

## ABSTRACT

**Title of Dissertation:** COUPLES COPING WITH LI-FRAUMENI SYNDROME: A MIXED-METHODS STUDY OF FAMILY STRENGTHS

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Using mixed methodology involving qualitative and quantitative data, this dissertation fills gaps in knowledge regarding psychosocial implications for families living with the genetically-transmitted Li-Fraumeni cancer susceptibility syndrome, specifically targeting couple dyads. An initial review of the existing literature on couples coping with heritable cancer syndromes identified gaps in knowledge, and pointed to future directions for research in this area. The three papers that comprise this dissertation provide multiple perspectives on the levels of distress, coping styles, and social support patterns of couples in which one partner is at high risk of cancer. The first paper investigates spousal distress and coping styles in relation to cancer worry for individuals with Li-Fraumeni Syndrome, using quantitative data from one of the largest existing collections of Li-Fraumeni Syndrome cases. The second paper identifies couples' coping and communication processes regarding cancer stressors, using semi-structured qualitative interviews of individuals with Li-Fraumeni Syndrome and their partners. The third paper utilizes a social network approach to illustrate shared patterns of emotional,

tangible, and informational support that couples report accessing. The integrated findings from these three studies indicate that these subjects are low in general distress but high in cancer-specific worry. Couples cope with this worry by balancing multiple roles, exercising flexibility in family dynamics, and utilizing extensive social support networks. This research provides significant information that can aid in development of effective interventions for couples as they face their ongoing threat of cancer. Recommendations for clinical work with this population include an integrated blend of couple therapy, genetic counseling, and oncology practice that is sensitive to the unique needs of individuals with heritable cancer syndromes and their partners.

COUPLES COPING WITH LI-FRAUMENI SYNDROME  
A MIXED-METHODS STUDY OF FAMILY STRENGTHS

by

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Dissertation submitted to the Faculty of the Graduate School of the  
University of Maryland, College Park, in partial fulfillment  
of the requirements for the degree of  
Doctor of Philosophy  
2018

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## DEDICATION

This dissertation is dedicated to couples and families who shared their vulnerabilities, strengths, and incredible life stories with me. I am honored to have been a part of these intimate conversations. My husband found this quote and it perfectly embodies the spirit of love, balance, and support that I observed in these couples, a phenomenon that I tried to represent in this work.

### **“A Marriage” by Michael Blumenthal**

You are holding up a ceiling  
with both arms. It is very heavy,  
but you must hold it up, or else  
it will fall down on you. Your arms  
are tired, terribly tired,  
and, as the day goes on, it feels  
as if either your arms or the ceiling  
will soon collapse.

But then,  
unexpectedly,  
something wonderful happens:  
Someone,  
a man or a woman,  
walks into the room  
and holds their arms up  
to the ceiling beside you.

So you finally get  
to take down your arms.  
You feel the relief of respite,  
the blood flowing back  
to your fingers and arms.  
And when your partner's arms tire,  
you hold up your own  
to relieve him again.

And it can go on like this  
for many years  
without the house falling.

## ACKNOWLEDGEMENTS

There are many people without whom this dissertation would not have been possible, and I wish to express my sincere gratitude and appreciation to them all.

First, I thank my dissertation chair, Dr. Norman Epstein. I am so grateful to have had such a dedicated and considerate advisor for my entire six years at the University of Maryland. How fateful it was to meet you at a dinner in Beijing so many years ago! You taught me so much about being a successful researcher, writer, and therapist. Thank you for always supporting me (even when you knew I was doing too much), giving me chips shaped like Wisconsin, and taking me to see puppies at WCC. Your calm and open approach to mentoring me was always so comforting. I will forever be grateful for your support and guidance during this journey.

Dr. Mark Greene, thank you for being an incredible mentor and guiding force during my time at NCI. My experience as a pre-doctoral fellow has provided me with opportunities I never could have imagined, conducting cutting-edge health research with talented clinical researchers. Thank you for your unwavering support of psychosocial research, for reading all my papers in incredible detail, and for challenging my imposter syndrome with your sincere belief in me and my work.

I also want to thank the other members of my committee for their insight and expertise: Dr. Allison Werner-Lin, thank you for taking me under your wing. Even from a distance, I always felt that you were involved and invested. I have learned so much from your creative mind, kind heart, and qualitative savvy. Dr. Amy Lewin, thank you for your positivity, encouragement, and reminding me that this is just another assignment. I deeply value our chats about balancing career and family life as a professional woman, you are an inspiration! Dr. Kevin Roy, thank you for sharing your love of qualitative research and theory. Your belief in me and help in this process has been invaluable. Dr. Greg Hancock, you are one of the best instructors I have ever had and I hope to someday emulate your passion for your students. Thank you for instructing me in structural equation modeling and welcoming all the family science students into your courses. Thanks for all Skype calls, statistical guidance, and much needed humor.

To Dr. Sharon Savage, Dr. Laura Koehley, Dr. Jennifer Loud, and Dr. Maria Isabel Achatz: without your leadership and support, I would have never had the opportunity to work on this important topic. Thank you for being such amazing pioneers and educators in your fields. To my dissertating partner in crime, Dr. Rotana Alsaggaf... WE DID IT! Having you next to me during every step of the process kept me grounded and sane. To the rest of my CBG friends and family: Renee (for keeping me hydrated with bubbly water), Payal, Megan, June, Kelvin, and Maria, thank you for always pleasantly distracting me, explaining genetics to me, and asking how you could help. Y'all are the best, most supportive co-worker group ever. Special thanks to Jenny, Jessica, Ashley, and Lori for their invaluable help in this research!

To my wonderful friends and PhD buddies: Emily, Leah, Joclynn, Shana, Jen, Rianna, Ally, Deirdre, Allison, Jenna, Lauren, Towanda, Diana, Kecia, Maya, Mama Cohen, and Martine, y'all are amazing, strong women and I am so grateful to have you as my friends. Shout out to my PhD guys: Ryan, Sam, and Shawn. I respect you for being the few men in the room and for venting, giggling, and struggling with me.

I will never be able to fully express my gratitude for the love and support of my family. To my father: my first academic advisor and always my strongest feminist supporter. Thank you for your jokes, stories, financial guidance, and lessons on how to live life in the way of the Buddha. To my mother: thank you for loving me so deeply and always making sure I am taking care of myself. I appreciate your phone calls, delicious meals, and the incredible culture and sense of family that you have surrounded me with. 收入后土田人前。 My success in life are all thanks to the gifts you two have given me. To my brother and best friend, Ricky: I don't know what I would do without you. You are always there for me when I need help, a drink, or for some yummy food adventures.

Lastly, to my little formed family: Demetrius, Chicken, and Egg. It has not been an easy road down the PhD path, but the brightness you all brought to it in our little Baltimore row home has filled my life with joy. Thank you, Demetrius, for everything. For your delicious creations, for cleaning the house, for being the best listener and giving me advice (when I would take it), and for always believing in me (I got the bug!). As we close this wonderful chapter of our life together, I'm so grateful I chose to experience it with you. Looking forward to many future adventures together in San Francisco!

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## CHAPTER 1: INTRODUCTION

### Statement of the Problem

Cancer genetics and inherited risk of developing cancer have significant health and psychological implications for individuals and their families. Inherited (germline) genetic mutations underlie 5-10% of all cancers, and researchers have identified more than 50 hereditary cancer syndromes that may predispose carriers to certain types of cancer (Berger, 2011; Lindor, McMaster, Lindor, & Greene, 2008). Within the field of heritable cancer syndromes, research has focused on the process of genetic testing, early screening, cancer prevention, and risk-reduction. A growing body of work regarding the psychological, relational, and emotional effects of genetically heritable cancer exists alongside this corpus of medical prevention and intervention research.

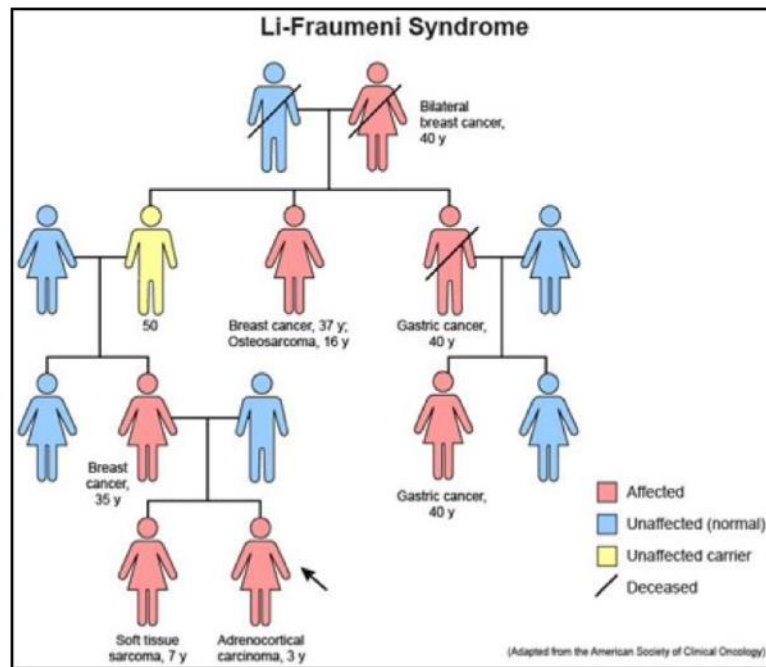
The nature of heritable cancer syndromes inherently lends itself to family studies. Not only are multiple family members across generations and genders at elevated risk of cancer; the family unit as a whole must cope with each new cancer diagnosis, genetic testing results, cancer treatment, and cancer prevention strategies. Family relationships among siblings, parents and children, cousins, spouses, *etc.* can all be affected, based on the course of the cancer diagnosis, treatment, and prevention strategies. However, research regarding the implications of cancer syndromes for family relationships is still in the formative stages. The limited research literature has shown that social support is very important in helping family members cope with cancer syndromes, and this includes support within families in terms of tangible assistance and emotional connections (Peters et al., 2016).



To best capture the complex nature and effects of genetically heritable cancer syndromes in the family context, this dissertation employed multiple research methods, including a quantitative study based on psychological assessment questionnaires, a qualitative study derived from semi-structured interviews with couples, and a social network analysis of quantitative data derived from interviews with individual partners about their social support networks. These three empirical studies and associated papers focused on one specific hereditary cancer susceptibility disorder, the Li-Fraumeni Syndrome (LFS), to best illustrate its effects on family relationships and the couples coping strategies associated with this challenging syndrome.

LFS is an autosomal dominant cancer predisposition syndrome, typically characterized by early age at cancer diagnosis and a high lifetime cancer risk. The overall cancer risk associated with LFS is estimated to be 50% by age 40 and as high as 90% by age 60 (Mai et al., 2016), with the most common cancers being early-onset breast cancer, osteosarcoma, soft tissue sarcoma, brain tumors, leukemia, and adenoid cystic carcinoma (more details about LFS can be found in the following chapter). Women with LFS have higher aggregate risks of all cancers combined due to the very high risk of female breast cancer. Individuals with LFS also have a substantial risk of multiple primary cancers, starting in childhood. Given the complexity of the syndrome and the stressors it creates for family members, to date there has been little research on its psychosocial effects on individuals and their families. The present dissertation was designed to help fill that gap in knowledge. Figure 1 below illustrates a typical LFS family pedigree.

**Figure 1. Illustrative Pedigree of an LFS Family**



Considering the limited amount of existing psychosocial research regarding LFS, the following review of literature focuses more broadly on couples' psychological and emotional coping with a member's cancer status in the context of newly diagnosed sporadic cancers, and other heritable cancer syndromes such as Lynch Syndrome, Von Hippel-Lindau (VHL), and Heritable Breast and Ovarian Cancer (HBOC). By broadening our attention to studies on family relationships and family functioning in other cancer syndromes, we may identify the unique aspects of individual and partner coping in LFS. In addition, HBOC is more common and more intensively studied, having a larger body of literature investigating dyadic processes. The goals of this literature review are twofold. The first is to identify specific gaps in existing couples research regarding heritable cancer syndromes and provide suggestions for future directions of study. The second goal is to synthesize the existing literature to propose clinical implications and provider recommendations for supporting these couples as they face a future that inevitably

involves dramatically elevated risks of cancer. This type of cancer syndrome requires life-long coping skills and social support. Many of the current psychological interventions focus on acute treatment once a patient has been diagnosed with a cancer. These skills are useful for people with a heritable cancer syndrome, but they do not address the more long-term complications and anticipatory emotional distress that can cause strain and burdens on a relationship. The literature review elaborates on the nuanced framework that is required for professional teams to develop adequate forms of care for people with heritable cancer syndromes and their families.

Since LFS is a rare syndrome, and related psychosocial research is limited, this investigator applied multiple research methods to investigate the dyadic experience of coping with an LFS diagnosis within couples. Quantitative research methods using relatively precise standardized measures with established reliability and validity have the most potential to produce findings that can be generalized, whereas qualitative studies can provide more in-depth understanding of individuals' life experiences, and generate novel hypotheses that warrant further investigation. Mixing qualitative and quantitative research methods may also provide deeper exploration of causal pathways, interpretation of meanings that individuals attach to their experiences, and contextual factors that may mediate or moderate the topic of study. Consequently, findings from this multi-method investigation of how stresses of heritable LFS influence couple relationships and how partners cope with cancer risk can broaden current knowledge and lead to evidence-based recommendations for clinicians working with couples affected by such syndromes. This set of studies emphasizes that cancer genetics is neither solely an individual nor biomedical matter, but rather a familial and psychosocial issue, and clinical practice and research must be expanded to look at the broader social and familial context.

## Theoretical Framework: Family Stress and Resilience

The family stress and resilience framework guided this investigation into the stressors (the threat of cancer, as well that associated with cancer screening and treatment procedures) and coping processes of couples facing LFS and how couple relationships are influenced by their ability to cope with such a significant set of stressors. According to Allen and Henderson (2017), family stress and resilience theory combines two important family theories: family stress theory and risk and resilience theory. Family stress theory (the ABCX model) focuses on how individuals experience and respond to life stressors that challenge their ability to cope, depending on their resources (*versus* vulnerabilities) and perceptions (Boss, 1987). According the ABCX model, *A* is the stressful event, *B* equals family resources or strengths, and *C* is the family's perception of the stressor event, or how they define or attribute meaning to the event (Hill, 1958). Stressor events can vary along a number of dimensions, such as acute *versus* chronic, and normative *versus* non-normative. Thus, an LFS diagnosis is a chronic stressor that is relatively non-normative or unusual.

In the ABCX model, if a couple or family lacks adequate resources for coping with a stressor and has negative perceptions of the stressor (*e.g.*, as overwhelming), this can lead to a crisis state of disequilibrium and deterioration in functioning (*e.g.*, debilitating individual anxiety and intra-couple conflict), the *X* component of the model. However, in the presence of effective resources (*e.g.*, good couple communication) and constructive perceptions (*e.g.*, “We will face this cancer threat together as a couple, and make wise decisions about the best medical procedures to use to stay healthy.”), a couple is more likely to weather the stressors, both as individuals and as a dyad. Individuals in a couple or family have their own personal resources, but the couple or family unit also has

resources as a group (*e.g.*, cohesiveness and mutual emotional support) that can help the members stay healthy and moving forward, even in the face of adversity (Patterson, 2002).

In response to a stressor, families develop specific strategies and roles for coping with the current challenges associated with that stressor. Coping in the context of a new cancer diagnosis involves the family's ability to adapt functionally to both the immediate distress of the diagnosis and treatment, and to make long-term adjustment to life changes (Burke, 2009). Family coping may involve shifts or changes in roles and responsibilities, communication, and how family members deal with conflict. Some family stressors that may interfere with successful coping could include loss of daily routine, physical symptoms, loss of confidence, feelings of isolation, loss of financial security, and feelings of guilt or resentment. A weakness with the ABCX model is its focus on specific, isolated stressors that require a family response. Given the long-term nature of life with LFS, it is important to consider how multiple coping styles may be employed at different time points in response to different stressors. Additionally, if families are carrying a low level of stress constantly (*i.e.*, cancer worry), they may need to develop regular or daily strategies for creating positive meaning in their lives. Some families may avoid the stressor developing into a crisis state of disequilibrium and deterioration by using coping resources that help them tolerate the stress and/or hold the degree of stress to a low level. However, in the stress and coping model, it is unclear how a family would cope with simultaneous acute (cancer diagnosis) and chronic stressors (constant vigilance and prevention actions). This dissertation aims to address this ongoing process of coping and family adaptation, utilizing aspects of family resilience theory, which extends theory and research on stress and coping.

The second component of the framework utilized in the present set of dissertation studies is the risk and resilience perspective (Demo, Aquilino, & Fine, 2005), which explores how families react to experiences in ways that can either produce negative outcomes (risks), as well as their ability to overcome life challenges and grow stronger (resilience). If families are able to cope and adapt in a dynamic manner, they can rebound positively within the context of adversity. Resilience is not simply innate in humans, but involves a complex interplay of multiple risk and protective processes that are influenced by individual, interpersonal, socioeconomic, and cultural factors (Walsh, 2012). Using this frame of reference, families that have genetic or social vulnerabilities, can counterbalance these risks with positive influences at multiple levels.

On the family level, supportive relationships can nurture individuals through attachment, support, and encouragement. Walsh (2007) discusses how the family resilience perspective moves away from the deficit-based lens of viewing families, to seeing families as having the potential to heal and grow from the challenges and adversities that they face. Over time, families transition and develop, and variable coping strategies must be employed for short-term crises or long-term chronic needs. This view of multiple, complex changes to the family system maps well onto families living with LFS. This dissertation will address how some families thrive by making meaning out of their adversity, maintaining flexibility and connectedness, and utilizing their social and economic resources (*i.e.*, mobilizing social networks, building financial security, and integrating into larger health systems). The processes for building and maintaining family resilience require clear communication, open emotional expression, and collaborative problem-solving.

Cancer experiences profoundly affect patients' and their relatives' lives. Much of the psychosocial literature has focused on the negative consequences of living with cancer; however, our study of resilience may enable providers to promote more positive psychosocial outcomes before, during, and after the cancer experience (Molina et al., 2014). For all phases of the cancer continuum, resilience descriptions in the literature have included preexisting or baseline characteristics of patients and their family members, such as demographics and personal attributes (e.g., optimism, social support), mechanisms of adaptation such as coping and constructive interactions with medical personnel (e.g., positive provider-family communication), as well as positive psychosocial outcomes including growth and improved quality of life after "bouncing back" from the initial negative impact of a cancer diagnosis. Families can provide their members a sense of stability and understanding that enables healing, particularly through the use of shared rituals, spirituality, and cultural or ethnic traditions (Walsh, 2007). For health services providers, promoting resilience is a critical element of patient psychosocial care.

Walsh (2012) posits that stressors and challenges are inherent in the human condition. Her concept of family resilience involves the potential for recovery, repair, and growth in families facing serious life challenges. Although some families are shattered by major stressors, disruptive transitions, or persistent hardship that develop into destructive crises, other families are, remarkably, able to emerge strengthened, more resourceful and better prepared to move forward with their lives.

Taken together, family stress and resilience theory addresses how families are prepared for, deal with, and learn from stress and risk (Allen & Henderson, 2017). This dissertation draws on key constructs from family stress theory and risk and resilience

theory to understand how couples living with LFS cope with the unique stressors of genetic testing, high cancer risk, intense cancer screening and the need to consider risk-reducing surgery.

The research questions and hypotheses of the present three studies were informed by tenets of family stress and coping theory and resilience theory. The first study examined the general distress, cancer-specific distress, and coping styles of individuals with LFS and their partners. From a family stress and coping perspective, the various types of stressors associated with an LFS diagnosis are likely to be associated with an increase in couples' levels of emotional distress and the risk of individual and relational problems in functioning. The ABCX model also suggests that the members of the couple will respond to the stressors with various specific coping strategies, so our study examined the degree to which both partners' coping styles may affect the LFS-diagnosed individual's functioning.

The second study investigated how couples cope with the challenges of LFS, paying particular attention to the shared strength or resilience that is built between two partners. This study explored some of the key processes in family resilience such as communication, problem-solving, and meaning-making (Walsh, 2007). This exploratory study considered whether there were any patterns of coping across couples, especially in the face of *ambiguous danger* related to cancer risk of family members. Family stress, coping, and resilience concepts emphasize the family preparation and response to life challenges. These constructs draw attention to how families learn from stressful events and how life lessons are communicated among family members. In the context of LFS, families may be faced with multiple stressors (genetic testing results, multiple acute cancers, risk-reducing surgery, frequent cancer screening), and this study assessed how



these stressors affected the quality of the couple relationship. Given the importance of multiple independent primary cancers in LFS, the study focused how couples coped and created shared belief systems across extended periods of time and multiple stressors.

The third study focused on family psychosocial distress and communal coping from a social networks perspective, exploring the shared supports and mutual exchanges of resources within couple dyads. The social network perspective is a social science which focuses on the joint activities and exchanges between participants in a social system (families in this study). Wasserman & Faust (1994) define a social network as a group of individuals and the relation or relations that define them. The core concepts of the social network perspective are: 1) “actors” are the main social unit and the core of social network analysis; in this study the actors are the two partners that are married to each other; and 2) “ties” capture how actors are connected to one another (behavioral interaction, physical connection) by marriage. Utilizing the “dual ego-centric” approach (Faust, 2007), a social network analysis tool commonly used to count directly the frequencies of relationship configurations in the data, we can visualize and quantify the actors and their ties to each other and the people around them.

A variety of protective factors may interact with risk factors to buffer couples from the negative effects of cancer(s), and the social network perspective focuses on the role of the partners’ social support resources. The aim of this study was to explore how much couples relied on their partners for various forms of support and how much their family and friend networks overlapped. It is not well understood whether or how mutual support between members of a couple, or the size of their shared networks, may contribute to the effectiveness of social support in reducing the level of distress of these couples. My study investigated whether higher levels of shared support and reciprocal

support in LFS couple relationships were associated with lower levels of distress. The utilization of these shared social resources may provide insight for organizational patterns that may be helpful to other families dealing with ambiguous cancer risks.

## CHAPTER 2: LITERATURE REVIEW

There multiple varieties of hereditary cancer syndromes, varying by age-at-onset, specific cancers implicated, mode of inheritance, *etc.* This chapter focuses on Hereditary Breast/Ovarian Cancer (HBOC) and LFS, summarizing the prevalence and penetrance of each syndrome, the unique psychosocial implications of each syndrome for individuals with the syndrome and their partner, as well as recommendations to health professionals for providing patient- and couple-centered care. The published literature regarding psychosocial functioning of couples affected by heritable cancer syndromes is sorely lacking, and consequently there exists a significant limitation in healthcare professionals' abilities to provide evidence-based care to these individuals and their partners. To address this gap in knowledge, and to help develop guidelines for the design of appropriate medical and psychological support structures, this review draws on the psychosocial literature on couples coping with cancer, research on cancer caregiver burden, and the specific research regarding functioning of couples with HBOC and LFS. I present an argument for conceptualizing and treating genetic cancer syndromes as conditions that are chronic, relapsing, or intermittent in nature, and as such it is crucial that on-going support structures be developed for people and families affected by them.

The field of heritable genetic cancer syndromes and psychosocial research has focused on the functioning of individuals with the germline genetic mutation that causes each disorder. Findings regarding the individuals' coping, stress levels, perceived ability to manage symptoms, and care have provided useful insights into how the medical community can best support them when they receive their genetic testing results. However, the main purpose of this review is to shed light on the impact that the genetic

diagnosis can have on the relationship dynamics between individuals with an elevated risk of cancer and their romantic partners. Long-term partners have been consistently identified in medical research as playing major influential roles in lives of individuals who have cancer or are recovering from cancer. The partner's own health behaviors, support for the individual with cancer, and the couple's relationship quality all play significant roles in the individual's emotional, social, and physical outcomes.

This review first considers the importance of a couple-specific contextual approach in heritable cancer syndrome research. Second, the existing literature on couple functioning in these two prototypic heritable cancer syndromes is described. Finally, recommendations are proposed for health care practitioners, mental health clinicians, and genetic counselors who work with these families, to facilitate their employing a more family-forward model of support and treatment. In this way, future research and interventions increasingly can be extended beyond the patient to their partner and family.

### **Couples and Cancer**

Traditionally, the focus of cancer care and its research has been on the individual experiences of patients or their spousal caregivers, but there has been a shift toward looking more closely at caregiver-patient dyads (Q. Li & Loke, 2014). This attention to the transactions between caregivers and patients as care partners can provide useful insights regarding the reciprocal nature of stress and support in these close relationships (Fletcher, Miaskowski, Given, & Schumacher, 2012). Several conceptual models have been identified that specifically target caregiver-patient dyads in the cancer population. The relationship intimacy model addresses the psychosocial adaptation of couples to cancer (Manne & Badr, 2008), and highlights the importance of the couple's relationship

and their engagement in communication styles that sustain and/or enhance the relationship during times of stress. Communication is defined as a transactional process in which individuals create, share, and regulate meaning; it is an essential part of the support that patients and caregivers provide for each other. Research suggests that this population has a desire for increased communication and openness.

In the other conceptual model, proposed by Fletcher et al. (2012), caregiver-cancer patient dyads are conceptualized as a functional unit, with their mutuality involving three dyad-level concepts: “communication,” “reciprocal influence,” and “caregiver-patient congruence.” Reciprocal influence refers to the effects that two members of a dyad have on each other. The concept of reciprocal influence has expanded previous literature that simply focused on the influence of the patient’s illness and need for assistance on caregivers. More recent findings illustrate how the stress process is reciprocal on multiple dimensions, and aspects such as caregiver and patient well-being, role adjustment, mental health, psychological distress, physical health, and quality of life appear to be interrelated (Bambauer et al., 2006; Chen, Chu, & Chen, 2004; Kim et al., 2008).

A third model, proposed by Sullivan (Sullivan, 2012), is the Communal Coping Model, which has previously been applied to pain communication. Communal coping refers to couple members holding a shared assessment of a health threat and vision of shared action about how to manage the event (Lyons, Mickelson, Sullivan, & Coyne, 1998). This model involves: a) one or both members of the couple holding the belief that a joint effort is advantageous, needed, or useful; b) partners communicating about the situation; and c) partners cooperating to solve problems (Lewis et al., 2006).

Caregiver-patient congruence emphasizes the synthesis of data from individual members of a relationship into a dyadic variable. For example, related terms such as agreement, concordance, or disparity address the level of congruence between a patient's and caregiver's experiences. One study used a promising conceptual approach, the Actor-Partner Interdependence Model, and structural equation modeling to explore the effect of partners' dissimilarity in distress on the caregiver's quality of life (Kim et al., 2008). Results from the latter study revealed that, although each person's psychological distress was the strongest predictor of their own quality of life, partner's distress and (dis)similarities in couple-related distress also played significant roles in one's quality of life. The present research also utilizes a version of the Actor Partner Interdependence Model that integrates the responses of individuals in a dyadic romantic relationship.

These models suggest that research into the caregiving experiences of families with cancer should go beyond just the caregiver or the cancer patient's experiences to look at the caregiver-patient dyad as a unit (Fletcher et al., 2012). Although these models help illuminate the cancer experience itself, genetically heritable cancer syndromes carry a lifelong burden of cancer risk beyond the single, acute occurrence. Therefore, research on these families must expand these models to incorporate dyadic coping during non-active cancer periods (during which cancer treatment is not a major activity) as well.

Relationship satisfaction is an important factor that modifies how successfully couples cope with cancer. One study found that relationship quality had a moderating effect on the secondary trauma stress symptoms that were exhibited by partners of cancer patients (Brosseau, McDonald, & Stephen, 2011). The researchers found that 23% of partners of cancer patients exhibited clinically significant levels of secondary traumatic stress, and that these partners had lower levels of relationship quality. They concluded

that relationship quality exhibited buffering effects only for the couples that reported higher levels of relationship quality, and this moderation was found for both the cancer patient and their partner.

There are several ways in which partners can show their support for an individual with cancer. Studies have examined the effects of three specific types of support (active engagement, protective buffering, and overprotection) on a variety of outcomes such as the marital satisfaction of both partners and whether these types of support were actually perceived as helpful by the cancer patient (Hagedoorn, Kuijer, et al., 2000), as well as the self-efficacy, physical health, and mental health of patients with a chronic illness (de Ridder, Schreurs, & Kuijer, 2005). *Active engagement* by partners means involving the patient in discussions and using constructive problem-solving methods; *protective buffering* by partners means hiding one's concerns to protect their spouse; and *overprotection* rests on an underestimation of the patient's capabilities, resulting in unnecessary help and excessive praise for accomplishments. Overall, partner protective buffering and overprotection behaviors have not been shown to improve the self-efficacy and marital satisfaction of the patient. Conversely, one study found a positive association between active engagement and the patient's marital satisfaction, especially for patients with high levels of psychological distress and more physical limitations (Hagedoorn, Kuijer, et al., 2000). These findings demonstrate the important process in which both partners should be actively engaged in care and utilize open communication.

Relationship satisfaction in couples confronted with colorectal cancer (Hagedoorn et al., 2011) was described in a sample of 29 female patients and 59 male patients and their partners, who participated in a study measuring the association between past and current spousal support and relationship satisfaction over time. The researchers found that,

in the short-term, spousal active engagement was positively associated with relationship satisfaction in patients and their partners, but this observed only occurred when past spousal support had been low. Spousal protective buffering was found to be negatively associated with relationship satisfaction in patients, again only when past spousal support was low. If past spousal support was high, participants reported their current relationship quality as high, regardless of partner's current support behaviors (Hagedoorn et al., 2011). These results demonstrate the buffering effect that high spousal support that existed before a cancer had on the marital relationship, as well as the positive impact of active engagement on the part of the spouse during colorectal cancer.

These studies illustrate both the effects of cancer on partners and the methods that partners use to support their sick spouse. The burden of cancer on both partners is well established; however, what is less well-known is how couples function when there is a constant risk of cancer in the future, or how couples cope with multiple separate primary cancers across the trajectory of their relationship. The next sections describe literature regarding the unique dyadic interactions that occur between people who carry mutations that increase their risk of cancer and their partners.

## **Hereditary Breast and Ovarian Cancer Syndromes**

### **Genetic Origin, Prevalence, and Penetrance**

Hereditary Breast and Ovarian Cancer Syndrome (HBOC) is an inherited genetic condition in which in which an elevated risk of breast and ovarian cancer is passed from generation to generation in a family. Two genes are associated with the majority of HBOC families: *BRCA1* and *BRCA2*, an acronym in which *BRCA* stands for BREast CANcer. Other, less common genes have also been associated with an increased risk of



developing breast and other cancers, such as mutations in the *TP53*, *PTEN*, *CDH1*, *ATM*, *CHEK2* or *PALB2* tumor suppression genes and many others. Blood tests now include many of these genes in a single, multiple-gene panel test. A mutation (alteration) in either *BRCA1* or *BRCA2* gives a woman a markedly increased lifetime risk of developing breast and ovarian cancer. Men with these gene mutations also have an increased risk of breast cancer and prostate cancer. There is a slight increase in the risk of other cancers, including pancreatic cancer and melanoma, among carriers of *BRCA1* or *BRCA2* mutations. Not all families with multiple cases of breast and ovarian cancer have mutations in *BRCA1* or *BRCA2*. Prevalence estimates of *BRCA1/2* among U.S. women range from 1:400 to 1:500 (excluding Ashkenazi Jewish populations) and it occurs in all ethnic and racial populations (NCI, 2018). The penetrance of the breast and ovarian cancer for women with a *BRCA1/2* pathogenic variant can be as high as 87%, and 20% for men, but varies for *BRCA1* and *BRCA2*. Risk of breast cancer within the general population is relatively low (risk of malignancy = 12%), compared with individuals carrying *BRCA1* (46-87%) or *BRCA2* (38-84%) mutations. The same applies to ovarian cancer, which is rare in the general population (1-2%) but which occurs at a much higher rate than for those with *BRCA1* (39-63%) or *BRCA2* (16.5%-27%).

### **Partnerships in the Context of HBOC**

The available literature on the psychological impact of being a partner of an individual diagnosed with a hereditary cancer syndrome has focused primarily on partners of women who carry (or are at high risk of carrying) the *BRCA1/2* gene mutation. These studies suggest that partners report distress levels that are similar to, if not greater

than, the distress levels of their mutation affected partners. There is very limited literature on men with the *BRCA1/2* gene mutation and their romantic relationships.

