surveillance that increase anxiety and distress levels in individuals affected with LFS and non-mutation carrier family members.

   a. *Hypothesis: Individuals with a personal history of cancer and/or a family history of cancer involving first-degree relatives experience higher levels of psychosocial distress than individuals with no personal history of cancer and/or a family history of cancer only in more distant relatives (for example, second- or third-degree relatives).*

   b. *Hypothesis: Individuals who are more actively involved in their own or a family member's LFS medical management experience higher levels of psychosocial distress associated with tumor surveillance than individuals who are less actively involved or not involved in LFS medical management.*

3. Compare and contrast non-mutation carrier family members' perceived benefits and drawbacks of comprehensive LFS surveillance to individuals with a diagnosis of LFS undergoing surveillance from survey/interview data and previous literature.

   a. *Hypothesis: Both populations will share similar perceived benefits and drawbacks of comprehensive LFS surveillance (for example, benefits may include early detection and peace of mind and drawbacks may include feeling overwhelmed, anxiety, and financial challenges).*

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4. Evaluate coping strategies and support resources utilized and desired by individuals with LFS and non-mutation carrier family members to manage emotional and pragmatic daily life challenges associated with comprehensive LFS tumor surveillance.

    a. *Hypothesis: Both populations utilize and desire similar coping strategies and support resources (for example, online and in-person support groups, professional counseling, and financial assistance).*

Overall, this study aims to provide insight into the psychosocial impact of comprehensive surveillance on LFS families as a whole (including non-mutation carrier family members), to describe this community's experience and to identify potential unmet needs for support or other resources. These insights are also critical for genetic counselors and other medical providers to better understand these families' experiences, identify possible barriers to obtaining surveillance, and provide support that could improve adherence.

CHAPTER 2: THE PSYCHOSOCIAL BURDEN OF LI-FRAUMENI SYNDROME TUMOR SURVEILLANCE ON MUTATION AND NON-MUTATION CARRIERS WITHIN FAMILIES [1]

2.1 Abstract

Individuals undergoing Li-Fraumeni syndrome (LFS) tumor surveillance are known to experience a significant psychosocial burden due to financial, emotional and logistical stresses. This study aims to increase understanding of the psychosocial impact of LFS tumor surveillance on both individuals with an LFS diagnosis and non-mutation carrier family members, expecting that both populations would experience similar burdens, to determine if there is an unmet need for support resources. We performed a mixed-methods study consisting of an online survey completed by 94 individuals with an LFS diagnosis and 29 non-mutation carrier family members and semi-structured phone interviews with 13 survey participant consisting of both mutation carriers (n = 9) and non-mutation carrier family members (n = 4). Regarding LFS-related support resources, only 20.7% of non-mutation carrier family member indicating utilizing online or in-person support groups and 51.7% reported desiring access to this resource, suggesting an unmet need in this population. When asked about top reasons for non-adherence to recommended LFS tumor surveillance, mutation carriers cited cost/insurance coverage and emotional/psychological reasons. Both groups had mean general anxiety (GAD-7) and cancer/tumor surveillance-related distress (IES-6) scores that were not statistically

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[1] Berenson, E., McGee, R.B., Hines-Dowell, S., Dobek, W. To be submitted to *Journal of Genetic Counseling*

significantly different (GAD7: p = .704, IES-6: p = .288). A statistically significant moderate positive correlation was identified between IES-6 scores and the number of years the participant or their family member has been undergoing LFS tumor surveillance (p = .001). A factor that led to statistically significant decreases in both GAD-7 and IES-6 scores was higher satisfaction with the amount of LFS-related support resources utilized (GAD-7: p = .038, IES-6: p = .028). A factor that led to a statistically significant decrease in IES-6 scores was the perception that LFS tumor surveillance is effective (IES-6: p =.030). Several themes emerged from interviews, most notably related to attitudes toward support resources, coping styles, and communication with family and friends. This study identified factors associated with LFS tumor surveillance that may guide healthcare providers in better managing their patients and family members using available support resources and knowledge of perceived barriers and drawbacks to tumor surveillance.

2.2. Introduction

Li-Fraumeni syndrome (LFS), caused by mutations in the *TP53* gene, is a rare, highly penetrant, autosomal dominant hereditary condition that leads to a predisposition for many types of cancer (Li & Fraumeni, 1969; Malkin et al., 1990). The cancers most commonly associated with LFS include premenopausal breast cancer, brain cancer, adrenocortical tumors, leukemia, and sarcomas (Malkin et al., 1990). More recently, increased rates of other cancer types including colon, pancreatic, stomach, kidney, endometrial, ovarian, prostate, lung, and skin cancers have been reported (Ruijs et al., 2010). Not only do individuals with LFS frequently develop cancer at younger ages, often during childhood, they are also more likely to develop multiple primary cancers throughout their lifetime (Hwang et al., 2003; Hisada et al., 1998).

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While cancer risk data varies, it is thought that the risk for cancer by age 31 is approximately 50% in females and 46% in males (Mai et al., 2016). The lifetime cancer risk for LFS is significantly higher in women (approximately 100%) than men (73%), primarily due to the increased risk for female breast cancer (Chompret et al., 2000). One study showed that individuals with LFS have a 57% risk to develop a second primary cancer and a 38% risk to develop a third primary cancer (Hisada et al., 1998). Initially thought to be a rare hereditary cancer predisposition syndrome, it is now thought that the prevalence of LFS may be anywhere from 1 in 5,000 to 1 in 20,000 individuals due to many individuals demonstrating less penetrant phenotypes (Gonzalez et al., 2009; Lalloo et al., 2003). Thus, these cancer risk estimates likely vary between individuals or different *TP53* variants.

In 2011, the first comprehensive clinical surveillance for people with LFS, often called the Toronto Protocol, was proposed (Villani et al., 2011). The goal of this comprehensive surveillance, involving both biochemical and imaging modalities such as whole-body MRI (WBMRI) and brain MRI, is to improve patient survival through early cancer detection and prevention. A recommendation for individuals with LFS is to avoid therapeutic radiation unless the benefits outweigh the risks due to increased sensitivity to radiation-induced cancers.

In the same study, the researchers investigated the effectiveness and feasibility of the proposed Toronto Protocol. Thirty-three individuals with confirmed *TP53* mutations participated, 18 of whom underwent surveillance. With the utilization of the proposed Toronto Protocol, 10 asymptomatic tumors (both small high-grade and low-grade or premalignant) were identified in 7 out of the 18 patients undergoing surveillance (39%).

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In the non-surveillance group, 12 high-grade, high-stage tumors developed in 10 patients. The three-year survival rate was 100% among those undergoing surveillance compared to 21% among the non-surveillance group (Villani et al., 2011). In 2016, this study was expanded with longer follow-up and a larger sample size. Eighty-nine confirmed *TP53* carriers participated, 59 of whom underwent surveillance. Forty asymptomatic tumors were detected in 19 (32%) of those 59 patients. Among the 49 patients who initially declined surveillance, 61 symptomatic tumors developed in 43 (88%) patients. The 5-year survival rate among those undergoing surveillance (88.8%) was statistically significantly higher than the 5-year survival rate among the non-surveillance group (59.6%) (Villani et al., 2016). The authors from both the 2011 and 2016 studies concluded that comprehensive tumor surveillance is feasible and should be incorporated into the routine management of LFS patients as it is associated with increased long-term survival due to earlier detection of cancers and tumors.

In 2017, the Toronto Protocol was revised by a international multi-disciplinary working group of experts focused on developing surveillance guidelines for pediatric cancer predisposition syndromes, including LFS (Kratz et al., 2017). NCCN has also published LFS surveillance recommendations that closely resemble those of the Toronto Protocol that focus primarily on adult management without specifically addressing recommendations for children (National Comprehensive Cancer Network, 2019). The revised Toronto Protocol includes surveillance recommendations for adrenocortical carcinoma (ACC), brain tumors, soft tissue and bone sarcomas, breast cancer, gastrointestinal (GI) cancer, and melanoma (Kratz et al., 2017).

Surveillance for LFS such as those recommended in the Toronto Protocol and by NCCN has been shown to provide patients with a better outcome in terms of early cancer detection and prevention. Recent literature has investigated the impact of tumor surveillance on individuals affected with various hereditary cancer syndromes. Gopie et al. (2012) performed a meta-analysis that investigated the psychosocial burden of surveillance for individuals with hereditary cancer syndromes such as LFS, familial adenomatous polyposis (FAP), Peutz-Jeghers syndrome (PJS), hereditary breast and ovarian cancer syndrome (HBOC), and Lynch syndrome. They identified 32 different studies and found that surveillance for most hereditary cancers was associated with positive psychosocial outcomes. However, surveillance for hereditary cancer syndromes where individuals are at a higher risk for multiple tumors in multiple organ systems, such as LFS, PJS, Von Hippel Lindau syndrome (VHL), FAP, and Multiple Endocrine Neoplasia (MEN) syndrome type 1 was found to be associated with higher levels of distress and a lower quality of life. Poorer psychological outcomes were associated with a personal history of cancer, female gender, having a family history of cancer in first degree relatives, negative illness perception, and coping style.

Individuals undergoing comprehensive surveillance for LFS experience a particularly significant psychosocial impact including significant burden and stress related to tumor surveillance such as logistical issues (e.g. insurance coverage, organization and navigation within hospital systems); feeling drained, exhausted; and negative emotions (e.g. anxiety, fear, and skepticism). These individuals also shared that they feel the tumor surveillance provides them with significant benefits, including peace of mind, early detection of cancers and tumors, having more knowledge, and a sense of

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control. Most of the individuals studied feel that, despite its burdens and drawbacks, the tumor surveillance is effective and they wish to continue participating in the screening (Jhaveri et al., 2015; Lammens et al., 2010; McBride et al., 2017; Ross et al., 2017).

McBride et al. (2017) demonstrated that patients with an LFS diagnosis experience a significant decrease in anxiety two weeks post-WBMRI when compared to baseline anxiety levels assessed prior to undergoing WBMRI. This decrease in anxiety immediately after WBMRI was not sustained, however. In addition, lack of social support, female gender and high perceived risk for developing cancer were associated with higher levels of distress and lower quality of life in individuals with LFS (Lammens et al., 2010).

1.4.2 Familial Impact of Tumor Surveillance

There have been several studies that have investigated how tumor surveillance for hereditary cancer syndromes psychosocially impacts non-mutation carrier family members and close non-kin of those undergoing the surveillance. Lammens et al. (2011) demonstrated that 28% of partners of individuals with an LFS or VHL diagnosis reported clinically relevant levels of syndrome-related distress (n = 14), which was significantly correlated with their affected partner's distress levels. Higher distress levels were also associated with younger ages and less social support. Seventy-six percent of partners felt that professional psychosocial support should be offered to them on a routine basis (n = 38).

Annual LFS tumor surveillance has led couples to experience feelings of significant stress and worry about receiving abnormal results and ongoing information about risk-reducing surgeries. (Young et al., 2018). In 2016, Peters et al. demonstrated

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that non-mutation carriers in LFS families and their close non-kin experience reportedly higher anxiety symptoms when compared to those with an LFS diagnosis. In a 2015 study by Kasparian et al., 15 individuals with VHL and 8 VHL caregivers reported experiences such as anxiety related to the possibility and uncertainty of future tumor development, difficulty in obtaining both satisfactory medical and psychosocial care, feeling the burden of needing to undergo lifelong tumor surveillance, frustrations related to finances, and stress related to taking on caregiver responsibilities. Previous literature highlighted the use of protective buffering (behavior and communication to shield and isolate others from negative psychosocial effects) by both LFS and VHL mutation carriers and their non-mutation carrier family members. (Young et al., 2018).

The majority of existing literature on the psychosocial burdens of comprehensive LFS surveillance, as described above, focuses on individuals with a diagnosis of LFS. Current literature on how LFS surveillance specifically impacts non-mutation carrier family members focuses primarily on partners and spouses and does not address other non-mutation carrier relationships (e.g. parent-child). Non-mutation carrier family members are defined as a family member who does not carry a pathogenic *TP53* mutation and therefore does not have a diagnosis of LFS. While non-mutation carrier family members are not undergoing the comprehensive tumor surveillance themselves, many of these individuals are actively involved in the management of their family member's LFS surveillance as a caregiver and/or significant source of support (emotionally, financially, and logistically) for their family member(s) with LFS. Additionally, watching a loved one go through frequent cancer screenings and/or risk-reducing surgeries and worrying about a loved one's cancer risk may bring about negative emotional reactions. They may

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experience a significant burden and could potentially benefit from additional psychosocial or logistical support.

Overall, this study aims to provide insight into the psychosocial impact of comprehensive surveillance on LFS families as a whole (including non-mutation carrier family members), to describe this community's experience and to identify potential unmet needs for support or other resources. These insights are also critical for genetic counselors and other medical providers to better understand these families' experiences; identify possible barriers to obtaining surveillance; and provide support that could improve adherence.

2.3 Materials and Methods

2.3.1 Participants

Participants included individuals 18 years of age and older who have a *TP53* mutation or who have a family member with a *TP53* mutation. Participants were recruited with permission form two United States-based patient advocacy groups, Living LFS and Li-Fraumeni Syndrome Association (LFSA). A study recruitment letter (Appendix A) was posted on two closed Facebook support groups curated by Living LFS: the Li-Fraumeni Support Group for individuals with a diagnosis of LFS and Li-Fraumeni Syndrome Family and Friends Support Group for family and friends of individuals with and LFS diagnosis. LFSA distributed a study recruitment letter to their members via their website, email blast, and social media pages on Facebook and Twitter. The letter included a description of the study and a link to the confidential online questionnaire (Appendix A). Participation was voluntary and respondents were not given any compensation. The

University of South Carolina Institutional Review Board (IRB) deemed this study exempt from the review in August 2019 (Pro00091625).