One study measured the specific needs of the spouses of who received genetic counseling for a positive *BRCA1/2* result (Metcalf, Liede, Trinkaus, Hanna, & Narod, 2002). The researchers surveyed 59 spouses of female mutation carriers. The mean relationship duration was 26 years (range: 2.5-50 years). All participants were supportive of their spouses' decision to undergo genetic testing and counseling. Four respondents stated that they wished that they had received additional support at the time of test disclosure, and 20% felt that their wives had received inadequate support. One-quarter of the spouses believed that their relationship had changed because of genetic testing; most felt that they had become closer to their wives. Husbands were most concerned about the risk of their wife dying of cancer (43%), followed by the risk of their spouse developing cancer (19%) and the risk that their children would test positive for the *BRCA* mutation (14%). Distress levels, measured by the Impact of Event scale, suggest that few spouses were experiencing clinical levels of distress.

The role of the partner without the mutation or who is not at elevated risk of cancer can be complicated. These partners must share their concerns with their partner regarding genetic testing and cancer screening for their children; however, they will never experience the testing or screening themselves. To evaluate how involved non-mutation carrying spouses are and how their level of involvement affects their mutation-positive partners and relationships, one study surveyed male partners of *BRCA1/2*-mutation positive women with children (DeMarco et al., 2010). Only 27% of fathers attended pretest cancer genetic counseling with mothers. Compared with fathers who did not attend the genetic counseling session, those who did attend had stronger parenting

alliances with mothers, were more likely to have sought out information about *BRCA1/2* testing, and felt more informed about testing. The conclusion that the researchers drew was that fathers who attend genetic counseling sessions may be better equipped to support mothers about making key decisions later on, including medical and family communication decisions. Additionally, helping fathers became more involved in the genetic counseling process, encouraging a stronger alliance between partners.

In conclusion, partners of women with a *BRCA1/2* mutation often request additional support for themselves and their partners. These partners are involved in the genetic testing process to varying degrees, which in turn affects the couple/parenting dyad. The literature on *BRCA1/2* mutation-positive women still lacks thorough research on the dyadic family planning processes and decision-making conversations that occur between partners. Hoskins (2008) conducted in-depth interviews with young *BRCA1/2* mutation-positive women regarding their romantic relationships and found that disclosure to a partner resulted in increased feelings of closeness and trust. This points to the importance of open communication and supportive partnerships; however, there is a need for research that can describe the full experience of the partner without the mutation, as well as interviews that systematically inquire about both partners' experiences.

## **Li-Fraumeni Syndrome**

### **Genetic Origin, Classification, Prevalence, and Penetrance**

LFS is an autosomal dominant cancer predisposition syndrome that can result in multiple cancer diagnoses across the course of an individual's life. Many individuals with LFS receive a cancer diagnosis in childhood or adolescence. LFS is a highly penetrant cancer syndrome, meaning the number of cancer occurrences as well as deaths from

cancer among mutation carriers is very high within LFS families (Becze, 2011). The risk of developing cancer by age 40 is estimated to be 50%, and is 90% at age 60 (Mai et al., 2016), meaning that 9 out of 10 *TP53* mutation-positive LFS patients will develop cancer at some point in their life. Germline mutations in the *TP53* tumor suppressor gene are the cause of LFS in about 70% of families (Schneider, Zelle, Nichols, & Garber, 1993). These mutations result in aberrant function of the *TP53* protein, and lead to inappropriate and abnormal cell growth. The most common cancer types in patients with LFS are female pre-menopausal breast cancer, bone cancer (osteosarcoma), soft tissue sarcomas, brain tumors, and cancer of the adrenal gland (adrenocortical carcinoma) (Mai et al., 2016).

There are diagnostic criteria through which an individual is clinically classified as having LFS. Classic LFS is defined by meeting all the following criteria: a proband with a sarcoma diagnosed before age 45, a first-degree relative with any cancer before age 45, and a first or second-degree relative with any cancer before age 45 or a sarcoma at any age (F. P. Li et al., 1988) According to the alternative Chompret criteria people can be classified clinically as having LFS if (1) the proband has a tumor belonging to the LFS tumor spectrum before age 46, and  $\geq$ one first- or second-degree relative with an LFS tumor before age 56 years; (2) probands have multiple independent tumors, two of which belong to the LFS tumor spectrum and the first of which occurred before the age of 46; (3) a proband has an adrenocortical carcinoma or choroid plexus tumor, regardless of family history. Studies have shown that 92-95% of people who tested positive for the *TP53* mutation also met the Chompret criteria for LFS (Ruijs et al., 2010).

Although LFS has been considered to be a rare hereditary cancer syndrome, recent data suggest that the frequency of a germline *TP53* mutation may be as high as 1:500 (Andrade et al., 2017).

Although LFS outcomes can be dire, cancer screening and early detection of cancers have shown promise in reducing cancer-related morbidity and mortality (Villani et al., 2016). Since women with LFS have been shown to have a 93% lifetime risk of developing breast cancer, medical practitioners recommend commencing breast MRIs, ultrasounds, and mammography starting at an earlier age than people at average risk of breast cancer. In order to screen for other cancers for both men and women, screening protocols are being developed that employ an annual full body MRI, blood tests, ultrasounds, colonoscopies, brain MRI, and physical exam (Kamihara, Rana, & Garber, 2014).

Genetic testing in families at risk is the first step in early cancer detection. When a family knows which specific *TP53* mutation they are carrying, testing previously untested family members is much cheaper and simpler, since it targets only the family-specific mutation), and they are equipped with knowledge that better prepares them to work with healthcare providers to establish a routine of cancer screening.

### **Partners in the Context of LFS.**

Couples with LFS face unique decision-making challenges regarding medical and genetic testing decisions, screening and prevention behaviors, and familial disclosure. This section describes strategies reported by patients as they handle those situations, and findings regarding the experiences of non-LFS partners and current gaps in the literature.

Peterson et al. (2008) found that several familial experiences with cancer were

correlated with cancer-specific distress that individuals experienced before receiving their genetic testing results for *TP53* mutations. Specifically, a higher number of cancer diagnoses and deaths in first-degree relatives were associated with greater cancer-specific distress in individuals from LFS families before they had their testing.

Overall, studies have shown that even after genetic education and counseling, patients with suspected *TP53* mutations are less likely to elect genetic testing than patients at risk of other genetically heritable cancer syndromes such as *BRCA1/2*, which is associated with increased risks of breast and ovarian cancer. This difference has been attributed to the fact that *BRCA1/2* mutation-carriers have specific surgical options available to decrease their risk of breast or ovarian cancer, whereas patients with *TP53* mutations have less specific options because the types of cancers they are at risk of are so varied (Parsons, 2011). These results demonstrate the conflict that individuals are faced with regarding genetic testing. Lower perceived self-efficacy regarding coping with the possibility of future cancer may prevent individuals from pursuing testing (Peterson et al., 2008). However, there are likely other variables in play that must be investigated. Other family members' beliefs regarding genetic testing have a large influence on the individual's behavior, but this relationship has not been studied previously in LFS patients.

One study in the Netherlands looked at distress in partners of individuals with LFS and Von Hippel-Lindau disease (VHL; another rare autosomal dominant cancer syndrome that results in higher risk of a broad range of tumors developing in early childhood or adulthood) (Lammens et al., 2011). In a study of 50 LFS or VHL affected individuals and their partners, the researchers found that 28% of the partners reported clinically relevant levels of distress related to the cancer syndrome. Levels of distress and

worry reported by the partner were significantly correlated with the distress levels of the high-risk spouse. The researchers also found that younger partners as well as partners with less social support in their lives reported higher levels of distress. Importantly, 76% of the partners who participated in the study believed that they, and not just their at-risk spouses, should be offered routine professional psychosocial support.

Since inheritance of a *TP53* gene mutation results in a nearly 100% lifetime risk of cancer, a prominent concern for young families is whether the mutation will be passed on to younger generations. There are a variety of options outside of natural conception that can be considered, such as adoption, surrogacy, or even pre-implantation genetic diagnosis (PGD), in which genetic testing for the family's *TP53* mutation is conducted on the embryo before it is implanted into the uterus. There are important ethical considerations that accompany each of these options, and it is recommended that prenatal testing only be done after thorough consultation with a team of clinicians that includes a pediatric oncologist, geneticist, psychosocial worker, prenatal care provider, and ethical representative. The major potential psychological benefit to the family of prenatal testing would be to reduce uncertainty in high-risk families.

Oftentimes adults learn that they are mutation-positive after they have already had children. In such cases, the next question they face is whether to test a child, and if so, at what age. (Alderfer et al., 2015) conducted a qualitative study to explore the decision-making process that parents undergo when deciding whether or not to test their child (who may or may not have already had cancer) for the *TP53* mutation. All of the families in the sample had at least one relative who had tested positive for the mutation and were involved in decision-making about whether to put their child through the process. Three types of decision-making styles emerged: *automatic decisions* involved little

consideration, with the family members citing the immediate benefits of knowing; *considered decisions* involved parents taking time to weigh the risks and benefits, but then reaching a conclusion easily; *deliberated decisions*, which were difficult and focused on psychosocial concerns such as not wanting to burden the child, adding unnecessary stress if the child never actually does have cancer, discrimination, and insurance issues. Across the board, *TP53* mutation testing interest was high (92%), with the vast majority of parents focused on the benefits of testing (Alderfer et al., 2015).

In summary, the themes that arose in the literature on LFS individuals and their partners focused on cancer-related distress, genetic testing for children, and patients' self-efficacy in the context of larger family history. Both individuals with LFS and their partners reported a need for increased mental health support, but tailored interventions for families coping with heritable cancer syndromes are still in beginning testing stages. The next section describes family interventions that may be adapted for this unique group.

## **Interventions**

Interventions vary in their goals and treatment style. Literature on chronic illness points to couple interventions that focus on couple relationship quality and functioning. Typically, such interventions focus on various methods to foster emotional expressiveness, reduce social isolation, prevent the disease from dominating couple and family life, help the individuals deal with loss of a loved one, promote collaboration among family members, improve empathy for all sides, deal with stigma, and resolve intra-family conflict (Medicine, 2001). Psychoeducation is often combined with couple relationship interventions, which might be more effective than psychoeducation alone,



especially as it relates to secondary prevention (encouraging regular exams and screening tests to detect disease in its earliest stages; e.g., mammograms to detect breast cancer).

A review of 10 different intervention studies targeted at female breast cancer patients and their partners found overwhelming benefits for both partners in some dimensions such as quality of life, psychological distress, relationship functioning and physical symptoms associated with cancer (Brandao, Schulz, & Matos, 2014). Although there was significant diversity in many of the characteristics and theoretical orientations underlying the interventions, all of the interventions included training in specific coping strategies, problem-solving, and communication skills. Other common elements included a significant psychoeducation component, promotion of emotional expression and social support, promotion of sexual and body adaptation, and promotion of benefit finding, post-traumatic growth, and a focus on sources of meaning in one's life. These results are in line with research findings for psychological interventions that have been found beneficial for couples dealing with other types of cancer (H. Badr & Krebs, 2013; Baik & Adams, 2011; Hopkinson, Brown, Okamoto, & Addington-Hall, 2012).

Relational coping and skills building are the foci of many studies looking at effects of psychosocial interventions with couples dealing with a current or recent cancer. However, couple interventions related to cancer can also be designed with a preventive goal in mind. An intervention study by Manne (2013) aimed to involve spouses in the colorectal cancer screening behaviors of their non-adherent spouse. The results indicated that using a couple-tailored print brochure resulted in higher intentions to engage in colorectal cancer screening as well as an increase in husbands' support for their wives' engagement in colorectal screening (Manne et al., 2013). Although there was no difference in post-test screening behavior between the control and the couple-tailored

intervention groups, there was an increased tendency for the couples who received the couples-tailored brochure to view colorectal cancer screening as having benefits for their marital relationship. Examples of these benefits included both partners having increased relational perspectives regarding cancer, support for spouse screening, and more discussions with one's partner about colorectal cancer screening. This type of prevention and screening study has direct relevance for couples in which one partner has a heritable cancer syndrome and is recommended to have regular cancer screenings starting at an early age. The challenge is that these couple-focused interventions have been developed for newly diagnosed sporadic cancer patients and their partners, and not much is known about how well those interventions can be transferred to couples with heritable syndromes.

### **Conclusion**

The importance of psychosocial and family issues in genetically heritable cancer syndromes has been widely recognized but under-researched. After an exhaustive search of relevant literature on this topic, only a handful of publications were found that dealt directly with couple relationships and/or the psychological effects of these syndromes on individuals and their partners. Because these syndromes are heritable, research on family communication and family functioning is very relevant. Despite the inclusion of family members as participants in many medical studies of heritable cancer syndromes, few researchers have looked at changes in family processes over time, and adaptation of family relationships under the stress of past, current, or future cancer. This static or short-term viewpoint on cancer does not lend itself to understanding the experiences of couples that face life-long risks of cancer due to their genetic mutations.

Psychological interventions designed to help couples dealing with cancer have been shown to have immediate benefits for both partners. Relational psychoeducation and communication skills building are psychological interventions that offer a framework for clinicians working with heritable cancer syndromes and the families with whom they work. Medical Family Therapy is a growing field that utilizes many of the traditional theories and techniques from different types of family therapy, but it also draws attention to the biopsychosocial nature of the human experience (Ruddy & McDaniel, 2016). Medical family therapists must be familiar with illnesses and their effects on individuals and families, understand the medical evaluation and treatment system and how to work collaboratively with medical providers, and be familiar with techniques that assist families in coping with the unique stressors that hereditary illness places on them. Increased numbers of trained medical family therapists working in conjunction with genetic counselors, oncologists, and clinical researchers who are familiar with the syndromes touched on in this review are desperately needed. These interdisciplinary teams can work together to increase the amount of targeted research on intervention and prevention, to provide the best support and outcomes for the whole family.

## CHAPTER 3: STUDY 1

### **Dyadic Coping Styles and Cancer Worry in Li-Fraumeni Syndrome Couples**

#### **Background**

After heart disease, cancer is the most common cause of death in the United States (CDC, 2015). According to the National Cancer Institute (2014), one's lifetime risk of developing any type of cancer is 40.37%. This risk probability varies based on a range of factors such as gender, age, and race. In addition, certain inherited genetic characteristics can put some people at a higher risk of cancer than the general population. More than 80 hereditary cancer syndromes have been described in the professional literature, with 5-10% of all cancers diagnosed in the United States developing from a hereditary genetic mutation (Lindor et al., 2008). The majority of these are genetic mutations that are inherited in an autosomal dominant fashion from parent to child and significantly increase a person's risk of developing cancer.

#### **Li-Fraumeni Syndrome**

Li-Fraumeni Syndrome (LFS) is an autosomal dominant cancer predisposition syndrome that can result in elevated risk of multiple cancers across the course of an individuals' life. Commonly, individuals with LFS receive a cancer diagnosis early in life, such as childhood or adolescence. The most common cancer types in patients with LFS are breast cancer, bone cancer, soft tissue sarcomas, brain tumors, and cancer of the adrenal gland (Mai et al., 2016). The number of cancer occurrences as well as deaths from cancer is very high within LFS families, and they face the possibility of a second or third independent primary cancers later in life (Becze, 2011). The risk of cancer by age

40 years is estimated to be 50%, and 90% at 60 years (Mai et al., 2016), meaning that 9 out of 10 people with LFS will develop cancer at some point in their life. Germline mutations in the *TP53* tumor suppressor gene cause LFS in about 70% of clinically-defined families (Schneider et al., 1993). The elevated risk of cancer can cause distress and elevated worry about cancer among individuals with LFS as well as their families. Fortunately, regular cancer screening and early detection of cancers have shown promise in reducing cancer-related morbidity and mortality (Villani et al., 2016).

### **Cancer Worry**

For individuals facing a high cancer risk due to a genetic diagnosis, the worry and anxiety related to future cancers can be overwhelming. Research on individuals diagnosed with LFS has shown that they experience psychological distress beyond the stress of daily functioning (Lammens et al., 2010). A study of 18 LFS families found that 23% of participants reported clinically relevant levels of LFS-related distress. This finding reflects a larger trend in the literature regarding cancer-specific distress in individuals who are at risk of hereditary cancers. For example, women with *BRCA1/2* mutations face higher chances of breast and ovarian cancer at younger ages than the general population, and research has found that these women typically have higher than average levels of emotional distress, especially in the months following genetic testing (Butow, Lobb, Meiser, Barratt, & Tucker, 2003; Ringwald et al., 2016).

To distinguish between general distress (such as general anxiety and depression) and cancer-specific distress, many studies have explored the concept of “cancer worry” in terms of how distressed a person is regarding risk of future cancers, and how much this worry interferes with daily functioning. Cancer-specific worry can disrupt one’s

functioning in a variety of areas such as job performance, enactment of family roles, and personal health maintenance (Wellisch, Ormseth, Hartoonian, & Owen, 2012). One study of women with a high risk of breast cancer showed that two-thirds reported that their worries about breast cancer interfered with their life functioning in multiple domains (Trask et al., 2001). In that study, the high-risk women who reported more cancer worry also reported greater anxiety and confusion, diminished mental health, and difficulty in performing their usual roles in and outside the home.

**Contributing factors to cancer worry, cancer worry's interference in functioning.** Some interventions such as genetic counseling can reduce worry about developing cancer, as shown in a group of women whose breast and ovarian cancer worry was measured before and after receiving genetic counseling (Bish et al., 2002). Unfortunately, beyond Lammens (2010) research on psychological distress, very little literature exists exploring cancer worry in this population, and there is even less research regarding how these individuals and their partners can cope with the future risk of cancer.

### **Partners' Cancer Worry**

Heritable cancer susceptibility disorders involve a cycle of intense psychological experiences not only for the at-risk individuals but also for their life partners. The relational implications of genetic risk may be examined within family systems theory (Peterson, 2005), in which events that affect an individual are predicted to also affect the whole family system. A genetic diagnosis and its implications, as in the case of hereditary tumors, are viewed not as a single event, but rather as an on-going dynamic process that may have repercussions for the family over time. Genetic conditions also pose a burden

on relatives, whether the results of each family member's genetic testing are positive (mutation-carrier) or negative (non-carrier); even those who are not at risk personally may experience significant worry about the results of genetic testing (Bowles Biesecker & Marteau, 1999).

Several studies have shown that the partners of people with rare hereditary cancer syndromes also exhibit high levels of psychological distress and worry (Hagedoorn, Buunk, et al., 2000; Lammens et al., 2011). However, the findings of studies on distress in cancer patients and their partners have been inconsistent. In several studies, intimate partners were found to be just as distressed as patients (Baider, Cooper, & Kaplan De-Nour, 1996; Baider & Kaplan De-Nour, 1997; Northouse & Swain, 1987; Oberst & Scott, 1988). In a study by Given and Given (1992), husbands of women with recurrent breast cancer reported even more depressive symptoms than their wives. Other studies of couples dealing with heritable breast cancer showed lower levels of distress for the husbands than for the patients (C. Hoskins et al., 1996; Northouse, Templin, Mood, & Oberst, 1998).

Lammens (2011) found that *TP53* mutation carriers were not significantly more distressed than non-carriers or those at risk but who did not undergo genetic testing. Additionally, those participants with a lack of social support were more prone to report clinically relevant levels of distress (Lammens et al., 2011). This study of LFS spouses also pointed out that many of the partners reported a desire for additional mental health or support services to help them cope with their *TP53* mutation-positive partner's risk of cancer. These studies demonstrate that spouses of individuals with LFS are also in need of psychosocial support from clinicians and may not receive adequate attention from research or health teams. Consequently, research using dyadic analysis methods that

account for interdependence between two partners' responses must be used to determine the pattern of cancer worry between partners.

### **Dyadic Coping**

To provide the most effective care, patients and their partners must develop effective coping skills together. Coping is defined by Folkman and Moskowitz (2004) as the thoughts and behaviors used to manage the internal and external demands of situations that are appraised as threatening. Coping with cancer is considered to be a dyadic process, with patients' adjustment and behaviors being affected by their partners' adjustments and behaviors, and *vice versa* (Berg & Upchurch, 2007). Partners of individuals with LFS are in a unique position, due to the nature of the syndrome. They may have been caretakers for their partners for past cancers, but they also have the potential to become a future caretaker for their partner, or potentially their children.

A study by Hagedoorn (2011) found that active spousal engagement in coping was positively associated with relationship satisfaction in patients with colorectal cancer, as well as in the partners. Spousal protective buffering, which involves hiding one's worries and fears and avoiding talking about the disease, was associated with lower relationship satisfaction in the patients. This relationship was only significant, however, when past spousal support (before cancer) was reported to be low. When past spousal support was high, then the participants rated the quality of their relationship relatively high, regardless of the partner's current types of support behaviors.

Breast cancer is an example of a dyadic stressor; i.e., a stressor that affects both members of a couple. The two primary objectives of dyadic coping are the reduction of stress for each partner and the enhancement of relationship quality. A coping process is



triggered when one partner communicates stress to the other either verbally or nonverbally. The other partner receives and interprets the stress signals and responds with some type of dyadic coping that is aimed at assisting the other person. Bodenmann (2005) broadly differentiates between positive and negative dyadic coping. The former includes supportive, delegated, and common dyadic coping. In supportive dyadic coping, one partner assists the other in his or her coping efforts, for example, by empathic understanding, practical advice, or expressing solidarity with the partner. In delegated dyadic coping, one partner takes over responsibilities and tasks to reduce the other's stress. Common dyadic coping occurs when both partners are similarly concerned about the stressor and participate more or less symmetrically in the coping process; for example, by joint problem-solving, joint information seeking, or relaxing together. In contrast, negative dyadic coping includes hostile, ambivalent, and superficial responses; that is, support that is accompanied by the partner distancing and showing disinterest, or support that is insincere or unwillingly provided.

Dyadic coping appears to have different effects for patient *versus* their partners. A longitudinal study of metastatic breast cancer patients and their spouses found the effects of common positive dyadic coping on cancer-related distress significantly differed for patients and their partners (Hoda Badr, Carmack, Kashy, Cristofanilli, & Revenson, 2010). Partners experienced lower levels of distress compared with the slightly higher levels of distress in patients. Although all participants who used more negative coping experienced significantly greater distress at all times, the association was stronger for patients than for their partners. Lastly, the study found that use of more common positive dyadic coping was beneficial for patients and partners, in terms of greater dyadic adjustment.

In the present study, each partner's individual coping styles were measured, and the strengths of both partners' coping styles were examined in relation to the degree of cancer worry reported by the spouse with LFS. This comparison allowed our model to integrate both members' styles of coping and their influences on the distress of the individual with regard to cancer.

### **Gender Differences in Response to Cancer**

The findings from studies on distress in cancer patients and their partners have been inconsistent. In several studies, intimate partners were found to be as distressed as patients (Baider et al., 1996; Northouse & Swain, 1987; Oberst & Scott, 1988). In one study, husbands of patients with recurrent breast cancer reported even more depressive symptoms than their wives (Given & Given, 1992). However, other studies among couples dealing with breast cancer showed lower levels of distress for the husbands than for the patients (C. Hoskins et al., 1996; Northouse et al., 1998).

In one study of 150 cancer patients and their romantic partners, the researchers explored whether the cancer patients and their partners differed on their levels of psychological distress and reported quality of life as a function of their gender-role identities (Pikler & Brown, 2010). Results from this study showed that individuals who ascribed to a masculine gender-role identity, regardless of whether they were a patient or a partner, were more at risk of developing depressive symptoms compared with those who ascribed to a feminine gender-role identity. Also, partners of cancer patients were more at risk of developing anxiety symptoms as compared with the cancer patients themselves, regardless of gender-role identity. The researchers found no significant differences among gender-role identities or role statuses in regard to quality of life (Pikler

& Brown, 2010). Building on that study, the present study included measures of general psychological distress such as anxiety, depression, and somatization as a possible contextual factor that influences cancer worry. We also anticipated higher amounts of psychological distress symptoms in our female participants, especially if they were the partner of an individual with LFS.

### **Objectives**

The goals of the current study were two-fold. First, it compared the psychosocial outcomes of spousal pairs to determine if there is a significant difference in the level of emotional functioning between LFS and non-LFS partners. Second, cancer-specific coping styles and psychological distress of the non-LFS partner were tested as predictors of the cancer worry of the LFS partner.

### **Hypotheses**

1. The general distress scores of non-LFS partners will be higher than LFS partners, with females having the highest levels of distress.
2. The cancer worry scores of LFS partners will be higher than non-LFS partners, with females having more cancer worry.
3. Mediation: For the LFS partner group, frequency of cancer worry will have a direct effect on how cancer worry impacts daily functioning; this direct effect will be mediated by how cancer worry impacts mood.
4. Moderation: The more adaptive coping the non-LFS partner reports, the less that the LFS partner's mood will affect their daily functioning.

## Methods

The current study analyzed data from the ongoing LFS study at the National Cancer Institute, National Institutes of Health (NCI Protocol #11-C-0255; NCT 00004007). The main goal of the larger LFS study is to investigate the clinical, epidemiologic, and genetic etiology of LFS, as well as to establish a national and international standard for cancer screening for individuals with or at risk of LFS. At its inception in 2011, the LFS study investigators conducted extensive recruitment by establishing a study website and disseminating information to a network of oncologists, genetic counselors, and the members of relevant specialty medical professional societies (the most common mode of referral to the study). The main recruitment strategy for the study has been through referrals from NIH clinicians, healthcare practitioners outside of the NIH, the NCI Cancer Information Service, interested laypersons, and other family members. Many of the participants had a high prevalence of cancer in the family medical history (cancer pattern reminiscent of LFS) and had either already received genetic counseling and genetic testing or were interested in starting the process. Previous publications on this research sample have shown that they are well-educated and predominantly white (Peters et al., 2016).

After contacting the research team and enrolling on the study, participants completed a rigorous consent process and the Individual Information Questionnaire (IIQ), which included baseline medical and psychosocial assessments. The psychosocial portion of the IIQ baseline assessment utilized multiple standardized psychometric instruments to capture the challenges that arise in navigating the wide range of individual and family issues related to this highly penetrant cancer disorder. I requested baseline data from the original research team to be analyzed for the current paper. Names and other personal

identifiers were removed from this dataset and replaced with coded participant ID numbers. The data file was stored on a secure NIH computer that was password-protected, and the Excel program document itself was also password protected.

### **Sample**

106 couple pairs were identified among study enrollees as having completed a baseline assessment. 30 of 106 couples included data from one or both partners who were deceased (other family members completed the assessment for them) and did not complete the psychosocial portion of the baseline assessment; data from both partners were removed from the analytic file. Two couples had one partner who did not complete the psychosocial portion of the IIQ, one couple disagreed on their marital status, and in 9 couples both partners were untested and it was unclear which partner had LFS. After these couples and the couples that included one or more deceased partners were removed, there were data from 64 couples (128 individuals) available for analysis. Among these 64 couples, 49 pairs included a female partner with a genetic test result that indicated that they were *TP53* mutation-positive or related by blood to the LFS mutation (at risk of the mutation). Fifteen couples were comprised of a male partner who was *TP53* mutation-positive at the time the survey was completed.

The participants' ages ranged from 22-80, with mean ages for women and men with LFS being 42.6 and 48.2, respectively, and for non-LFS women and men being 47.5 and 45.3, respectively (see Table 1, which summarizes demographic characteristics of the sample). Participants were well educated (70% had a college degree or higher) and had high levels of income (63% of participants reported annual household income over \$70,000). All participants identified as white, and one couple also identified as Hispanic.

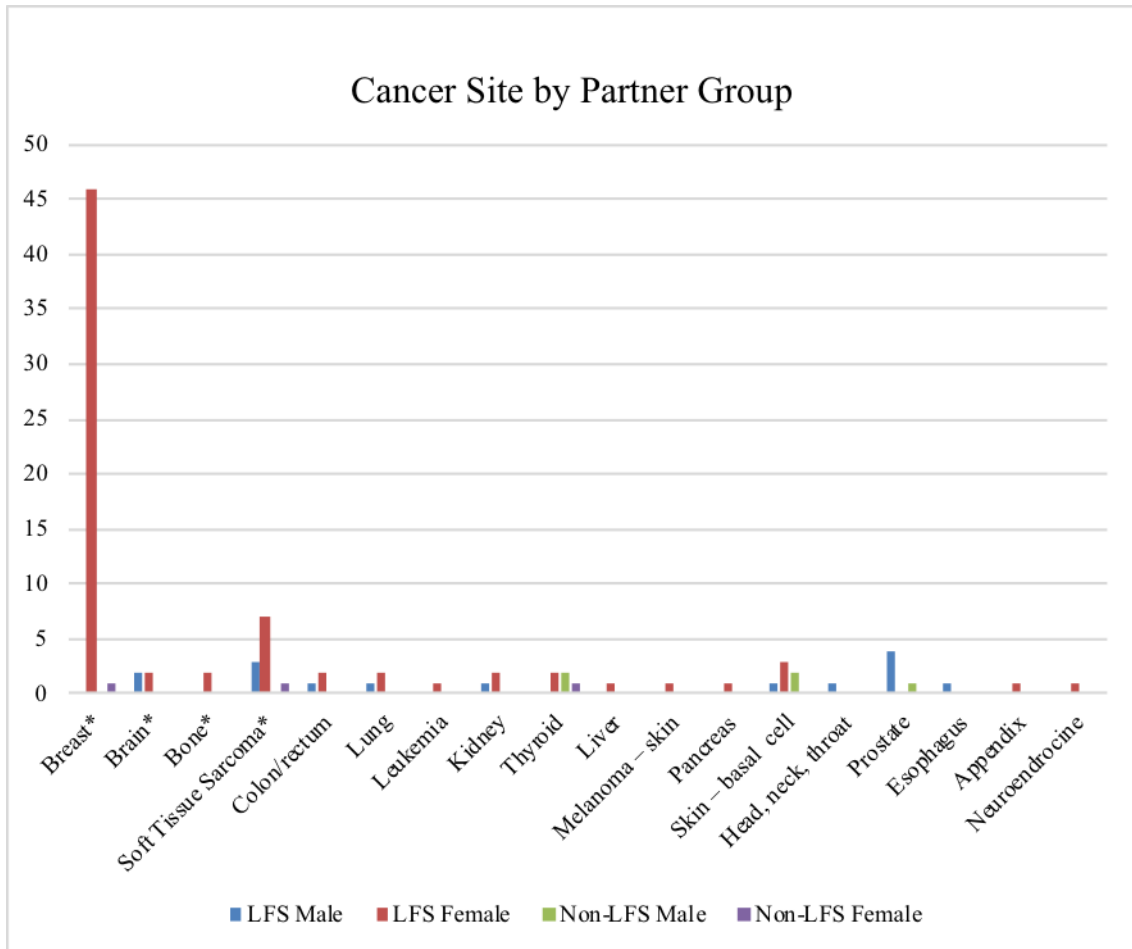
Four women with LFS, one man with LFS, and four non-LFS men identified as Ashkenazi Jews.

The majority of participants had at least one child; only nine couples had no children. Forty-four couples reported having a child with cancer, and 28 couples reported having a child with LFS.

Table 2 summarizes the cancer histories of the participants, as well as the cancer histories of first- and second-degree relatives of LFS partners. Sixty percent of LFS men and 88% of LFS women had a personal history of cancer, and the types of cancer that the participants had are described in Figure 2. Overall, breast cancer incidence in the women with LFS was very high, with 46 reported cases of breast cancer in the LFS cancer group. There were three cases of soft-tissue sarcomas in LFS men and seven in women. Four men also reported a history of prostate cancer.

The LFS participants also had many first-degree relatives with a cancer history (see Table 3). Thirty-six LFS participants reported a mother with cancer, and 17 of whom died from cancer. Thirty-four LFS participants reported a father with a cancer history, 21 of whom fathers died from cancer. Sixty-one of the participants' siblings had a cancer history, 31 of whom died from cancer. Finally, eighteen of the participants' children had cancer, and three had died from cancer.

**Figure 2. Total Number of Participant Cancers by Cancer Site**



\* Indicates cancers most commonly associated with LFS.

## Measures

Several questions included in the original study’s Individual Information Questionnaire (IIQ) were intended to assess the psychological and social functioning of adult participants at the time of enrollment. These four measures were standardized, validated scales used widely in cancer genetics research and in other NCI studies to characterize the baseline functioning of adult participants and for the purposes of comparison across conditions. This study employed the Brief Symptom Inventory, Cancer Worry Scale, Perceived Stress Scale, and Brief COPE to document baseline

depression and anxiety symptoms, cancer worry, stress, and coping strategies of participants.