2.3.2 Materials/Measures

This study utilized mixed methodology consisting of an online questionnaire and an optional semi-structured phone interview. Two online questionnaires (one for individuals with a diagnosis of LFS and one for non-carrier family members) incorporated skip logic and were developed through Qualtrics (Appendix B and C). Both questionnaires were reviewed and approved by board members of Living LFS and the LFSA. The online questionnaire contained questions about demographics, personal and family history of cancer, and experiences regarding LFS tumor surveillance, and it was comprised of multiple choice, Likert scale, and open-ended text entry questions.

To measure baseline anxiety, participants in both study groups completed the Generalized Anxiety Disorder-7 or GAD-7 questionnaire (Spitzer et al., 2006) that used a seven-item Likert-scale (1 = not at all; 4 = nearly every day) on topics relating to anxiety, fear, and nervousness (Spitzer et al., 2006). Higher numerical scores represent higher levels of general anxiety. The scale had a high level of internal consistency, as determined by a Cronbach's alpha of 0.919.

To measure distress specifically associated with cancer/tumor surveillance, participants in both study groups completed the Impact of Event Scale-6 or IES-6, an abbreviated version of a widely used measure of the psychological impact of a specific event (Bauml et al., 2016). The IES-6 uses a seven-item Likert-scale measure (1 = not at all distressing; 5 = extremely distressing). Higher numerical scores represent higher

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levels of distress. The scale had a high level of internal consistency, as determined by a Cronbach's alpha of 0.920.

The semi-structured interviews were conducted and recorded by phone by a single researcher (E.B.) and included approximately 11 prompts and questions from an interview guide (Appendix D) related to attitudes toward LFS-related support resources, coping strategies utilized to manage the burden of LFS tumor surveillance, and communication strategies with friends and family about fears and worries related to LFS tumor surveillance.

2.3.3 Methods

The questionnaires (Appendix B and C) were administered online through Qualtrics. The introduction to the questionnaire outlined the goals of the study and participants gave their consent to participate by clicking "Yes" to the first question. Participants were able to skip any question with the exception of the first two questions that determined study eligibility. They were also able to leave the questionnaire at any time. Non-mutation carrier family member participants were asked to pick one family member with whom they are more knowledgeable/involved to answer the LFS tumor surveillance-related questions throughout the questionnaire.

Upon completion of the online questionnaire, respondents had the option to provide their contact information (name, email, and phone number) for a semi-structured telephone interview. The participants who provided their contact information were contacted via email to determine a time for the interview. Verbal consent for participation and recording was obtained at the beginning of each interview. Interviews were recorded on the interviewer's password protected computer via Windows Voice Recorder and

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transcribed verbatim. Audio-recordings were destroyed following transcription. Data was collected from August 2019 to February 2020.

Microsoft Office Excel software was used for descriptive statistical analysis. For quantitative analysis, Statistical Package for Social Sciences (SPSS) Version 26 was used. A p-value of 0.05 was considered significant for statistical tests performed in this study. The Chi-square Test for Independence was used to analyze associations between categorical variables. Pearson correlation was used to evaluate the linear relationship between two continuous variables. Finally, ANOVA was utilized to determine any statistically significant differences in the means of two or more independent groups.

Qualitative thematic analysis with a grounded theory approach was utilized to identify and analyze reporting patterns within responses from open-text entries from the online questionnaire and from the semi-structured interviews (Mays & Pope, 2000). After the raw data was read several times, emergent themes that were grouped into categories based on their similarities were independently developed by two researchers (E.B. and W.D.). Responses relevant to each category were examined using constant comparison, a process where each item is compared with the rest of the data to establish analytical categories. Identified themes were compared by both researchers and refined until common coding and categorization was agreed upon. Categories were added as needed to reflect the nuances of the data. Quotations were extracted and classified to their corresponding theme and reported on their frequency. Kappa coefficients were calculated to determine inter-rater reliability. Data was analyzed from February 2020 to April 2020.

2.4 Results

2.4.1 Demographic Information

A total of 123 individuals participated in our study; 94 mutation carriers with a personal diagnosis of LFS and 29 non-carrier family members. Because participants were able to skip questions, there is variation in completion rate for the online questionnaire. Due to confidentiality of the questionnaires, we were unable to connect/pair responses from mutation carriers with their non-mutation carrier family members.

Demographic characteristics of the participants in each study group (mutation carriers and non-mutation carrier family members) are summarized in Table 2.1. The sample population consisted of mostly Caucasian females individuals (80.5%; n = 99) with a mean age of 41.5 years old (age ranged from 19 to 70 years). A majority reported having at least a bachelor's degree or graduate degree (64.2%, n = 79). Nearly one-third of participants reported an income of greater than $100,000 (32.5%, n = 40). Over half of participants reported having private or employer-based health insurance (59.3%, n = 73). Those who selected "Other" to the question about health insurance most often stated that they are from another country with socialized medicine or national health system (74.1%, n = 20). Approximately two-thirds of participants stated that they are currently living in the United States (66.7%, n = 82). In addition, over half of participants reported being married (59.3%, n = 73). Almost all participants reported having a family history of cancer in a first or second-degree relative, a spouse or partner, or a step or adopted relative (91.9%, n = 113), and over half have a personal history of cancer (60.1%, n = 74). When answering the question about their occupation, 18.7% responded that they were in the healthcare field (n = 23). Those who selected "Other" for their occupation

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most often stated that they were self-employed (10.5%, n = 4), disabled (10.5%, n = 4), or a homemaker (13.2%, n = 5). The average age of LFS diagnosis for mutation carrier participants and non-mutation carriers' family member with LFS (n = 113) was 33.7 years (age ranged from 2 to 68 years). The average age of a first cancer diagnosis for participants (n = 72) was 33.4 years (1-63 years). The average number of years the mutation carriers and non-mutation carriers' family member with LFS have undergone LFS tumor surveillance (n = 111) was 4.5 years (1-41 years).

2.4.2 Support Resources

The type of support resources utilized and the type of support resources desired is summarized in Figure 2.1 and 2.2, respectively. Mutation carriers were most likely to utilize online or in-person support groups as a support resource (47.9%, n = 45) while non-mutation carrier family members were most likely to indicate that they did not utilize any formal support resources (41.4%, n = 12). There was a statistically significant association between participant mutation status (being a mutation carrier vs. a non-mutation carrier family member) and utilization of online or in-person support groups with mutation carriers being more likely these support groups than non-mutation carrier family members (p = .009). There was no other statistically significant difference between the two study groups in what support resources were utilized. The most common "Other" response entered for a utilized support resource by both mutation carriers and non-mutation carrier family members was family and friends as a source of support (43.8%, n = 7).

In assessing what support resources participants desired, mutation carriers most often indicated financial support (34.0%, n = 32) while non-mutation carrier family

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members indicated online or in-person support groups (51.7%, n = 15). There was a statistically significant association between participant mutation status (being a mutation carrier vs. a non-mutation carrier family member) and desire for access to online or in-person support groups with non-mutation carrier family members being more likely to desire access to these support groups than mutation carriers (p = .008). There was no other statistically significant difference between the two study groups in what support resources were desired. The most common "Other" response for a desired support resources by both mutation carriers and non-mutation carrier family members was health insurance advocacy (33.3%, n = 3).

Participants in both study groups were asked about their satisfaction with the amount of support resources utilized. Participants had the following choices: very unsatisfied (n = 7), unsatisfied (n = 13), neutral (n = 49), satisfied (n = 32), and very satisfied (n = 16). Satisfaction scores ranged from a minimum score of 1 (very unsatisfied) to a maximum score of 5 (very satisfied) with a mean score of 3.31 (n = 118). The mean satisfaction scores for both the mutation carrier (n = 90) and the non-mutation carrier family member (n = 28) groups are summarized in Figure 2.3 and demonstrated no statistically significant difference between the two study groups (p = .274), with both reporting relatively neutral satisfaction.

2.4.3 Perceived Effectiveness of LFS Tumor Surveillance

Participants in both study groups were asked if they perceived LFS tumor surveillance to be effective (n = 108) or not effective (n = 11). There was no statistically significant difference in perceived effectiveness of LFS tumor surveillance between the

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two study groups (p = .746), with the majority of participants (90.7%) indicating that they felt it is effective.

2.4.4 Involvement in LFS Tumor Surveillance Management

Participants in both study groups were asked if they felt they were not involved (n = 4), somewhat involved (n = 33), or very involved (n = 79) in their own or a family member's LFS tumor surveillance management. Involvement scores ranged from a minimum score of 1 (not involved) to a maximum score of 3 (very involved) with a mean score of 2.64 (n = 117). There was no statistically significant difference in mean involvement scores between the mutation carrier group (mean score = 2.69) and the non-mutation carrier family member group (mean score = 2.50)

Participants in the non-mutation carrier family member group were asked if they considered themselves to be a primary caregiver or guardian of an individual with an LFS diagnosis. Approximately half of respondents indicated that they do not consider themselves to be a primary caregiver or guardian (46.4%, n = 15) while approximately half of respondents indicated that they do consider themselves to be a primary caregiver or guardian (53.6%, n = 13).

Finally, participants in the non-mutation carrier family member group were asked whether they considered themselves to be logistically involved in their family member's LFS tumor surveillance management. This could include scheduling appointments, driving to appointments, and assisting financially with medical care costs. The majority of respondents (64.3%, 18 of 28 respondents) indicated that they considered themselves to be logistically involved in some way.

2.4.5 Personal and Family History of Cancer

Participants in both study groups were asked if they had ever been diagnosed with cancer. The majority of participants, 60.7%, responded "yes" (n = 74) while 39.3% of participants responded "no" (n = 48). Of those with a personal history of cancer, 94.6% were mutation carriers (n = 70) while 5.4% were non-mutation carrier family members (n = 4). Participants in both study groups were also asked about their family history of cancer. Participants were classified into three groups: no family history of cancer (9.8%, n = 12), family history of cancer that includes a first degree relative and/or spouse/partner (80.5%, n = 99), family history of cancer that includes only non-first-degree relatives (9.8%, n = 12).

2.4.6 Adherence to Recommended LFS Tumor Surveillance

Participants in both study groups were provided with a list of tumor surveillance recommendations based on the Toronto protocol and asked about the amount of that recommended tumor surveillance they or their family member have undergone, the results of which are summarized in Figure 2.4. Participants could choose: none (n = 6), few (n = 7), some (n = 12), most (n = 38), all (n = 60). Most respondents reported that they or their family member with LFS followed all or most of the recommendations (79.7%, n = 98). Participants who indicated that they do not follow all of the LFS tumor surveillance recommendations (51.2%, n = 63) were asked why they do not follow them, the results of which are summarized in Figure 2.5. The most common reasons for not following all of the LFS tumor surveillance recommendations besides "other" were due to issues with cost/insurance coverage (30.2%, n = 19) and emotional or psychological concerns (19.1%, n = 12). Reasons for choosing "Other" often included it not being

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recommended by their doctor (22.2%, n = 14), living in another country where different recommendations are followed (6.4%, n = 4), and currently undergoing treatment for cancer (4.8%, n = 3).

2.4.7 General Anxiety and Cancer/Tumor Related Distress

Scores on GAD-7 of 12, 17, and 22 represent cut-points for mild, moderate, and severe anxiety, respectively. In this study, GAD-7 scores ranged from a minimum score of 7 to a maximum score of 28 with a mean score of 14.8 (n = 122). The mean GAD-7 scores for both the mutation carrier and the non-mutation carrier family member groups are summarized in Figure 2.6 and demonstrated no statistically significant difference between the two study groups, with both reporting mild levels of anxiety.

Scores on IES-6 of 14, 21, and 28 represent cut-points for mild, moderate, and severe distress, respectively. IES-6 scores in this study ranged from a minimum score of 6 to a maximum score of 30 with a mean score of 14.3 (n = 118). The mean IES-6 scores for both the mutation carrier and the non-mutation carrier family member groups are summarized in Figure 2.7 and demonstrates no statistically significant difference between the two study groups, with both reporting mild levels of distress.

2.4.8 Factors that Influence GAD-7 and IES-6 Scores

A Pearson correlation test indicated that there was no statistically significant correlation between GAD-7 scores and the number of years the participant or their family member has been undergoing tumor surveillance (p = .197). However, there was a weak positive correlation between IES-6 scores and the number of years the mutation carrier of the non-mutation carrier's family member has been undergoing LFS tumor surveillance (p = .001) with IES-6 scores increasing as the number of years undergoing tumor

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surveillance increases. Additionally, a Pearson correlation test also indicated that GAD-7 and IES-6 score were both weakly negatively correlated with the level of participant satisfaction with the support resources utilized with scores increasing as satisfaction levels decreases (GAD-7: p = .006, IES-6: p = .036). GAD-7 and IES-6 scores were not correlated with age at LFS diagnosis (GAD-7: p = .454, IES-6: p = .270) or age of participant (GAD-7: p = .372, IES-6: p = .145).

A one-way ANOVA was also conducted to determine if GAD-7 and IES-6 scores were different between participants who do and do not believe LFS tumor surveillance is effective. There was no statistically significant difference in GAD-7 scores between participants who do and do not believe LFS tumor surveillance is effective (p = .289). Participants in the group that indicated they felt LFS tumor surveillance is effective, however, had a statistically significantly higher mean IES-6 score than the group that indicated they felt that LFS tumor surveillance is not effective (p = .030).