**Psychological Distress:** The Brief Symptom Inventory (BSI-18) is an 18-item short form of a psychometrically validated self-report instrument that is used to measure psychological distress within the past 7 days in the domains of depression, anxiety and somatization (Derogatis, 2001). This assessment has been successfully and broadly used in medical and clinical research. Global distress and 3 sub-scale scores are calculated and compared with appropriate norms in the general population. The BSI-18 is sensitive to relatively recent changes (1 week) in mood that may accompany difficult recent events in self or relatives. In a study of men and women who received genetic testing for *BRCA1/2* mutations, the BSI-18 was used to measure general distress, and was found to have a reliability coefficient between .89 and .91 at different longitudinal time points (Graves et al., 2011). The BSI-18 was found to be highly reliable for the LFS sample ( $\alpha = .88$ ) and the non-LFS sample ( $\alpha = .88$ ). Normative T-scores derived from general population norms were computed for each BSI-18 subscale. According to the BSI-18 manual, respondents who have a t-score  $\geq 63$  on any two symptom scales or on the summary GSI scale should be classified as having clinically significant distress. For a copy of the BSI-18 with instructions and questions, please see Appendix A.

**Perceived Stress:** The Perceived Stress Scale (PSS) is a widely used, 10-item, self-report instrument for measuring individual perception of stress, *i.e.*, the degree to which situations in one's life are appraised as stressful (Cohen, Janicki-Deverts, & Miller, 2007). Previous studies have shown strong reliability and validity, and in a study of breast cancer patients the researchers found a range of .86 to .92 alpha coefficients at different



time points (Golden-Kreutz, Browne, Frierson, & Andersen, 2004). The questions in the PSS ask about feelings and thoughts during the last month, including a number of direct queries about current levels of experienced stress. Items assess how unpredictable, uncontrollable, and/or overloaded the respondents found their lives, especially important in LFS syndrome with so many unanswered questions about medical assessment and management. For the full PSS with instructions and questions, please see Appendix B.

**Cancer Worry:** We used a modified Lerman Breast Cancer Worry Scale to assess cancer-related worry (Lerman, Daly, Masny, & Balshem, 1994). The breast cancer version has high internal consistency and is widely utilized in the field of cancer research (Caruso, Vigna, & Gremigni, 2017; Custers et al., 2014). Higher worry scores have been associated with poor adherence to screening in at risk women (Brain et al., 2002; Lerman et al., 1994; Lerman et al., 1995). The questions were modified to focus on general cancer worry on a 4-point scale (1 = “not at all or rarely” to 4 = “a lot”) regarding the frequency with which cancer worry affects one’s thoughts, feelings and ability to perform daily activities. Lammens et al. (2011) adapted the same tool to assess cancer worry in families with LFS and Van Hippel Disease (VHL). They found high reliability for *TP53*-positive spouses (.90) and in the current study, we also found high reliability for participants with LFS ( $\alpha = .78$ ) The Cancer Worry Scale can be found in Appendix C.

**Brief COPE:** To measure the type of coping employed by each partner, the Brief COPE scale was used (Carver, 1997). The Brief COPE is a 28-item measure of coping strategies that was created to measure the coping reaction to a stressful situation, in this case, elevated cancer risk. The Brief Cope was developed as a shorter, alternative version to

the full COPE scale (Carver, Scheier, & Weintraub, 1989), which included 60 items, and 15 coping strategies (4 items per coping strategy). The Brief COPE has two items for each of 14 strategies (active coping, planning, positive reframing, acceptance, humor, religion, using emotional support, using instrumental support, self-distraction, denial, venting, substance, behavioral disengagement, and self-blame). Participants rated how often they had been using each type of coping on a scale of 1-4, with 1 = I haven't been doing it at all, 2 = I have been doing it a little bit, 3 = I have been doing this a medium amount, and 4 = I have been doing this a lot. There is no "overall" composite coping score for all scores combined; it was designed evaluate each coping strategy separately. A study of cancer survivors ranged in reliability from .50 to .90 for each subscale (Schmidt, Blank, Bellizzi, & Park, 2012). In our study, the reliability for LFS partners ranged from .49 to .97 for each subscale. The reliability for non-LFS partners ranged from .45 to .91 for each subscale. The Brief COPE can be found in Appendix D.

## **Analyses**

Analyses were conducted using statistical software SPSS version 21 (IBM Corp, 2012) and Mplus version 8 (Muthen & Muthen, 1998-2017). Un-weighted descriptive statistics were obtained for categorical and continuous variables, including socio-demographics, BSI global distress, anxiety, depression, somatization, perceived stress, cancer risk perception, cancer worry, and coping styles. Bivariate analysis was conducted using independent t-tests to compare baseline demographic characteristics. Pearson correlation coefficients were used to estimate linear correlations in *post-hoc* analyses. Correlation coefficients of 0.10, 0.30 and 0.50 indicated small, moderate and large effect sizes, respectively. An exploratory factor analysis for the LFS and non-LFS groups were

run in SPSS to reduce the Brief COPE, and then a Confirmatory Factor Analysis (CFA) was run in Mplus to test the structure of the factors. Lastly, we ran two path analysis models. To test hypothesis 3, we ran a mediation path analysis with bootstrapping in Mplus, and to test hypothesis 4, we ran a moderated mediation analysis with bootstrapping in Mplus. Mediation effects can be completely, partially, or inconsistently mediated (Ledermann, Macho, & Kenny, 2011). Complete mediation occurs when the direct effect (c) is zero and the indirect effect is nonzero.

## Results

First, descriptive statistics for the sample were calculated and are reported in Tables 1-3. The results for all for groups on the BSI, PSS, and Cancer Worry Scale for four groups are reported in Tables 4, 5, and 6. The four categories include male and female LFS participants, and male and female non-LFS participants. Independent *t*-tests were run to compare male and female participants within the LFS and the non-LFS participants to determine if there were significant differences in their scores on these measures. Additional tests were run to compare members of the same gender across LFS groups. The results of the *t*-tests for the BSI and PSS showed that we did not have the statistical power to detect significant differences across LFS groups or gender. This did not support the hypothesis that general distress would be higher for the non-LFS group, and specifically in women.

The results of independent *t*-tests showed that men with LFS reported higher mean perceived cancer risk than men without LFS ( $t(60) = -3.80, p < .001, d = .70$ ), male with LFS:  $M = 7.53, SD = 2.75$ ; male no LFS:  $M = 5.00, SD = 2.08$ ), and women with LFS with report higher perceived risk than women without LFS ( $t(61) = -10.27, p$

< .001,  $d = 2.65$ , female with LFS:  $M = 8.98$ ,  $SD = 1.28$ ; female no LFS:  $M = 4.80$ ,  $SD = 1.66$ ). These high mean scores indicate that men and women with LFS report perceiving that they will almost definitely get cancer in the future. Within the LFS group, female participants reported higher perceived cancer risk than men ( $t(61) = -2.82$ ,  $p < .01$ ,  $d = .84$ ), female with LFS:  $M = 8.98$ ,  $SD = 1.28$ ; male with LFS:  $M = 7.53$ ,  $SD = 2.75$ ) (Tables 5 and 6).

Similarly, there was also a significant difference in cancer worry based on whether participants had LFS or not (Table 5). Men with LFS had significantly more frequent thoughts of cancer than people of the same gender without LFS ( $t(60) = -3.71$ ,  $p < .001$ ,  $d = .58$ , male with LFS:  $M = 1.73$ ,  $SD = .79$ ; male no LFS:  $M = 1.15$ ,  $SD = .42$ ), and these thoughts of cancer more frequently affected their mood ( $t(60) = -4.77$ ,  $p < .001$ ,  $d = .56$ , male with LFS:  $M = 1.33$ ,  $SD = .49$ ; male no LFS:  $M = 1.00$ ,  $SD = .00$ ). Women with LFS had significantly more frequent thoughts of cancer than people of the same gender without LFS ( $t(60) = -5.14$ ,  $p < .001$ ,  $d = 1.52$ , female with LFS:  $M = 2.42$ ,  $SD = 2.42$ ; female no LFS:  $M = 1.13$ ,  $SD = .35$ ), and thoughts of cancer more frequently affected their mood ( $t(60) = -3.11$ ,  $p < .001$ ,  $d = .92$ , female with LFS:  $M = 1.66$ ,  $SD = .82$ ; female no LFS:  $M = 1.00$ ,  $SD = .00$ ), and these thoughts of cancer more frequently affect their daily functioning ( $t(60) = -3.86$ ,  $p < .001$ ,  $d = .63$ , female with LFS:  $M = 1.35$ ,  $SD = .635$ ; female no LFS:  $M = 1.00$ ,  $SD = .00$ ).

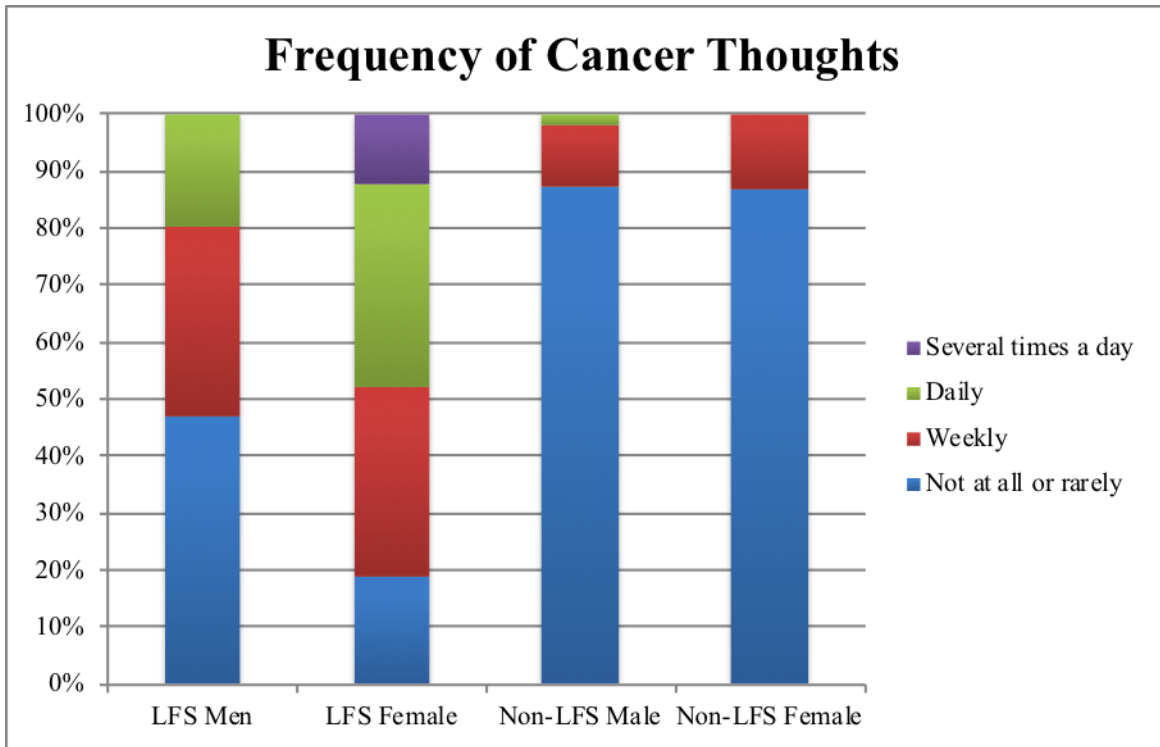
There was also a gender difference for cancer worry within the LFS group. Women with LFS had significantly more frequent thoughts of cancer than men with LFS ( $t(61) = -2.54$ ,  $p < .01$ ,  $d = .82$ , female with LFS:  $M = 2.42$ ,  $SD = .942$ ; male with  $M = 1.73$ ,  $SD = .799$ ), and thoughts of cancer more frequently affected their daily functioning than men with LFS ( $t(61) = -2.15$ ,  $p < .05$ ,  $d = 1.14$ , female with LFS:  $M = 1.35$ ,  $SD = .64$ ;

male with LFS:  $M = 1.00$ ,  $SD = .00$ ). (see Figures 3, 4, and 5, which illustrate the differences in cancer worry across groups).

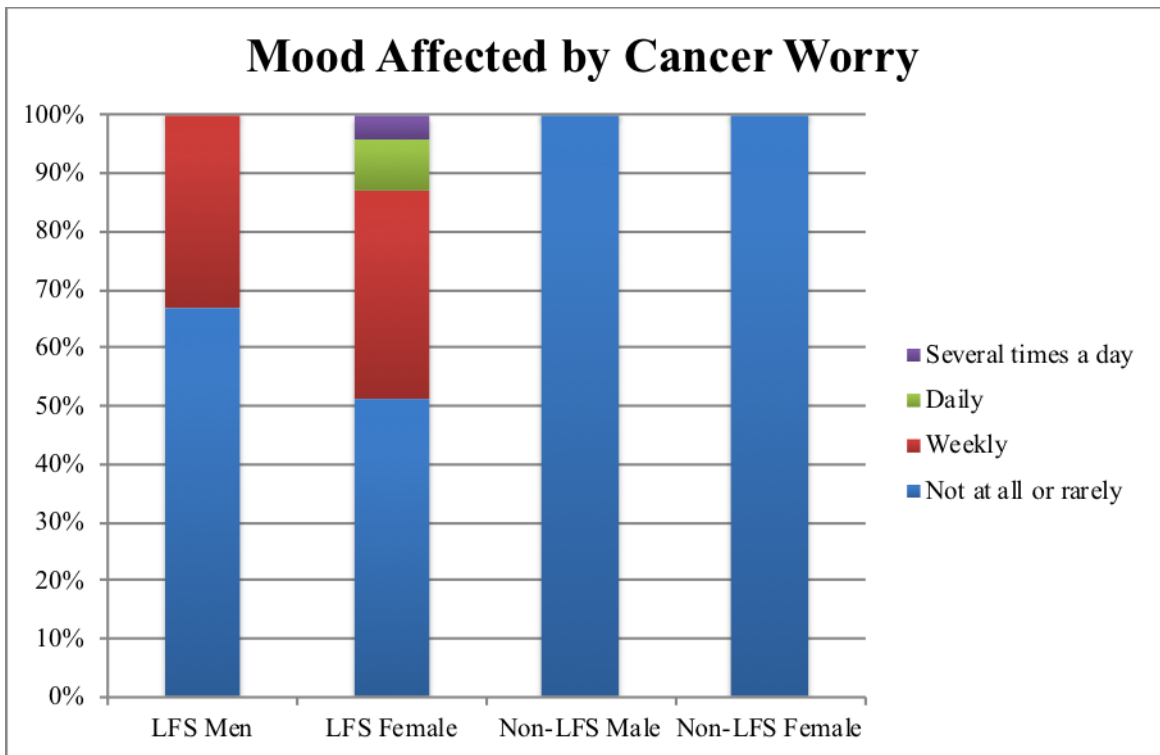
These findings did support the hypothesis that the cancer worry scores of LFS partners would be higher than non-LFS partners, with females having higher frequency of cancer worry. These mean levels of cancer worry demonstrate that some women with LFS have thoughts of cancer several times a day, with the majority of men and women with LFS thinking about cancer on a weekly or daily basis.

*Post-hoc* analyses demonstrated that for participants with LFS, the number of total cancers they had personally developed was positively correlated with the perception of cancer risk ( $r(63) = .24$ ,  $p < .05$ ), but was not significantly correlated with cancer worry frequency. These results indicated that the stronger their prior cancer history, the higher they believed their chances were of getting another cancer. Additionally, age of the participants with LFS were significantly negatively correlated with their reported comparative cancer risk ( $r(63) = -.40$ ,  $p < .01$ ), perceived cancer risk ( $r(63) = -.26$ ,  $p < .05$ ), frequency of cancer worry ( $r(63) = -.38$ ,  $p < .01$ ), and frequency that mood was affected by cancer worry ( $r(62) = -.31$ ,  $p < .05$ ). These results indicated that older participants worried less about cancer, and their own perception of their risk was lower than younger participants.

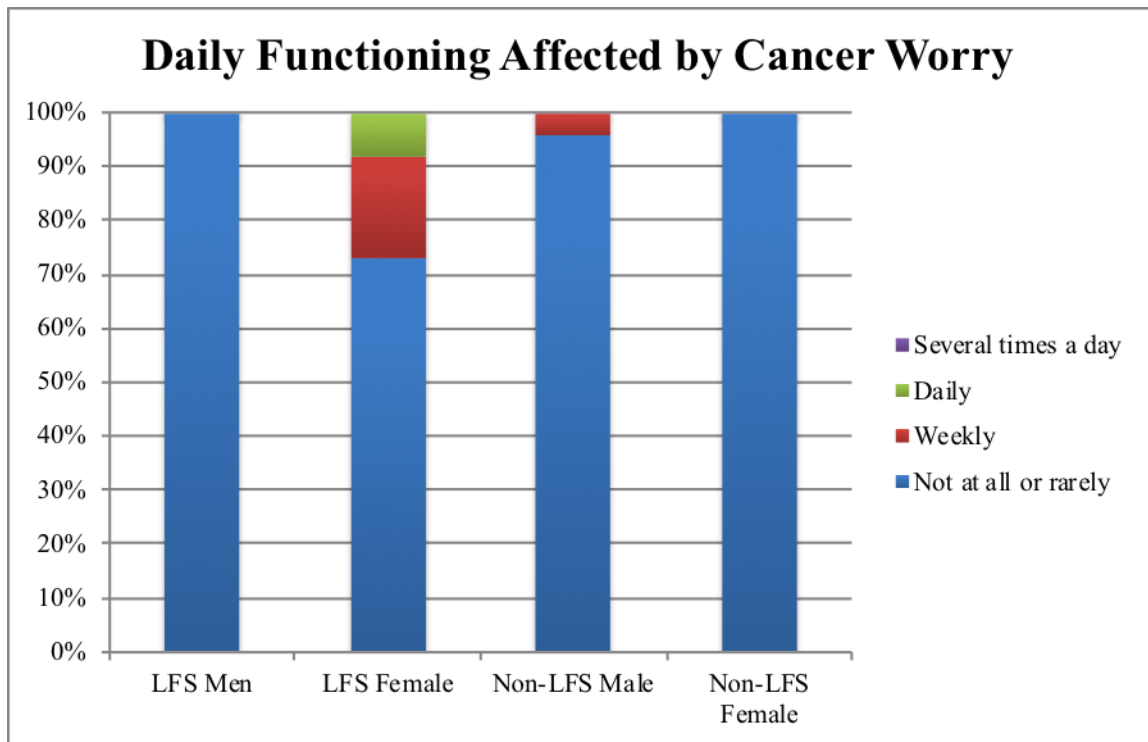
**Figure 3. Frequency of Thoughts of Getting Cancer**



**Figure 4. Frequency of Cancer Thoughts Affecting Mood**



**Figure 5. Frequency of Cancer Thoughts Affecting Daily Functioning**



### **Partners' Coping Styles**

First, we ran a comparison of female and male use of the 14 coping styles through independent t-tests. Within the LFS group, women reported using emotional support, venting, positive reframing, and planning significantly more than men (see Table 7). In the non-LFS group, women reported higher levels of coping using emotional support, instrumental support, religion and self-blame. I then reduced the number of coping style variables to use in the path analysis model with cancer worry.

**Data Reduction and Analysis of Coping Styles.** The Brief COPE data were screened for univariate outliers; no out-of-range values were identified. LFS group and non-LFS group were analyzed separately. The minimum number of cases for factor

analysis was low, with a final sample size of 64 (using listwise deletion) for each group, providing a ratio of >4 cases per variable.

Initially, the factorability of the 14 Brief COPE items was examined. It was observed that for both groups all 14 items correlated at least .3 with at least one other item, suggesting reasonable factorability. Additionally, the communalities for 12 items were all above .3, confirming that each of those items shared some common variance with other items. However, two items “substance use” and “religion” had communalities under .3 for both LFS and non-LFS partners, and these two items were dropped. Given these indicators, factor analysis was deemed suitable with 12 items.

An oblimin form of oblique rotation using a Principle Analysis Factoring extraction was selected to identify and compute composite scores for the factors underlying the short version of the COPE scale. For the LFS group, initial eigenvalues indicated that the first two factors explained 36% and 15% of the variance, respectively. The two-factor theoretical model, which explained 51% of the variance for the LFS group, was supported empirically by the data for the LFS group. Similarly, initial eigenvalues indicated that the first two factors for the non-LFS group explained 34% and 20% of the variance, respectively. Thus, the two-factor solution, which explained 54% of the variance was also selected for the non-LFS group.

Composite scores were created for each of the two factors for the two groups, based on the mean of the items that had their primary loadings on each factor. Higher scores indicated greater use of the coping strategy.

For the LFS group, the first factor (8 items, eg. “self-distraction, venting, planning, humor”) was named “Adaptive Coping” and the second factor (3 items, “denial,



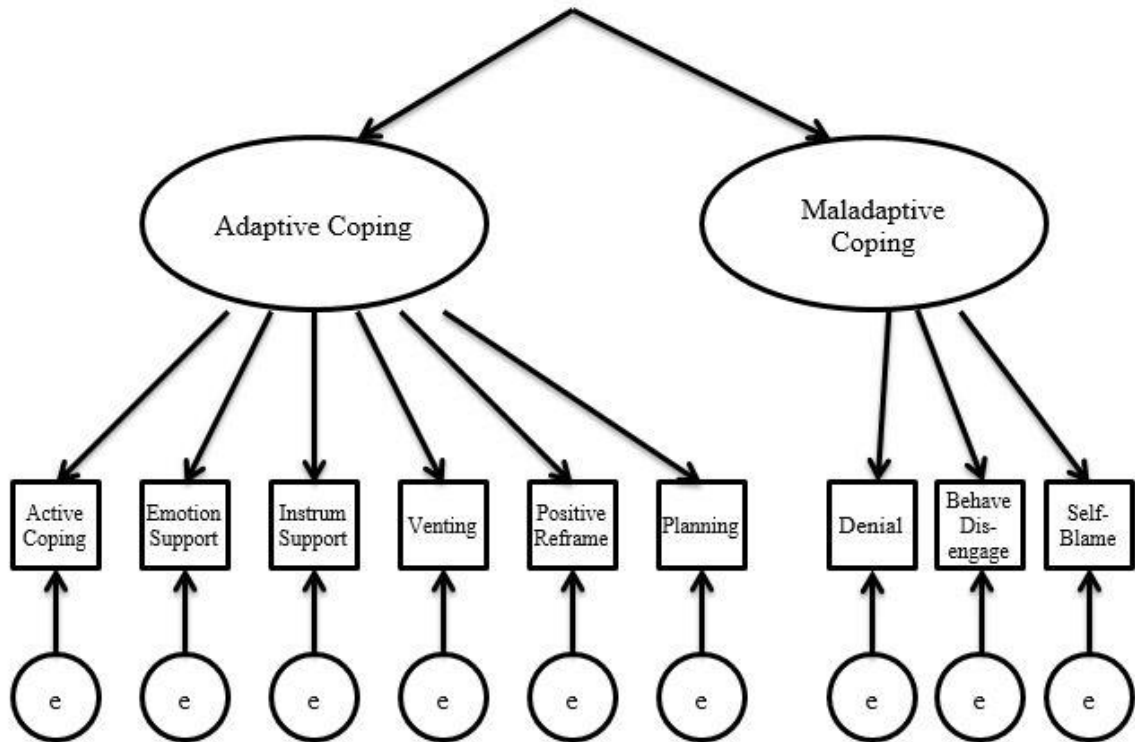
behavioral disengagement, self-blame”) “Maladaptive Coping”. Adaptive Coping was the factor that participants reported using the most.

For the non-LFS group, the first factor (6 items, eg. “active coping, use of instrumental support, use of emotional support”) was similarly named “Adaptive Coping”, however two items (self-distraction and humor) were dropped from the final factor solution due to low factor loading scores. The second factor was comprised of the same three items as the bloodline group and similarly named “Maladaptive Coping”.

Table 7 presents the loadings of each item on the rotated two-factor solution. The “Adaptive Coping” factor was finally comprised of the six items that were shared across LFS and non-LFS groups: active coping, use of emotional support, use of instrumental support, venting, positive reframing, and planning. The “Maladaptive Coping” factor was comprised of three items: denial, behavioral disengagement, and self-blame.

A Confirmatory Factor Analysis (CFA) was conducted in Mplus to verify the factor structure of the observed variables. This analysis was run to test the hypothesis that the latent constructs of adaptive and maladaptive coping were related to the specified observed indices.

**Figure 6. Latent Variable Factor Structure**



For the LFS group, the reliability coefficient for adaptive coping was  $\omega = .84$ , and for maladaptive coping it was  $\omega = .57$ . For the non-LFS group the reliability coefficient for adaptive coping was  $\omega = .82$ , and for maladaptive coping it was  $\omega = .78$ .<sup>1</sup>

The maladaptive coping scales were dropped due to very low variance scores for both partners. The data indicate that very few participants (29% of the sample) reported any use of the maladaptive coping styles, leading to the low variance. In addition, the two latent variables were not significantly correlated with one another indicating an issue with fit. The model was then reduced to one latent variable: adaptive coping for LFS and non-LFS participants.

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<sup>1</sup> McDonald's  $\omega$  was used to calculate the reliability of the latent variables developed in this study because McDonald's  $\omega$  addresses the relation between question items and latent variables. In the "Methods" section of this paper, Cronbach's  $\alpha$  was used to compare reliability in this sample to other studies.

## Mediation Model

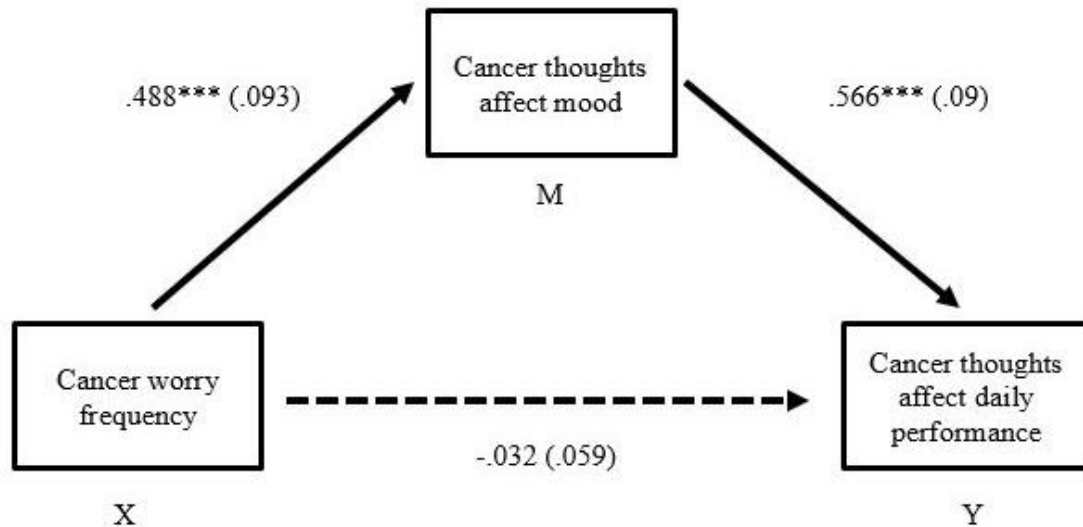
The next step in the analysis was to run a mediation model for cancer worry for the LFS spouse. To do so, we estimated a path model using maximum likelihood within Mplus. This was done to test the hypothesis that the frequency of LFS partner's worries about cancer (X) affected their ability to perform daily activities (Y), which is mediated by the how often their cancer worry affects their mood (M). A path analysis model in Mplus was used to test this mediation model in which cancer worry's effect on daily functioning (Y) and cancer worry's effect on mood (M) were endogenous variables, and cancer worry frequency (X) is an exogenous variable. The estimated path model is shown in Figure 7. All three of these variables were observed, so rectangles rather than circles were used to represent the variables.

Results indicated that worry frequency (X) was found to be a significant predictor of worry's effect on mood (M),  $b = .49$ ,  $SE = .09$ ,  $p < .001$ , and that effect on mood (M) was found to be a significant predictor of worry's effect on daily functioning (Y),  $b = .55$ ,  $SE = .08$ ,  $p < .001$ . These results support the mediational hypothesis. When controlling for the mediator, cancer worry frequency (X) was no longer a significant predictor of worry's effect on daily functioning (Y),  $b = .57$ ,  $SE = .09$ , ns ( $p = .59$ ), consistent with full mediation. The indirect effect was tested using a bootstrap estimation approach with 10,000 samples. These results indicated the indirect coefficient was significant ( $b = .28$ ,  $SE = .07$ ,  $CI = .14, .42$ ) indicating a significant mediation effect.

These results did support the study's mediation hypothesis, *i.e.*, that for the LFS group the frequency of cancer worry would have a direct effect on the degree to which cancer worry affected daily functioning, and that this direct effect was mediated by how cancer worry affects one's mood. Based on this model, the more frequent the individual's

thoughts of cancer, the more their daily functioning is affected adversely, but this is a function of cancer worry affecting moods.

**Figure 7. Cancer Worry Mediation Model**



**Moderated Mediation Model**

The final step in model testing was to assess whether the coping styles of the LFS partner themselves and the coping style of their partners moderated the relationship between cancer worry and cancer worry affecting daily functioning. This part of the analysis plan employed a path analysis model to test for partner effects of coping style on cancer worry. Other studies have stressed the importance of analytic strategies that recognize that data from members of couples are non-independent (they are linked and correlated) (Brandao et al., 2014). Path analysis captures both the direct and indirect effects between partners while simultaneously accounting for partner interdependencies in the data (Cook & Kenny, 2005).

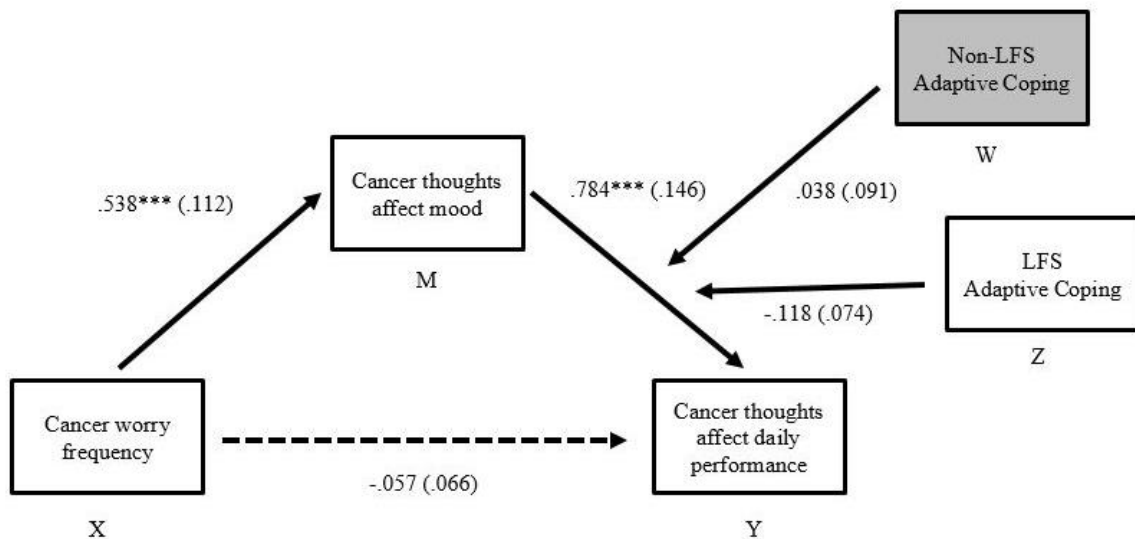
Using Mplus software, we analyzed each partner’s scores on each of the coping styles as predicting the LFS partner’s level of cancer worry affecting their daily functioning. Interaction terms between the two partners’ coping styles (four factors) and

frequency of cancer worry affecting one's mood were created. The moderators (adaptive coping for LFS and non-LFS) were calculated as measured variables for the final model because of the small sample size.

*Gender*

The moderated mediation model was run separately for gender, with one analysis specific to the model for female LFS partners and another analysis for the model for male LFS partners. There was a variance of zero in the male LFS score for the outcome variable and therefore that model would not run. We continued the analysis with data from only female LFS participants and their male non-LFS partners.

**Figure 8. Moderated Mediation Model Women with LFS and Partners**



The full moderated mediation model for LFS women is presented in Figure 8. Interaction terms were created by multiplying the mediator with each of the moderators. If the interaction term were significant, that would indicate a joint effect of MW or MZ, and a significant moderation effect. In this study, no significant interaction terms were observed, indicating that adaptive coping for the non-LFS spouse did not significantly moderate the relationship between the LFS spouse's cancer worry affected mood and

their cancer worry affected daily performance, as shown by nonsignificant interactions  $b = .038$ ,  $SE = .09$ , ns ( $p = .68$ ). These findings do not support the hypothesis that the more adaptive coping the non-LFS partner reports, the less that the LFS partner's cancer worry affected mood would affect their daily functioning. Additionally, the LFS partner's own adaptive coping did not moderate the relationship between cancer worry affected mood and daily functioning,  $b = -.12$ ,  $SE = .074$ , ns ( $p = .11$ ).

### **Discussion**

The purpose of the current cross-sectional study was to examine the relationship between general distress, coping, and cancer-specific distress for couples in which one partner had LFS. We used baseline data from participants with LFS and their spouses in the NCI's LFS Cancer Screening Study to compare each partner's general distress level, cancer-specific distress, and coping styles. One of the goals of this study was to test for significant differences between partners in general distress and cancer-specific distress in couples coping with LFS. The second goal of this study was to identify coping strategies of both partners that can alleviate the cancer-specific distress of a LFS partner. This dyadic-level goal specifically examined the relationship between cancer worry and mood and daily functioning among individuals with LFS, and also identified potential protective coping styles that partners employ that may be associated with reducing cancer worry's impact on daily functioning.

We hypothesized that (1) general distress (depression, anxiety, somatization, and perceived stress) would be higher for the non-LFS group, and specifically in women. The data did not support that hypothesis, and we did not find significant differences across LFS groups or gender. We also hypothesized that (2) the cancer-specific distress of LFS

partners would be higher than non-LFS partners, with females having more cancer worry. Our data supported this second hypothesis, with LFS females having the most cancer worry and highest perception of cancer risk, followed by LFS men, and lastly by non-LFS men and women. These results are what one would expect from a high-risk cancer sample, and the gender difference also appropriately parallels the higher cancer penetrance in women with LFS.

The present study also found a significant cancer worry mediation model for women with LFS only. For these LFS women, the frequency of cancer worry had a direct effect on how frequency of cancer worry affected their daily functioning, and this direct effect was mediated by how cancer worry affects individuals' mood. These results partially supported the hypothesis for LFS partners, but the outcome variable, cancer worry affecting daily functioning, had very little variation for male LFS participants and therefore was dropped from the model. Using just the female LFS partners, we tested the final hypothesis that the more adaptive coping the non-LFS partner reported, the less that the LFS partner's mood will affect their daily functioning. The data did not support this moderated mediation hypothesis, with neither the LFS partner's own adaptive coping nor their non-LFS partner's adaptive coping moderating the relationship between cancer worry affected mood and daily functioning. The methodological limitations of the data set may have contributed to the ambiguity of the findings for the moderator variables. The following section of this paper discusses some potential explanations for the lack of a moderating effect of coping on cancer worry.

## **Strengths and Limitations**

This sample size of 67 couples was both a study strength and limitation. Although the sample size is small, this study represents the largest sample of couples with LFS in the world. The only other study of couples with LFS had 17 couples in their sample (Lammens, 2011). Our small sample size was due to the rarity of LFS, as well as to the small number of spouses who enrolled and participated in the LFS screening study. There were also significantly fewer LFS men with female partners enrolled in the study (15 couples). This small male LFS sample is representative of the disproportionately high number of women with LFS enrolled (about two-thirds female participants) in the LFS Screening Study. The reasons for oversampling of women with LFS may be due to the fact that breast cancer is the most commonly occurring cancer in LFS, and consequently cancer occurrence/risk is higher for women. Additionally, women in general are likely to seek health care services (Thompson et al., 2017), health information (Stefan, 2015), and to engage in cancer screening (Davis, Buchanan, Katz, & Green, 2011). Future follow-up data collection and recruitment efforts will focus on enrolling more men with LFS and their female partners in the LFS Study cohort.

This study was subject to several other limitations that deserve consideration. First, the sample was limited in terms of racial, educational, and economic diversity. All participants were white, highly-educated, and wealthy, and thus do not represent the social and economic makeup of the United States. The participants' mental health and coping skills were sound, and these individuals were highly motivated to engage in research. Our participants were highly motivated and able to participate in a rigorous research study protocol that included hours of paperwork, visits to local doctors, regular medical testing, and annual trips to the NIH Clinical Center in Bethesda, MD, which



requires taking off time from work and/or finding childcare, although travel costs were underwritten by the study. They must also have been sufficiently savvy about the US health care system to successfully navigate genetic testing, insurance coverage for a rare syndrome, taking out a life insurance policy, and compiling medical records from all of the relevant procedures or screenings. This unique sample clearly is subject to significant selection bias; our results cannot be reliably generalized to the US population at large. Future research must include community-based recruitment and focus on oversampling, non-white, lower education and lower SES-status families. This can be accomplished by collaborating with health institutions that provide community-level care for a more diverse range of people seeking genetic testing, genetic counseling, and cancer screening. My/our data document that these study participants comprise a high-functioning group, with excellent coping skills. The maladaptive coping factor dropping out of the model may be due to this aspect of their positive coping.

Our data rely on self-reports, potentially subject to implicit or explicit biases. Social desirability may have played a role in under reporting distress or maladaptive coping styles. This may be due to the nature of LFS, in which families go through periods of relative normality while the partner with LFS is cancer-free; but when a cancer is diagnosed, there is a large adjustment and shift in the family that occurs. When the participants enrolled in the study and completed the questionnaires, they were not actively being treated for a cancer at that time (a requirement of the study). This limitation can be addressed in future analyses that combine both the quantitative results with some of the descriptive coping styles identified in Study Two of this dissertation. Mixing these findings may aid in the identification of LFS-specific coping styles.

A second limitation was the poor fit of the Brief Cope confirmatory factor analysis. This may be due in part to cross loadings of specific items on the two factors, adaptive and maladaptive coping. Contrary to our expectation, coping styles of members of married couples were only weakly correlated, which may illustrate the collaborative nature of couple coping, in which each partner specializes in different coping behaviors that are complementary, rather than mirroring the same coping behaviors. This measure simply asks respondents about frequencies of use of coping styles, but does not establish the processes that contribute to each partner's use of particular coping styles (e.g., an intent to protect one's partner from emotional distress regarding LFS). Thus, responses to the coping measure shed limited light on the dyadic interaction of partners' coping styles. We did not test the interaction of two partners' coping styles as a potential moderator, an approach that may be a valuable next step in research on couple coping with LFS.

Future research in this area might benefit from using different measures of coping, for example, moving away from measures of individual coping styles to using dyadic coping measures such as the Dyadic Coping Inventory (DCI) (Burri, Blank Gebre, Bodenmann, 2008: *Dyadic Coping Inventory Test Manual*). This measure has been used in studies of couples coping with chronic pain and other health conditions, but may also be applied to cancer and heritable cancer risk. The DCI may also address the lack of moderation effects on LFS partner's cancer worry. It is possible that an individual-level coping assessment may not be an accurate method for capturing the complex and interpersonal nature of dyadic coping. Additionally, the use of qualitative research methods has the potential to explore the unique coping styles that these couples employ in the face of cancer risk. The next paper in this dissertation explores dyadic coping from a Grounded Theory perspective and follows up on some of the questions that were raised

in this study. Social network analysis, used in Study 3, also helps broaden understanding of social support in this population. The Brief Coping only includes two indices of support: emotional and instrumental, and many participants reported high levels of these types of support.

A third limitation is the phrasing of the Cancer Worry scale for non-LFS spouses, which asked them to report the frequency with which they thought about their own risk of cancer (even though they are assumed to be at a lower risk of cancer than their LFS spouse). Therefore, future questionnaires could utilize a cancer worry scale that captures the degree or frequency of worry that non-LFS spouses report about their *partner's* cancer risk, rather than their own cancer worry.

Lastly, this study was cross-sectional, with the Individualized Information Questionnaires administered at baseline rather than longitudinally at various time points. Thus, results need to be interpreted with caution, especially given the small sample size. Future studies could either employ longitudinal data collection or utilize information gained from the qualitative paper of this dissertation regarding the unique coping styles of this population and their ongoing, low-level stress. The qualitative findings could be used to construct more appropriate measures of coping and distress, that then could be validated using a similar process of exploratory and confirmatory factor analysis.

In spite of these limitations, the present study makes several important contributions to the literature on couples coping with LFS. Most valuable, this is the first study that compared married partners' responses on multiple measures of distress, cancer worry, and coping in an LFS population. We obtained detailed medical and family histories, and used standardized and study-specific psychosocial measures. Second, the results of this study indicate that individuals with LFS and their partners were not

experiencing clinically-indicated levels of depression, anxiety, or somatization at the time of study enrollment. This is significant because the questionnaire was administered during the time when many families recently discovered the presence of *TP53* mutation in their family or they are about to receive genetic testing results. The results of the current study do not address how levels of distress or cancer worry vary once the participants enroll in the study and begin intensive screening. Study Two of this dissertation addressed this evolution of emotional experiences, since interviews occurred after enrollment and during their visits to the clinical center.

### **Clinical Implications**

Clinicians working with this population of LFS-affected families can utilize the information from this study in several ways. First, it may be helpful to consider that although there are gender differences in the level of perceived cancer risk, cancer worry, and cancer worry impacting mood and daily functioning, men and women with LFS both have frequent thoughts about their risk for cancer. More importantly, these thoughts occur on a daily or weekly basis and can influence the mood and daily functioning of patients.

People with LFS and their partners have multiple strategies for coping with this worry that are adaptive or maladaptive. Clinicians may want to make note of family members that are engaging in maladaptive behaviors such as behavioral disengagement, denial, or self-blame. Specifically, women married to men with LFS are more likely to engage in self-blame than men. Clinicians or mental health experts can remind both partners that they are similarly stressed and that it may be helpful to participate in joint problem-solving, joint information seeking, or relaxing together. Since LFS will be a part

of their lives for the long-term, couples may do well do recognize that coping styles may change over time and should seek professional help to them manage stress and health care concerns.

### **Conclusion**

In conclusion, although we had speculated that our participants might be very distressed and withdrawn due to the many physical, emotional and social challenges associated with LFS, this study generally found the opposite. Specifically, most participants reported few psychosocial symptoms, indicating low general distress, with only five participants meeting the criteria for clinically significant distress. The results of the present study indicate that LFS partners with LFS experience significantly more cancer-specific worry than non-LFS partners. Some women with LFS had thoughts of cancer multiple times a day, and most men and women with LFS were thinking about cancer with a daily/weekly frequency, which then affects their mood and daily functioning, especially for women with LFS. Although these couples employed multiple methods for coping with the stress related to finding out that they or a family member were at increased risk of cancer, these coping styles do not necessarily protect against the impact of cancer worry on mood and on daily functioning of people with LFS. Our findings show that although people with LFS are worried about cancer, this worry does not translate to significant levels of distress for themselves nor their partners. These subjects demonstrated remarkable resilience despite being challenged by one of the most complex cancer susceptibility syndromes.

## Tables

**Table 1. Descriptive Statistics of Analytic Sample**

	<u>LFS Partner</u>		<u>Non-LFS Partner</u>	
	Men (N = 15)	Women (N = 49)	Men (N = 49)	Women (N = 15)
Average age (years)	48.2	42.6	45.3	47.5
Age range (years)	27-84	22-65	27-71	27-80
<b>Educational level <i>n</i> (%)</b>				
Less than high school	1 (6.7%)	0 (0%)	0 (0%)	1 (6.7%)
HS grad or GED	1 (6.7%)	2 (4.1%)	3 (6.1%)	1 (6.7%)
Vocational/trade school	2 (13.3%)	2 (4.1%)	3 (6.1%)	0 (0%)
Some college	2 (13.3%)	6 (12.2%)	7 (4.3%)	1 (6.7%)
College graduate	2 (13.3%)	21 (42.9%)	13 (26.5%)	7 (46.7%)
Some graduate school	3 (20%)	2 (4.1%)	6 (12.2%)	1 (6.7%)
Masters or doctoral degree	4 (26.7%)	13 (26.5%)	14 (28.6%)	4 (26.7%)
<b>Income (&gt;\$50,000)</b>	80%	80%	77%	93%
<b>Children</b>				
<b># Children</b>				
0	1 (6.7%)	8 (16.3%)	8 (16.3%)	1 (6.7%)
1	3 (20%)	7 (14.3%)	8 (16.3%)	2 (13.3%)
2	4 (26.7%)	25 (51%)	25 (51%)	5 (33.3%)
≥3	7 (46.7%)	9 (18.3%)	8 (16.3%)	7 (46.7%)
Child average age	15.4	15.4	15.4	15.4
Child with LFS	9	19	19	9

*Note:* *n* = the number of participants, % = the percent of each LFS status and gender group that are in each category.

**Table 2. Personal Cancer History (all cancers combined)**

# of cancers	<b><u>LFS Partner</u></b>		<b><u>Non-LFS Partner</u></b>	
	Men (N = 15)	Women (N = 49)	Men (N = 49)	Women (N = 15)
0	6 (40%)	6 (12.2%)	43 (87.8%)	12 (80%)
1	5 (33.3%)	23 (46.9%)	5 (10.2%)	3 (20%)
2	2 (13.3%)	12 (24.5%)	1 (2%)	0
≥3	2 (13.3%)	8 (16.3%)	0	0

**Table 3. Cancer History in First-Degree Relatives of Participants with LFS**

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	<u>Male LFS</u>	<u>Female LFS</u>
<b>Family members had cancer (<i>n</i>)</b>		
Mother	5	31
Father	5	29
Sibling	24	37
Child	11	9
<b>Family died of cancer (<i>n</i>)</b>		
Mother	5	12
Father	3	18
Sibling	9	22
Child	2	1

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**Table 4. Participants' General Distress Scores**

	<b><u>LFS Partners</u></b>		<b><u>Non-LFS Partners</u></b>	
	Men (N = 15)	Women (N = 49)	Men (N = 49)	Women (N = 15)
<b>Brief Symptom Inventory - Mean (SD)</b>				
Global Distress	46.87 (9.93)	46.13 (9.47)	44.79 (9.10)	45.27 (10.35)
Anxiety	49.07 (8.46)	46.85 (9.39)	47.29 (7.83)	45.60 (8.71)
Depression	49.07 (9.57)	48.52 (8.38)	47.23 (7.25)	49.20 (9.73)
Somatization	44.87 (5.38)	45.92 (7.83)	44.15 (5.79)	45.73 (8.36)
<b>Perceived Stress Scale Global Score</b>				
Mean (SD)	12.60 (5.01)	14.57 (7.25)	12.29 (5.79)	15.53 (7.17)

*Note:* SD = standard deviation

**Table 5: Participants' Cancer-Specific Distress (perceived cancer risk and worry)**

	<u>LFS Partners</u>		<u>Non-LFS Partners</u>	
	Men (N = 15)	Women (N = 48)	Men (N = 47)	Women (N = 15)
<b>1) Compared with other people your age, what are your chances of getting cancer (or another cancer) in your lifetime?</b>				
	M = 4.20 <sup>a</sup> SD = 1.207	M = 4.88 <sup>b</sup> SD = .334	M = 2.64 <sup>c</sup> SD = 1.131	M = 3.00 <sup>c</sup> SD = .655
<b>2) Compared with other people your age, what are your chances of getting cancer (or another cancer) in your lifetime?</b>				
0 = no chance that I'll get cancer; 5 = I may or may not get cancer; 10 = I will almost certainly get cancer in my lifetime				
	M = 7.53 <sup>a</sup> SD = 2.748	M = 8.98 <sup>b</sup> SD = 1.28	M = 5.00 <sup>c</sup> SD = 2.075	M = 4.80 <sup>c</sup> SD = 1.656
<b>3) How often have you thought about your own chances of getting cancer (or another cancer)?</b>				
	M = 1.73 <sup>a</sup> SD = .799	M = 2.42 <sup>b</sup> SD = .942	M = 1.15 <sup>c</sup> SD = .416	M = 1.13 <sup>c</sup> SD = .352
<b>4) How often have thoughts about your chances of getting cancer (or another cancer) affected your mood?</b>				
	M = 1.33 SD = .488	M = 1.66 SD = .815	M = 1.00 SD = .0 Missing = 2	M = 1.00 SD = .000
<b>5) How often have thoughts about cancer affected your ability to perform your daily activities?</b>				
	M = 1.00 <sup>a</sup> SD = .000	M = 1.35 <sup>b</sup> SD = .635 Missing = 1	M = 1.04 SD = .204 Missing = 2	M = 1.00 SD = .000

*Note:* Means for cancer risk perception (questions 1 & 2) and cancer worry (questions 3, 4, & 5) were compared with non-independent *t*-tests. Means that have different superscripts are significantly different.

**Table 6. Detailed Responses of Perceived Cancer Risk and Worry**

	<u>LFS Partners</u>		<u>Non-LFS Partners</u>	
	Men (N = 15)	Women (N = 48)	Men (N = 47)	Women (N = 15)
<b>1) Compared with other people your age, what are your chances of getting cancer (or another cancer) in your lifetime?</b>				
Much less (1)	1 (6.7%)	0 (0%)	9 (18.4%)	0 (0%)
A little less (2)	0 (0%)	0 (0%)	10 (20.4%)	3 (20%)
About the same (3)	3 (20%)	0 (0%)	21 (42.9%)	9 (60%)
A little more (4)	2 (13.3%)	6 (12.2%)	3 (6.1%)	3 (20%)
Much more (5)	9 (60%)	42 (85.7%)	4 (8.2%)	0 (0%)
<b>3) How often have you thought about your own chances of getting cancer (or another cancer)?</b>				
Not at all or rarely	7 (46.7%)	9 (18.4%)	41 (83.7%)	13 (86.7%)
Weekly	5 (33.3%)	16 (32.7%)	5 (10.2%)	2 (13.3%)
Daily	3 (20%)	17 (34.7%)	1 (2%)	0 (0%)
Several times a day	0 (0%)	6 (12.2%)	0 (0%)	0 (0%)
<b>4) How often have thoughts about your chances of getting cancer (or another cancer) affected your mood?</b>				
Not at all or rarely	10 (66.7%)	24 (49%)	47 (100%)	15 (100%)
Weekly	5 (33.3%)	17 (34.7%)	0 (0%)	0 (0%)
Daily	0 (0%)	4 (8.2%)	0 (0%)	0 (0%)
Several times a day	0 (0%)	2 (4.1%)	0 (0%)	0 (0%)
<b>5) How often have thoughts about cancer affected your ability to perform your daily activities?</b>				
Not at all or rarely	15 (100%)	35 (72.9%)	45 (95.7%)	15 (100%)
Weekly	0 (0%)	9 (18.8%)	2 (4.3%)	0 (0%)
Daily	0 (0%)	4 (8.3%)	0 (0%)	0 (0%)
Several times a day	0 (0%)	0 (0%)	0 (0%)	0 (0%)

**Table 7. Participants' Coping Styles**

<b>Coping Styles</b> M (SD)	<b>LFS Partners</b>		<b>Non-LFS Partners</b>	
	Men (N = 15)	Women (N = 49)	Men (N = 49)	Women (N = 15)
1. Self-Distraction	4.87 (2.03)	5.10 (1.77)	3.88 (1.55)	4.27 (1.22)
2. Active Coping	4.47 (2.10)	5.45 (1.84)	4.88 (1.86)	4.93 (1.79)
3. Denial	2.52 (1.13)	2.16 (0.55)	2.18 (0.67)	2.60 (1.24)
4. Substance Use	2.07 (0.26)	2.69 (1.34)	2.73 (1.50)	2.53 (0.83)
5. Use of Emotional Support	3.87 (1.64) <sup>a</sup>	5.37 (1.74) <sup>b</sup>	3.63 (1.83) <sup>c</sup>	4.93 (2.02) <sup>d</sup>
6. Use of Instrumental Support	3.47 (1.30)	4.43 (1.90)	3.18 (1.58) <sup>a</sup>	4.53 (1.81) <sup>b</sup>
7. Behavioral Disengagement	2.13 (0.83)	2.33 (0.90)	2.24 (0.72)	2.47 (1.19)
8. Venting	3.00 (1.20) <sup>a</sup>	3.65 (1.20) <sup>b</sup>	2.82 (1.25)	3.27 (1.28)
9. Positive Reframing	4.53 (2.03) <sup>a</sup>	5.73 (1.95) <sup>b</sup>	4.39 (1.82)	4.93 (2.12)
10. Planning	4.20 (1.97) <sup>a</sup>	5.49 (1.86) <sup>b</sup>	4.59 (1.89)	5.07 (1.83)
11. Humor	3.93 (2.37)	4.22 (1.90)	2.73 (1.20)	3.27 (1.34)
12. Acceptance	6.40 (2.41)	6.86 (1.44)	6.22 (1.84)	6.47 (1.41)
13. Religion	3.87 (2.64)	4.84 (2.55)	3.35 (1.94) <sup>a</sup>	4.87 (2.33) <sup>b</sup>
14. Self Blame	2.73 (1.58)	2.69 (1.25)	2.49 (0.98) <sup>a</sup>	3.27 (1.34) <sup>b</sup>

*Note:* Means were compared with non-independent *t*-tests. Means that have different superscripts are significantly different.

**Table 8. Rotated Factor Analysis Pattern Matrices**

<b><u>LFS Partners</u></b>	<b><u>Factor 1</u></b>	<b><u>Factor 2</u></b>
Self-distraction	.369	.112
<b>Active coping</b>	<b>.691</b>	.008
<b>Denial</b>	.110	<b>.728</b>
<b>Use of emotional support</b>	<b>.560</b>	-.040
<b>Use of instrumental support</b>	<b>.609</b>	-.016
<b>Behavioral disengagement</b>	-.364	<b>.421</b>
<b>Venting</b>	<b>.616</b>	.226
<b>Positive reframing</b>	<b>.688</b>	-.106
<b>Planning</b>	<b>.822</b>	.011
Humor	.417	.133
Acceptance	.562	-.516
<b>Self-blame</b>	.234	<b>.404</b>

<b><u>Non-LFS Partners</u></b>	<b><u>Factor 1</u></b>	<b><u>Factor 2</u></b>
Self-distraction	.404	.360
<b>Active coping</b>	<b>.616</b>	-.019
<b>Denial</b>	-.084	<b>.769</b>
<b>Use of emotional support</b>	<b>.784</b>	-.017
<b>Use of instrumental support</b>	<b>.675</b>	-.025
<b>Behavioral disengagement</b>	-.136	<b>.819</b>
<b>Venting</b>	<b>.649</b>	.356
<b>Positive reframing</b>	<b>.602</b>	-.061
<b>Planning</b>	<b>.660</b>	.000
Humor	.428	.335
Acceptance	.365	-.237
<b>Self-blame</b>	.162	<b>.733</b>

*Note:* Bolded loadings indicate coping styles that were included in the final two-factor solution.

## CHAPTER 4: STUDY 2

### **In-depth Interviews with Couples Affected by Li-Fraumeni Syndrome**

#### **Background**

Li-Fraumeni Syndrome (LFS) is a rare hereditary genetic condition, and is most often caused by a deleterious mutation on the *TP53* gene (a tumor suppressing gene) (Lindor et al., 2008). A mutation in the gene results in an almost 100% lifetime risk of developing one cancer, and a 45% possibility of a second cancer developing later in life (Mai et al., 2016). Nearly half of affected individuals have a cancer diagnosis before the age of 40, and many individuals develop multiple cancers over the course of their life (Kratz et al. 2017). The *TP53* mutation is autosomal dominantly inherited, so parents have a 50-50 chance of passing the gene mutation on to their children. In many cases, cancers associated with Li-Fraumeni syndrome develop in children or young adults, but they can occur during any stage of life. People with Li-Fraumeni syndrome are typically younger when they develop cancer compared with healthy individuals in the general population. Thus, when a family member is tested and determined to be positive for LFS, lifelong cancer screenings are recommended to prevent and catch cancer early enough to avoid death.

#### **Psychosocial Impact of LFS Diagnosis on Families**

There are several routes to the identification of LFS and proof that the diagnosis is correct. One possibility is when a family member is diagnosed with cancer, the diagnosed individual's doctor or oncologist notices a strong prevalence of cancer in the family history, including the marked heterogeneity of age at affection and site-specific origin of

the cancers which characterize this syndrome. The combination of early-onset breast cancer and sarcoma in family members was the original finding that triggered the investigation of this disorder. Certain very rare cancers, such as adrenal cortical carcinoma and choroid plexus tumors represent a very strong clinical clue to the presence of LFS. the patient's doctor then recommends genetic testing. A family member who tests positive for deleterious germline mutations in the *TP53* gene confirms the diagnosis, but about 30% of patients with a clinical picture suggestive of LFS do NOT have detectable mutations in this gene. Presumably, there are other undiscovered genes which account for that minority of cases.

A mutation-positive family member with LFS may decide to spread the word to parents, siblings, cousins, aunts, and uncles, who are definable risks of themselves being carriers of the family's mutation, *i.e.*, 50% probability among first-degree relatives, 25% probability among second-degree relatives. From there, some families engage in cascade testing for the specific mutations in other family members begins, and multiple generations of *TP53* mutation-positive individuals are identified (McBride et al., 2017).

The degree of open communication about genetic testing differs from family to family. Given the nature of modern family relationships and the complexity of genetic information itself, communication of testing results can be difficult or even impossible in some circumstances (Patenaude, 2006). Patients bear primary responsibility for sharing their information with relatives, but various factors (*i.e.*, infrequent communication, poor relationship quality, or fear of the other relative's reaction) may prevent a patient from sharing the genetic testing information with potentially affected relatives.

Another complexity to the LFS story is the fact that approximately 14% of people with LFS are affected by a "*de novo*" (new) mutation. The ancestors and siblings of such

a person will not carry this mutation, nor will they have a strong family history of cancer. However, the descendants of a *de novo* carrier can transmit the mutation to their own children (Renaux-Petel et al., 2018). Regardless of whether a person inherits a mutation or the mutation occurs for the first time in a person, that person has a 50% chance of passing on either their own normal copy of the *TP53* gene and a 50% chance of passing on their mutated copy of the gene to his/her child.

The *TP53* test, unsurprisingly, often contributes to psychological distress for the person undergoing the testing. Peterson et al. (2008) examined the psychosocial functioning of individuals undergoing genetic testing for LFS. They found that greater cancer-specific distress for *TP53* mutation carriers was associated with factors such as a lower quality of life and a higher number of first-degree relatives with cancer. Additionally, even without a personal cancer diagnosis, individuals who reported a higher perceived risk of having the *TP53* mutation reported significantly more cancer-specific distress. A case study examined the experiences of an individual female with multiple independent primary malignancies and explored the benefits and burdens of ongoing cancer screening (Jhaveri et al., 2015). The researchers used this case to point out that although aggressive cancer screening can provide temporary relief when no cancers are found, the emotional trade-off is the anxiety of a possible cancer diagnosis that exists leading up to the screening, as well as any “false positive” scan results that have to be followed up with a biopsy or additional scans.

The cancer-related implications of *TP53* mutations have been studied for the past two decades, and medical protocols for close monitoring and full body cancer screening have been developed (McBride et al., 2014).(McBride et al., 2014). The screening protocols developed in the past five years have shown significant survival benefits for



individuals with LFS (Villani et al., 2011). One example of a comprehensive screening protocol is the Toronto Protocol (Kratz et al., 2017), which combines annual brain magnetic resonance imaging (MRI), annual rapid whole-body MRI, annual breast MRI for female patients, physical exams every 6 months (including blood and urinalysis), and colonoscopies every 2-5 years.

Although the main goal of screening is to increase survival for patients with LFS by detecting cancers at an earlier stage in their natural history, at point in time when the cancer may still be curable. These screening protocols require significant investments of time and resources, and can be emotionally exhausting for the patients and their families. A meta-analysis of 578 participants with LFS from 13 cohorts in 6 countries found that at first baseline MRI-based cancer screen, the overall detection rate of new cancers was 7% (Ballinger et al., 2017). An LFS screening program at MD Anderson Cancer Center evaluated the benefits and drawbacks of intense early detection cancer screening (Ross et al., 2017). They found that participants reported the perceived drawbacks (logistical issues, difficulty navigating the system, screening being draining, negative emotional reactions) did not outweigh the benefits (peace of mind, centralized screening, knowledge as power, screening making LFS more livable). The study found that despite significant benefits of screening, there are still notable drawbacks that may limit engagement in screening protocols. Many of the participants in the study also mentioned that the screening protocol had a large impact on their families and that family emotional and pragmatic supports were important to comply with the screening process. Yet, the precise impact of screening on multiple family members, with or without LFS, is not yet well understood, largely because these protocols are relatively early in their development. The risk perceptions and family beliefs of non-LFS family members regarding genetic testing

and screening utility are important in understanding their decisions for making shifts in family resources in response to a perceived threat. The family members' joint perspectives and influence on a patient's screening behaviors have not been explored. This indicates a need for further research on the family implications of LFS cancer screening that includes the viewpoints of multiple family members.

The medical community's focus on the patient or individual with LFS ignores the risk of LFS for family members, caregiving burden, shared anticipation of a diagnosis, and the psychological impact that LFS can have on family members. Having a heritable form of cancer risk can strain the resources of individuals and families because of the nature of cancer (van Oostrom et al., 2007). Families with heritable cancer often deal with multiple aspects of cancer treatment and prevention for several family members over time, often simultaneously. Cancer diagnosis and treatment, recovery from cancer, and continued anticipation of cancer can all have significant mental health effects on the individual with LFS as well as his or her family members and other loved ones (Harris et al., 2010).

This study applied tenets of a family systems framework to the context of couple experiences with LFS, consistent with prior research demonstrating the significant role that spousal relationships play in cancer experiences and high cancer risk syndromes. Using Family Systems and Family Resilience frameworks, we applied qualitative research methods of data collection, coding, and validation to identify themes from interviews of couples affected by LFS, with an emphasis on how couples' relationships shift in response to threats to their health and the well-being of their family.

## **Family Experiences with Li-Fraumeni Syndrome**

In the general medical oncology community, the term “affected” refers to an individual who has had cancer. In the cancer genetics community, individuals with a germline mutation in a known cancer susceptibility gene are at varying degrees of cancer risk, although they may not (yet) have developed a cancer themselves. In a genetic sense, such a person could be described as “affected” as well.

In this paper we expand this definition. We assume that cancer and the not yet manifest cancer susceptibility affects the individual with cancer, the person’s spouse/partner, the rest of their family, and potentially their social, networks; *i.e.*, the whole family system is affected. Family systems theory suggests that individuals cannot be understood in isolation from one another, but rather as a part of their family, as the family is a socio-emotional unit (Bowen, 1978). As a result, we use the term “affected” to indicate any person or relationship that has been touched by the increased risk of cancer or a cancer experience. Research shows that the family system can greatly influence the members’ degrees of distress and worry regarding each cancer occurrence, because these emotional experiences are interrelated (Hagedoorn, Buunk, et al., 2000). The literature has shown mixed results regarding the psychological and emotional functioning of these families. Participants with LFS in (Peters et al., 2016) study of emotional, tangible, and spiritual forms of social support did not report a lack of support or confidants in their lives. In contrast, another study of distress in people with LFS found that both LFS partners and non-LFS partners had clinically significant levels of distress (depression, anxiety, somatization) and reported a desire for increased mental health support for themselves and their partners (Lammens, 2010). It is important to investigate these

contradictory findings to better address the emotional, social support, and mental health needs of families faced with a high burden of cancer risk.

The psychosocial research related to genetically heritable forms of cancer has not been expanded beyond the study of individuals with heritable diseases, and studies looking at multiple family members with LFS are still needed. Currently, the majority of the qualitative research in this area focuses on the individual family member with the diagnosis, but this overly simplifies a complex family process over a lifetime. Family dynamics and systemic reactions to stress are important parts of the LFS experience. The analysis of this phenomenon must be expanded beyond the individual level to the family level. Specifically, research that integrates assessments of how multiple family members are affected by LFS and how they deal with this diagnosis together would more accurately capture their collective experience and could better serve clinicians working to support these families.