There were no statistically significant differences in GAD-7 and IES-6 scores between participants who:

- Are male and female (GAD-7: p = .684, IES-6: p = .732)

- Do and do not have a personal history of cancer (GAD-7: p = .220, IES-6: p = .979)

- Do or do not consider themselves a guardian/primary caregiver of a mutation carrier family member (GAD-7: p = .772, IES-6: p = .478)

- Do or do not consider themselves logistically involved in the care of a mutation carrier family member (GAD-7: p = .934, IES-6: p = .246)

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There were also no statistically significant differences in GAD-7 and IES-6 scores based on:

- The amount of recommended tumor surveillance the participant or their family member has undergone (GAD-7: $p = .783$, IES-6: $p = .234$)

- The participant's perceived level of involvement in their or their family member's LFS tumor surveillance (GAD-7: $p = .487$, IES-6: $p = .313$)

- Family history of cancer (GAD-7: $p = .325$, IES-6: $p = .444$)

2.4.9 Qualitative Results

Qualitative results were analyzed from free-response questions on the online questionnaire and 13 phone interview transcripts. On average, the interviews lasted 23 minutes (range 10 - 61 minutes). Data regarding emerging themes associated with LFS tumor surveillance-related support resources, coping strategies, and communication with family and friends from these interviews are summarized in Table 2.2.

Support Resources

Several themes emerged regarding participants' thoughts and experiences with LFS-related support resources. The first major theme was that online and in-person support groups provided participants with a sense of belonging and fewer feelings of isolation. These individuals expressed that it was helpful to be in a supportive environment where they could feel like they were not the only one going through the hardships associated with an LFS diagnosis. The evocation of strong emotions was another theme that emerged when discussing attitudes towards LFS-related support resources. Some participants indicated that they felt that online and in-person support groups could be overwhelming, depressing, and have a negative impact on their mental

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state such that they would need to step away and take a break at times. Another theme identified regarding LFS-related support resources was passive participation. These are individuals who are a part of an in-person or online support group and prefer to remain silent and not actively participate in the conversation as they are most comfortable observing and listening to what others have to say. A final theme that came up related to LFS-related support resources was access to knowledge and information. Several participants expressed that they appreciated that support groups provided them with information about ongoing research, cancer treatment and management, and others' experiences with LFS.

Coping Strategies

Several themes emerged related to coping strategies to manage the psychosocial impact of tumor surveillance. The first major theme included self-care/active strategies. These individuals utilize coping strategies that involve doing something deliberately to alleviate stressful circumstances and take care of their mental, emotional, and physical health (i.e. researching or reading information about LFS, helping others, exercise, meditation) as it provides them with a sense of control. The support of friends and family to help cope with the burden of tumor surveillance was another theme that emerged.

Another theme related to coping strategies was religion. These individuals utilize their faith practices (such as participating in Bible study or asking family and friends to pray for them or a family member) to help manage the anxiety and stress that is associated with LFS surveillance. Several participants indicated that having a strong healthcare team helps them to cope with tumor surveillance. Finally, allowing for a mindset adjustment was another theme that emerged as a coping strategy. Examples

include allowing themselves to have an occasional "pity party," thinking about LFS tumor surveillance as a job, or reminding themselves about how grateful they are to have the knowledge of their LFS diagnosis.

Communication

Several themes emerged related to communicating about anxieties and other negative emotions associated with LFS surveillance to family and friends. The first major theme was that of isolation. Mutation carriers expressed that they often feel as though others cannot understand what they are going through and experience feelings of loneliness and isolation. Non-mutation carrier family members expressed similar feelings of isolation with their friends and other non-relatives.

Another theme was protective buffering. Protective buffering occurs when an individual does not share anxieties and other negative emotions with a certain person to keep that person from experiencing additional burden. Non-mutation carrier family members often expressed that they did not want to further burden or add stress to their family members with LFS. In addition, mutation carriers often did not want to share their own anxieties and negative emotions to prevent transferring those feelings onto their family members.

In contrast to protective buffering, another communication theme that emerged was openness and honesty. These individuals expressed that they don't keep their feelings bottled up, rather, they share information about their scans and cancer treatments with others. A final theme was specific people with whom participants share their LFS surveillance-related anxieties of fears. Some participants said they prefer to speak with

their significant others, while someone else prefers to speak with their non-mutation carrier siblings.

Perceived Benefits, Drawbacks and Challenges Associated with LFS Tumor Surveillance

A free -response questionnaire item asked participants what they perceive to be the benefits, drawbacks, and challenges of LFS tumor surveillance. The most frequent responses in both the mutation carrier group and the non-mutation carrier family member group for perceived benefits of LFS tumor surveillance included early detection of cancers and tumors (35%, n = 41), a higher life expectancy (11.1%, n = 13), peace of mind (11.1%, n = 13) and a sense of control (6.8%, n = 8). Several participants also indicated that they felt the LFS tumor surveillance is very thorough and complete (12%, n = 14) and that it provides powerful knowledge (4.3%, n = 5). The most frequent responses in both the mutation carrier group and the non-mutation carrier family member group for perceived drawbacks of LFS tumor surveillance included feelings of stress and anxiety (42.5%, n = 51), financial burden (23.3%, n = 28) and that it is time-consuming (15.8%, n = 19). Several participants also expressed that a challenge associated with LFS tumor surveillance were logistics with scheduling (7.5%, n = 9).

2.5 Discussion

2.5.1 Support Resources, Coping Mechanisms, and Communication Styles

One notable conclusion obtained from interviews with participants is that support resources, coping strategies, and communication techniques with family and friends related to LFS tumor surveillance that may be beneficial for one person and may not be beneficial for someone else. Several participants indicated that online support groups

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provide them with a sense of belonging and less isolation while other participants emphasized that being in that environment was too overwhelming and depressing at times.

Additionally, in relation to coping strategies, several participants mentioned that they relied heavily on their faith and religion, which previous research has shown can provide individuals with a sense a hope and comfort (Costa et al., 2019) while other participants indicated that they placed an emphasis on utilizing self-care and active strategies such as exercise, meditation, and researching information about LFS.

Finally, there were contrasts in how participants handle communication about negative emotions (fear, anxiety, and stress) related to LFS tumor surveillance with family and friends. Similarly to Young et el., (2018), several participants indicated that they practiced protective buffering and would not typically discuss their negative emotions with family and friends. Other participants emphasized that they heavily value openness and honesty with everyone. Even more, some participants mentioned that they would tend to discuss their negative emotions only with certain individuals (e.g. spouses, boyfriends, non-mutation carrier siblings).

Another important result obtained from this study was related to the utilization of and desire for specific LFS-related support resources by both mutation carriers and non-mutation carrier family members. Non-mutation carrier family members' most common response (41.4% of respondents) was that they did not utilize any formal support resources. As 51.7% and 35.4% of non-mutation carrier family members respectively indicated that they desired access to online or in-person support groups and professional

counseling, results suggest that there could be a need and desire for support resources among non-mutation carrier family members that is not currently being met.

These results collectively suggest that clinicians and other medical providers should take a personalized approach when recommending LFS-related support resources and coping strategies in addition to making referrals to mental healthcare professionals. This study has highlighted that attitudes toward support resources, coping strategies, and communication styles are very personal and unique to each individual; therefore clinicians should also be prepared with different options and suggestions for these resources when discussing what may be most beneficial for the patient and their family members. Additionally, it is important that clinicians and other healthcare providers do their best to include non-mutation carrier family members in the conversation about support resources to better ensure that lack of access to and awareness of these resources is not a barrier to appropriate mental healthcare for these individuals. This may place an additional burden on the individual with an LFS diagnosis as the responsibility of relaying information about support resources to their non-mutation carrier family members may fall on them. Perhaps a healthcare provider having a ready-made list of certain nationwide support resources that a mutation carrier could pass on to a non-mutation carrier family member could help ease that burden.

2.5.2 Impact of Perceived Benefits, Drawbacks, and Barriers to LFS Tumor Surveillance on Patient Adherence

This study also highlighted the most significant perceived benefits and drawbacks associated with LFS tumor surveillance for both mutation carriers and non-mutation carrier family members. The most common perceived benefits (early detection of cancers

and tumors, a higher life expectancy, a sense of control, peace of mind, having more knowledge) and drawbacks (financial burden, feelings of stress and anxiety, time-consuming) of LFS tumor surveillance identified in this study were similar to those identified in other studies (Lammens et al., 2010; Ross et al., 2015). These perceived benefits add further evidence that LFS tumor surveillance can have a positive effect on families' overall wellbeing and quality of life. It is also important for clinicians and other healthcare providers to be aware of the perceived drawbacks to LFS tumor surveillance as these may impact adherence to screening. For example, being aware of the time-consuming nature of attending multiple surveillance appointments over several days in different locations annually brings to light the significance of developing centralized locations for LFS tumor surveillance. If patients can do all of their tumor surveillance in one day at one location, they may be more likely to be compliant as it eases the burden of logistical complications like requesting time off of work and the amount of travel required.

Approximately a quarter of the participants who are not adherent with all LFS tumor surveillance recommendations cited cost and insurance coverage concerns as a contributing factor. This finding is further strengthened by the fact that while only 8.5% of mutation carriers reported receiving financial support, approximately a third of mutation carriers said that they did not receive but desired financial support. These concerns about cost are consistent with results from a previous study that found most participants expressed loss of insurance coverage as being the largest barrier that might prevent them from continuing screening (Ross et al., 2015). This same study also reported that insurance coverage was the biggest logistical issue that participants faced.

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Additionally, Villani et al. (2016) indicated that the most frequently cited reason for patients declining LFS surveillance was an absence of insurance coverage. This steady concern over insurance coverage may be due to several reasons such as lack of reimbursement for health insurance companies, unique Medicare guidelines, and procedure code issues and should be investigated further.

Additionally, some participants who indicated that they or a family member did not partake in all of the recommended LFS tumor surveillance cited emotional and psychological reasons such as fear and anxiety as a factor. Addressing or acknowledging these factors with families may mitigate the psychological barriers to accessing LFS tumor surveillance. A factor associated with both decreased GAD-7 and IES-6 scores was increased satisfaction with the amount of LFS-related support resources utilized while factors associated with decreased IES-6 scores were fewer years undergoing LFS tumor surveillance and the perception that LFS tumor surveillance is effective. Individuals who feel that the LFS tumor surveillance is effective are likely to be more confident that it will catch cancers and tumors at an earlier stage and prolong their life. This may provide these individuals with peace of mind and reassurance which in turn lessens their feelings of anxiety and distress.

We hypothesized that more involvement (including logistical involvement) in one's own or a family member's LFS care and identifying as a primary caregiver or guardian of a family member with LFS would be associated with higher anxiety and scan-related distress scores; however, our findings did not support this. Data from qualitative interviews suggests that non-mutation carrier family members may feel obligated or that it is their duty to care for and help their mutation carrier family members

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(such as feeling responsible for advocating for them and researching information about LFS that may help them). Fulfilling this need by being more involved in the care of a family member with an LFS diagnosis may give these non-mutation carriers a feeling of satisfaction and a sense of purpose and control that helps alleviate negative emotions related to tumor surveillance. This idea is further strengthened by Teschendorf et al. (2007) demonstrating that family caregivers of adult cancer patients experienced a sense of satisfaction from their work and involvement. There were also no statistically significant differences in anxiety and scan-related distress scores between individuals who did and did not have a first-degree relative with cancer. This suggests that the degree of relative affected with cancer may not have the impact on general anxiety and distress that we hypothesized.

Understanding the reasons why mutation carriers are not adhering to the recommended LFS tumor surveillance identify potential barriers to care. Clinicians and other healthcare providers may be able to help alleviate negative emotions associated with LFS tumor surveillance by regularly assessing their patients' need for support resources throughout their lifetime, even years after initial tumor surveillance has begun. Additionally, as finances and insurance coverage have consistently been identified as a barrier to LFS tumor surveillance, mutation carriers and their family members may benefit from a referral to a patient advocate, social worker, or billing specialist who may be able to assist them in navigating the health insurance realm and identify possible financial assistance programs (such as those currently available to help cover the cost of breast MRIs for high-risk women).

2.5.3 Limitations

Our study population was primarily composed of highly educated Caucasian women with an LFS diagnosis. Due to this uniformity in participant demographics, our findings may not generalize to other populations. People of different sexes, races and education levels may have different experiences, satisfaction and receptiveness to LFS tumor surveillance and support. Obtaining a more diverse sample group may be achieved by recruiting participants from both a clinical setting and support organizations. In addition, our sample size of non-mutation carrier family members was relatively small. Factors that influence general anxiety and scan-related distress scores may be better seen in a larger sample.

Another limitation of this study is that we cannot know if higher GAD-7 scores are due to LFS-related worries and anxieties or due to other unrelated stressful events going on in their lives. The GAD-7 scores were able to provide valuable information such as whether individuals who are more anxious are more or less likely to find the LFS tumor surveillance effective, have higher or lower satisfaction, regarding the amount of support resources utilized. The cancer/tumor surveillance-related distress scale, however, was more specific to LFS-related feelings.

Additionally, due to the anonymous nature of this study, we were not able to responses and interviews from mutation carriers with their family members who may have also completed the surveys and interviews. Analysis of perspectives from multiple family members may provide new information on how an LFS diagnosis impacts families as a whole. Finally, as participants were recruited from patient advocacy groups, this study was selecting for motivated and engaged patients and families with a likely high

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adherence to tumor surveillance recommendations. Individuals who are not involved in these groups may have different attitudes toward and adherence to tumor surveillance recommendation that are not representative of results from this study.

2.5.4 Future Research and Directions

All interviews of participants (both mutation carriers and non-mutation carrier family members) were interviewed individually. We believe there is more that could be learned about how LFS tumor surveillance impacts families as a whole if families are interviewed together. This may provide additional insight about families' communication styles with each other and how LFS tumor surveillance impacts them similarly or differently.