### **Cancer and Couple Relationships**

One of the most important relationships in a family is the spousal dyad, which serves as the foundation for family formation in traditional family structures. Studies have shown that intimate partner relationships are the single largest source of happiness in a person's life, as well as the largest source of distress and violence (Rakovec-Felser, 2014). The quality of couple relationships has a large impact physical and mental health and well-being (Berkman, 2000). The daily transactions of social support between intimate partners affect psychological functioning of each individual partner, their health behaviors, as well as their health outcomes (Sarma et al., 2018).

The present study is the first to our knowledge to qualitatively study couples coping with LFS. The scope of this paper has been narrowed to focus on dyadic partner

relationships between heterosexual individuals with LFS and their married partners. Focusing our attention on married couples is a starting point for understanding the development of the entire family. The rarity of psychosocial studies on people with LFS and their families presents a unique opportunity to apply a family systems lens to the challenges faced by couples and move beyond individual-level data.

Couples who learn of an LFS diagnosis for one of the partners must learn how to negotiate new roles, create new meaning in their lives in the context of LFS, and cope together with the diagnosis. Partners of individuals with LFS may be unsure how to best support their partner and the rest of the family. As the non-LFS partner, they may struggle with finding appropriate ways to be involved in medical treatment, prevention, and advocacy of their LFS-positive partner. They also may underreport the impact that the LFS diagnosis and the risk of cancer have on their partner, as well as on their own psychological and emotional well-being, because a common style of coping by spouses of cancer patients is *protective buffering*, in which a spouse hides his or her concern and emotional distress from the patient in an effort to protect them from further worry (Hagedoorn, Kuijer, et al., 2000). The individual covers up their own distress as an attempt to protect the sick partner, but this does not mean that the non-LFS partner is unaffected by the diagnosis. As a result, the couple may no longer engage in the open communication required for them to share their innermost thoughts and feelings without fear of hurting the other. Consequently, it is important to explore factors that influence a couple's tendency to engage in protective buffering, especially when they are living with a major stressor such as LFS for the rest of their life.

One study of individuals with LFS and their partners (Lammens et al., 2011) found that many LFS participants reported a serious need for mental health support

services for their non-LFS spouses and partners. The researchers examined distress in 50 partners of individuals with LFS and Von Hippel-Lindau disease (VHL)<sup>2</sup> and found that 28% of the partners reported clinically relevant levels of distress related to the cancer syndrome (Lammens et al., 2011). Levels of distress and worry reported by the partner were significantly correlated with the distress level of the high-risk spouse. The researchers also found that younger partners as well as partners with less social support reported greater distress. 76% of the partners who participated in the study believed that they, and not only their at-risk spouses, should be offered routine professional psychosocial support. From this research, we can conclude that the distress and support systems of non-LFS spouses are important to consider both for their own well-being and the well-being of the spouse with LFS. However, this prior research did not evaluate dyadic models in which the distress levels of two partners interact and, due to the small sample sizes that are unavoidable in rare diseases, the results solely consisted of correlations and linear regression analyses, rather than multilevel modeling.

To build a conceptual model for the present inquiry into dyadic effects of LFS, we extrapolated from results of studies regarding the variety of roles that non-bloodline partners may inhabit when their partner is experiencing a newly-diagnosed sporadic cancer; i.e., support person, co-parent, decision-maker, health proxy, and caregiver (Q. P. Li, Mak, & Loke, 2013). Data on the cancer experiences of couples coping with sporadic cancers can shed light on the range of psychosocial challenges that LFS couples might face. One study by (Manne et al., 2004) examined associations among couple communication regarding cancer, psychological distress, and relationship satisfaction of

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<sup>2</sup> Von Hippel-Lindau disease is another rare autosomal dominant cancer syndrome that results in higher risk of a broad range of tumors developing in early childhood or adulthood.

women diagnosed with early stage breast cancer. A sample of 148 couples completed a videotaped discussion of a cancer-related issue and a general issue in their relations, as well as measures of psychological distress and relationship satisfaction. Videotapes were coded with the Rapid Marital Interaction Coding System (Heyman et al., 2001). The researchers' analysis focused on partner responses to patient self-disclosures. During the cancer-specific discussions, patients reported less distress when partners responded to disclosures with reciprocal self-disclosure and humor and when partners did not immediately propose solutions for the other's problem. The researchers found that when couples were discussing a general issue, the link between partner responses to patient self-disclosures and patient distress was weaker than when they were discussing cancer. The results suggested that male partner openness in their responses played a role in helping women adapt to breast cancer, specifically increasing reciprocal self-disclosure, using humor appropriately, and reducing problem-solving attempts, which may improve adaptation and relationship intimacy during and after this stressful life event (Manne et al., 2004). Overall, these findings on bi-directional communication and humor suggest that couples dealing with a stressful illness experience find support in open discussions regarding the breast cancer of the female partner. Yet, these studies do not address the ways in which communication styles vary over time for couples who face multiple cancers, and the experience of men with a cancer diagnosis and their unaffected female partners.

Studies of other heritable cancer syndromes, such as Hereditary breast and Ovarian Cancer associated with mutations in the *BRCA1/2* genes, provide insight into how couples cope with high risk of cancer. A study by Metcalfe et al. (2002)(Metcalfe et al., 2002) measured the specific needs of the spouses of individuals who received genetic

counseling for a positive *BRCA1/2* result. The researchers surveyed 59 spouses of female mutation carriers. The mean length of relationships was 26 years (range: 2.5-50 years). All participants were supportive of their spouses' decision to undergo genetic testing and counseling. Four respondents stated that they wished that they had received additional support at the time of test disclosure, and 20% felt that their wives had received inadequate support. One-quarter of the spouses believed that their relationship had changed because of genetic testing; most felt that they had become closer to their wives. Husbands were most concerned about the risk of their wife dying of cancer (43%), followed by the risk of their spouse developing cancer (19%) and the risk that their children would test positive for the *BRCA* mutation (14%). Distress levels, measured by the Impact of Event scale, suggested that few spouses were experiencing clinically elevated levels of distress, compared with the general population at the time of data collection. Specifically, distress was measured by the level of intrusion that genetic testing results had on their lives, as well as how much the partners avoided the event. Men with a high school education or less displayed significantly higher levels of distress than more educated men, but age and cancer status of their female partners was not associated with varying distress levels. The researchers suggested that the gender discrepancies regarding reported distress may be due to male partners minimizing their distress in order avoid worrying their partners or a general gender difference regarding reports of clinical distress, with women more likely to admit distress than men due to socialization into culturally-specific gender roles. The impact of genetic testing varies by couple, but these findings indicate important gender differences, and encouraging results about the increased closeness of couples after a genetic test. Regarding limitations of the study, there was a lack of follow-up questions and an opportunity for interviews with the



male partners. In addition, the study only assessed one time point in the experiences of one partner. When applied to the experiences of couples with heritable cancer syndromes, the study only utilized individual-level analysis at the beginning of living with the cancer syndrome and did not include dyadic-level analyses.

Prior studies that have examined participants' perceptions of relationships in heritable cancer syndromes have focused on heterosexual, mostly male partners of mutation-positive individuals. Hoskins et al. (2008) conducted in-depth interviews with 11 young women who learned before marriage that they had a high risk of early-onset breast and ovarian cancer due to their *BRCA1/2* mutation status. The narratives that were collected through the interviews illustrated the complexity that the women faced in forming a relationship with a new partner, with regard to sharing information about their mutation. An opportunity for relationship-building was highlighted when they shared their experiences of disclosing their *BRCA* mutation status to partners. Although the disclosure was often preceded by feelings of fear and anxiety, many participants reported that doing so had positive effects on their relationships. If the partner was able to respond with interest, empathy, and affection, the participants reported increased future intimacy and increased attachment (L. M. Hoskins, Roy, Peters, Loud, & Greene, 2008). (L. M. Hoskins et al., 2008). Thus, interviews represent a more comprehensive and potentially beneficial approach to gaining information about relationships of couples affected by LFS.

The complexity of couple dynamics in the context of heritable syndromes has yet to be captured in a study that involves both partners in an in-depth discussion about the syndrome and their relationship patterns and changes in relation to the syndrome. Prior studies have provided valuable information about communication patterns and

perceptions of each individual partner, but very rarely were both partners included in the discussion, and dyadic processes of coping were not the focus of those studies. The present study paper takes a family systems and strengths perspective to investigating the multifaceted dyadic process of living with LFS.

### **Theoretical Framework**

The Family Resilience Framework (Walsh, 2012) guided this study of couples' processes of coping processes with LFS. This framework is part of a movement in recent decades to shift away from an overemphasis on pathology and family deficits to more attention on family strengths. Family resilience, in this model, is defined as how a family adapts, works through, and learns from stressful situations, developing personal resources as a result of being challenged. One of the basic premises guiding this framework is that stressful events and persistent challenges influence the whole family, and in turn, specific family processes mediate the level of recovery and development of resilience of each family member and the entire family as a whole. Interventions that employ this framework are aimed at building family strengths when addressing problems, thereby reducing vulnerability to future stressors. Hopefully, as families become increasingly resourceful, their ability to meet future challenges will be improved. Family resilience is not the same for every family, but there are some common characteristics that have been found to distinguish families that can successfully cope from families that are unable to regroup after a major stressful event such as an LFS diagnosis. One of the common strengths is the ability to seek out emotional support and tangible practical support from each other as well as from the family's external support network when under duress from life stressors. If families are not equipped with the resources to mitigate the various

stressors associated with diagnosed cancer risk, those stressors may have a detrimental impact on the emotional quality of their relationships, their communication, and family cohesiveness.

The Family Resilience Framework has been used to explore family challenges such as a mental illness diagnosis, divorce, and deployment in military families (Walsh, 2002). In the context of LFS, people do not always define their situation as presently severe, unless they are currently being treated for a cancer. However, the challenges of living with LFS may not always be so immediately and clearly observable; rather, they may manifest as chronic, ongoing, and changing over time, such as the anticipation and stress of possible future cancer diagnosis or loss of a family member to cancer. These types of anticipated losses fall into the category of what Riskind (1998) has described as “looming vulnerability” in which individuals and other family members are experiencing the anticipatory danger of significant losses and grief over the ambiguous expectancy that sometime in the future the diagnosed person may die from cancer. Thus, since resilience does not mitigate a family’s risk of cancer, resilience must be applied to the family’s preparation for future events that may threaten their family functioning. Rolland (2006) has emphasized the utility of using the concept of anticipatory loss, defined as “the experience of living with possible, probably, or inevitable loss,” (p.140) as a framework for investigating the emotional experiences and meaning-making processes of families dealing with LFS.

### **Objectives**

**Research Question:** How do couples in which one partner has LFS cope with their own/their partner’s elevated cancer risk and the possibility of premature mortality?

This study involved in-depth qualitative interviews with couples in which one partner had *TP53* mutation-positive LFS, to identify the challenges unique to couples coping with LFS, to explore what coping strategies and resources couples use to manage the emotional, pragmatic challenges, and to assess the natural history of resilience. For this purpose, couple resilience was defined as role flexibility, dyadic adaptation, and balancing of responsibilities. Specifically, this study focused on couple dynamics, as well as the ways in which married partners discuss LFS as a shared burden, the extent to which couples approach cancer treatment and prevention together, and how the couples handle cancer-risk related issues regarding their children (genetic testing, discussing cancer with them, etc.). The goal of the study was to contribute to an ongoing effort to help families affected by LFS navigate changes to their daily life and outlook on the future.

Living with heightened vigilance regarding cancer can have a range of psychological and emotional effects on families with LFS. Using a Family Resilience framework, this study was designed to identify the strategies that couples describe using in response to ongoing challenges that couples face, either as the person with LFS or married to a person with LFS. Specifically, this study explored specific processes of joint coping that couples have used, as well as the values, attitudes, and beliefs that they hold regarding how to best cope with the ongoing threat of cancer.

## **Methods**

This study was part of the Li-Fraumeni Syndrome Cancer Screening Study (11-C-0255, ClinicalTrials.gov; Identifier NCT01443468; [www.lfs.cancer.gov](http://www.lfs.cancer.gov)) conducted at the National Cancer Institute and approved by the NCI Clinical Center Institutional Review

Board. The main goal was to investigate the clinical, epidemiologic, and genetic etiology of LFS, as well as to establish a national and international standard for cancer screening for individuals with or at risk of LFS. To establish a standard routine physical screening for people with LFS, a cohort of participants has been invited to the National Institutes of Health (NIH) Clinical Center to do full body, brain, and breast MRIs (for female participants who still have intact breasts), complete physical exams, and psychosocial interviews. The psychosocial interviews are conducted with each member of the family individually and with all presenting members together.

### **Data collection**

From its inception in 2011, the LFS study conducted extensive recruitment by establishing a study website and disseminating information to a network of oncologists and genetic counselors, and the membership of relevant medical professional societies (the most common mode of referral to the study). Prospective patients and their families were referred to the Clinical Genetics Branch (CGB) by NIH clinicians and other healthcare professionals from outside NIH, the NCI Cancer Information Service, interested laypersons, and family members themselves. Interested individuals contact the CGB. A CGB Referral Team research nurse then conducts a telephone interview with the patient or another member of the family to collect cancer history information on the individual and family. Such information includes enumeration of extended family members, type of tumors, ages at diagnosis, number of multiple primary tumors, vital status, number of affected and unaffected individuals, etc. Once it is established that the person has met the clinical criteria for LFS and does not have an active cancer at the time of enrollment, they are enrolled and provided with consent information. Additionally, family members related either by blood or through marriage were allowed to participate

in the study, though if they were not at high risk for cancer, they did not participate in the cancer-screening portion. For more detailed information regarding the inclusion and exclusion criteria, please see Mai et al. (2016). Participants who enrolled in the study underwent a rigorous baseline evaluation, which included both medical and mental health history assessments. After the baseline evaluation was completed, participants are assigned to the clinical and field cohort. The non-clinical field cohort is followed over time by the researchers and provided recommendations for care as well as annual newsletters and questionnaires. This cohort may engage in recommended screening locally, but are monitored to observe their healthcare actions. The clinical cohort travels to the NIH Clinical Center annually for a 1-2 day visit that includes a range of MRIs, blood tests, and interviews.

Participants are allowed to bring one support person during their visit to the Clinical Center, and these support people range from siblings to friends to parents to spouses. Participants are not required to bring a support person, and often the friend or family member who travels with them varies from year to year. Support persons who consent to enroll in the study agree to complete the same psychosocial and medical history assessments as the LFS patients. Participants, their support people (if considered a family member), and/or a family member who is also enrolled in the study are invited to complete a family interview.

The participants first completed an individual Colored EcoGenetic Relationship Map (CEGRM) interview with a genetic counselor, a healthcare professional with specialized training in medical genetics and counseling. The CEGRM is a novel counseling tool, a simple method of obtaining detailed social exchange information through an interactive process that produces a concise, visual representation of selected

social exchange domains (information, tangible, emotional, and spiritual/religious support) with color-coded symbols applied to the genetic pedigree, to increase the understanding of communication and support within cancer-prone families (Kenen & Peters, 2001; Peters et al., 2016). After completing the CEGRM, couples met together with a Marriage and Family Therapist for the family interview.

Interviews lasted approximately one hour and were audio recorded with the permission of the participants. Transcripts of the interviews were requested from the research team to be analyzed for the current study. Participant names and other personal identifying information were removed from this dataset and replaced with pseudonyms prior to analysis, and all identifying information has been removed from the transcripts. The transcripts were stored on a secure NIH computer that is password protected, as was the data analysis file in the Dedoose qualitative analysis software was also password-protected.

## **Sample**

A total of 64 family interviews were conducted between 2012 and 2017 during annual coordinated care visit to the NIH Clinical Center. Of these 64 interviews, 26 included couple pairs (52 individuals). Although sexual orientation and marital status were not part of the exclusion criteria for this study, all couples were heterosexual and married. Of those 26 couples, 21 included a female partner with LFS. Participants' ages ranged from 22-61 years. 17 of the 25 couples included a partner with an LFS-cancer history. Table 8 presents a complete description of the demographics of the participant sample.

Of 18 couples that reported their level of education, over 60% had a college degree and many have a graduate degree. Out of the 18 couples that reported their income level, 50% have an annual income of over \$100,000, well above the national median household income in 2016 of \$57,617 (Guzman, 2017). For the 21 couples that reported marriage duration, the average length of marriage was 15 years and the range was 2-32 years. These participants possessed a high-level of familiarity with healthcare systems, since the LFS Screening study requires an intense amount of paperwork to enroll and to continue to participate annually. After visits to the National Institutes of Health Clinical Center, frequent follow up is required, either at home or at the Center, to assess if a finding from the MRI could be a possible cancer. In addition, participants must have the ability to take several days off work each year to come to the Clinical Center for the screening, as well as to schedule doctors' appointments every four months for blood draws. Over half of the sample reported a religious affiliation, including: Catholic, Protestant, Jewish, LDS/Mormon, and Methodist.

Most of the couples have had at least one child. Of those, only four couples had not tested any of their children for the familial *TP53* mutation at the time of the interviews. Out of the total 47 children of participants, 79% had undergone genetic testing for the *TP53* mutation and 34% tested positive. Three couples had a child who had died due to cancer. See Table 10 for information on couples' children.

### **Design: Grounded Theory and Interpretive Description**

The data analysis used the tenets of grounded theory (GT) (Charmaz, 2006; LaRossa, 2005) and interpretive description (ID) (Thorne, 2008). GT is an iterative



method in which data collection and analysis occur simultaneously. ID uses GT as its foundation, and has its methodological roots in nursing research, which contextualizes biomedical and psychosocial experiences in preexisting empirical and practice knowledge.

### **Interview Protocol**

Multiple members of the LFS research team at the NCI collaborated to build the interview guide, including a family therapist, genetic counselor, social work consultant, and oncology medical staff. The interview guide included a semi-structured protocol, modified for the constellation of family members attending the annual visit. The goal of the family interview protocol was to focus on intra-family communication issues, reproductive decision-making, couple relationships, cancer prevention behaviors, and choices regarding genetic testing for adults and children.

### **Data Analysis**

Transcripts were analyzed using the inductive analysis steps of thematic, axial, and open coding, informed by grounded theory methodology. The coding team was comprised of four researchers trained in qualitative methods with experience working with medical transcript data. During the initial readings of the interviews, three coders conducted open blinded coding on three transcripts individually, identified significant content, and noted personal reactions and reflections. Researchers used Dedoose software to conduct open thematic coding toward the development of a codebook, and initial coding identified sensitizing concepts such as “partnering, family development, and

parenting”. At this point, the team’s first qualitative codebook was developed to outline and define each theme.

Two researchers then blinded six transcripts and coded them independently using the first codebook to check for inter-coder differences regarding code length and code definitions. Discrepancies were resolved through discussion, and selective coding for specific themes began. After half of the transcripts were coded by one person, three codes were determined to be too broad (family of origin, parenting, and coping), and the first author used thematic coding again to create child codes that fell underneath the three larger parent codes. These additional child codes were added to the codebook, and transcripts were recoded using this second, refined version of the codebook. The codebook was modified and finalized, and two researchers independently coded all transcripts. In the final analysis phase, the coding team met to discuss interpretations and synthesize findings into recurring themes.

Linguistic analysis was employed to tag specific phrases and words that reflected aspects of participants’ identity. Included in the codebook was a theme regarding pronoun use, and plural versus singular identifiers were coded on a scale from 0 “I” to 10 “we”. A code of 5 was used when a speaker alternated use of “I” and “we” in the same sentence.

### **Data Quality**

This study employed the following methods to maximize rigor and trustworthiness of the findings:

**Group process data analysis.** A team-based approach to coding and synthesizing findings was used during the data analysis stage of this study. First, two coders checked

each other's findings and established consistency across individual findings. Second, a seasoned qualitative researcher and medical provider with expertise in hereditary cancer genetics provided mentorship and additional feedback regarding the thematic findings of the study. These strategies facilitated the validation of the data and findings through cross-verification from multiple sources.

**Team debriefings.** The Li-Fraumeni Syndrome Screening clinical research team met weekly to discuss upcoming meetings with families that were coming to the clinic and to review most recent visits to the clinical center. The researcher who served as interviewer on this project participated in these weekly debriefing sessions as well as one-on-one debriefing with the genetic counselor that conducted the individual interviews. The purpose of these meetings was to discuss any concerns regarding the mental health of the participants, follow up on questions, and cross check information gathered from multiple sources. In addition, peer debriefings with another qualitative researcher who observed family interviews provided a preliminary direction for the analysis process.

**Prolonged exposure and time in the field.** Over the course of three years, the primary interviewer conducted over 60 family interviews with multiple configurations of family members, such as sibling pairs, couples, parent-child groups, *etc.* During this extended period of time, the interviewer became intimately familiar with these families and developed familiarity with some of the common challenges and strategies employed by families in the face of LFS. The semi-structured nature of the interview allowed the interviewer to probe regarding specific issues or clarify family coping processes. This technique and the time invested allowed the researcher to develop relationships and rapport with family members and aid in the co-construction of meaning between researcher and members of the LFS community.

## Findings

Couples across the study described living with a sense of *ambiguous danger* due to the persistent threat that disease could manifest itself suddenly and pose great threat to the individual's well-being and survival, yet they did not have clues as to onset, course, or outcomes. As a result, couples remained in a constant state of apprehension. Here Bert illustrates what it is like to know his wife's family history with cancer:

*Bert: We're both worried. After you've seen it [cancer] happen, and you've seen it happen to her, her father, her sister. You know where you finish the race, you just don't know when you're finishing the race.*

From this description, Bert demonstrated how he shares his fear with his wife and her family regarding the uncertain nature of the cancer timeline and how cancer's inevitability makes them feel worried that his wife will get cancer and die early.

## Ambiguous Danger

Like Bert and his wife, couples participating in the screening study discussed coming to the NIH in hopes that screening would detect cancer at an early stage so that they have a higher chance of survival. Yet, the annual intense screening also came at an emotional cost. Some spouses described the cycle of stress regarding annual cancer screening and the fear of finding an abnormal result or learning about another preventative surgery that might help reduce the risk of future cancer. The spouses were very attuned to the anticipation of results that could come out of a screening visit, and partners without LFS were perceptive of their partners' anxiety leading up to the visit. Tim says of his wife's annual screening, "We play Russian roulette once a year, but the

game is never over.” This is a statement that expresses the lifelong burden of worry and anticipation specific to the cancer screening that they participate in every year. Tim and his wife Jackie must wait for days after the screening test results come back to learn whether or not a new cancer has developed. For these couples, annual screenings add to the chronic nature of LFS, and are combined with an ongoing sense of ambiguity related to the potential stressor of cancer.

Thematic coding of the 26 transcripts revealed two prominent typologies of coping with the screening and disease burden associated with LFS. First, nineteen couples *coped in connection*, in which both partners identified LFS as a shared challenge. Partners in this category used language to indicate mutuality and shared identity as their approach to living their lives with LFS. Second, nine couples *coped independently* and regarded the stress of LFS as affecting them individually. Partners in this category frequently used bi-directional protective buffering to shield their partner from distress. Withholding these emotional reactions and experience often increased isolation and disconnection within the relationship.

### **Coping in Connection**

The majority of couples engaged in cohesive coping styles that reinforced a sense of togetherness through uncertainty and demonstrated the value of the relationship. Three specific behaviors served as indicators of mutuality. First, in the shared interview, both partners revealed concerns about the threat of cancer to their lives and family, indicating their engagement in open dialogue. Joe and Veronica found out that Veronica had LFS during their engagement period, while they were planning their wedding and their life together:

*Veronica: It put us into a position that we didn't have a choice but to be strong and hold on together. We're dealing with something serious and we don't have time to worry about little, stupid things. We reached a different level in our relationship.*

*Joe: It put things in perspective. My thing was, "Stay focused." Do what we need to do. Get married. Live the rest of our lives.*

Second, these couples viewed LFS as a "We-stress" and used plural pronouns to address themselves when talking about LFS. Third, these couples provided examples of how they were attuned to each other's needs and alternated sharing the burden of LFS-related stress.

**"We" versus "I".** Couples' deliberate and specific use of "we" served as a proxy for the sense of joint ownership over managing and coping with LFS. The frequent use of "we" by non-LFS spouses indicated a high level of involvement in care. The use of "we" in the following example captures the intensity with which the non-LFS partner takes responsibility for and part in the health and care of the LFS-partner:

*Tim: Well, we've been very blessed with a clean bill of health now repeatedly. And I think a part of me, knowing that we've been granted sort of a reprieve, we've been given another clean bill, and not that we might not be still given one, but we're going to have – and that's fine. We'll deal with whatever has to happen, and the timing of that, and how it affects whatever. We'll just make a plan, and we'll do it.*

Tim uses "we" to describe his wife's past and present health status, as well as their future plans. This demonstrates his perspective on a joint front in the face of potential cancer and his pragmatism in response to his wife's distress.

**Balance/taking turns.** Partners also demonstrated a shared commitment to a joint approach to coping by alternating emotional caregiving and taking roles. They described a process in which one would serve as the emotionally “strong”/capable/ supportive partner while the other expressed a need to emotionally grieve/process and withdraw momentarily from family responsibility. Based on timing and life events, partners switched roles of who leaned on whom for strength. For example, the news that Veronica was positive for the *TP53* mutation was difficult for her to handle. To support her initial adaptation and relieve her of the burden, her husband Joe made phone calls to share the news with family members:

*Veronica: Our parents knew I was getting tested; they knew there was a chance.*

*Joe: I probably made the phone calls.*

*Veronica: Yeah. I don't remember.*

*Joe: You probably didn't do it. I probably made the phone calls.*

*Interviewer: And told everyone?*

*Joe: Yeah. I don't think it was – you weren't in a good state of mind.*

*Veronica: No.*

Here Joe exhibited that he was attuned to Veronica's mood and could complete the necessary task at hand in a way that helped relieve her burden. This demonstrated how couples must adjust their daily lives and roles to compensate for adjustment to the illness. The lack of clear recollection of who took on what task also points to Joe and Veronica not keeping score of who did what when for whom. Instead they seamlessly switch roles of responsibility for certain LFS-related duties. For several of these couples, partners encouraged each other and maintained hope and positivity as a balance to the

distress that the other partner felt. Jared looked out for Liz and encouraged her to take the steps that she needs to do to stay healthy:

*Liz: He's always my protector...you really shouldn't be getting the x-ray*

*Jared: I keep telling her that there is going to be a tomorrow...that's my job.*

*Liz: So, I think sometimes it's more of that struggle around, "Gosh, like, it's really hard," and I just don't want to go through that. Or I'll feel, like, upset about, like, gosh, not knowing, or finding out that something's there. You know, ignorance is kind of blissful. But he does a really good job just encouraging me and telling me that it has to be done. And he's right. I agree.*

Liz described the struggle of constantly having to seek information that may turn out to be bad news, but also gratitude toward Jared for boosting and motivating her when she does not feel able to manage the stress of potential cancer findings. Jared took on the role of health behavior monitor for Liz, and his pragmatism balanced her desire to remain ignorant of any potential health issues.<sup>3</sup> Another aspect of the health protector role was to maintain vigilance toward the prevention or cancer-risk reducing behaviors that their partners should be engaging in, including x-ray exposure, sun exposure, exercise, and healthy eating habits.

Lisbeth described a support process that many couples experienced when visiting the clinical center. Partners with LFS described the comfort of having their partner with them while they were undergoing stressful medical tests.

*Interviewer: And how has it been for you coming like and being the support person during this process.*

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<sup>3</sup> Individuals with LFS have a higher sensitivity to radiation, and it is recommended that they avoid x-rays whenever possible.



*Steve: It's been good she doesn't require a lot of support (\*laughter\*). I just like to spend time with her and being with her during this situation.*

*Lisbeth: I always like having him with me because I think too that part of this study there is always a scan and it's a long scan and so on top of scanning anxiety in general, so it's just nice to have him along. I'm really tired and he finds his way around. (\*laughter\*)*

This passage demonstrates how the shared comfort that each partner feels in the presence of the other can aid in relieving anxiety they have regarding screening.

### **Coping Independently**

Couples who coped independently viewed LFS as an individual stressor and were less internally consistent in their story. They coped with events in ways that relied on individual strengths and vulnerabilities, and focused on their own individual plot or perspective. Three specific themes indicated emotional distance between partners, including use of “I” language, protective buffering, and disconnection in their experiences. Some partners had a gap between their beliefs about what they perceived as a challenging life experience, and this gap in beliefs caused distance between the partners. For example, the partner with LFS often perceived that their spouse was worse off because it is easier to be the person with cancer than watch a loved one go through it. On the flip side, the non-LFS partner possessed a heavy burden of fear regarding losing their spouse or a child to cancer that they did not often share with the LFS carrier spouse. These communication patterns expressed that they did not share the fear or burden with their partner.

**“I” versus “We”.** Compared with connected coping, independently oriented couples coped in a simultaneous, parallel, and distinct manner. Most often the person with LFS used “I” in the context of describing their experience with cancer, demonstrating their independent identity in coping with the diagnosis, treatment, and recovery. Several couples did not share a narrative of coping, nor did they seek support from each other during times of high stress. When asked about a team approach to tackling stress or health problems, stated that they found their own roles in the family, but that it was not focused on support or empathy and focused on individual responsibilities instead.

*Bill: We didn't really cope, because she pretty much just takes care of herself. It's not my decision what she does with her body or medical because pretty much everything I say probably she's going to say is stupid or blame me, like scapegoat type stuff. So I stay out of it. I just took care of the kids and everything else and let her try and get healthy.*

In the above example, Bill described feeling like his primary role is in supporting aspects of daily life rather than her health care and emotional well-being. The members of the couple each found areas in which they could balance their family life by taking on other necessary roles beyond the healthcare responsibilities. Bill framed the healthcare aspects of LFS as his wife's challenge to deal with, and not their shared challenge. His partner Harriet is a nurse, and her response confirms Bill's statement in that she describes herself as a “controlling” person, and someone who has a hard time accepting help or listening to other people (including doctors). This couple had an internally consistent narrative regarding each of the partners' roles. Bill's language demonstrates a sense of being rejected from any medical process and a lack of a role in Harriet's healthcare.

Instead, Bill focused his attention on taking care of the kids in order to help Harriet devote her attention to getting healthy. This couple openly articulated that they coped separately during Harriet's breast cancer and stated that if it were not for their children, they may not have stayed together for so long. How this lack of connection is related to the cancer experiences is unclear; however, the language of independent coping is related to the disconnection that the couple felt.

Another couple, Fred and Rebecca discussed the death of their son from an LFS-related brain tumor:

***Fred:*** *I kind of dealt with it on my own terms, the good days and the bad days.*

***Rebecca:*** *I don't know if I could have handled it, I'm still having a rough time.*

This couple was very much in sync with each other, and still felt that their relationship was strong, even through their son's multiple cancers. However, on an emotional level, the death of their son was too raw an event to cope together. The couples that coped independently from each other found a rhythm and pattern of distinct coping that did not rely on their spouse. For some, coping alone was easier than having conversations with their partner that forced them to face painful emotions of grief, fear, and anxiety. Lucy and Phil described their team process before and after screening:

***Lucy:*** *I withdraw before and after the test. "Don't give me one more thing to do.*

*Don't mess with me until this is over." Because I tend to cognitively slow down.*

*The things that I have to do just take longer, so I just want to put everything off until this is handled.*

***Phil:*** *I have to deal, process wise, what's the contingency plan.*

This woman with LFS described the struggle of anticipating bad news but expressed gratitude to her husband for taking on more of the planning and decision-

making responsibilities. Many couples agreed that the process of experiencing cancer risk or being diagnosed with LFS tested their relationship but made them stronger as a family.

**Protective buffering.** Partners often engaged in protective buffering behaviors to shield their spouse from stress related to cancer worries or prevention behaviors. This process of protective buffering was bi-directional, meaning that both partners used this tactic. Not only were the non-LFS partners (who can be considered equivalent to the caregivers in other studies) engaging in protective buffering; also, the people with LFS themselves were also frequently hiding their worries and fears, or avoiding talking about the disease out of consideration for their “healthy” partner.

**LFS partner protective buffering behaviors.** LFS partners used multiple methods of behavior and communication to shield and isolate their partner from the effects of LFS. Many of the women with LFS expressed guilt and frequently said “he has it the worst” because their husbands might 1) serve as the caregiver for them and possibly their children and 2) outlive multiple family members. In some cases, LFS partners delayed making specific health decisions out of consideration for their partner’s circumstances. For example, Jessica and Andrew were in agreement that Jessica should get genetic testing to see if she had LFS. Andrew believed that they were on the same page and wanted it to happen right away, but he thought that Jessica was dragging her feet because she did not want to know the results. During the family interview, Jessica revealed that she had postponed the testing because she wanted to avoid adding stress to Andrew’s life.

*Jessica: I pulled back and I stopped talking about it because he was under a lot of stress. And he never asked me to. I probably could've moved forward with the study and said, "Okay, I'm ready to test." But I was nervous, because I knew the next 6 months he was under a lot of stress at work, and I thought, "This might not be the right time."*

Andrew reacted with surprise when Jessica told him that she had delayed her genetic testing because of his work stress. This was not the only couple to reveal protective buffering behaviors for the first time during the family interview. In this case, Jessica knew that there was a potential for additional stress to their lives if the genetic test revealed that she had the *TP53* mutation. Most partners believed that the person at risk had the right to choose whether or not to complete genetic testing, and the timing of genetic testing became a topic of shared interest between partners because of the various implications that the results might have for their joint lives.

After Jessica completed testing and found out that she had the *TP53* mutation, the idea of having LFS was constantly at the forefront of her mind. She would sometimes share her thoughts and feelings with her husband Andrew, but she also wanted to give him space if his thoughts about LFS were not as frequent as hers. In this quote, she talked about how she held back from discussing her concerns with him:

*Jessica: When you first get your diagnosis, it's on your mind 24/7. And you feel this weight and burden all the time. I would watch him watching a football game, and it's on my mind, and I want to talk about it, but I would see, "Oh, he's having a moment that's LFS free. He's getting to escape it for a minute, I don't want to take that from him." I'd be hesitant to interrupt, so sometimes where I'd just wait a couple hours.*

Jessica was simultaneously protecting her partner and giving him a reprieve from the reality of LFS even though she is in need of support. This type of break that Jessica provided Andrew was not a result of a request from Andrew, but was intended as an unspoken expression of her caring about him that meant sacrificing her own needs.

Many couples had invested years of their relationship to cancer treatment, recovery from surgery, or cancer screening. Some of the LFS partners felt guilt for the time their partners spent caring for them or at hospital visits and tried to relieve their spouses from those health-specific responsibilities. Michelle has LFS, and together the couple has two children, both of whom have LFS. In the following example, Michelle discussed how involved Sam has been in her care:

***Michelle:** Every one of [my chemo treatments], he'd be sitting there in a hard chair at the end, four hours later. I'm like "That's really pathetic, honey. You don't have to come." "Yes I do. I want to be there."*

***Sam:** But these appointments, I don't-*

***Michelle:** These ones you don't. I usually tell him no. Like I'll deal with it. I don't like him having to deal with it...I mean, it sucks. So, I don't like him having to come to all of it. You know? I try and schedule the kids' stuff.*

Sam's consistent company during Michelle's chemotherapy treatments demonstrated his commitment to her and his involvement in her cancer treatment, even with her protests that he did not have to be with her. Since then, Michelle has taken over the scheduling of doctors' appointments for herself and their two children, because she is trying to shield Sam from the experience. Sam agreed that it has been hard to participate in these events, but that the emotional difficulty never prevented him from being present.

Regarding the strain that Michelle feels around screening, Sam said, “I can see it’s stressing her, so I’m happy to take over a lot of it,” demonstrating that he’s willing to be a part of her cancer care and prevention.

**Non-LFS partner protective buffering behaviors.** For some couples the non-LFS partner felt the need to spare the other undue emotional pain to avoid increasing the fear or stress that their partner was experiencing. Further, non-LFS partners protected themselves from experiencing additional worry by minimizing open dialogue with their LFS spouses. For some, this strategy created barriers to communication and increased discord. One woman’s description of the interaction pattern outlined the harmful consequences of protective buffering within a couple that was dealing with the wife’s breast cancer. Her husband, Gilbert was holding back his emotional turmoil in an effort to shield his wife, but it ended up increasing isolation from each other.

*Gilbert: Some of the huge things, I always felt if I told her I was worried it would cause her to worry more. I thought, she had enough on her plate. I didn’t want to add to it. I couldn’t let myself do that. So I went into my box and just hid from her.*

*Cordelia: A lot of his struggles that he was thinking and feeling, again because he didn’t want to burden me with them, he kind of hid them pretty well. So I wasn’t really aware of a lot of the things he was feeling...I thought to myself, “Well if I could have someone that I could cry with, that would make me feel so much better. So Gilbert, why can’t you do this?” I feel like that caused a lot of tension between us. So the distance kind of became even more.*

The couple discussed seeking psychotherapy, in which Gilbert learned how to tell Cordelia about his fears, and she learned how to ask Gilbert for support. Gilbert said that

he can “trust in her that when I talked about my fears it wasn’t gonna make her fears worse.” Cordelia still has some reservations about this new pattern of interaction because “I have LFS, the chance of me getting another cancer is kind of high. Is this gonna happen all over again?”

Statements from the next couple, Adam and Eve, refer to hiding worries/news/cancer-related thoughts and concerns from one’s spouse or partner as a means to shield them from stress and pain.

*Eve: When you don’t want to talk about it and I want to is the only time it’s hard*

*Adam: I probably don’t want to be sad (\*laughter\*)*

*Eve: He is more positive, more of an optimist and I’m more of a realist and so you don’t like it when I’m realistic about things because he is more like, “You are never going to get cancer” (\*laughter\*) Or at least you say stuff like. “You don’t have to worry about it.” You don’t think so?*

*Adam: Well she calls it optimism, and I think that she is just really negative sometimes.*

In this conversation, Eve called Adam the optimist and herself the realist in the relationship. This type of terminology was employed frequently by couples in the independent coping style category. Often these couples had discrepant perceptions of risk or were less cohesive in how they manage their worry about cancer. These patterns solidified over time and couples reported these patterns were hard to change. The different risk perceptions that couples held made it more challenging to discuss topics that involved cancer, because one person wanted to talk more about it as a way to prepare or gather information, and the other person wanted to minimize the risk. The protective buffering behaviors that non-LFS partners employed emerged from a sense of



compassion and sympathy for their partner's position, but made (not always accurate) assumptions about what their partner needed.

**Male partner unique experiences.** Gender differences played a role in the findings. Many male partners of females with LFS described wanting to act but feeling helpless when there was no way for them to support or provide tangible assistance to their partners. For example, Gilbert described how he was feeling during his wife's breast cancer, "I felt guilty asking for help, didn't even talk to anybody about it, because nothing was wrong with me." The experience of being interviewed about these issues often provoked strong emotional reactions, especially for these men, who focused their attention heavily on their spouse as the person suffering and in need of support.

## **Discussion**

This qualitative study highlights the ongoing and understudied challenges faced by couples dealing with LFS. In the review of 26 interview transcripts, the overall conclusion was that spouses of individuals with LFS were considerably engaged and knowledgeable in the care and decision making-processes with their partner. Additionally, couples were mostly cohesive in their relationships regarding health care, family planning, and parenting goals. Through focused coding, we developed themes and identified specific processes that were only relevant to the couples' relationship and coping styles. The 26 couples all identified ways in which LFS has affected their lives and their relationship. Many couples reported that the process of experiencing cancer risk or being diagnosed with LFS was a test of their relationship and made them stronger as a family. A few couples described serious emotional strain on the relationship due to the damaging

effects of protective buffering. The partners mirrored the negative emotions previously described by people with LFS in other studies, in which there exists an ongoing elevated degree of cancer worry that affects their daily functioning (Lammens, 2010). Participants frequently discussed their anxiety regarding potential cancer diagnoses, using language that resembled a perception of “looming vulnerability” in which the danger of cancer was dynamic and multidimensional (Riskind, 2005).

### **Protective Buffering**

Literature on cancer patients and their caregivers suggests that spouses often hide their concern and emotional distress from the partner with cancer. This is an attempt to cover up their own distress to help the person with the illness, but it can be associated with lower relationship satisfaction in patients (Hagedoorn, Kiujer, et al. 2000; Langer, 2010; Langer, Brown, & Syrjala, 2009). The research has shown that it is commonly the spouse in the caregiving role who is more often engaging in protective buffering behaviors. In the present study, we found the opposite. In this study, protective buffering occurred more strikingly on the part of the individual with LFS. These partners often wanted to shield their families from their own stress about getting cancer or wanted their spouses to be free from having to constantly support them. Similar to the findings from Lammens (2011) study of partners of people with LFS and Von Hippel-Lindau (VHL) disease, this study found that the non-LFS partner experienced a moderate amount of LFS-related stress. This was rarely discussed between the partners at home, but during the interviews many of the male partners of women with LFS expressed grief and sadness about past cancer hardships and the possibility of future cancers. Many of the women in this study also revealed a concern about the burden that their husbands carry due to being

the spouse that will most likely outlive them and potentially their children if the offspring also develop cancer. Men, though, used protective buffering to hide their feelings of inadequacy and frustration for not being able to take action and do something to fix the situation.

### **Resilience in Couples Coping with LFS**

The family resilience framework outlines processes regarding how families can dynamically adapt and cope with adversity (Walsh, 2012), and the findings of this paper support the hypothesis that families living with LFS can cultivate resilience in multiple ways, the first of which is to focus on “living with” LFS, rather than focusing on “getting past” a particular event. In addition, by addressing ambiguous information such as cancer risk through open communication and consistent messages, couples made meaning of their situation and developed a shared sense of purpose. Additionally, couples coped with the stress of screening by staying connected and using open emotional expression such as sharing painful feelings, empathizing, and using humor.

Strength and resilience among these couples derives from their ability to develop long-term dyadic strategies for managing LFS and its ongoing logistical hardships and emotional stresses. The sharing of this burden helped couples cope with the disease. Members of the couples in this sample elaborated on what it meant to be a supportive spouse and provided some concrete examples of how the partners balance the burden between the two of them. The flexibility of roles in the ongoing, life-long experience of living with LFS is the main strength of these families. There are times when one partner may take on more of the burden than the other, and in these times of imbalance, one

person can sometimes internally shut off their own distressed thoughts and emotions out of protection and love for their partner.

The couples' flexibility in roles and identities in relation to health was mirrored in their language and the pronouns that they used to describe their experiences. The use of "We" versus "I" language in their process of coping from a relational perspective has been explored in previous cancer literature (Kayser, Watson, & Andrade, 2007). When couples coping with cancer viewed the cancer as a dyadic stressor or a "we-stress", they were of the philosophy that they were in it together, and they talked more openly about the cancer. In the current study, the greater use of "we" by non-LFS spouses often indicated a higher level of involvement in care.

This study did not explore the broader sense of "we-ness" for these couples that existed in the context of their extended family or other family members who have LFS. Future research can expand this definition of "we" by looking at the larger family system and identifying when the non-LFS partner may feel like an "outsider" because he or she does not have LFS, and how this influences the couple's relationship.

### **Implications for Practice**

Living with LFS is a challenging, ongoing, and shifting process for families, and mental health practitioners in psychosocial oncology must be aware of the evolving and transforming coping styles that couples employ. To contribute to family well-being, clinicians should support partners' mutual disclosure of distress as one means to facilitate shared coping over time. For example, when couples are engaging in protective buffering as a means of coping, clinicians can identify these behavioral patterns, draw the couple's attention to them, and help the partners explore the reasons why they are engaging in

these behaviors. It may be helpful for the clinician and couple to understand how protective buffering is related to the emotional distress of one or both partners and what types of emotion regulation strategies may help them “live with” the distress. This practice can prevent couple conflict that might arise when an individual’s protective buffering efforts backfire due to incorrect assumptions he or she has made about the partner’s needs.

Additionally, facilitated conversation between couples was deemed “healing”, “helpful”, “insightful”, and “revealing” by participants and provided further evidence for a systemic approach to handling this unique syndrome and the intense cancer screening that people choose to engage in to catch cancer early. Communication and relationship training or coaching can be integrated into systems of care, especially when families first find out about LFS or when they are diagnosed with cancer. Clinicians can pay attention and utilize language that mirrors the pronouns that patients use when referring to themselves or their families, and employ more “we” or “you both” to include both partners linguistically. The skills and management strategies offered by medical family therapists, a less well-recognized but invaluable set of resources, can supplement the services available through genetic counselors, nurse practitioners, and appropriately-trained physicians.

### **Study Strengths and Limitations**

Findings from some prior studies have provided descriptions of the perspective of individuals with LFS, but rarely have the voices of their partners, who are also living through the experience, been revealed. The present dataset represents the richest and largest representation of couples dealing with LFS. An unforeseen advantage to the

family interview was the timing; for many participants, the family interview was the last activity on their schedule, and they were processing a lot of the information that they had received from other clinicians on the team. They had begun to think about next steps and beginning to face going home to either think about prophylactic surgery or returning to normal life until they heard the results of their screening. This primed the couples to have thoughts about the effects of LFS on their individual and shared lives at the forefront of their minds when the qualitative interviewer asked the prompting questions.

The procedures used in obtaining the sample for this study clearly had effects on the characteristics of the participants who were included. For couples to participate in the family interview, the spouse of an individual with LFS must have gone through rigorous consent and assessment procedures, leading to a self-selected sample. Spouses that attended clinic may have been more highly involved in LFS related care or more supportive than spouses who did not come to clinic. In addition, a disproportionate number of couples included a female partner with LFS; in only four couples did the male partner have LFS. Additionally, the sample was almost entirely White, well-educated, and had a high level of socio-economic status. These both reflect limitations within the larger LFS Screening Study. There are more female participants enrolled, and female participants are more likely to attend their annual clinic visits with family members than are male participants. Although the exact prevalence of LFS across racial and ethnic groups in the United States is unknown, it is assumed to be equal across ancestral groups and not predominantly found in White families. Therefore, future research must engage a more diverse group of participants to better characterize the experiences of couples who identify with other ethnic or racial groups and are more representative of the heterogeneous US population. For example, couples' coping styles may be influenced by

the resources available to them based on their socioeconomic status, whether they have children, how many of the children or other family members have LFS, and how many cancer diagnoses they have experienced.

Another factor that may have influenced the data is that there were three different interviewers who worked with couples. Five interviews were conducted by the first interviewer, one was conducted by a second interviewer, and the first author conducted the following 20 interviews. Different interviewers may have slightly different styles of interacting with participants, and with a semi-structured interview script there is freedom to ask follow-up questions, of which many might have varied across interviewers. Thus, interviewers' own prior knowledge and assumptions regarding LFS and effects of cancer on families may have influenced the line of questioning and the topics that members of the couples discussed. The assumptions and potential biases of interviewers and coders were addressed through regular clinical and research supervision, collaboration in an interdisciplinary team, and guidance of a seasoned qualitative mentor. These methods were utilized to maintain objectivity and maximize credibility.

## **Conclusion**

Partners often made health care decisions together, with shared goals for ongoing health and wellbeing. Yet, with inherited, highly penetrant cancer syndromes this is not always the case, since high disease burden, limited screening utility, and ongoing distress changed the styles in which couples cope with each aspect of the disease. The findings from this study strengthen the argument for additional mental health supports for partners of individuals with LFS, and for specific attention to couple relationship dynamics. Couple and family assessments can be integrated into medical screening for broader

issues that may be interfering with a couples' ability to cope well together. Subsequent appropriate referrals for couples therapy can be made for families that are struggling and need additional skills and support. Additional research is needed to establish the best assessments for family mental health and coping strengths for this population, as well as targeted mental health and family systems interventions, including psychoeducation, communication and problem-solving skills training, and enhancement of dyadic coping.



## Tables

**Table 9. Demographic Characteristics of the Sample**

<b>Sample Characteristics</b>	<b><u>Female (n = 26)</u></b>	<b><u>Male (n = 26)</u></b>
Average age (years)	40	43
Age range	22-57	23-72
TP53-mutation-positive	21	4
<b>Highest education achieved</b>		
<i>(missing data from 8 couples)</i>		
High school diploma	0	1
Vocational/trade school	1	3
Some college	1	2
Bachelor's degree	9	4
Some graduate school	1	3
Masters or doctoral degree	6	5
<b>Total household annual income</b>		
<i>(missing data from 8 couples)</i>		
\$10,000 to \$19,999	1	0
\$30,000 to \$39,999	0	2
\$40,000 to \$49,999	1	1
\$50,000 to \$69,999	4	2
\$70,000 to \$99,999	3	4
\$100,000 or above	9	9
<b>Race/Ethnicity</b>		
White	26	26
Hispanic/Latino	1	1
<b>Religion</b>		
<i>(missing data from 7 couples)</i>		
Catholic	3	3
Protestant	7	4
Jewish	2	2
LDS/Mormon	3	3
Methodist	2	0

**Table 10. Couple Level Demographics on Children**

<b>Number of Children</b>	<b>Number of couples</b>	<b>Total children</b>	<b>Children tested for mutation</b>	<b>Children untested</b>	<b>Children tested positive for mutation</b>
0	3	0	N/A	N/A	N/A
1	7	7	6	1	1
2	10	20	18	2	12
3	4	12	9	3	1
4 or more	2	8	4	4	2
		47	37 (79%)	10 (21%)	16 (34%)

## CHAPTER 5: STUDY 3

### Embedded Social Networks of Couples Coping with Li-Fraumeni Syndrome

#### Introduction

The evolution of cancer genetics has shifted medical practice and research from an individual-focused stance to a more family-focused perspective. Cancer in a family member affects multiple people close to them psychologically, emotionally, and concretely (H. Badr & Krebs, 2013). Although not connected genetically, couples are the core dyadic relationship in family systems, and partners of people with cancer are often the main support person and caregiver for the one with cancer (Hagedoorn, 2011). Although couple relationship research points to romantic partners as each other's primary secure attachment and support person, couples often reach out to others (extended family, family of origin, friends, social groups, co-workers) for additional support. These extended networks have multiple roles in the couples' lives, at times providing hands-on, tangible support, and at other times providing emotional connection and empathy. These networks can be especially important sources of resources as members of a couple strive to cope with cancer.

Li-Fraumeni Syndrome (LFS) is a hereditary syndrome with a high lifetime risk of cancer. LFS is mostly caused by germline *TP53* mutations and follows an autosomal dominant pattern of inheritance (Malkin et al., 1990). Individuals with LFS have a 90% lifetime risk of developing cancer and a 50% chance of a second, independent primary cancer. The most prevalent LFS tumors are early-onset breast cancer, sarcomas, leukemia, adrenal carcinomas, and brain cancer (Mai et al., 2016). Onset of cancer risk is in childhood, creating unique psychosocial challenges for parents and their affected children

compared with adult-onset inherited cancer syndromes. Couples in which one partner has LFS must confront the likelihood of future cancer diagnoses and potential early cancer mortality. The only preventive option for LFS patients is prophylactic mastectomy to reduce the risk of breast cancer. To detect expression of the disease at an early stage, regular surveillance is recommended.

Hereditary cancer syndromes, and specifically LFS, are family matters that not only pose a considerable threat to the well-being of high-risk family members but also to the partners (Lammens et al., 2011). Partners are confronted not just with the cancer susceptibility of their spouse but also with the possibility of their children or future children may also be at increased risk of cancer (Metcalf et al., 2002; Mireskandari et al., 2006). This can lead to life-changing decisions (i.e., family planning) and in the cases where cancer does occur, a significant amount of caregiving responsibility being placed on other family members. The worry regarding future cancers may have an effect on the psychosocial distress of the both partners, especially because the timing of a diagnosis is so difficult to predict, and families must develop methods for coping and constant health preparation.

### **Social Support, Integration, Social Networks and Health**

Intimate relationships and communities play important roles in shaping health outcomes in the general population (Berkman, 2000). Berkman and colleagues proposed that social networks shape individual health and health behaviors primarily through (1) social support (e.g., sharing resources such as information, funds, and emotional support) that foster individuals' positive health behaviors; (2) social influence on individuals' health-related choices (e.g., comparison with peers, pressure from publicized societal

norms); (3) social participation and engagement (e.g., the individual's choices to engage in healthy or unhealthy activities and connecting with friends); (4) person-to-person contact (e.g., exposure to disease); and (5) access to material resources and goods (e.g., healthcare, housing). However, despite evidence for the important influences of social networks on individuals' health, there have been limited social network analyses in health research, especially for cancer cases.

A few studies have established the power of emotional support in intimate relationships, finding that lack of emotional support is associated with worse mortality and health outcomes for people who have experienced cancer (Sarma et al., 2018), heart attacks, and stroke (Fiorillo & Sabatini, 2011). Similarly, smaller social networks and social isolation have also been associated with higher mortality risks in several health conditions (Ikeda & Kawachi, 2011). Some researchers have concluded that when individuals are socially isolated, they are less able to buffer the impact of health stressors and are at greater risk of negative health outcomes (Smith & Christakis, 2008).

The specific mechanisms that underlie the relationship between social network size and health have been explored in several studies of healthy and ill participants. One study found that individuals with larger support networks considered potential stressors to be less threatening, which led to a reduced level of stress symptoms and a better subjective health condition (Fiorillo & Sabatini, 2011). These findings indicated that individuals with larger trust and support networks considered potential stressors to be less threatening, which leads to a reduced level of stress symptoms and a better subjective health condition. This has important implications for the perception of cancer risk for families coping with LFS, in that individuals with larger support networks may be less stressed or have reduced psychological distress related to the possibility of future cancers.

In the field of hereditary cancers, social network members have been found to play an important role in providing social resources and promoting health behaviors. In particular, one study of families with Lynch Syndrome found that older adults (over age 60) were more likely to be nominated as providing instrumental support, emotional support, help in a crisis situation, and dependability when needed (Ashida et al., 2011). Older family members were also more likely than younger family members to be described as encouragers of colon cancer screening.

Social support is believed to contribute to reducing the perception of new incidents as stressful and the avoidance of stressful events, as well as improving the ability to cope with events and their consequences. For example, one study of sisters in hereditary breast and ovarian cancer families found that social integration, or the size of a person's emotional support network, was negatively associated with anxiety (Koehly et al., 2008). The impact of social support appeared to have both a psychological and practical function. Psychologically, the presence of a strong social support network can change the way that people appraise a stressor/health issue by making a health problem feel more manageable when a person is surrounded by emotional supports that build up their self efficacy and self-esteem. Practically, structural and tangible support can buffer the impact of a health issue on a person's life by spreading the burden of care across multiple people (Åslund, Larm, Starrin, & Nilsson, 2014; Friedman & King, 1994; Roohafza et al., 2014). Looking beyond the ill person, social support has also been shown to buffer negative impacts of psychological distress among caregivers of people with cancer (Pinquart & Sorensen, 2007).

Resource transfer through personal networks may be most important in populations with high healthcare needs, such as families with LFS. It is recommended

that families with LFS engage in intensive cancer screening to diagnose cancers early, when they might be easier to treat. Current cancer risk management guidelines for individuals with LFS from the National Comprehensive Cancer Network (NCCN) include yearly physical examinations with blood tests, dermatologic exams, and brain magnetic resonance imaging (MRI) of body and brain. Colonoscopies are also recommended every 2-5 years starting at age 25. Additional recommendations are based on the family history of type and age at onset of cancers. Women also have additional breast cancer screening, which includes annual breast MRIs starting at age 20. These exams require frequent visits to the doctor, and when a cancer is diagnosed or a person is undergoing treatment, they require a large amount emotional and tangible support.

### **Couple Coping Using Dual Ego-Centric Social Networks**

Couples do not exist in isolation, but rather they are embedded in social networks. The members of a couple may share common network members, and over time they may increasingly invest in each other's extended friend and family networks (Felmlee, 2001). Although individuals' friendship networks become smaller over the life course, when couples move in together, their shared friendships and joint contacts grow and become more strongly related (Kalmijn, 2003). These shared networks can provide resources to the couple or can drain resources away when members of the network need assistance from the couple (Bryant & Conger, 1999).

Couples engage in dynamic coping processes when faced with an initial threatening event such as learning about Li-Fraumeni Syndrome status through genetic testing. This is a stressful process that includes experiencing cognitive, physiological, and emotional changes, which then require the couple to take action to cope with the threat

using their available resources. When faced with a shared health threat (i.e., cancer risk), family members may cooperate using a reciprocal exchange of support from each other or may use commonly shared support resources. Research is needed to explore how families employ interactive support processes to cope with a shared threat.

Prior studies of social support in couple relationships have not actually collected social network data, and instead rely on global assessments of network characteristics, such as a static social support metric that asks individual how much support they are receiving in general from categories of people (not specific individuals). These assessments are generally not customized to couples and do not allow for the classification of overlapping networks between partners. Also, studies that have explored the intersection of partners' social networks have relied on reports from only one member of the couple, which likely are biased and do not adequately capture the perspectives of both partners (Cornwell & Waite, 2012).

To test existing theories of how social networks affect a couple's functioning requires assessing and examining the properties of the partners' "*dual ego-centric social networks*", which are the combined network of relationships that surround a couple (Kennedy, Jackson, Green, Bradbury, & Karney, 2015). A couple's network includes members who either have shared ties with both partners of the dyad or ties that are primarily linked to one partner and not the other. Collecting data about such ties from both partners can minimize the amount of missing or inaccurate network information. In addition, an assessment of duo ego-centric couple networks is developed using data gathered from both individuals, but the aggregated result may reveal features that lie outside the awareness of either partner (Coromina, Guia, Coenders, & Ferligoj, 2008).



Previous literature on social support in LFS families is scarce and has focused on describing the individual-level support networks of people with LFS (Peters et al., 2016). However, an assessment that provides a full view of the interdependent nature of coping with cancer or the risk of cancer requires methods that can capture and characterize the connections among those multiple individuals who are coping together. Thus, the present paper used social network analysis of the dual ego-centric networks of individuals with LFS and their spouses. The social network approach provides a framework for quantifying and visualizing these interpersonal relationship patterns and their effect on the couple's behavior.

### **Social Network Analysis**

The history of social network analysis is rooted in social theory, empirical research, and formal mathematics and statistics. The social network perspective defines relationships by the interactions and linkages among units. Using a social network framework, a social environment can be expressed as patterns or regularities in relationships among interacting units (Kennedy et al., 2015). These regular patterns in relationships are called *structure*. Some of the underlying assumptions of the social network perspective relevant to the present study are: 1) actors and their actions are viewed as interdependent rather than independent, and 2) relational ties between actors are channels for the flow of resources (material or nonmaterial) (Wasserman & Faust, 1994). Social network analysis employs statistical analyses and visual diagrams to map relationships, resource exchanges, and interactions; i.e., patterns of social connections.

Social network analysis may be used for hypothesis development and phenomenological description, as well as hypothesis testing. The processes of model development in network analysis begins with describing the social network using

qualitative or count data and creating visual representations of a network (which includes multiple people and the ties between them). From there, researchers make observations about the relational counts or visualizations (ie. identifying patterns regarding size and configurations of social networks) and move on to model specification and testing using quantitative methods. Network models may also be used to test theories about relational processes or communication patterns. Such theories posit specific outcomes such as health behaviors or health outcomes, which may then be evaluated against observed network data regarding communicated health risks.

In this study, we explored two specific aspects of LFS couples' social networks: *shared supports* and *reciprocal support*. Shared supports are defined as a ratio of how many people both partners nominated as providing support, over the number of total people that the couple nominated as providing support. Reciprocal support is defined as the level of exchanges of support between partners, and the four levels ranging from no reciprocity to full reciprocity (mutuality) are illustrated in Figure 11. These two aspects of LFS couples' social networks were analyzed in conjunction with cancer occurrences and three psychosocial symptoms: depression, anxiety, and somatization. Specifically, we explored how couples communally coped with cancer using reciprocal support and their shared social networks.

### **Objectives**

This study used social network methodologies to quantify social support across married spouses, one of which is at high risk of cancer, and its relation to each partner's psychological distress in the context of cancer risk. These methods captured the degree of social integration (the size of the individual's social network), reciprocity, and shared

resource constructs. After exploratory consultation between three psychosocial researchers on the results of couples' "dual ego-centric networks," four main hypotheses were developed. Specifically, we investigated whether individual social integration, partners' shared supports, or reciprocal spousal support enhance psychological adaptation in couples living with LFS.

Below are the specific hypotheses that we tested:

- 1) The number of cancers reported by the partner with LFS will be associated with higher psychological distress symptoms for both partners.
- 2) The number of cancers reported by the partner with LFS will be associated with larger dual ego-centric support networks.
- 3) The percent of shared support that couples report will predict individual psychological distress symptoms, with more shared support predicting fewer symptoms.
- 4) The typology of the dyad (mutual, asymmetric, or null, see Fig. 11) will predict differences in psychological distress symptoms between partners, with mutually supportive couples reporting smaller differences in BSI scores as compared with couples who report asymmetric support exchange or no support exchange.

## **Methods**

### **Sample Characteristics**

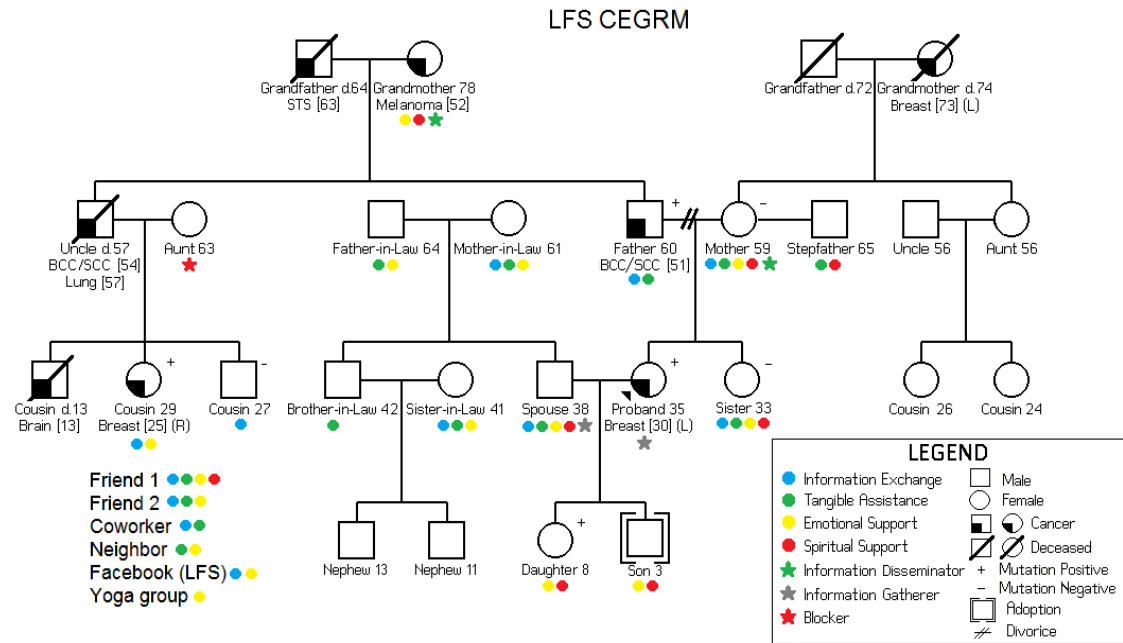
The present sample included 20 heterosexual couples from families with a known deleterious *TP53p53* mutation. The twenty partners with LFS were selected from a larger pool of 146 individual participants with LFS in an IRB-approved National Cancer Institute (NCI) protocol that is investigating new Li-Fraumeni Syndrome screening

methods. All of the 40 participants were non-Hispanic Caucasian, and their ages ranged from 27 to 71, with a mean age of 41. Sample characteristics are presented in Table 11. The sample was well educated; 75% of participants had at least a college degree. The sample was also wealthy, with almost 60% of participants reporting over \$70,000 as their annual household income. All of the couples have at least one child, with the median number of children being 2. Fifteen of the LFS partners reported at least one cancer in the past (the highest was five cancers), and two of the non-LFS partners had a cancer previously. None of the participants had an active cancer at the time of data collection (one of the requirements to enroll in the study). This group of 20 LFS participants and their partners was representative of the larger screening cohort.