Future research may also focus on how general anxiety or cancer/tumor surveillance-related distress levels differ based on where in the surveillance process an individual is. Determining these levels shortly before a scan and after a scan (both before and after they receive results) may be helpful in determining if certain time frames of the surveillance process are more stressful or anxiety-provoking than others.

With many participants indicating that one of the biggest challenges with LFS tumor surveillance involves logistics with scheduling, one area of future research may be the development of a smart phone application to help patients and their family members with surveillance scheduling. This application may reduce the number of missed surveillance appointments by having everything documented in one central application. Individuals would be able to see what has been scheduled and what still needs to be scheduled to better ensure that they are following the surveillance recommendations.

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Finally, with the knowledge that many non-mutation carrier family members desire access to an LFS-related online or in-person support group, future research may focus on the creation of more support groups specifically for this population to fill the need. Understanding how participation in support groups specifically tailored for non-mutation carrier family members impacts their overall wellbeing (including anxiety and cancer/tumor surveillance-related distress levels) may guide healthcare professionals in better managing the care of LFS families as a whole.

2.5.5 Conclusion

As uptake in *TP53* genetic testing has occurred due to increased multi-gene panel germline testing and somatic tumor testing, more patients are being diagnosed with LFS than in years past. With this increasing recognition and awareness of LFS, it is more important than ever to consider the psychosocial impact that LFS tumor surveillance has on both those with a diagnosis of LFS and their non-mutation carrier family members. It is also important to understand what barriers to LFS tumor surveillance exist. Both the psychosocial impact of and perceived barriers to LFS tumor surveillance can lead to non-adherence. This study shows that mutation carriers and non-mutation carrier family members experience a similar psychosocial impact from LFS tumor surveillance based on similar mean general anxiety and scan-related distress scores. In addition, both groups expressed that they experience similar challenges associated with LFS surveillance, including negative emotions (stress, anxiety, and fear), a financial burden, insurance coverage concerns, and logistical concerns (time and transportation). Given these results, it is important for mutation carriers to be offered or made aware of various support resources, including online and in-person support groups, professional counseling, health

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insurance advocates, and appointment coordination assistance. In addition, immediate non-mutation carrier family members may benefit from the same support resources due to the similar impact they experience with a family member's LFS diagnosis and tumor surveillance.

Table 2.1 Demographic characteristics of study participants

Characteristic	Mutation Carriers (%)	Non-Mutation Carrier Family Members (%)	Total (%)	p-value*
Age (n=123)				0.249
18-24	6.4	0	4.9	
25-34	24.5	17.2	22.8	
35-44	38.3	27.6	35.8	
45-54	21.3	20.7	21.1	
Over 54	9.6	31	14.6	
Prefer Not to Say	0	3.4	0.8	
Biological Sex (n=123)				0.817
Male	10.6	13.8	11.4	
Female	87.2	82.8	86.2	
Prefer Not to Say	2.1	3.4	2.4	
Ethnicity (n=123)*				
White	91.5	89.7	91.1	
Hispanic/Latino	4.3	6.9	4.9	
Black/African American	1.1	0	0.8	
Native American/Alaskan Native	0	0	0	
Asian/Pacific Islander	1.1	0	0.8	
Other	5.3	0	4.1	
Prefer Not to Say	2.1	3.4	2.4	
Education (n=123)				0.836
No Formal Education	2.1	0	1.6	
Some High School	1.1	0	0.8	
High School Degree or Equivalent	11.7	6.9	10.6	
Some College	12.8	10.3	12.2	
Associate Degree	8.5	10.3	8.9	

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Bachelor's Degree	33	44.8	35.8	
Graduate Degree	29.8	24.1	28.5	
Prefer Not to Say	1.1	3.4	1.6	
Annual Household Income (n=123)				0.088
Less than $25,000	3.4	17	13.8	
$25,001-$50,000	6.9	16	13.8	
$50,001-$75,000	13.8	8.5	9.8	
$75,001-$100,000	6.9	16	13.8	
More than $100,000	48.3	27.7	32.5	
Prefer Not to Say	20.7	14.9	16.3	
Health Insurance (n=123)				0.073
Private or Employer Based	56.4	69	59.3	
Medicare/Medicaid	9.6	10.3	9.8	
No Insurance	3.2	0	2.4	
Other	26.6	6.9	22	
Prefer Not to Say	4.3	13.8	6.5	
Relationship Status (n=123)				**0.009**
Single, Never Married	20.2	0	15.4	
Single, Living with Significant Other	9.6	3.4	8.1	
Married	54.3	75.9	59.3	
Domestic Partnership or Civil Union	0	0	3.3	
Widowed	0	6.9	1.6	
Divorced/Separated	10.6	10.3	10.6	
Prefer Not to Say	1.1	3.4	1.6	
Occupation (n=123)				0.633
Science/Technology	6.4	3.4	5.7	
Service/Retail	3.2	0	2.4	
Media/Communications	3.2	3.4	3.3	

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Government/Non-profit	7.4	6.9	7.3	
Business	9.6	6.9	8.9	
Healthcare	18.1	20.7	18.6	
Manufacturing	2.1	3.4	2.4	
Education	9.6	17.2	11.4	
Other	34	20.7	30.9	
Prefer Not to Say	6.4	17.2	8.9	
Geographical Location (n=123)				0.129
United States	62.8	79.3	66.7	
Canada	8.5	0	6.5	
Europe	16	13.8	15.4	
Africa	1.1	0	0.8	
Other	11.7	3.4	9.8	
Prefer Not to Say	0	3.4	0.8	
Family History of Cancer (n=123)**				
Yes-blood/biological relative	92.6	82.8	90.2	
Yes-spouse/partner, adopted relative, step-relative	2.1	31	8.9	
No	6.4	10.3	7.3	
Not sure	2.1	3.4	2.4	
Personal History of Cancer (n=122)				< .001
Yes	74.5	14.3	60.7	
No	25.5	85.7	39.3	

*p-value was calculated to determine associations between demographic characteristics and mutation carrier status (mutation carrier vs. non-mutation carrier family member)

**Participants were able to select more than one option for these questions, allowing the percentage to add up to more than 100 and therefore p-value could not be calculated

Table 2.2 Thematic analysis of participants' responses (n = 13) focusing on support resources, coping strategies, and communication strategies related to LFS-tumor surveillance

Topic and response themes	Verbatim	Participants whose responses reflected each theme (N)
Support Resources		
Sense of belonging/fewer feelings of isolation	"It felt like for so long I was falling apart, like I was always sick and I didn't know why. Now I feel like it wasn't just me, it wasn't my bad medical luck. It was that I actually have something wrong with me that a lot of people have wrong with them."— 40 year old (y.o) female mutation carrier (participant 2) "I have found them to be so supportive, just in making me feel like I was not alone in the challenges. That some stuff that felt really weird and isolating was actually really normal."— 35 y.o. female non-mutation carrier family member (participant 3)	6
Evocation of strong emotions	"I've seen some people disappear for periods of time and come back and say 'sorry I haven't been around.' They just needed a break because it was a little too emotional for them. Like say they recently have a diagnosis and then it's hard for them to see everybody else and take on their stress so they just kind of bow out for a little while."— 44 y.o. female non-mutation carrier family member (participant 1) "Honestly, it can be overwhelming and very depressing. Um, so, sometimes I'll just like turn off notifications on that on Facebook. Because um, especially with kids dying, it's so much."— 43 y.o. female mutation carrier (participant 7)	3
Passive participation	"I stay very behind the scenes. I don't make comments because I'm not the one who has the gene. So I don't think it's appropriate for me to make any comments."— 57 y.o. female non-mutation carrier (participant 10)	3

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Access to knowledge and information	"They help you keep updated on like what's the latest…like some of the latest research on LFS."— 56 y.o. female mutation carrier (participant 6) "They have been helpful with some information about like, um, surgery recovery and whatnot."— 43 y.o. female mutation carrier (participant 7)	5
Coping Strategies		
Self-care/active strategies	"When I fall down the anxiety spiral I just start researching and reading. My most common way of coping is by over researching, and over analyzing, and hanging out on PubMed for long stretches of time."— 40 y.o. female mutation carrier (participant 4) "I like to exercise and I like to do different things including you know…like yoga for instance is one thing I'll do. So making sure that I pretty much get daily exercise."— 29 y.o. male non-mutation carrier family member (participant 8)	5
Utilization of friends and family	"I reached out to a lot of family and friends just to sort of ask can you sort of send your prayers, send your love, send your support in whatever form."— 35 y.o. female non-mutation carrier family member (participant 3) "Having friends and family be there and support me was helpful even though sometimes it was like they don't fully get it. But just knowing I have a support network and people who care…they might not be able to fully understand everything but they still like want to help…that was helpful."— 27 y.o. female mutation carrier (participant 11)	3
Religion	"I have a Bible study…that was another very supportive forum, a group of people where I could share everything and then we would pray for each other…"— 27 y.o. female mutation carrier (participant 11)	4
Strong healthcare team	"Just having a really good team of doctors that knows, understands and knows what it's all about and makes all of that a priority, too."— 44 y.o. female non-mutation carrier (participant 1)	3

Mindset adjustment	"I do have my own pity parties every once in a while. I don't have them real often but I have them once in a while."— 56 y.o. female mutation carrier (participant 6) "I just keep saying thank you to myself. 'I don't like this, but thank you for this lesson.' I am so grateful that I know I have LFS. I don't want it, but I am so grateful to know I have it."— 70 y.o. female mutation carrier (participant 12)	4
Communication		
Isolation	"There are not that many people who have it, so it is somewhat isolating. My friends already don't get it. You're so alien to them that honestly I don't talk about that much with people."— 40 y.o. female mutation carrier (participant 4). "As much as your family and friends are close to you and want to help, it's very lonely. It doesn't matter sometimes if I share or not. I still have that feeling of being isolated."— 41 y.o. female mutation carrier (participant 9)	5
Protective buffering	"I talk with my daughter constantly, but I always try to talk in a positive way. She doesn't need any more burden than she already has. When your child is an adult, I think it's really important to express your frustrations but always…with anybody…keep a positive attitude, too."— 57 y.o. female non-mutation carrier family member (participant 10) "A lot of times when I'm dealing with a lot of anxiety, I won't tell my parents right away because my mom gets anxious, too."— 27 y.o. female mutation carrier (participant 11)	6
Openness and honesty	"I think it's really important to be super open and honest about it with everybody, including family members and friends…everybody…"— 57 y.o. female non-mutation carrier family member (participant 10)	3

| Speaking to specific individuals | "I share it with my husband, mainly. Not so much with my relatives because I feel like I end up kind of like downplaying the stress with them."— 43 y.o. female mutation carrier (participant 7)