## **Procedures**

The Li-Fraumeni Screening Study is an ongoing cohort study of families with LFS that were recruited between 2010 and 2017. Couples for this study were selected if one partner had undergone genetic testing and received a diagnosis of LFS, and their spouse also enrolled in the study. Participants of the study come to the Warren G. Magnusen Clinical Center of the National Institutes of Health once annually to participant in rigorous cancer screening that includes full-body, brain, and breast MRI. Participants are allowed to bring one support person to the screening, and if the spouse chose to enroll in the study they were considered for this analysis. A clinician obtained informed consent and conducted a medical history and physical examination. During this visit, participants completed questions regarding their psychological distress as well as the Colored Eco-Genetic Relationship Map (CEGRM).

**Figure 9. Illustrative Colored Eco-Genetic Relationships Map (CEGRM)**



The CEGRM (see Figure 8) is a visual research tool to assess social interactions and support exchanges between family members and friends of participants (Kenen & Peters, 2001). An investigator administered a 20 to 30-minute semi-structured interview using a genetic pedigree<sup>4</sup> as a template; a copy of the interview protocol can be found in Appendix F. Participants were asked to list the first names of family members, friends, and groups with whom they feel close and who were not on the pedigree. In the next step, participants operationalized social support resources by placing stickers onto the pedigree next to the relevant individuals whom they felt provided those support resources. The types of social supports provided by family and friends to participants included exchanges such as LFS information, tangible aid, spiritual support, and emotional support. The finished CEGRMs were scanned into digital images and social exchange data were

<sup>4</sup> A genetic pedigree displays a family tree, and shows the members of the family who are affected by a genetic trait.

coded into databases for subsequent social network analyses. All digital images and data files were stored on secure servers at the National Institutes of Health. Data files containing CEGRM sticker counts and demographic information were all de-identified using participant ID numbers, and these numbers also served to match spousal pairs. Audio files and investigators' hand-written comments on the CEGRM scripts were used to clarify unclear sticker placement.

The first (baseline) CEGRM interviews that participants completed were selected for analysis because it was the first time that participants completed this activity, and those interviews cover their social networks up to that point; therefore, they have the richest relational data. Subsequent CEGRMs are focused on an annual update of the information collected from the baseline interview. There were four couples in which baseline CEGRMs from the two partners were completed one or two years apart. This often arises from a situation in which the non-LFS spouse was either not enrolled in the study or not present at the LFS spouse's first screening visit. Often, non-LFS spouses (who are not undergoing the intense LFS full body screening) will enroll as participants at a later point in the study and will complete their consent forms, baseline paper work, and baseline CEGRM at the LFS-partner's second or third visit.

## **Measures**

**Demographic data** included age, race/ethnicity, education, income, number of children, and cancer history. Demographic information was collected at baseline, before beginning the screening study, through a paper-pencil Individual Information Questionnaire (IIQ). There were four couples missing IIQ data due to non-LFS partner enrolling later in the study and not completing an IIQ.

**Psychological distress** was measured using the Brief Symptom Inventory (BSI-18), which was administered at each visit to the Clinical Center immediately preceding any evaluations. The BSI-18 is a psychometrically validated self-report instrument that is used to measure psychological distress within the past 7 days in three domains: depression, anxiety, and somatization (Derogatis, 2001). Normative T-scores derived from general population norms were computed for each BSI-18 subscale. For a copy of the BSI-18 with instructions and questions, please see Appendix A. For the visualizations, BSI global and subscale scores were calculated into quartiles, with lighter colors representing lower BSI scores (yellow, orange) and darker color representing higher BSI scores (red, purple). The cut-off scores can be found in Table 12. Additionally, we calculated the difference in scores between partners for each BSI subscale. Because this study did not directly measure qualities of the couple relationship, discrepancies in distress scores between partners were utilized as a dyad-level variable that provides information about the relationship. Previous studies have shown that smaller differences in psychological distress between partners were related to higher marital satisfaction and more similarity in health behaviors (Lewis et al., 2006; Manne et al., 2004).

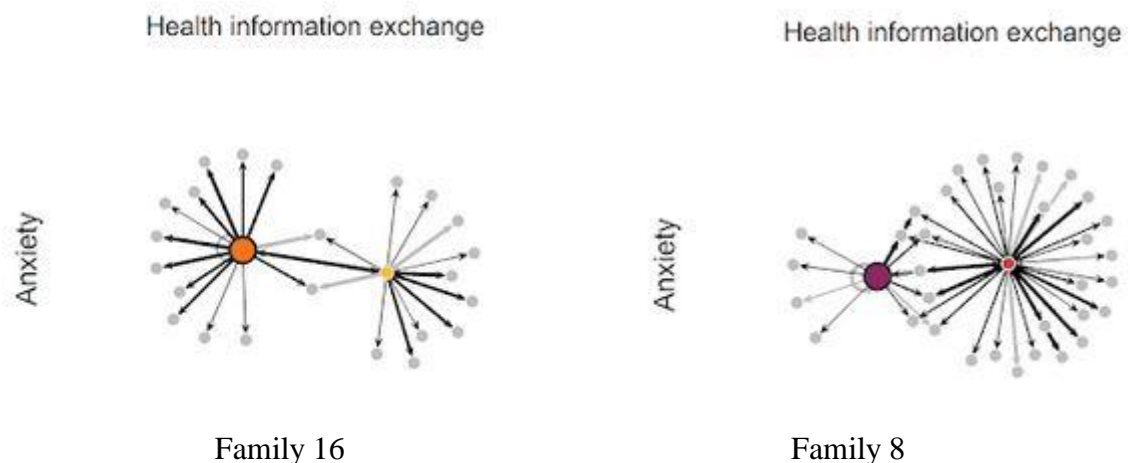
## **Data Analysis**

Descriptive statistics were used to describe participants' psychosocial features and their social support networks' structural characteristics. There were no missing BSI or CEGRM data, but four couples had incomplete demographic information. Visualizations of the social networks were obtained using R software (RCoreTeam, 2014), and the creation of dyadic and social network variables, as well as the quantitative analysis of the

dyadic network data, were also conducted in R packages sna (Butts, 2016) and lme4 (Bates, Maechler, Bolker, & Walker, 2015).

The first step of the analysis was to create visual representations or “Dual Ego-Centric Networks” of the CEGRM and BSI data for dyad pairs. The term “Ego” here refers to the participant who was completing the CEGRM, and the combination of data from related spouses including is called a “Dual Ego-Centric Network.” The grey circles to which the arrows are pointing to comprise the “Alters”, which refers to the people that the “Egos” nominated as a person within their social network. The two circles with colored centers represent the two members of the couple. Colored circles encircled by a bold line represent the partner with LFS. The colors in the center of these circles indicate the BSI global and subscale scores of the participant (see Table 12). The arrows pointing outward indicate a friend or relation that the participant nominated as providing a specific type of support. Grey arrows mean that this friend or relation was not nominated for that type of support. Thickness of the arrow line indicates degree of relation, with thicker lines indicating first-degree relation and thinner lines indicating second degree or friendship. Please see Appendix G for the full list of visualizations by family.

**Figure 10. Example of Dual Ego-Centered Networks**

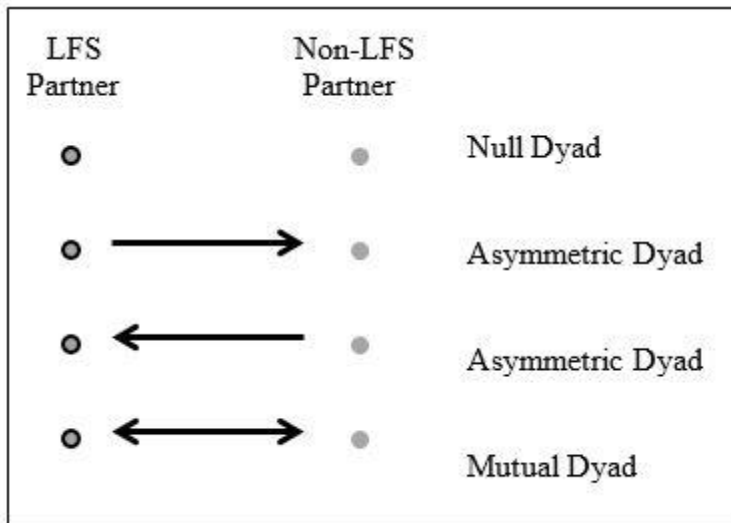




Visualizations of dual ego-centered networks can provide insight for developing hypotheses and interpreting results (Kennedy et al., 2015). Three psychosocial researchers met to review the visualizations and describe observed patterns of social support (see Appendix H for comparisons of Dual Ego-Centered Networks). All of the researchers had experience working with family-level data, and two were experts in social network analysis. Observations of the visualizations were recorded and formed into hypotheses to be tested statistically.

Social integration and communal coping characteristics were derived from the CEGRM process described above. We considered three structural types of social exchanges. The first, *reciprocity*, is a family-level variable that indicates whether or not spouses selected each other as providing a given type of support. In this study we categorized each couple according to three types of dyadic reciprocity: full, asymmetric, or null (see Figure 11). *Full reciprocity*, also called *Mutuality*, indicates that both spouses selected each other as people who provide a specific type of support. *Asymmetrical reciprocity* indicates that only one spouse nominated their partner as providing a type of support. *Null reciprocity* indicates that neither spouse selected the other as providing one type of support.

**Figure 11. Four Types of Dyadic Reciprocity**



The second type of social exchange considered in this study was *social integration*, an ego/individual-level variable that measured the size of a participant’s social support networks (the number of people providing each type of support). Lastly, this study measured *shared supports* between partners, which is a dyad-level variable that indicates the number of persons providing support to both partners. This variable was count based, and was also transformed to a percentage that represented how many people were nominated by both partners as providing the same type of support (numerator) over the total number of people nominated by each partner for that type of support (denominator). Shared support denominators were conditional on all the people that were nominated by either partner.

Once the social network variables were calculated, we employed Welch’s *t*-tests to examine group differences on BSI global and subscale scores, and individual ego-centric social network sizes for the four types of support. Correlations were employed to establish any associations between number of cancers the LFS partners reported and the BSI scores of both partners. For models in which the outcome variable was continuous

and at the individual level, we used generalized linear mixed models clustered on the dyad to account for dependence between partners. For models in which the outcome variable was at the dyad level, we used regressions appropriate for the distribution of the outcome variable (Bates et al., 2015).

Regression analyses addressed three main hypotheses. First, we expected that mutual dyadic support for each of four support types (emotional support, health information exchange, tangible support, and spiritual support) would predict smaller differences between partners in overall BSI scores as well as on each BSI subscale (anxiety, depression, and somatization). We tested this hypothesis using a series of Poisson regressions (to approximate the half-normal distribution) in which couple mutuality predicted the absolute value of the difference in partners' scores on the general BSI and subscales.

Second, we hypothesized that individuals embedded in couples who exchanged mutual support would have lower scores on the general BSI as well as on the subscales. We used a series of generalized linear mixed models clustered on the dyad to test whether mutual support at the dyad level predicted individual BSI scores. Third, we hypothesized that the amount of overlap in supports (that is, the proportion of people who were named by both partners as providing a particular type of support out of the total set of individuals who provided that type of support to either partner) would predict lower general BSI and subscale scores. We tested this via a series of linear and Poisson regressions.

## Results

### Psychological Distress

On average, study participants did not appear to be psychologically distressed when compared with general population norms (Table 13). Only two participants, one female with LFS and one male without LFS (not related to one another), had clinically significant levels of distress based on BSI norms (Global BSI score  $\geq 63$ ). Using two-tailed independent *t*-tests, there were no significant differences between the BSI scores across genders (i.e., men with LFS vs without LFS) or within LFS groups (women with LFS vs men with LFS) on the BSI global and subscale scores.

### LFS Cancers and Psychological Distress

We found trends suggesting that the number of cancers that the partner with LFS reported was negatively correlated with their depression score ( $r(18) = -.40, p = .07$ ), but not with their partner's depression score ( $r(18) = .06, p = .82$ ). Similarly, there was a trend pointing for the number of cancers a person with LFS had to be negatively correlated with their anxiety score ( $r(18) = -.42, p = .07$ ) but this trend was not found for their partner's anxiety score ( $r(18) = -.26, p = .27$ ). Unexpectedly, these trends provide some evidence that partners with LFS who have had more cancers tend to have *less* depressive and anxiety symptoms.

Correlational analysis revealed no significant relationship between the LFS partner's number of cancers and either their own somatization symptoms ( $r(18) = .24, p = .32$ ) or the non-LFS partner's somatization symptoms ( $r(18) = -.21, p = .37$ ).

Correlational analysis also revealed no significant relationship between the LFS partner's number of cancers and their own global distress symptoms ( $r(18) = -.28, p = .23$ ) nor the

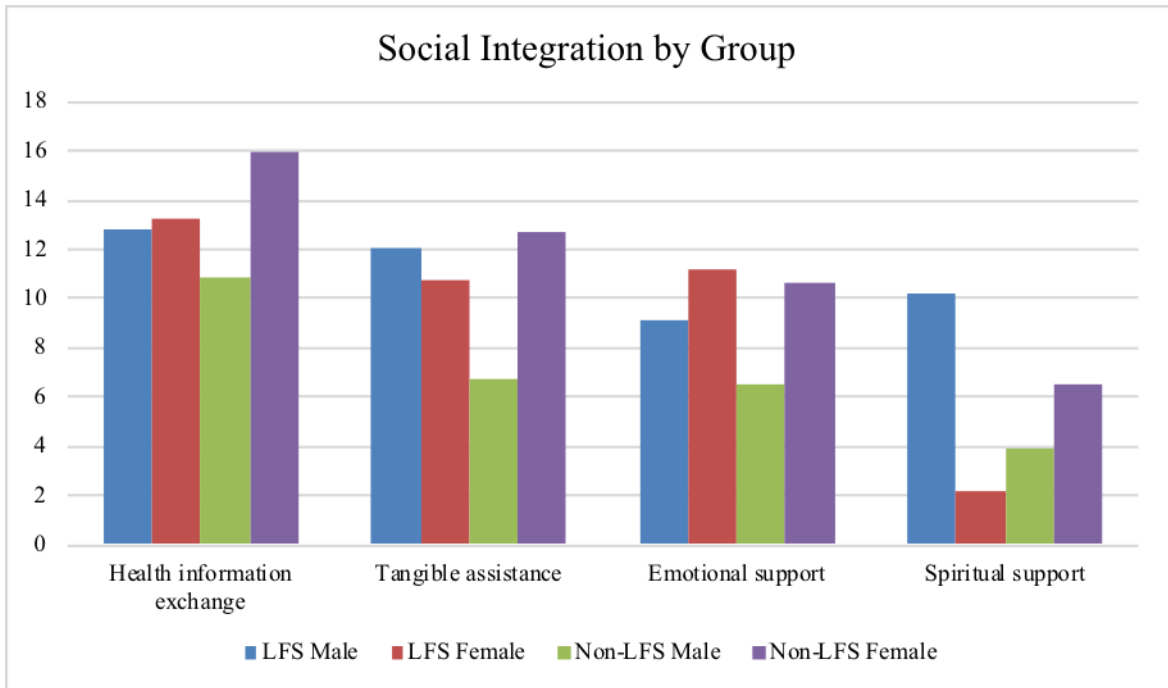
non-LFS partner's global distress symptoms ( $r(18) = -.27, p = .37$ ). These results only did not support our hypothesis that the number of cancers reported by the partner with LFS will be associated with higher BSI scores for both partners. Future analysis will aim to increase the sample size, which may strengthen the correlations, but if the negative correlations are maintained, this would counter our hypothesis.

### **Social Network Size**

Participants discussed LFS with more members of their support network than the number from whom they received tangible assistance or emotional support (Table 14). There were four couples in which both partners nominated zero people for spiritual exchanges and four couples in which only one partner nominated people as providing spiritual exchanges.

Using independent *t*-tests, we assessed for group mean differences (men with LFS vs. men without LFS, women with LFS vs. women without LFS, men vs. women with LFS, men vs. women without LFS) in conditional social network size for the four types of support. Although it appears that there may be some patterns related to how males cope with risk (LFS males' support networks appear larger than non-LFS males), we did not find any significant difference between. In addition, there were no other significant differences by gender or LFS group regarding the size of their network for each type of support.

**Figure 12. Social Integration by Group**



### **Shared Social Networks**

On average, couples had health information exchanges with 20 people, and 19% of those people were shared supports between the two partners (see Table 15). This indicated that out of the total number of people who were nominated by either partner as providing health information to either partner, around 19% were the same person for both partners. Sixty-five percent of couples also both nominated each other as providing health information.

Tangible assistance was provided to couples by an average of 16 people, of which 17% (about 3 people) were nominated as providing that support to both partners. Only 7 out of the 20 couples indicated mutual tangible assistance, lower than any other category of support.

Members of couples were very emotionally supportive with each other, with 17 of the 20 couples providing reciprocal emotional support, but couples only had an overlap of 8% in their emotional support networks. These results indicate that partners received extensive emotional support from each other, but that they each relied on unique friends and family to provide additional emotional support.

When analyzing spiritual support, the four couples who indicated that they had no people with whom they had spiritual exchanges were removed from the group. Of the 16 remaining couples, 10 couples provided full reciprocal spiritual support, and had 11% overlap in their shared social network.

### **LFS Cancers and Dual Ego-Centric Social Network Size**

We tested the correlation between the number of cancers that the partner with LFS had and the size of the couple's dual ego-centric support networks. Correlational analysis indicated trends that showed the number of LFS cancers was negatively associated with the size of the couple's emotional support network ( $r(18) = -.40, p = .08$ ) and tangible support network ( $r(18) = -.41, p = .07$ ), but not the couple's informational exchange network ( $r(18) = -.77, p = .45$ ) or their spiritual network ( $r(18) = -.07, p = .76$ ).

These results do not support the hypothesis that the number of cancers reported by the partner with LFS will be associated with larger dual ego-centric support networks. The trends in the findings suggest that the opposite may be true, that couples who have experienced more LFS cancers have fewer people that they rely on for emotional and tangible support.

### **Shared Support and Psychological Distress**

Linear models were run to determine whether there was a significant relationship between percent shared supports and the BSI scores of participants. None of these models revealed significant results, indicating that the amount of shared support between partners was not related to psychological distress of individuals in our sample. These results do not support the hypothesis that more shared supports would be associated with less psychological distress. Possibly due to power issues, we did not find a relationship between percent shared support and individuals' psychological distress.

### **Reciprocity and Difference in Psychological Distress**

Poisson regression models were employed to test whether couple mutuality in support was related to the difference in BSI scores between partners (see Table 17). Asymmetric and null ties pooled together as the reference group and mutuality was the predictor. The results showed that if couples reported mutuality on tangible, emotional and spiritual support, their differences on BSI global, somatization, and depression scores were significantly smaller (see Table 17). When couples reported mutuality on health information exchange and emotional support, their difference on anxiety symptoms was significantly smaller. Thus, these results generally support the hypothesis that mutuality would be associated with smaller difference in psychological distress between partners.

## **Discussion**

This social network analysis represents a novel method for understanding the interplay between the social support networks that surround couples and the psychological functioning of the couple themselves. These social support networks



provided crucial care to families that were at high-risk of cancer, but previously they often have been difficult to assess in studies. Mapping these social support networks is important for understanding how families cope with the possibility of multiple cancers.

These findings are consistent with research that has indicated that a minority of individuals with LFS and their partners experienced heightened levels of psychological distress (Lammens, 2011; Peters, 2016). Our correlational trends suggested that partners with LFS who have had more cancers tended to have less depressive and anxiety symptoms. This may indicate that with each cancer people with LFS were adjusting better and developing less psychological distress. This is in line with resilience theory that has been supported in the population in the other studies in this dissertation. It is also possible that this effect is not linear; for example, there may be a large increase in psychological distress symptoms after the first cancer diagnosis, and subsequently smaller decreases in distress for each subsequent diagnosis. The LFS screening study is collecting longitudinal psychological distress data, CEGRMs, and medical data, and in the future a longitudinal analysis of the process of psychosocial adjustment may be possible. In addition, trends in the data suggest that couples who have experienced more LFS cancers have fewer people that they rely on for emotional and tangible support. This may be explained by the “pruning down” of a network during and after a cancer experience. Many families that have survived cancer described how they “found out who their real friends were” due to a loss of friends, either from support fatigue or the family not asking for help.

The findings of this study indicate that there are different patterns of support within couples as well as around couples. We found that the amount of reciprocal support that couples reported within their relationship varied by support type. Partners most

frequently mutually nominated each other as providing emotional support, followed by health information exchange, spiritual exchange, and lastly tangible assistance. When support was asymmetric, the LFS partners more often nominated the non-LFS spouse as providing tangible, informational, and emotional support, and this pattern was stronger for tangible support. These findings may point to the caregiving role that the non-LFS spouse would take on if their partner had cancer.

Interestingly, we found that although couples are mutually very emotionally supportive, they do not have many shared emotional supports outside the relationship, indicating that partners seek out each other, but seek other people when they need emotional support. This is an encouraging sign that individually partners have a broad network of support outside of the relationship. Couples do not rely wholly on one or two shared persons for their various support needs. Mutuality in the four types of support had strong associations with smaller differences in psychological distress between partners. This points to a level of connection and congruency of emotional function in couples that are mutually supportive.

### **Strengths and Limitations**

This study is the first of its kind to investigate the social context of couples living with LFS. Utilizing social network analysis, qualitative, and quantitative data, we were able to identify the specific sharing of resources between married partners as well as how often they support each other. Our findings included descriptions and visual representations of the couples' shared support networks. The analysis described the rich quantitative social network data collected through a qualitative, semi-structured interview. A strength of the duocentric-network approach is that it allows each partner's individual

perceptions of the network to be combined into a description of the social context that utilizes data from multiple network participants. Building on the findings from the previous two studies, this social network analysis captured both individual and dyad level use of support as a coping style, as well as information about the patterns of support within the couple relationship. The CEGRM has been used to measure the social networks of individuals and families from other hereditary disease populations, and the findings of this study can be compared to those studies using similar tools.

Several limitations of this study should be noted. First, due to the cross-sectional nature of this study, it was not possible to draw conclusions regarding causality, but only statistical associations. Second, although we attempted to capture the experiences of as many people with LFS and their partners as possible, the sample size available for this study was relatively small. The small sample size limited our ability to detect significant between-group differences in BSI scores or social network size or to fit more complex models due to a lack of power. Third, the structure of the CEGRM interview may have biased some of the results. For example, a pedigree from the partner with LFS was used for the placement of stickers nominating support people. This pedigree does not include the family of origin for the person without LFS; therefore, if a partner without LFS had significant non-family support people in their life, they would have had to add this information to the CEGRM manually. This extra step may have dissuaded some participants from adding all of their support people. Our analysis did not, however, detect any group differences in the size of each support network. Finally, the structure of the CEGRM interview was to first nominate people with whom participants have discussed LFS or cancer. Using this as the starting place for the interview primed the participants to consider the people they nominated as “informational exchanges” for other categories.

We believe our preliminary results presented herein warrant additional research in several areas. Future research can look at the size of couples' shared support networks as potential moderators for the mediation model outlined in Paper 1, regarding cancer worry and its impact on their mood and daily functioning. Future studies will also incorporate family interview data and social network data to flesh out more specific descriptions of dyadic coping styles and how those typologies relate to patterns of social support. In addition, it is important to explore how reciprocity patterns of the type found between partners also can be identified as operating with support people outside of the couple dyad. In this study, although our multi-informant network visualizations included information about the degree of relation for support people, we did not use these data in our analysis. In the future we would like to utilize these data that captures the degree of closeness between participants and relatives (degree of relation) or friends to analyze how mutuality predicts which friends or family members individuals go to beyond their partner. This type of study would also help shine light on individuals' choices to seek support from others who have a better understanding of the syndrome (related by blood or who also have LFS) versus friends and relatives who are not as familiar with the unique needs of this population.

As the LFS study continues, multiple cancers are diagnosed each year of the study, and, as we collect outcome data on their cancer survival outcomes, we can incorporate the social network data as a predictor of health outcomes. Using this study as a model, we can collect longitudinal information about social networks to explore how different types of couples (couples with children, children who have or have not had cancer, couples who have or have not had cancer, *etc.*) are coping with Li-Fraumeni Syndrome by using their social support networks. With each time point's data collection, we can assess

changes in social networks, especially in relation to life events associated with LFS, such as a new cancer.

Lastly, this sample is not nationally representative with regard to race, education, or income; future research must integrate perspectives of a more diverse population. Specifically, these 20 couples all have strong medical support as part of their participation in the LFS screening study. They can meet regularly with experts in the field of heritable cancer syndrome and do not have to pay for intensive cancer screening procedures (e.g., MRIs). This is compared with a cohort of people who must navigate a health care system outside of the National Institutes of Health. The psychosocial experiences of families with LFS who are not part of the LFS study screening cohort are likely to be very different from the experience of this study's sample.

### **Clinical Implications**

Mutual support in these LFS couple dyads has been shown to have positive associations with psychological distress. Research on survivors of cancer continues to elucidate informational and emotional needs during their long-term survivorship (Vivar & McQueen, 2005) and people with LFS may have similar needs across the life course. It may be helpful for clinical teams to utilize relationship assessments and interventions that focused on the health and functioning of newly diagnosed partners, with survivors providing informational and emotional support. To our knowledge there is no specific intimate partner support intervention for families living with LFS. This type of intervention could profitably focus on quality of life for both the person with LFS and their spouse.

We recommend that all health professionals seeing patients and families with LFS consider expanding their discussions about management of risk to include topics of social

and emotional supports. Early identification of areas of concern could guide ongoing support and help anticipate future interventions that might be needed. Genetic counseling training could also incorporate training in systems-based counseling and research to address the social factors involved in living with LFS.

## **Conclusion**

This study represents an important early step in examining a dyadic framework for understanding coping with hereditary disease. Coordinated support resources within couples may be indicative of either adaptive processes, as in shared emotional supports, or maladaptive when considering the exchange of hereditary risk information. Although we anticipated higher numbers of cancers to be associated with more psychological distress, we found trends that suggested the opposite to be true. These trends indicate that partners with LFS who have had more cancers tended to have less depressive and anxiety symptoms over time, which points to the resilience and strength of this population. The couples in this study were emotionally supportive of each other and had a large range in shared social network size.

Families are complex social systems that can facilitate or impede the coping process; the data presented herein suggest there may be real value in elucidating the social context in which support processes occur. These results have important implications to health-care providers as they facilitate adaptation for at-risk sisters and their families. The insight gained from prospective, follow-up studies hold genuine promise for improving clinical management of the complex psychological and behavioral issues occurring not only in families where sisters are at risk for developing breast/ovarian cancer but also for families at increased risk for other inherited cancers as well.

## Tables

**Table 11. Descriptive Statistics of Analytic Sample**

Characteristic	Descriptive Statistics ( <i>N</i> =40)
Age, years <i>M</i> (range)	41 (27-71)
# women with <i>TP53</i> mutation	14
Education level ( <i>N</i> = 30)	
High school degree	1
Vocational/trade school	4
Some college	1
College degree	11
Some graduate	5
Masters or doctoral degree	8
LFS partner with cancer	75%
Non-LFS partner with cancer	10%
Couples with children	100%
Spirituality	
Catholic	7
Protestant	8
Jewish	4
Mormon (Latter Day Saints)	4
Methodist	1
None	6

**Table 12. Cutoff Scores for BSI Quartiles**

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	<b><u>Yellow</u></b>	<b><u>Orange</u></b>	<b><u>Red</u></b>	<b><u>Purple</u></b>
BSI Total	34-39	40-44	45-51	52-66
Anxiety	36-42	43-46	47-54	55-66
Depression	40	40-41	42-48	49-68
Somatization	39	40-42	43-48	49-61

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Note: Lower scores indicate fewer symptoms. General population norms: M = 50, SD = 10.



**Table 13. BSI Scores by Group**

<b>Psychological Distress* M (SD)</b>	<b>LFS Male</b>	<b>LFS Female</b>	<b>Non-LFS Male</b>	<b>Non-LFS Female</b>
Anxiety	53.17(9.47)	47.21 (8.21)	48.29 (7.95)	48.33 (7.00)
Somatization	43.83 (4.21)	46.00 (7.79)	45.93 (8.34)	47.67 (8.48)
Depression	49.83 (7.96)	43.57 (7.15)	46.29 (7.10)	48.33 (8.36)
BSI Global	50.50 (6.28)	45.07 (7.35)	45.64 (10.15)	47.67 (8.45)

Note: M = mean; SD = standard deviation.

\*General population norms: M = 50, SD = 10.

**Table 14. Social Integration by Group**

<b>Support Type</b> M (SD)	<b>LFS</b> <b>Male</b>	<b>LFS</b> <b>Female</b>	<b>Non-LFS</b> <b>Male</b>	<b>Non-LFS</b> <b>Female</b>	<b>Average</b> <b>Individual</b> <b>Network</b> <b>Size</b>
Health info	12.83	13.29	10.86	16.00	15.33
exchange	(7.36)	(4.38)	(7.8)	(9.21)	(7.77)
Tangible assistance	12	10.79	6.79	12.67	12.00
	(6.69)	(5.73)	(6.19)	(7.97)	(7.32)
Emotional support	9.17	11.14	6.57	10.67	11.73
	(9.47)	(5.39)	(8.03)	(8.91)	(8.82)
Spiritual support	10.17	2.21	3.92	6.50	8.32
	(10.87)	(8.47)	(4.46)	(5.58)	(8.33)

Note: M = mean; SD = standard deviation.

**Table 15. Couple-level Social Support**

<b>Support Type</b>	<b>Couple Network Size M (SD)</b>	<b>Reciprocity N (%)</b>	<b>Shared supports %</b>
Health information exchange	20.15 (8.35)	13 (65)	18.55%
Tangible assistance	15.60 (8.67)	7 (35)	16.67%
Emotional support	14.90 (9.95)	17 (85)	8.43%
Spiritual support (16 couples)	13.01 (9.58)	10 (63)	10.99%

Note: M = mean; SD = standard deviation.

**Table 16. Mutuality and Difference in BSI Scores between Partners (Raw Scores)**

	Couples <i>n</i>	Anxiety Difference M	Somatization Difference M	Depress Diff M	BSI Global Diff
<b>Health Information exchange</b>					
Mutual	13	5.69	7.38	6.23	5.92
Non-LFS nominated	4	11.00	12.50	7.00	6.25
LFS nominated	2	6.00	1.00	3.00	3.50
Null	1	8.00	6.00	2.00	8.00
<b>Tangible Assistance</b>					
Mutual	7	6.43	6.14	4.43	4.29
Non-LFS nominated	10	7.90	8.70	7.40	7.20
LFS nominated	1	4.00	1.00	4.00	1.00
Null	2	5.00	11.5	4.00	7.00
<b>Emotional Support</b>					
Mutual	17	6.29	7.18	4.88	4.64
Non-LFS nominated	2	11.50	13.00	16.00	15.00
LFS nominated	0	-	-	-	-
Null	1	8.00	6.00	2.00	8.00
<b>Spiritual Support</b>					
Mutual	10	6.70	6.40	4.90	4.20
Non-LFS nominated	1	11.00	21.00	2.00	5.00
LFS nominated	2	3.00	9.50	2.00	4.50
Null	7	7.71	7.14	8.86	8.71

Note: “Non-LFS nominated” indicates that the partner with LFS nominated their spouse as providing a specific type of support.

**Table 17. Mutuality and Difference in BSI Scores between Partners (Model Estimates)**

	<b>Anxiety Difference</b>	<b>Somatization Difference</b>	<b>Depression Difference</b>	<b>BSI Global Difference</b>
	<i>β</i> (SE)	<i>β</i> (SE)	<i>β</i> (SE)	<i>β</i> (SE)
<b>Mutual Health Info Exchange</b>	-.47*** (.12)	-.12 (.12)	.19 (.14)	.03 (.14)
<b>Mutual Tangible Assistance</b>	-.11 (.13)	-.33** (.13)	-.40** (.15)	-.45** (.15)
<b>Mutual Emotional Support</b>	-.40*** (.14)	-.40** (.14)	-.84*** (.14)	-1.00*** (.14)
<b>Mutual Spiritual Support</b>	-.06 (.12)	-.34** (.12)	-.33* (.13)	-.58*** (.14)

Note: \*\*\*p < 0.001, \*\*p < 0.01, \*p < 0.05

## **CHAPTER 6: CONCLUDING DISCUSSION**

Using data from the LFS screening study at the NIH, the three studies comprising this dissertation illuminate the psychosocial functioning and coping styles of couples in which one partner has LFS. Each study investigated different facets of dyadic coping of high cancer risk, including individual-level coping styles, cohesive *versus* independent coping, and couple coping utilizing social networks. Below, I briefly summarize the main contributions of each of the studies, their limitations and suggestions for future research, and the overarching implications for policy and practice.