"Talking to my other siblings who also don't have LFS-that can be helpful, because they can relate to that situation."— 29 y.o. male non-mutation carrier family member (participant 8) | 4 |
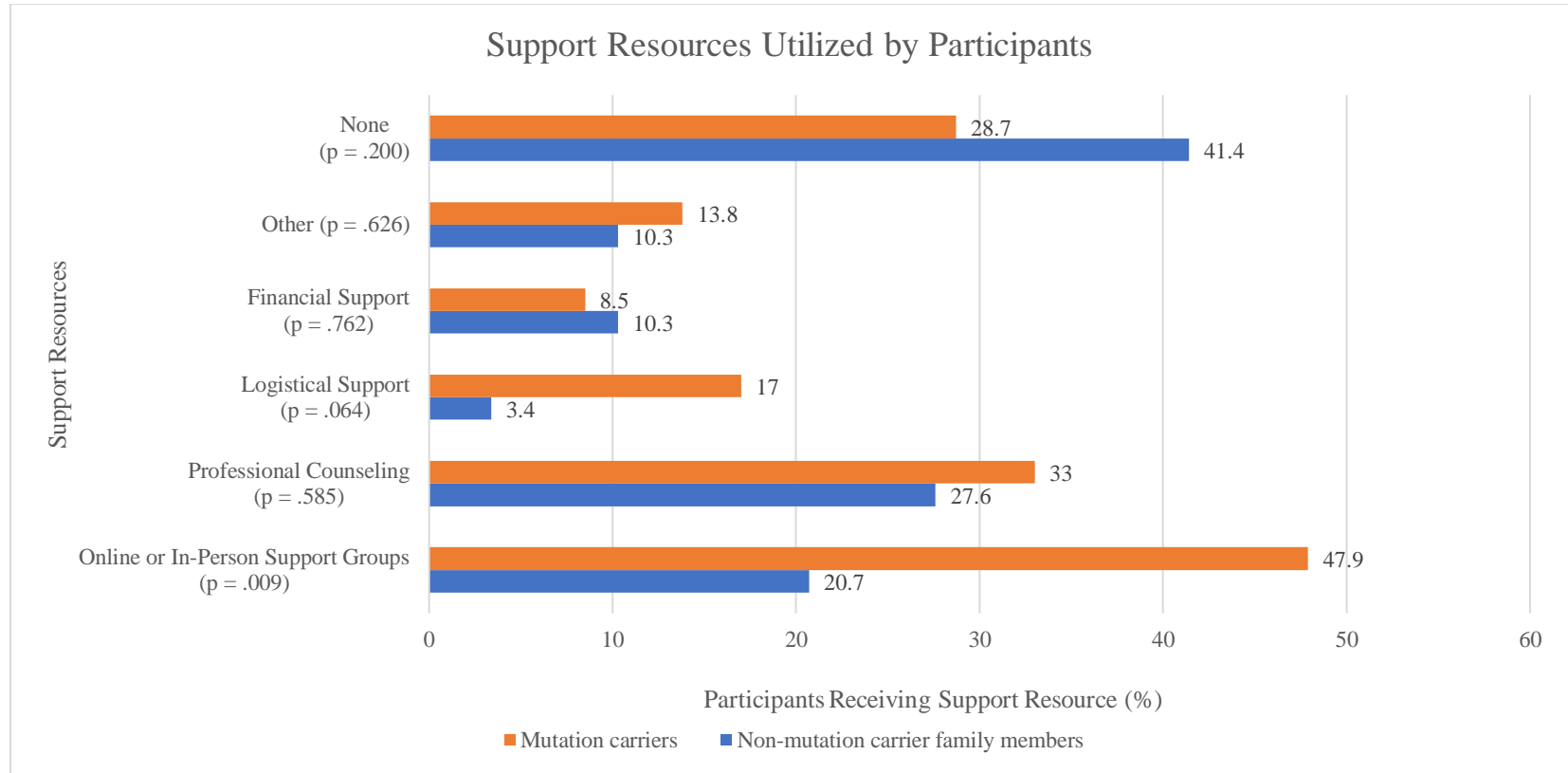
Figure 2.1 Percentage of study participants utilizing various LFS-related support resources (participants were able to select more than one option for this question, allowing the percentage to add up to more than 100.
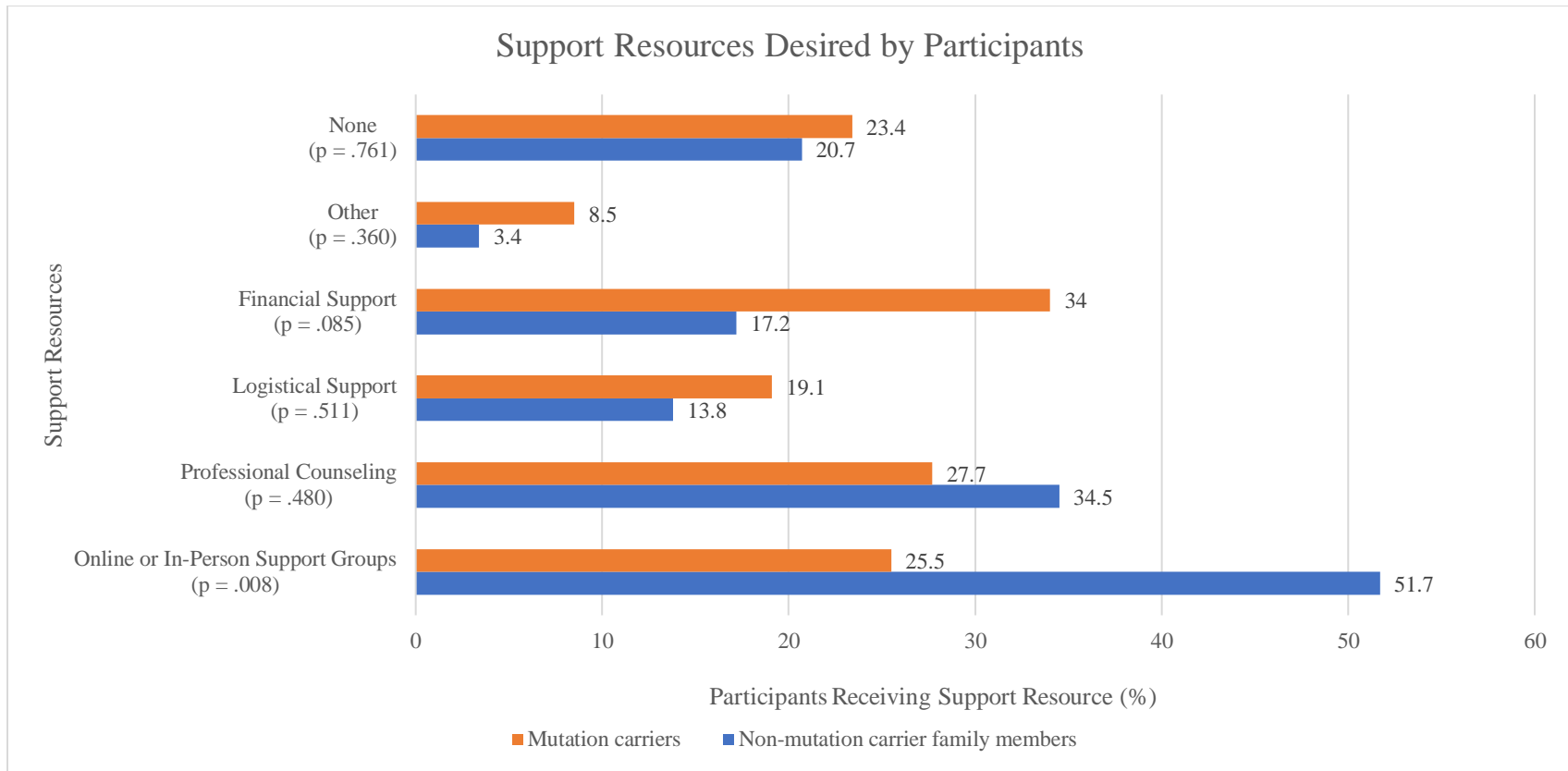
Figure 2.2 Percentage of study participants desiring various LFS-related support resources (participants were able to select more than one option for this question, allowing the percentage to add up to more than 100
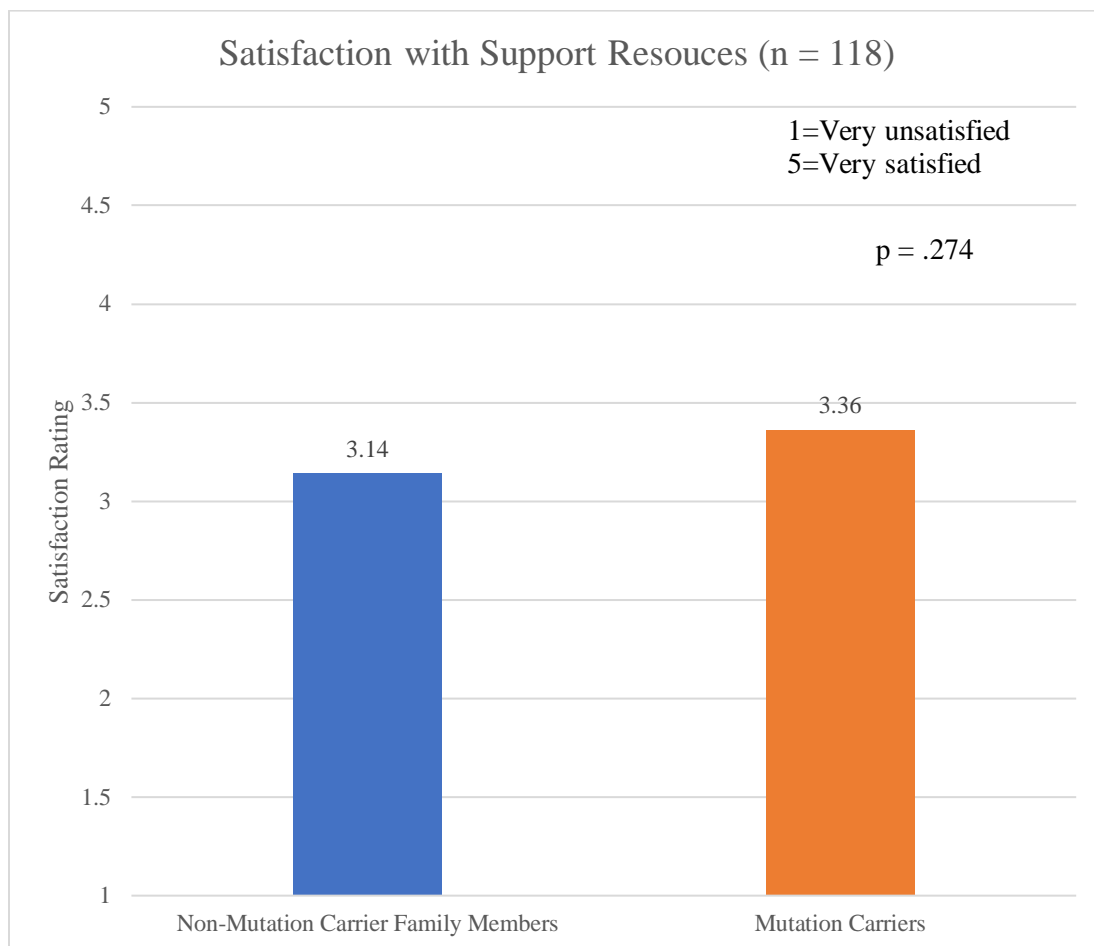
Figure 2.3 Overall satisfaction with the amount of support resources utilized between mutation carriers and non-mutation carrier family members
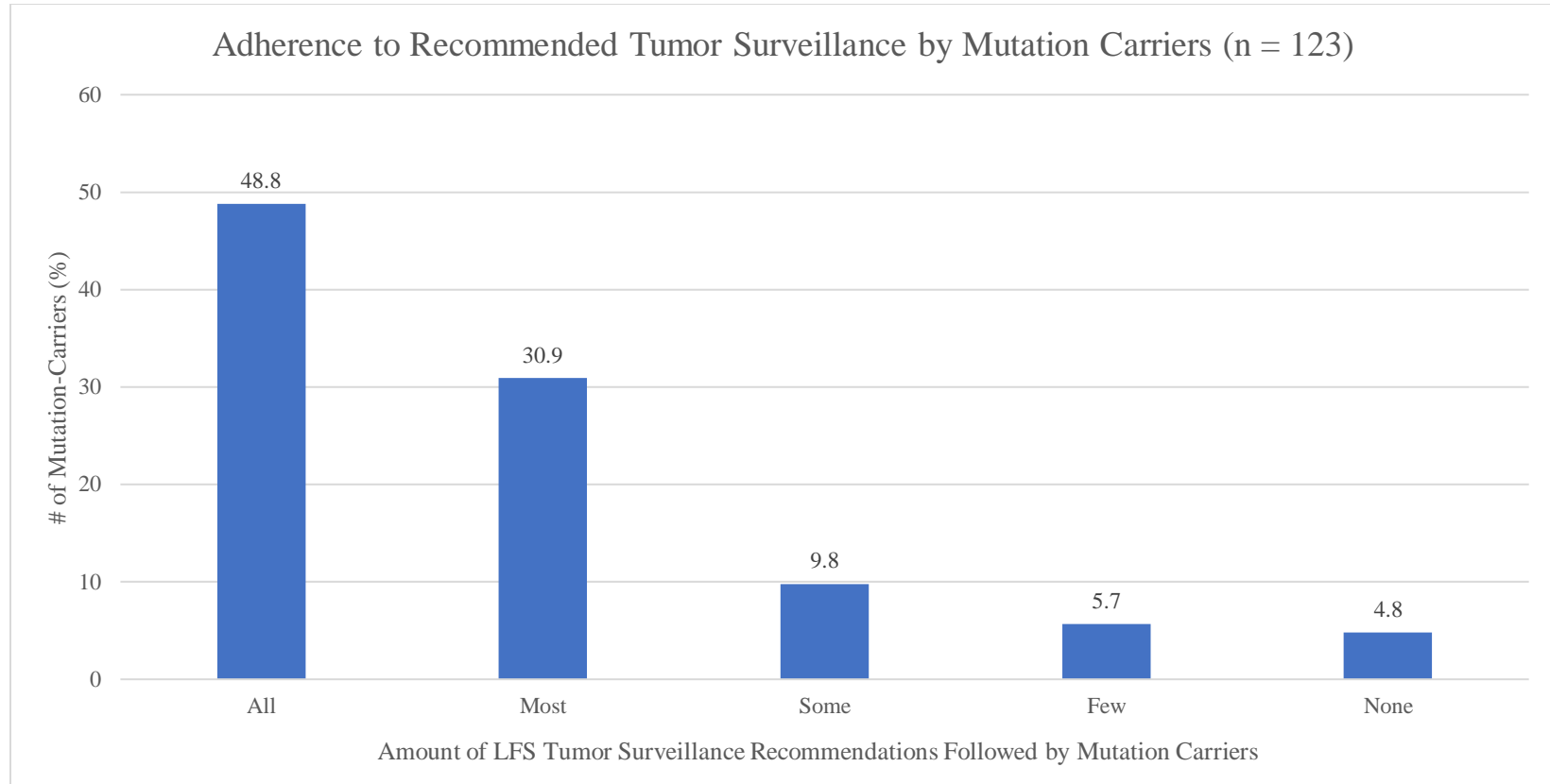
Figure 2.4 Adherence of mutation carriers to recommended LFS tumor surveillance as reported by mutation carriers or non-mutation carriers on behalf of their relative with LFS
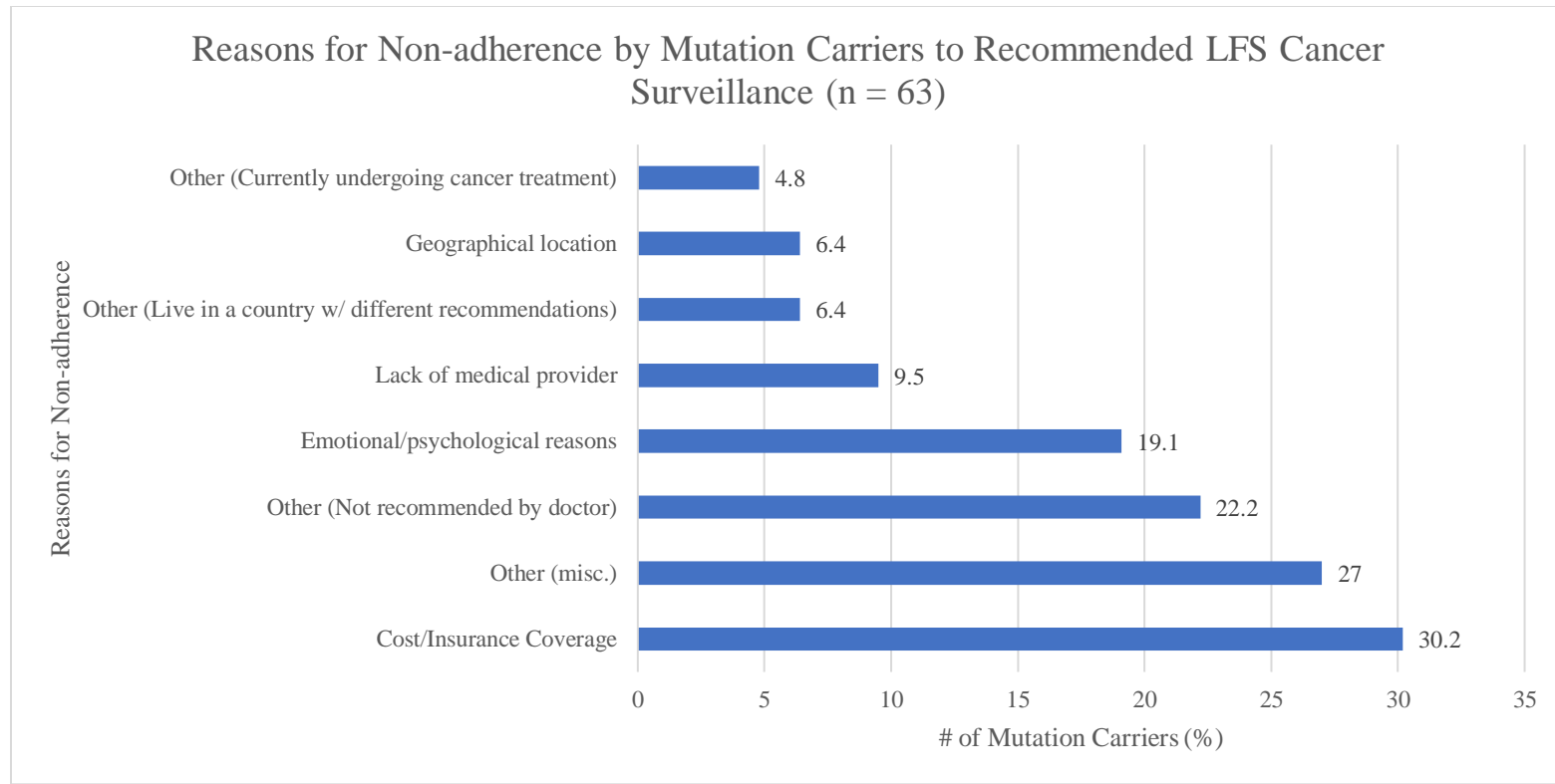
Figure 2.5 Reasons for non-adherence of mutation carriers to recommended LFS tumor surveillance as reported by mutation carriers and non-mutation carriers on behalf of their relative with LFS who indicated that did not adhere to all recommended LFS tumor surveillance recommendations (participants were able to select more than one option for this question, allowing the percentage to add up to more than 100)
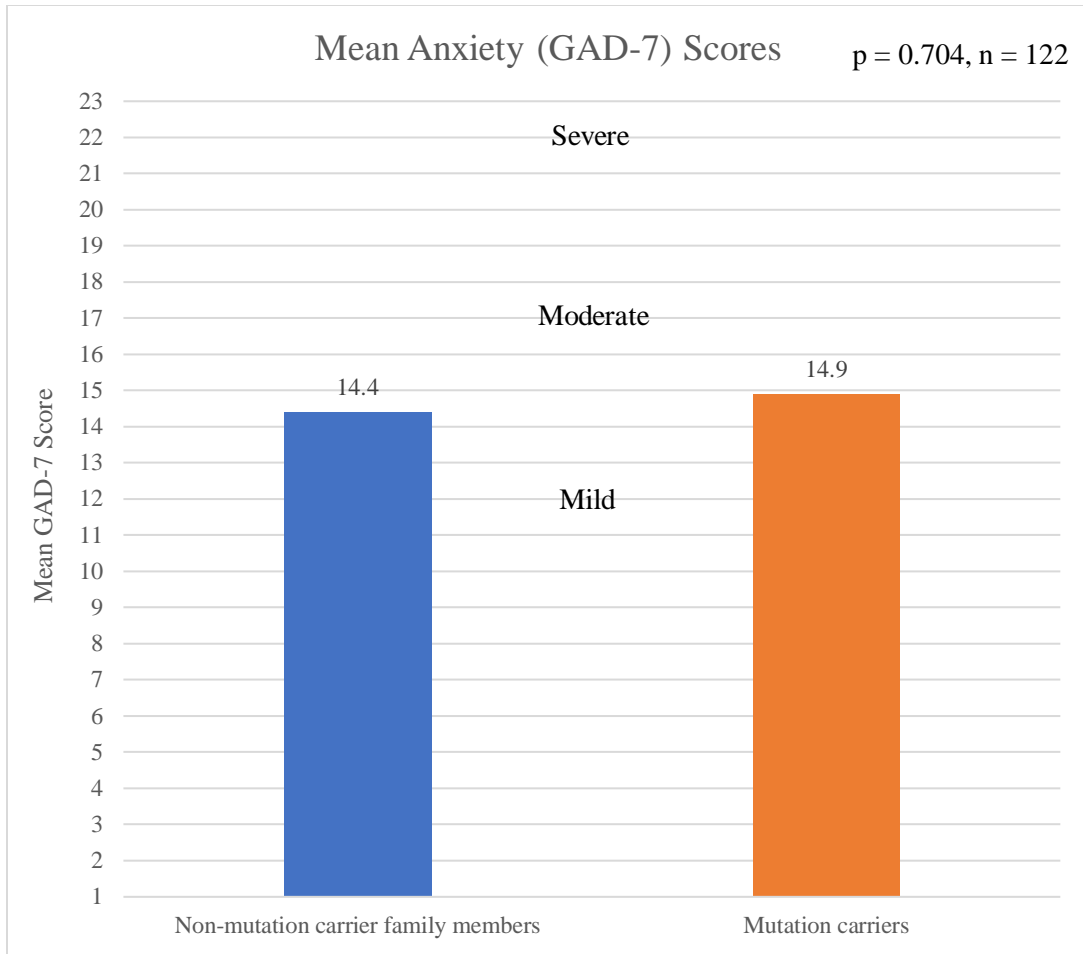
Figure 2.6 Mean general anxiety (GAD-7) scores between mutation carriers and non-mutation carrier family member
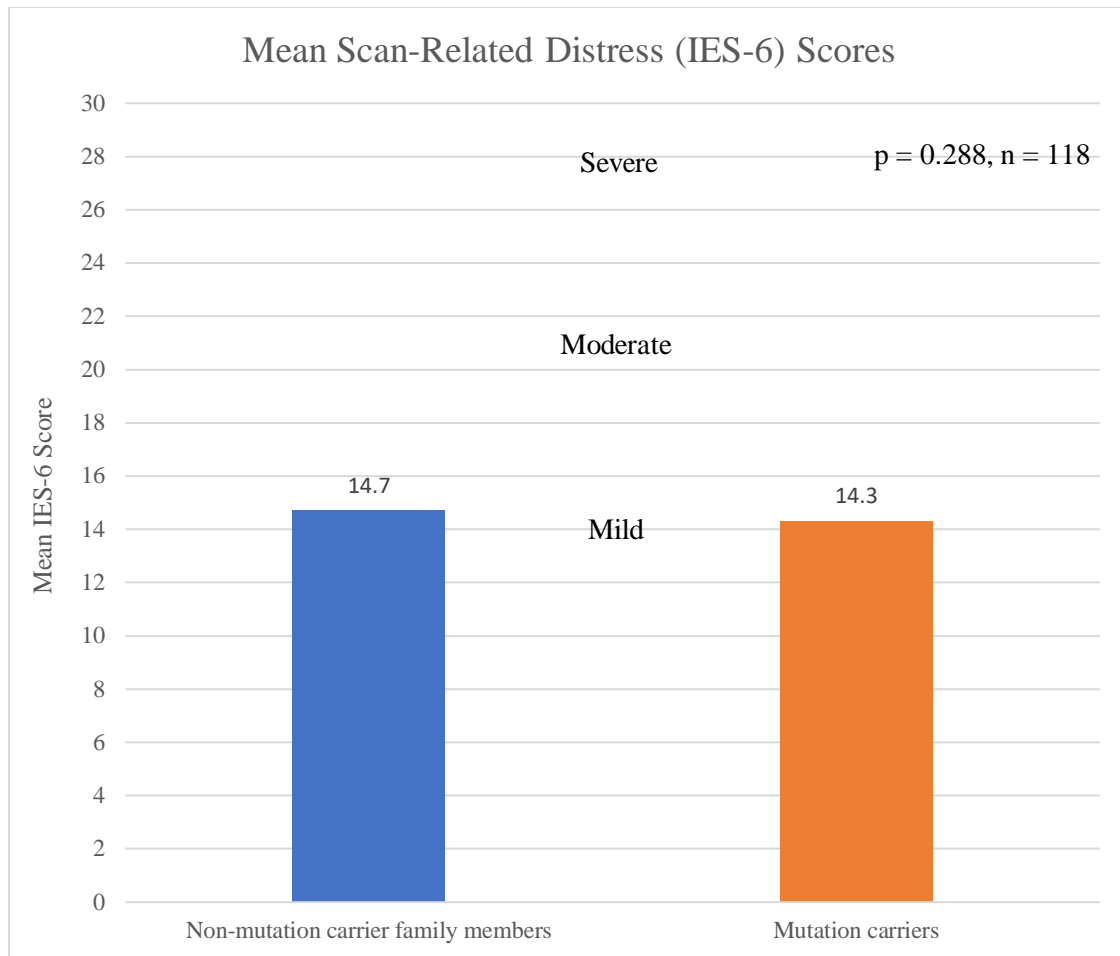
Figure 2.7 Mean scan-related distress (IES-6) scores between mutation carriers and non-mutation carrier family member

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APPENDIX A: STUDY RECRUITMENT LETTER

Hello,

My name is Emily Berenson and I am a genetic counseling student interested in the psychosocial/emotional impact of the currently recommended Li-Fraumeni syndrome (LFS) cancer/tumor surveillance on both those with a diagnosis of LFS and their family members. With the support of the Li-Fraumeni Syndrome Association and Li-Fraumeni Syndrome Association, I am conducting an 10-15 minute online survey to learn more about your experiences with LFS tumor/cancer surveillance. Please consider participating if you are over the age of 18 and have a diagnosis of LFS or if you have a family member with a diagnosis of LFS. We also strongly urge you to consider sharing the below survey links with your family members so that they may also have the option to participate in this study. Your thoughts on this important topic are very much appreciated! This study has been approved by the University of South Carolina Institutional Review Board (Pro00091625).

Please use the following link if you have a diagnosis of LFS:
https://uofsc.co1.qualtrics.com/jfe/form/SVcBEypQQiBrMUha5

Please use the following link if you do not have an LFS diagnosis but have a family member with a diagnosis of LFS:
https://uofsc.co1.qualtrics.com/jfe/form/SV_aVK051GwabcczAh

Sincerely,

Emily Berenson
Genetic Counseling Student
University of South Carolina-Columbia

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APPENDIX B: MUTATION CARRIER QUESTIONNAIRE

Thank you for your interest in participating in my master's research project. Please review the study details below prior to completing this survey.

PURPOSE AND BACKGROUND:

You are being asked to participate in our research study because you have Li-Fraumeni syndrome (LFS) or have a family member with LFS. The purpose of this study is to assess the psychosocial burden of comprehensive LFS surveillance on those with a diagnosis of LFS and their family members.

CONSENT:

By completing this anonymous survey, you are consenting to its use in this study and any future research, presentations, or publications. However, you may withdraw your consent at any time by contacting the individuals listed below.

BENEFITS/RISKS: The risks of participating in this study are minimal: you may experience negative emotions when recalling your or your family members' cancer surveillance experience. There is no direct personal benefit to participating in this study; however, your input may contribute to improved understanding of the psychosocial impact of cancer surveillance on individuals with LFS and their family members.

DURATION:

Participation in the study will take approximately 10-15 minutes.

PAYMENT TO PARTICIPANTS:

You will not be paid for participating in this study.

VOLUNTARY PARTICIPATION:

Your participation in this study is voluntary. You are free not to participate and you can choose to leave the study at any time for any reason without negative consequences. You can choose to skip (not answer) individual questions in the survey. Your answers will be anonymous (your responses cannot be linked to your personal identity) unless you provide contact information for further interview and confidential (your responses will be

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stored securely, and only accessible to members of the research team conducting the study). In the event that you do withdraw from this study, the information you have already provided will be discarded.

If you have any questions, please contact Emily Berenson, the primary investigator of the study, by email at emily.berenson@uscmed.sc.edu, or Whitney Dobek, CGC by email at whitney.dobek@uscmed.sc.edu.

End of Block: Welcome/Consent

Start of Block: Age of Participant

Q1 Are you 18 years of age or older?

○ Yes

○ No

Skip To: End of Survey If Q1=No

End of Block: Age of Participant

Start of Block: Phx/Fhx of LFS

The following questions are about your personal and family history of Li-Fraumeni syndrome.

Q2 Do you have a diagnosis of Li-Fraumeni syndrome?

○ Yes

○ No

Skip To: End of Survey If Q2=No

Display This Question:
*   If Q2 = Yes*

Q3 At approximately what age were you diagnosed with Li-Fraumeni syndrome?

_____

Q4 Do you have a family member with a diagnosis of Li-Fraumeni syndrome (select all that apply)?

○ Yes

○ No

○ Not sure

End of Block: Phx/Fhx of LFS

Start of Block: Phx of Cancer

The following questions are about your personal history of cancer.

Q5 Have you ever been diagnosed with cancer?

○ Yes

○ No

Skip To: End of Block If Q5 = No

Display This Question:

If Q5 = Yes

Q6 What type(s) of cancer were you diagnosed with?

_____

Display This Question:

If Q5 = Yes

Q7 At what age(s) were you diagnosed with cancer?

_____

End of Block: Phx of Cancer

Start of Block: Fhx of Cancer

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The following questions are about your family history of cancer.

Q8 Do you have a family history of cancer?

☐ Yes-blood/biological relative

☐ Yes-spouse/partner, adopted relative, step-relative

☐ No

☐ Not sure

Skip To: End of Block If Q8 = No
Skip To: End of Block If Q8 = Not sure

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Q9 Who in your family has been affected with cancer (select all that apply)?

☐   Biological parent

☐   Biological sibling

☐   Biological child

☐   Biological second-degree relative: aunt/uncle, niece/nephew, grandparent, grandchild (specify relative):

_____

☐   Spouse/partner

☐   Adopted relative (specify relative):

_____

☐   Step-relative (specify relative):

_____

Q10 Has anyone in your family passed away from cancer (select all that apply)?

☐ Yes-blood/biological relative

☐ Yes-spouse/partner, adopted relative, step-relative

☐ No

☐ Not sure

Q11 Who in your family has passed away from cancer (select all that apply)?

☐ Biological parent

☐ Biological sibling

☐ Biological child

☐ Biological second-degree relative: aunt/uncle, niece/nephew, grandparent, grandchild (specify relative):

_____

☐ Spouse/partner

☐ Adopted relative (specify relative):

_____

☐ Step-relative (specify relative):

_____

The following questions are about your involvement in your Li-Fraumeni syndrome surveillance.

The following are the surveillance protocols recommended by experts in Li-Fraumeni syndrome for both children and adults:

Children (birth until age 18)

-Physical exams and ultrasounds of the abdomen and pelvis every 3-4 months

-Annual brain and whole-body MRIs

Adults

-Physical exams every 6 months

-Annual brain MRIs, whole-body MRIs, mammograms/breast MRIs, ultrasounds of the abdomen and pelvis, and dermatology (skin) examinations

-Colonoscopies and upper endoscopies every 2-5 years

-Bloodwork checking for cancers of the blood (leukemia/lymphoma) every 4 months

Q12 How much of the recommended surveillance do you participate in?

○ All of these surveillance recommendations

○ Most of these surveillance recommendations

○ Some of these surveillance recommendations

○ Few of these surveillance recommendations

○ None of these surveillance recommendations

Skip To: Q15 If Q12 = All of these surveillance recommendations
Skip To: Q14 If Q12 = Most of these surveillance recommendations
Skip To: Q14 If Q12 = Some of these surveillance recommendations
Skip To: Q14 If Q12 = Few of these surveillance recommendations
Skip To: Q13 If Q12 = None of these surveillance recommendations

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Q13 Please indicate the reason(s) for not participating in any of the Li-Fraumeni syndrome cancer surveillance.

☐   Cost/insurance coverage

☐   Geographical location

☐   Lack of medical provider who can provide surveillance

☐   Emotional/psychological (for example, fear, anxiety, skepticism, exhaustion)

☐   Other (please specify):
_____

Skip To: End of Block If Q13 = Cost/insurance coverage
Skip To: End of Block If Q13 = Geographical location
Skip To: End of Block If Q13 = Lack of medical provider who can provide surveillance
Skip To: End of Block If Q13 = Emotional/psychological (for example, fear, anxiety, skepticism, exhaustion)
Skip To: End of Block If Q13 = Other (please specify):
Skip To: End of Block If Q13(Other (please specify):) Is Not Empty

Q14 Please indicate the reason(s) for not participating in parts of the Li-Fraumeni syndrome cancer surveillance.

☐ Cost/insurance coverage

☐ Geographical location

☐ Lack of medical provider who can provide surveillance

☐ Emotional/psychological (for example, fear, anxiety, skepticism, exhaustion)

☐ Other (please specify):

_____

Q15 For approximately how many years have you been undergoing surveillance for Li-Fraumeni syndrome?

Q16 How involved do you feel you are in the management of your Li-Fraumeni syndrome cancer surveillance?

○ Not involved

○ Somewhat involved

○ Very involved

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Q17 What kind of emotional and logistical support associated with the management of your LFS surveillance have you received (please check all that apply)?

☐ Online or in-person support groups

☐ Professional counseling

☐ Logistical support (for example, transportation, scheduling appointments, etc.)

☐ Financial support

☐ Other (please specify):

_____

☐ None

Q18 What kind of emotional and logistical support associated with the management of your LFS surveillance (that you have not utilized) would you have an interest in receiving (please check all that apply)?

☐ Online or in-person support groups

☐ Professional counseling

☐ Logistical support (for example, transportation, scheduling appointments, etc.)

☐ Financial support

☐ Other (please specify):

_____

☐ None

Q19 Are you satisfied with the amount of support associated with the management of your LFS surveillance that you have received?

$\bigcirc$ Very unsatisfied

$\bigcirc$ Unsatisfied

$\bigcirc$ Neutral

$\bigcirc$ Satisfied

$\bigcirc$ Very satisfied

The following questions ask about your thoughts and opinions on LFS surveillance.

Q20 Do you believe that the recommended Li-Fraumeni syndrome surveillance is effective?

$\bigcirc$ Yes (please explain): _____

$\bigcirc$ No (please explain): _____

Q21 Do you believe the benefits of the recommended Li-Fraumeni syndrome surveillance outweigh the burdens?

$\bigcirc$ Yes (please explain): _____

$\bigcirc$ No (please explain): _____

The following are the surveillance protocols recommended by experts in Li-Fraumeni syndrome for both children and adults:

Children (birth until age 18)

    -Physical exams and ultrasounds of the abdomen and pelvis every 3-4 months

    -Annual brain and whole-body MRIs

Adults

    -Physical exams every 6 months

    -Annual brain MRIs, whole-body MRIs, mammograms/breast MRIs, ultrasounds of the abdomen and pelvis, and dermatology (skin) examinations

    -Colonoscopies and upper endoscopies every 2-5 years

    -Bloodwork checking for cancers of the blood (leukemia/lymphoma) every 4 months

Q22 When you read the above description of the recommended cancer surveillance for Li-Fraumeni syndrome, what reactions and/or emotions come to mind first?

_____

Q23 When you read the above description of the recommended cancer surveillance for Li-Fraumeni syndrome, what **benefits or positive aspects** of the surveillance come to mind?

_____

Q24 When you read the above description of the recommended cancer surveillance for Li-Fraumeni syndrome, what **downsides or negative aspects** of the surveillance come to mind?

_____

End of Block: Free response questions

The following questions ask about aspects of your personality.

Q25 Over the last 2 weeks, how often have you been bothered by the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious or on edge	○	○	○	○
Not being able to stop or control worrying	○	○	○	○
Worrying too much about different things	○	○	○	○
Trouble relaxing	○	○	○	○
Being so restless that it is hard to sit still	○	○	○	○
Becoming easily annoyed or irritable	○	○	○	○
Feeling afraid as if something awful might happen	○	○	○	○

Q26 Below is a list of difficulties people sometimes have after stressful life events. Please read each item, and then indicate how distressing each one has been for you during

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the past 7 days with respect to your most recent Li-Fraumeni syndrome-related scan (for example, ultrasound, bloodwork, MRI).

	Not at all distressing	Little bit distressing	Moderately distressing	Quite a bit distressing	Extremely distressing
I thought about it when I didn't mean to	◯	◯	◯	◯	◯
I felt watchful or on-guard	◯	◯	◯	◯	◯
Other things kept making me think about it	◯	◯	◯	◯	◯
I was aware that I still had a lot of feelings about it, but I didn't deal with them	◯	◯	◯	◯	◯
I tried not to think about it	◯	◯	◯	◯	◯
I had trouble concentrating	◯	◯	◯	◯	◯

Q27 Please let us know below if there is any additional information you would like us to know about how your LFS surveillance has impacted you?

_____

End of Block: GAD-7/ISE

The following questions ask about your demographics. This section helps to classify responses among subsets of the population and will not be used in any attempts to identify you.

Q28 What is your age?_____

Q29 What is your biological sex?

○ Male

○ Female

○ Prefer not to say

Q30 What is your ethnicity?

☐ White

☐ Hispanic or Latino

☐ Black or African American

☐ Native American or Alaskan Native

☐ Asian/Pacific Islander

☐ Other (please specify):
_____

☐ Prefer not to say

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Q31 Which of the following best describes your current relationship status?

○ Married

○ Divorced/Separated

○ Widowed

○ In a domestic partnership or civil union

○ Single, but living with a significant other

○ Single/Never married

○ Prefer not to say

Q32 What is the highest degree or level of school you have completed?

○ No formal education

○ Some high school

○ High school degree or equivalent

○ Some college

○ Associate degree

○ Bachelors degree (e.g. BA, BS)

○ Graduate degree

○ Prefer not to say

Q33 What was your total household income last year?

○ Less than $25,000

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○ $25,001-$50,000

○ $50,001-$75,000

○ $75,001-$100,000

○ More than $100,000

○ Prefer not to say

Q34 What type of health insurance do you have?

○ Private insurance plan (Ex. Aetna, Cigna, etc.)

○ Medicaid/Medicare

○ No insurance

○ Other (please specify): _____

○ Prefer not to say

Q35 What is your occupation?

○ Science/technology

○ Service/retail

○ Media/communications

○ Government/non-profit

○ Business

○ Healthcare

○ Manufacturing

○ Education

○ Other (please specify): _____

○ Prefer not to say

Q36 In what part of the world do you currently reside?

○ United States

○ Canada

○ Latin America

○ Europe

○ Africa

○ Asia

○ Middle East

○ Other (please specify): _____

○ Prefer not to say

End of Block: Demographics

Start of Block: Interview Request

If you are willing to participate in a short phone interview, please provide your name, phone number, and email address in the spaces below so that we may contact you. Your name, phone number, and email address will not be used for any purpose other than to

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contact you for a follow up. This is optional and will not eliminate you from this study should you not want to be interviewed. Your participation is greatly appreciated!

Name

_____

Phone number

_____

Email address

_____

End of Block: Interview Request

Start of Block: End of Survey Notification: COMPLETED SURVEY

Thank you for taking the time to complete this survey. We hope the information that you and other participants provided will be of value to the Li-Fraumeni syndrome community. Your interest in this study is very much appreciated!

End of Block: End of Survey Notification: COMPLETED SURVEY

Start of Block: End of Survey Notification: DO NOT MEET INCLUSION

CRITERIA

Thank you for taking the time to complete this survey. Unfortunately, you do not meet the criteria for this study. Your interest is very much appreciated!

End of Block: End of Survey Notification: DO NOT MEET INCLUSION CRITERIA

APPENDIX C: NON-MUTATION CARRIER FAMILY MEMBER QUESTIONNAIRE

Thank you for your interest in participating in my master's research project. Please review the study details below prior to completing this survey.

PURPOSE AND BACKGROUND:

You are being asked to participate in our research study because you have Li-Fraumeni syndrome (LFS) or have a family member with LFS. The purpose of this study is to assess the psychosocial burden of comprehensive LFS surveillance on those with a diagnosis of LFS and their family members.

CONSENT:

By completing this anonymous survey, you are consenting to its use in this study and any future research, presentations, or publications. However, you may withdraw your consent at any time by contacting the individuals listed below.

BENEFITS/RISKS:

The risks of participating in this study are minimal: you may experience negative emotions when recalling your or your family members' cancer surveillance experience. There is no direct personal benefit to participating in this study; however, your input may contribute to improved understanding of the psychosocial impact of cancer surveillance on individuals with LFS and their family members.

DURATION:

Participation in the study will take approximately 10-15 minutes.

PAYMENT TO PARTICIPANTS:

You will not be paid for participating in this study.

VOLUNTARY PARTICIPATION:

Your participation in this study is voluntary. You are free not to participate and you can choose to leave the study at any time for any reason without negative consequences. You can choose to skip (not answer) individual questions in the survey. Your answers will be

anonymous (your responses cannot be linked to your personal identity) unless you provide contact information for further interview and confidential (your responses will be stored securely, and only accessible to members of the research team conducting the study). In the event that you do withdraw from this study, the information you have already provided will be discarded.

If you have any questions, please contact Emily Berenson, the primary investigator of the study, by email at emily.berenson@uscmed.sc.edu, or Whitney Dobek, CGC by email at whitney.dobek@uscmed.sc.edu.

End of Block: Welcome/Consent

Start of Block: Age of Participant

Q1 Are you 18 years of age or older?

○ Yes

○ No

Skip To: End of Survey If Q1=No

End of Block: Age of Participant

Start of Block: Fhx of LFS

The following questions are about your family history of Li-Fraumeni syndrome.

Do you have a family member with a diagnosis of Li-Fraumeni syndrome (select all that apply)?

☐ Yes-blood/biological relative

☐ Yes-spouse/partner, adopted relative, step-relative

☐ No

☐ Not sure

Skip To: End of Survey If Q2=No

Q3 Which family member(s) have a diagnosis of Li-Fraumeni syndrome (select all that apply)?

☐   Biological parent

☐   Biological sibling

☐   Biological child

☐   Biological second-degree relative: aunt/uncle, niece/nephew, grandparent, grandchild (specify relative): _____

☐   Spouse/partner

☐   Adopted relative (specify relative): _____

☐   Step-relative (specify relative): _____

Q4 **Think of the one relative for whom you are most involved in and/or familiar with their care.** At approximately what age was your family member diagnosed with Li-Fraumeni syndrome?

_____

Q5 Germline genetic testing is a type of medical test (usually involving a blood or saliva sample) that identifies changes or mutations in genes, such as the *TP53* gene associated

with Li-Fraumeni syndrome, that a person is born with. The results of a genetic test can confirm or rule out a genetic condition.

Have you had germline (blood or saliva) genetic testing to confirm that you do NOT have Li-Fraumeni syndrome?

○ Yes

○ No

○ Not sure

End of Block: Fhx of LFS

Start of Block: Phx of Cancer

The following questions are about your personal history of cancer.

Q6 Have you ever been diagnosed with cancer?

○ Yes

○ No

Skip To: End of Block If Q6 = No

Display This Question:
If Q6 = Yes

Q7 What type(s) of cancer were you diagnosed with?

_____

Display This Question:
If Q6 = Yes

Q8 At what age(s) were you diagnosed with cancer?

_____

End of Block: Phx of Cancer

Start of Block: Fhx of Cancer

The following questions are about your family history of cancer.

Q9 Do you have a family history of cancer (select all that apply)?

☐ Yes-blood/biological relative

☐ Yes-spouse/partner, adopted relative, step-relative

☐ No

☐ Not sure

Skip To: End of Block If Q9 = No
Skip To: End of Block If Q9 = Not sure

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Q10 Who in your family has been affected with cancer (select all that apply)?

☐   Biological parent

☐   Biological sibling

☐   Biological child

☐   Biological second-degree relative: aunt/uncle, niece/nephew, grandparent, grandchild (specify relative): _____

☐   Spouse/partner

☐   Adopted relative (specify relative): _____

☐   Step-relative (specify relative): _____

Q11 Has anyone in your family passed away from cancer (select all that apply)?

☐   Yes-blood/biological relative

☐   Yes-spouse/partner, adopted relative, step-relative

☐   No

☐   Not sure

Q12 Who in your family has passed away from cancer (select all that apply)?

☐ Biological parent

☐ Biological sibling

☐ Biological child

☐ Biological second-degree relative: aunt/uncle, niece/nephew, grandparent, grandchild (specify relative): _____

☐ Spouse/partner

☐ Adopted relative (specify relative): _____

☐ Step-relative (specify relative): _____

End of Block: Fhx of Cancer

Start of Block: LFS Surveillance

The following questions are about your involvement in your family member's Li-Fraumeni syndrome surveillance.

When answering these questions, please think of the one relative with Li-Fraumeni syndrome for whom you are most involved in and/or familiar with their care.

The following are the surveillance protocols recommended by experts in Li-Fraumeni syndrome for both children and adults:

Children (birth until age 18)
-Physical exams and ultrasounds of the abdomen and pelvis every 3-4 months

-Annual brain and whole-body MRIs

Adults

-Physical exams every 6 months

-Annual brain MRIs, whole-body MRIs, mammograms/breast MRIs, ultrasounds of the abdomen and pelvis, and dermatology (skin) examinations

-Colonoscopies and upper endoscopies every 2-5 years

-Bloodwork checking for cancers of the blood (leukemia/lymphoma) every 4 months

Q13 How much of the recommended surveillance does your family member participate in?

○ All of these surveillance recommendations

○ Most of these surveillance recommendations

○ Some of these surveillance recommendations

○ Few of these surveillance recommendations

○ None of these surveillance recommendations

Skip To: Q16 If Q13 = All of these surveillance recommendations
Skip To: Q15 If Q13 = Most of these surveillance recommendations
Skip To: Q15 If Q13 = Some of these surveillance recommendations
Skip To: Q15 If Q13 = Few of these surveillance recommendations
Skip To: Q14 If Q13 = None of these surveillance recommendations

Q14 Please indicate the reason(s) for your family member not participating in any of the Li-Fraumeni syndrome cancer surveillance.

☐ Cost/insurance coverage

☐ Geographical location

☐ Lack of medical provider who can provide surveillance

☐ Emotional/psychological (for example, fear, anxiety, skepticism, exhaustion)

☐ Other (please specify): _____

☐ Not sure

Skip To: End of Block If Q14 = Cost/insurance coverage
Skip To: End of Block If Q14 = Geographical location
Skip To: End of Block If Q14 = Lack of medical provider who can provide surveillance
Skip To: End of Block If Q14 = Emotional/psychological (for example, fear, anxiety, skepticism, exhaustion)
Skip To: End of Block If Q14 = Other (please specify):
Skip To: End of Block If Q14(Other (please specify):) Is Not Empty
Skip To: End of Block If Q14 = Not sure

Q15 Please indicate the reason(s) for your family member not participating in parts of the Li-Fraumeni syndrome cancer surveillance (select all that apply).

☐   Cost/insurance coverage

☐   Geographical location

☐   Lack of medical provider who can provide surveillance

☐   Emotional/psychological (for example, fear, anxiety, skepticism, exhaustion)

☐   Other (please specify): _____

☐   Not sure

Q16 For approximately how many years has your family member been undergoing surveillance for Li-Fraumeni syndrome?

Q17 Are you the guardian and/or sole caregiver for any of your family members diagnosed with Li-Fraumeni syndrome?Yes

○ No

Q18 Are you logistically involved in the surveillance of a family member with Li-Fraumeni syndrome in any way (i.e. scheduling appointments, driving to appointments, assisting financially with medical care)?

○ Yes (please specify involvement): _____

○ No

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Q19 How involved do you feel you are in the management of your family member's Li-Fraumeni syndrome cancer surveillance?

○ Not involved

○ Somewhat involved

○ Very involved

Q20 What kind of emotional and logistical support associated with the management of your family member's LFS surveillance have you received (select all that apply)?

☐ Online or in-person support groups

☐ Professional counseling

☐ Logistical support (for example, transportation, scheduling appointments, etc.)

☐ Financial support

☐ Other (please specify): _____

☐ None

Q21 What kind of emotional and logistical support associated with the management of your family member's LFS surveillance (that you have not utilized) would you have an interest in receiving (select all that apply)?

☐ Online or in-person support groups

☐ Professional counseling

☐   Logistical support for example, transportation, scheduling appointments, etc.)

☐   Financial support

☐   Other (please specify): _____

☐   None

Q22 Are you satisfied with the amount of support associated with the management of your family member's LFS surveillance that you have received?

◯ Very unsatisfied

◯ Unsatisfied

◯ Neutral

◯ Satisfied

◯ Very satisfied

End of Block: LFS Surveillance

Start of Block: Perceived Effectiveness of LFS Surveillance

The following questions ask about your thoughts and opinions on LFS surveillance.

Q23 Do you believe that the recommended Li-Fraumeni syndrome surveillance is effective?

◯ Yes (please explain): _____

◯ No (please explain): _____

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Q24 Do you believe the benefits of the recommended Li-Fraumeni syndrome surveillance outweigh the burdens?

○ Yes (please explain): _____

○ No (please explain): _____

The following are the surveillance protocols recommended by experts in Li-Fraumeni syndrome for both children and adults:

Children (birth until age 18)

-Physical exams and ultrasounds of the abdomen and pelvis every 3-4 months

-Annual brain and whole-body MRIs

Adults

-Physical exams every 6 months

-Annual brain MRIs, whole-body MRIs, mammograms/breast MRIs, ultrasounds of the abdomen and pelvis, and dermatology (skin) examinations

-Colonoscopies and upper endoscopies every 2-5 years

-Bloodwork checking for cancers of the blood (leukemia/lymphoma) every 4 months

Q25 When you read the above description of the recommended cancer surveillance for Li-Fraumeni syndrome, what reactions and/or emotions come to mind first?

_____

Q26 When you read the above description of the recommended cancer surveillance for Li-Fraumeni syndrome, what **benefits or positive aspects** of the surveillance come to mind?

_____

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Q27 When you read the above description of the recommended cancer surveillance for Li-Fraumeni syndrome, what **downsides or negative aspects** of the surveillance come to mind?

_____

The following questions ask about aspects of your personality.

Q28 Over the last 2 weeks, how often have you been bothered by the following problems?

	Not at all	Several days	More than half the days	Nearly every day
Feeling nervous, anxious or on edge	○	○	○	○
Not being able to stop or control worrying	○	○	○	○
Worrying too much about different things	○	○	○	○
Trouble relaxing	○	○	○	○
Being so restless that it is hard to sit still	○	○	○	○
Becoming easily annoyed or irritable	○	○	○	○
Feeling afraid as if something awful might happen	○	○	○	○

Q29 Below is a list of difficulties people sometimes have after stressful life events. Please read each item, and then indicate how distressing each one has been for you during the past 7 days with respect to your family member's most recent Li-Fraumeni syndrome-related scan (for example, ultrasound, bloodwork, MRI).

	Not at all distressing	Little bit distressing	Moderately distressing	Quite a bit distressing	Extremely distressing
I thought about it when I didn't mean to	○	○	○	○	○
I felt watchful or on-guard	○	○	○	○	○
Other things kept making me think about it	○	○	○	○	○
I was aware that I still had a lot of feelings about it, but I didn't deal with them	○	○	○	○	○
I tried not to think about it	○	○	○	○	○
I had trouble concentrating	○	○	○	○	○

End of Block: GAD-7/ISE-6

Start of Block: Demographics

Q30 Please let us know below if there is any additional information you would like us to know about how your family members' LFS surveillance has impacted you?_____

The following questions ask about your demographics. This section helps to classify responses among subsets of the population and will not be used in any attempts to identify you.

Q31 What is your age?_____

Q32 What is your biological sex?

○ Male

○ Female

○ Prefer not to say

Q33 What is your ethnicity (select all that apply)?

☐ White

☐ Hispanic or Latino

☐ Black or African American

☐ Native American or Alaskan Native

☐ Asian/Pacific Islander

☐ Other (please specify): _____

☐ Prefer not to say

Q34 Which of the following best describes your current relationship status?

○ Married

○ Divorced/Separated

○ Widowed

○ In a domestic partnership or civil union

○ Single, but living with a significant other

○ Single/Never married

○ Prefer not to say

Q35 What is the highest degree or level of school you have completed?

○ No formal education

○ Some high school

○ High school degree or equivalent

○ Some college

○ Associate degree

○ Bachelors degree (e.g. BA, BS)

○ Graduate degree

○ Prefer not to say

Q36 What was your total household income last year?

○ Less than $25,000

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○ $25,001-$50,000

○ $50,001-$75,000

○ $75,001-$100,000

○ More than $100,000

○ Prefer not to say

Q37 What type of health insurance do you have?

○ Private insurance plan (Ex. Aetna, Cigna, etc.)

○ Medicaid/Medicare

○ No insurance

○ Other (please specify): _____

○ Prefer not to say

Q38 What is your occupation?

○ Science/technology

○ Service/retail

○ Media/communications

○ Government/non-profit

○ Business

○ Healthcare

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○ Manufacturing

○ Education

○ Other (please specify): _____

○ Prefer not to say

Q39 In what part of the world do you currently reside?

○ United States

○ Canada

○ Latin America

○ Europe

○ Africa

○ Asia

○ Middle East

○ Other (please specify):_____

○ Prefer not to say

End of Block: Demographics

Start of Block: Interview Request

If you are willing to participate in a short phone interview, please provide your name, phone number, and email address in the spaces below so that we may contact you. Your name, phone number, and email address will not be used for any purpose other than to

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contact you for a follow up. This is optional and will not eliminate you from this study should you not want to be interviewed. Your participation is greatly appreciated!

Name

_____

Phone number

_____

Email address

_____

End of Block: Interview Request

Start of Block: End of Survey Notification: COMPLETED SURVEY

Thank you for taking the time to complete this survey. We hope the information that you and other participants provided will be of value to the Li-Fraumeni syndrome community. Your interest in this study is very much appreciated!

End of Block: End of Survey Notification: COMPLETED SURVEY

Start of Block: End of Survey Notification: DO NOT MEET INCLUSION CRITERIA

Thank you for taking the time to complete this survey. Unfortunately, you do not meet the criteria for this study. Your interest is very much appreciated!

End of Block: End of Survey Notification: DO NOT MEET INCLUSION CRITERIA

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APPENDIX D: PHONE INTERVIEW GUIDE

<u>Interview Questions:</u>

Support/Resources

How did you come to join the Living LFS support group? (first question in interview)?

- Tell me about your experience with any other support groups, professional counseling, or other support resources that you have participated in or utilized.

-What has been the most helpful aspect, the most unhelpful aspect of these support resources?

Coping Mechanisms/Styles

When you are feeling overwhelmed or stressed about your or your family member's LFS management/surveillance, how do you typically handle it?
-What helps? What doesn't help?

Protective buffering:

Noncarrier-How do you communicate with your family member(s) with LFS about any negative emotions/frustrations/fears you have related to surveillance?

Affected with LFS-How do you communicate with your family members without LFS/with LFS (if applicable) about any negative emotions/frustrations/fears you have related to surveillance?

Noncarriers-What advice do you have for people dealing with family members going through LFS surveillance?

Affected with LFS-What advice do you have for people going through LFS surveillance?

Can you expand on your answer to question _____ from the survey?

FINAL QUESTION: Is there anything you would like to add or have we missed something you think is important?