### **Contributions**

The three studies that comprise this dissertation expand the scope of research on LFS beyond the individual that has the syndrome to the rest of the family that is affected. Each study builds on levels of closeness to the individual, with the first study analyzing individual-level variables that were collected from both partners. The second study included both members of the couple to create collaborative and shared narratives about how they coped together with LFS. The third study developed a social context of friends and families that support and surround the couple. Taken together, these three studies provide a complex and comprehensive review of couple functioning.

The first study explored the psychosocial functioning of couples that are faced with increased risk of cancer(s) for one partner. One of the major findings of this study was that people with LFS frequently worry about their chances of getting cancer, some even having thoughts about cancer multiple times per day. This finding was significantly stronger for women with LFS. Additionally, this cancer worry frequency influenced their

daily function as a function of how cancer worry affected their mood. People who more frequently worried about cancer also reported that their mood and daily functioning were affected by these thoughts. We expected that some of the coping strategies that these individual and their partners employ to deal with LFS would moderate this process, and that more adaptive coping styles would be associated with less cancer worry affecting daily functioning. The results of the study did not show that individual coping styles of either the person with LFS nor their partner moderated this cancer worry process.

The second study explored the ways that couples coped together in the face of intense surveillance and significant cancer worry. Utilizing a modified grounded theory approach, analysis of the semi-structured interviews revealed several prominent themes. First, couples shared a sense of ambiguous danger related to the threat of cancer and when to expect a diagnosis. To cope with this ambiguity, couples developed several strategies for communicating and adapting. Many couples described resilient processes such as role flexibility, connectedness, and utilization of social and economic resources. Communication processes varied by couple, with some people engaging in protective buffering behaviors or individual problem-solving in an effort to spare their partner any unnecessary pain or stress. Other couples openly shared their fears and engaged in empathy and collaborative problem solving.

Many participants and collaborators pointed out the utility of psychosocial interviews as a major contribution to the LFS screening study at the NIH. The screening at NIH is a unique experience for the families, and many of the couples used this time during the family interview to discuss worrisome symptoms leading up to the visit to Bethesda because heightened the potential that a new cancer would be found. The family interviews also gave couples a chance to debrief with a mental health clinician at the end

of a stressful experience. Many of the couples comfortably gave feedback about the process of screening at NIH to the interviewer, who was then able to relay the feedback to the research team, who then made appropriate adjustments (example: how to discuss mastectomies with women). At the conclusion of the interviews, many couples said they had never discussed LFS in the context of their family to this depth, or in such an open manner, and that they appreciated the opportunity to be enlightened regarding their partners' perceptions and experiences.

The third study employed a novel approach to exploring couples' social support structures. Utilizing a social network framework, visual representations of familial and friend supports were created via a semi-structured interview and quantitative analyses were performed. One of the most important findings of the study was that the sample of couples was highly mutually supportive, emotionally, but less so when it came to providing tangible support, which was found to be slightly unequal (non-LFS partner provided more tangible support). In addition, the number of cancers that the person with LFS had was negatively associated with distress, meaning people who had experienced more cancers were less distressed. Couples who had experienced more cancer also reported smaller emotional and tangible support networks, possibly pointing to how after having cancer people may lose peripheral friends but bonds with close friends may be strengthened. Lastly, the differences in BSI scores were smaller when the partners reported mutual support, indicating a cohesion and collective mentality about distress and support. The integration of two participant perspectives in this manner provided insight into how these couples used their available human resources to cope with their high risk of cancer.



The three papers each had their various strengths and weaknesses, but viewed as a whole, they provide a more complete picture of the functioning of couples with LFS. The first and second studies utilized distinct methods for measuring partner coping styles, and the results of the Brief COPE and the qualitative typologies of dyadic coping integrate the perspectives of both partners when the data collection is done both individually and with the two partners together. The third paper captures individual psychological distress at a different time and provides more detail about how members of couples utilize their support networks to cope with the demands of a complex health situation.

### **Limitations and Suggestions for Future Research**

LFS is rare syndrome and although this study represents the largest study of couples living with LFS to date, the relatively small sample size decreased our statistical power, which limited our ability to apply more complex analytic tools in hopes of detecting an effect when there was one. Therefore, without sufficient statistical power, the quantitative studies may be subject to Type 1 and Type 2 errors. We attempted to address this limitation by simplifying our analysis with fewer variables, rather than utilizing more complex predictive modeling. Future research on families that are affected by LFS can build upon this dataset and increase the sample size to improve the power of the study.

An important limitation of this study is that the findings are not likely to be generalizable to a broader US population from which the respondents were not systematically drawn, in this case, to all married individuals with LFS and their partners. Recruitment methods were unique to this study, and they yielded a particular group of couples that produced these particular results. These families had a long history of participation in one or more NIH-sponsored research projects over time. These families

commonly had multiple affected family members and had made extensive use of genetic testing and LFS cancer screening. Thus, the population described here is heterogeneous in terms of age, relationship length, longevity of knowledge of mutation status, and cancer experiences, while being relatively homogeneous with regard to race, socioeconomic status, sexuality, level of education, etc. Therefore, these findings provide little insight regarding how families who differ on these characteristics might experience their lives when affected by LFS. Further qualitative and quantitative studies should focus on these other subgroups within the LFS population to increase our understanding of what kind of variation might exist that we could not capture. Additionally, since our studies were biased towards female mutation carriers and their male partners, a larger sample of men with LFS and their female partners or a sample of non-heterosexual couples may further enrich and clarify the findings of the current study.

A possible deficiency of this study is the discrepancy between the qualitative and quantitative studies with regards to negative experiences. Studies 1 and 3 found participants' levels of distress were relatively low; however, Study 2 uncovered a range of negative emotions related to the LFS experience and the cancer screening experience. These negative experiences were not captured in the quantitative studies, suggesting that the measures that were used may not be appropriate for this population. Future studies of couples in LFS can employ measures that are more focused on family relationships and dyadic coping.

### **Implications for Policy and Practice**

Promoting resilience is a critical element of psychosocial care for people with LFS and their families. There has been little analysis to date on the nature of the families' experience with heritable cancer syndromes and what implications are regarding the

unique features of family relationships and interactions in the context of LFS. Specific features of the families' experience with cancer were examined in this dissertation with the goal of developing approaches to care that recognize and incorporate the interconnectedness of family responses and the considerable needs of family members for emotional and practical support (Yates, 1999).

Although the absolute risk of cancer is not affected by the couples' resilience, their state of mind or outlook can certainly modulate the experience of risk. This is a valuable accomplishment on the behalf of the couples, and holds an important message that they can pass along to their children or other family members about how they choose to live with LFS. The resilience of these families should be not be underestimated and clinicians working with this population should focus on principles of strength instead of deficit for clinical and community-based practice. Taking a relational view of human resilience means including family members in the process of screening and communication of results. Clinicians can also evaluate families for their community, cultural, and spiritual resources, and connect them to in-person or online support groups, the LFS Family Association, or the LFS bi-annual symposium for families and researchers. It is important to acknowledge that every family has a different pathway and style for coping. There is huge variation in LFS families related to their specific health challenges, pile-up of symptoms, and immediate versus long-term stressors. Clinicians must consider the unique situations and family beliefs of their patients, and can point out developmental phases or generational patterns that adds context to the coping of the family.

The implications of this research can help promote and encourage open conversations about the uncertainties of living with a high-risk cancer syndrome. Medical

care and genetic education are crucial resources that are not distributed equally across the United States in general, and for families with LFS in particular. This sample represents a highly motivated group of participants who values modern healthcare and constant medical monitoring. However, there are many people with LFS who may not have access to information about LFS or the cancer risk management options available to them, or who hold different opinions about how to manage their cancer risk, which helps define additional needs that are not currently being met.

Amidst a deluge of information about genetic testing, cancer risk, risk-reduction strategies and cancer screening, couples felt overwhelmed, but were able to form cohesive beliefs about the best ways to balance risk-management and maintaining their family goals. Individuals with LFS also emphasized that the presence of the spouse helped relieve anxiety and distress during the screening procedures. This is in line with couples' research that has shown that the physical presence and empathetic stance of a partner can reduce the levels of reported pain that the other person feels (Goldstein, Shamay-Tsoory, Yellinek, & Weissman-Fogel; Younger, Aron, Parke, Chatterjee, & Mackey, 2010). In addition, a support person can manage, share and distribute the healthcare responsibilities to mitigate the very real burdens of day-to-day living that is felt by the family. This research underscores the need for a systemic and relational view of the health care for families who are affected by LFS. Although some families are more vulnerable or face more hardships than others, all families have the potential for positive growth as they face health challenges. Services focused on coping skills, adaptation, and competence that build off underlying resilience can empower families, bring hope, and strengthen family connections.

## APPENDICES

### Appendix A: Brief Symptom Inventory

Derogatis, L. R. (2001). *BSI 18, Brief Symptom Inventory 18: Administration, scoring and procedures manual*. Minneapolis, MN: NCS Pearson, Inc.

Below is a list of problems people sometimes have. Read each one carefully and circle the number that best describes how much that problem has distressed or bothered you during the past 7 days, including today.

Circle only one number for each row.

During the past 7 days, how much were you distressed by:	Not at all	A little bit	Moderately	Quite a bit	Extremely
A. Faintness or dizziness	1	2	3	4	5
B. Feeling no interest in things	1	2	3	4	5
C. Nervousness or shakiness inside	1	2	3	4	5
D. Pains in the heart or chest	1	2	3	4	5
E. Feeling lonely	1	2	3	4	5
F. Feeling tense or keyed up	1	2	3	4	5
G. Nausea or upset stomach	1	2	3	4	5
H. Feeling blue	1	2	3	4	5
I. Suddenly scared for no reason	1	2	3	4	5
J. Trouble getting your breath	1	2	3	4	5
K. Feelings of worthlessness	1	2	3	4	5

L. Spells of terror or panic	1	2	3	4	5
M. Numbness or tingling in parts of your body	1	2	3	4	5
N. Feelings of hopelessness about the future	1	2	3	4	5
O. Feeling so restless that you couldn't sit still	1	2	3	4	5
P. Feeling weak in parts of your body	1	2	3	4	5
Q. Thoughts of ending your life	1	2	3	4	5
R. Feeling fearful	1	2	3	4	5

## Appendix B: Cancer Worry Scale

Custers, J. A., van den Berg, S. W., van Laarhoven, H. W., Bleiker, E. M., Gielissen, M. F., & Prins, J. B. (2014). The Cancer Worry Scale: Detecting fear of recurrence in breast cancer survivors. *Cancer Nursing*, 37(1), E44-50.

During the past month, how often have you thought about your own chances of getting cancer (or another cancer)?

- Not at all or rarely .....  1
- Weekly .....  2
- Daily.....  3
- Several times a day .....  4

During the past month, how often have thoughts about your chances of getting cancer (or another cancer) affected your mood?

- Not at all or rarely .....  1
- Weekly .....  2
- Daily.....  3
- Several times a day .....  4

During the past month, how often have thoughts about cancer affected your ability to perform your daily activities?

- Not at all or rarely .....  1
- Weekly .....  2
- Daily.....  3
- Several times a day .....  4

### Appendix C: The Brief COPE Scale

Carver, C. S. (1997). You want to measure coping but your protocol's too long: Consider the Brief COPE. *International Journal of Behavioral Medicine*, 4(1), 92-100.

The following questions ask about ways you've been coping with the stress in your life since you found out that you or a family member had cancer, or may be at increased risk of having cancer. There are many ways to try to deal with problems. These items ask what you've been doing to cope with this one. Each item says something about a particular way of coping. We want to know to what extent you've been doing what the item says. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Please circle the response that best describes how often you have been doing a certain thing to cope.

	<b>I haven't been doing it at all</b>	<b>I have been doing it a little bit</b>	<b>I have been doing this a medium amount</b>	<b>I have been doing this a lot</b>
A. I've been turning to work or other activities to take my mind off things	1	2	3	4
B. I've been concentrating my efforts on doing something about the situation I'm in	1	2	3	4
C. I've been saying to myself "This isn't real."	1	2	3	4
D. I've been using alcohol or other drugs to make myself feel better	1	2	3	4
E. I've been getting emotional support from others	1	2	3	4
F. I've been giving up trying to deal with it	1	2	3	4
G. I've been taking action to try to make the situation better	1	2	3	4
H. I've been refusing to believe that it has happened	1	2	3	4
I. I've been saying things to let my unpleasant feelings escape	1	2	3	4
J. I've been getting help and advice from other people	1	2	3	4
K. I've been using alcohol or other drugs to help me get through it	1	2	3	4
L. I've been trying to see it in a	1	2	3	4



	<b>I haven't been doing it at all</b>	<b>I have been doing it a little bit</b>	<b>I have been doing this a medium amount</b>	<b>I have been doing this a lot</b>
different light, to make it seem more positive				
M. I've been criticizing myself	1	2	3	4
N. I've been trying to come up with a strategy about what to do	1	2	3	4
O. I've been getting comfort and understanding from someone	1	2	3	4
P. I've been giving up the attempt to cope	1	2	3	4
Q. I've been looking for something good in what is happening	1	2	3	4
R. I've been making jokes about it	1	2	3	4
S. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping	1	2	3	4
T. I've been accepting the reality of the fact that it has happened	1	2	3	4
U. I've been expressing my negative feelings	1	2	3	4
V. I've been trying to find comfort in my religion or spiritual beliefs.	1	2	3	4
W. I've been trying to get advice or help from other people about what to do	1	2	3	4
X. I've been learning to live with it	1	2	3	4
Y. I've been thinking hard about what steps to take	1	2	3	4
Z. I've been blaming myself for things that happened	1	2	3	4
AA. I've been praying or meditating	1	2	3	4
BB. I've been making fun of the situation	1	2	3	4

### Appendix D: Cohen Stress Scale

Golden-Kreutz, D. M., Browne, M. W., Frierson, G. M., & Andersen, B. L. (2004).  
Assessing stress in cancer patients: A second-order factor analysis model for the  
Perceived Stress Scale. *Assessment, 11*(3), 216-223.

The following questions ask you about your feelings and thoughts during the past month.  
In each case, please circle the choice that best describes how often you felt or thought a  
certain way.

During the past month...	Never	Almost never	Sometimes	Fairly often	Very often
A. How often have you been upset because of something that happened unexpectedly?	0	1	2	3	4
B. How often have you felt that you were unable to control the important things in your life?	0	1	2	3	4
C. How often have you felt nervous and “stressed”?	0	1	2	3	4
D. How often have you felt confident about your ability to handle your personal problems?	0	1	2	3	4
E. How often have you felt that things were going your way?	0	1	2	3	4
F. How often have you found that you could not cope with all the things that you had to do?	0	1	2	3	4
G. How often have you been able to control irritations in your life?	0	1	2	3	4
H. How often have you felt that you were on top of things?	0	1	2	3	4
I. How often have you been angry because of things that were outside of your control?	0	1	2	3	4
J. How often have you felt difficulties were piling up so high that you could not overcome them?	0	1	2	3	4

## Appendix E: Semi-Structured Interview Protocol (Family Interview)

### INTRODUCTION

*Interviewer:* Thank you all so much for your willingness to participate in this interview study. I'd like to tell you a bit more about the purpose of this study. I am interested in learning about the experiences of both individuals and families with increased hereditary cancer risk, and specifically about how living with that risk impacts and is impacted by your relationships with each other. Through this research, I'm hoping to explore and better understand the experiences of individuals and families affected by *TP53* mutations. Someone on our team has already spoken to each of you about your individual experiences related to the mutation in your family; now, I'd like to learn how you talk about and collectively understand what's happening within your family, relative to your genetic predisposition to cancer.

I want to remind you that whatever you say here is completely confidential; I will not use your real names or any personal identifying information when reporting our findings. Each of you has already chosen individual pseudonyms to be used in place of your first names in anything we write from this study. Is there a **fictitious last name** that we could use to refer to all of you as a family?

I also want to reassure you that, as a mental health professional who works with individuals and families facing medical and genetic challenges, I am deeply and personally committed to understanding your unique and personal experiences as members of families faced with hereditary cancer risk, and how that might impact other important aspects of your lives.

The results generated using the information provided by you and other study participants, may help inform the body of knowledge about psychosocial issues affecting mutation carriers and families, as well as the manner in which these challenges are understood by physicians, genetic counselors, and therapists with whom they interact in a variety of healthcare settings.

Do any of you have any questions for us about the purpose of the study or what we hope to do with the results?

OK, let's get started. Please remember that if you don't feel comfortable answering any of the questions, just let us know and we can skip them. Does that sound OK?

## **SECTION A: DEMOGRAPHICS AND FAMILY RELATIONSHIPS**

Great. First we'd like to get some basic information about all of you as a group.

1. How are the [three, four, five, etc.] of you related?
2. Tell us about how the [three, four, five, etc.] of you chose to participate in the study together, or to be here as support persons.
  - a. *Is there anyone you wish were here who isn't?*
  - b. *How do you make sense of that absence?*
3. [Get a sense of family structure]
  - a. *[if siblings are present] Who is the oldest sibling? Youngest? Are there other siblings who aren't here today?<sup>5</sup>*
  - b. *In families in which there has been a death, follow-up about how that has been handled. How have other family members stepped in to fill the role of a lost loved one? How has the loss been dealt with?*
  - c. *Who is the closest? Who has a more distant relationship?*
4. Tell me about how you all communicate and interact with each other. How do you keep in touch?

## **SECTION B: FAMILY HISTORY OF CANCER AND TP53 MUTATIONS**

OK. Next, we'd like you to tell us about how you became aware of the *TP53* mutation in your family. Can you tell us that story?

*Please tell me about who has had cancer in your family and what those experiences have been like.*

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<sup>5</sup> Italicized questions are "probes," which serve as reminders for the interviewer to gather this information; these items will not be directly requested unless the interviewees do not talk about them in their answers to the broader questions.

1. *When did the family first become aware that cancer might be hereditary?*
2. *How did genetic testing come to happen in your family?*
3. *Who was the first to be tested? How did information about genetic testing spread from that person to other family members?*
4. *What challenges have you faced in talking about cancer risk as a family, or addressing cancer-related issues that have surfaced within the family since genetic testing? How has the family dealt with those?*

## **SECTION C: GENETIC TESTING**

Next, we'd like to know about how your family communicates about **genetic testing** specifically.

1. Is there a family belief about whether/when/which people should get tested?
2. What are the various ways this message has been communicated? Have you found some ways more or less effective than others?
3. How are decisions about genetic testing made by individuals in your family?
4. To what extent were each of you involved in each others' genetic testing processes? In what ways did you participate?
5. What has happened in the family when someone gets tested and receives her/his results? (How) are those results communicated to other family members?
6. How has your family responded to members who choose not to get tested?

## **SECTION D: RISK MANAGEMENT**

The next several questions will focus on how members of the family are involved in each others' **risk management decisions and experiences**. Is there a traditional way or family expectation about how people who carry the mutation should manage their risk? By manage, I mean any behaviors that people do in response to their cancer risk, in an attempt to monitor for and/or avoid cancer.

1. Which specific management options have the members of your family considered or used?
2. How do you communicate with each other about risk management?
  - a. *Positive experiences?*
  - b. *Negative experiences?*
3. How do you support each other with regard to risk management issues?

4. What happens when individuals make different choices about how to manage their cancer risk? For example, if one family member decides to participate in screening and one opts not to?
5. What happens when family members disagree with each other about how one person should manage her/his cancer risk?
6. Is there a family authority or “leader” when it comes to risk-management? Who, and why that person? Is there a person to whom others turn for advice or information? Why this person? Has this been an effective way to handle these decisions?

## SECTION E: THE NEXT GENERATION

Next we’d like to know about how information regarding the *TP53* mutation and cancer risk has been or will be communicated to and handled with the next generation – young people in your family who aren’t old enough yet to fully understand this issue, maybe your kids or grandkids.

1. Tell us about who in the family fits in this group.
  - a. *What is the gender distribution – how many boys, how many girls?*
  - b. *How old are the kids in the next generation?*
  - c. *How many are children of known carriers? Children of people who have tested negative? Children of family members who haven’t been tested?*
  - d. *Is the next generation pretty much complete, or are new babies still coming into the family?*
2. What has happened in your family with regard to testing minors for the mutation?
  - a. *How are any cases of childhood cancer relevant to this question?*
  - b. *What has happened when different children within the family have different mutation statuses?*
  - c. *How have family members reacted to decisions about testing minors?*
3. Thinking specifically about older kids who are capable of understanding the idea of being tested, tell me what information about the LFS and/or cancer and cancer risk has been shared with members of this next generation?
  - a. *How have these conversations gone?*
  - b. *Is there a family consensus about whether/when this information should be shared? What happens when people disagree?*
4. Have any untested family members under age 18 expressed an interest in being tested for the mutation? How has that been handled?
5. Have issues related to having a *TP53* mutation come up as members plan pregnancies?
  - a. *How are these issues handled?*
  - b. *What strategies have family members considered relative to influencing the likelihood of passing the mutation along to a child? (e.g., adoption, donor gametes, PGD, PND, etc.)*

- c. *Has anyone utilized, or is anyone planning to utilize, these options? What was the response from the family?*
  - d. *What happens when people disagree?*
  - e. *Have you learned anything specific from your own experiences, either helpful or not helpful, that you would want to pass along to younger family members?*
6. What are your hopes for the next generation with regard to *TP53* and cancer?

## **SECTION F: INTERVIEW WRAP-UP**

1. What else do you think is important for me to know about your family that I didn't ask you about?
2. What has it been like being interviewed together about these issues?
3. Anything else you'd like to tell me?
4. Do you have any questions for me?

Thank you so much for your help. If I have more questions for you that come up later, is it alright for me to contact you?    YES    NO

And, if you think of anything else that you forgot to say or if you think of something else you'd like to tell me regarding your experience, please call or e-mail me – I'd love to hear from you.

I will be e-mailing my study findings –interpretations and conclusions – to participants to get their feedback and reactions. Would you be willing to read those findings and get back to me with comments?                      YES    NO

OK. And if in the future I decide to collect some follow-up data through a survey, interview, or questionnaire, would you be willing to participate?    YES NO

Okay. Everything you've shared today has been very helpful, and I truly appreciate your taking the time to talk with us today. I will be looking forward to talking with you again when the results have been analyzed, to get your feedback on our interpretation of the data.

This is the end of the interview with the [NAME] family.

## Appendix F: CEGRM Script

Name: \_\_\_\_\_ CEGRM Case #: \_\_\_\_\_  
Date: \_\_\_\_\_ Time: \_\_\_\_\_ CEGRM number: 1 2 3 4  
Administered by: JP LH Other \_\_\_\_\_

### **Introduction:**

Researcher Roles:

- Genetic counselor: any questions from prior counseling?
- Researcher interested in study participants as people, beyond just the medical.

Description and purpose:

- Getting to know you in the context of family and friends.
- Collaborative effort between us, since you are the expert.

Show paper and legend

Verbal consent- get permission to do CEGRM together

Confidentiality

### **Pedigree:**

Review pedigree and symbols

Update as needed

Explain how we will use pedigree as the basis of the CEGRM by adding symbols

First let's add symbols and first name of other people in your life with whom you feel close. This may include friends, neighbors, doctors, ministers, church members, co-workers, parents of kid's friends, and even pets.

Types of People:

Friends

Neighbors

Doctors

Minister/Rabbi/Priest, etc.

Co-Workers

In-Laws

Others

Do you have a **confidante**?  No  Yes (specify with \*) \_\_\_\_\_

Particular **Groups**, Teams, Support Groups, Clubs that you relate to mainly as a group?

**Blue Circles = Information exchanges**



Let's use a blue circle to identify anyone in the family and among your friends with whom you've talked specifically about cancer in the family or the genetic testing that you underwent (skip if no genetic testing)

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- In-Law(s)
- SDR, TDR (specify)
- Friends
- other (specify)

Who did you talk to first about genetic testing? And then.....

Is there a primary person with whom you discuss new cancer or genetic information? Why that person?

How does the information get disseminated, i.e., how do these conversations come about?

Are the exchanges mutual? E.g., they call you when they have something to tell and you call them when you have news?

Are the people with whom you discuss general cancer issues the same people with whom you discuss cancer in your family and genetic issues? How are those groups the same or different?

Do you feel as though you are able to talk about cancer and genetic issues with friends and family members as much as you need to (i.e., do you get the informational support that you need?)

**Silver Stars = Information Gatherer(s)/Researcher(s)**

We can use a silver star to identify a person who takes on the job of looking for new information about cancer or genetic testing. They might do this by searching online, doing a lot of reading, or putting themselves in touch with other people going through similar experiences. Is there someone in your family who fits that description?

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- Self
- In-Law(s)

- SDR, TDR (specify):
- Friends
- other (specify)

What does that person/those people do to gather that kind of information?

What do you think motivates that person/those people to do this?

**Green Stars = Information Disseminator(s)**

Are there one or two main people in the family or among close friends who spread genetic and cancer information to all the others and who try to get everyone talking about cancer risk and sharing information with each other? E.g., like the hub of a wheel?

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- Self
- In-Law(s)
- SDR, TDR (specify)
- Friends
- other (specify)

How does that person/those people go about the job of dissemination?

What do you think motivates that person/those people to do this?

**Red Stars = Information Blocker(s) / Private Person(s)**

This person or people might be sort of like the opposite of the green star person. In some families, there are people who are very private and don't seem to want to talk about these health issues.

Who in the family or among friends (or maybe even yourself) doesn't want to hear about or be involved in conversations about the cancers and genetic risk?

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- Self
- In-Law(s)
- SDR, TDR (specify)
- Friends

other (specify)

How do they show that they don't want to talk about it?

What do you think is behind this?

Is this person's reluctance to talk specific to the issues of cancer and genetic testing, or is that something that happens with other topics as well?

**Green Circles = Tangible Help**

When you need something, like a favor or some help with something, whom do you count on?

e.g., doctor's visit, ride to the airport, watch the kids, feed the pets, run errands, etc.

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- In-Law(s)
- SDR, TDR (specify)
- Friends
- other (specify)

What kinds of favors do these individuals do for you?

Are these favor exchanges mutual? If so, how do you help them?

Do you feel as though you get the right amount of this type of support? Or do you sometimes feel like you could use some more of this type of support?

**Yellow Circles = Emotional Exchanges**

Who do you call/see when you get good news or bad news or just feel like you need a little support?

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- In-Law(s)
- SDR, TDR (specify)
- Friends
- other (specify)

Who is the primary person that you count on for this kind of support? Why that person?

Do you find that you are able to be both a giver and a receiver of this type of support? i.e., in situations or at times when you find yourself needing emotional support, are you still able to be an emotional support to others? Tell me about how that works for you.

Do you feel as though you get the right amount of this type of support? Or do you sometimes feel like you could use some more emotional support?

**Red Circles = Spiritual Exchanges**

You have already mentioned/or I noticed that you haven't mentioned exchanges in regards to spiritual or religious resources. I wonder whether you feel that spirituality is an important part of your social world?

- yes
- no
- can't say
- other:

Do you or have you in your life affiliated yourself with a particular religious group?

- In family of origin: \_\_\_\_\_
- In adulthood: \_\_\_\_\_

Are there particular people with whom do you feel especially spiritually connected?

- Parent(s)
- Sibling(s)
- Child(ren)
- Spouse/Partner
- In-Law(s)
- SDR, TDR (specify)
- Friend(s)
- other (specify)

By what means do you connect?

- attend the same church, synagogue, bible study group
- pray together or for each other
- socialize in church-sponsored events
- spend time with yourself/introspective/journal/nature
- other: \_\_\_\_\_

Do you feel as though you get the right amount of this type of support? Or do you sometimes feel like you could use more spiritual support or sharing?

### **Ending/Closing/Changes over Time**

\_\_ **Transition:** That does it for my part. Thanks for sharing all of this with me. It definitely helps me understand better your experience as you've been dealing with all of this. I have a better sense of how your family and friends work together.

\_\_ **Summarize:** Let me just review what you've told me the main events been going on in your life recently, e.g., health issues, work, moving, relationships....

\_\_ **Stressors:** Are there other things that have been stressful or challenging?

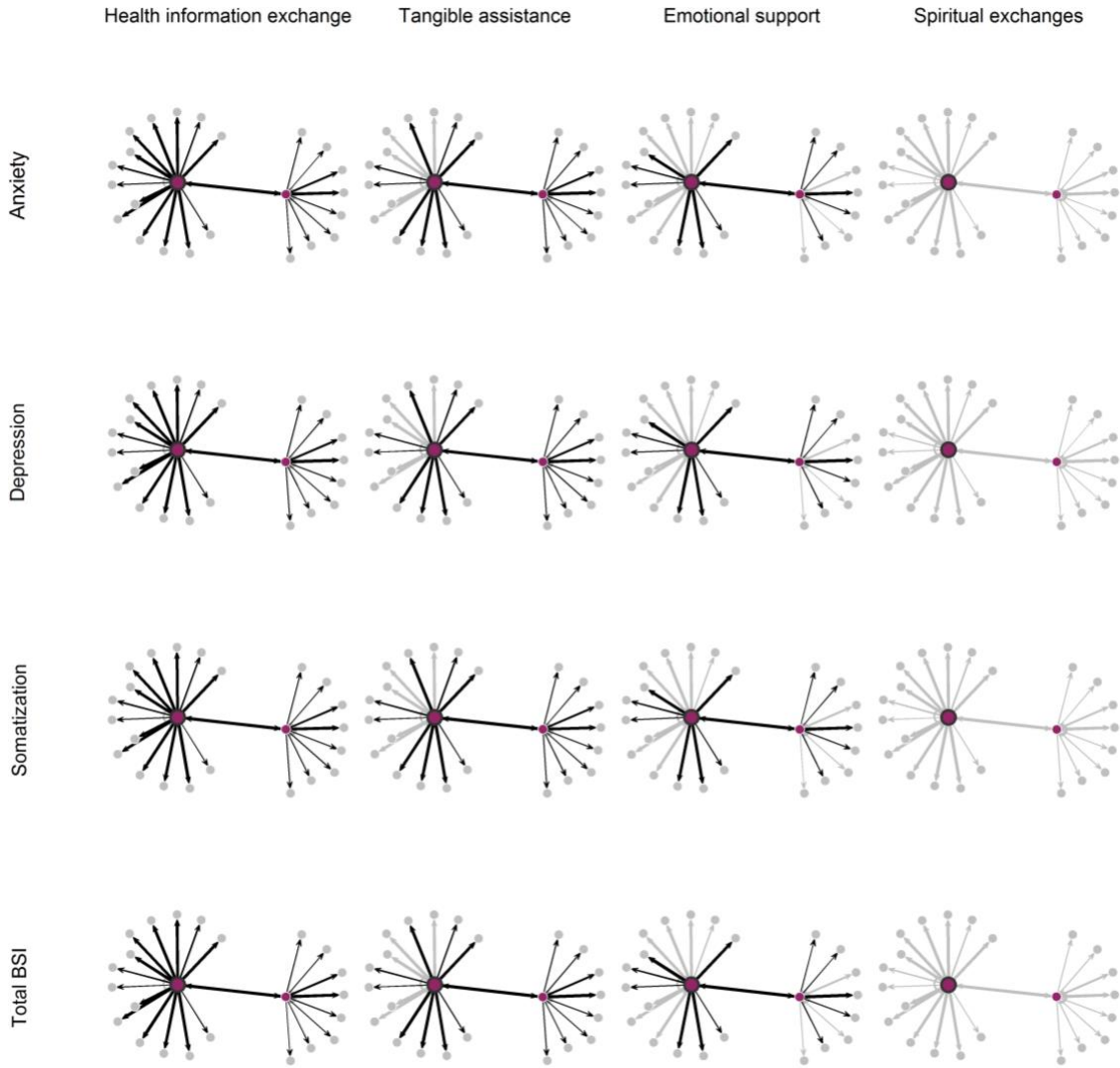
\_\_ **Other Missing:** Is there anything else or anyone else that we missed this year? i.e., Is there anything else that you would like to tell me about your experiences with the dealing with the cancers or cancer risk in yourself or your family?

\_\_ **Impression:** As we pause for a moment and look at your family CEGRM, what do you see? i.e., How would you describe your social world as you've shown it to me here?

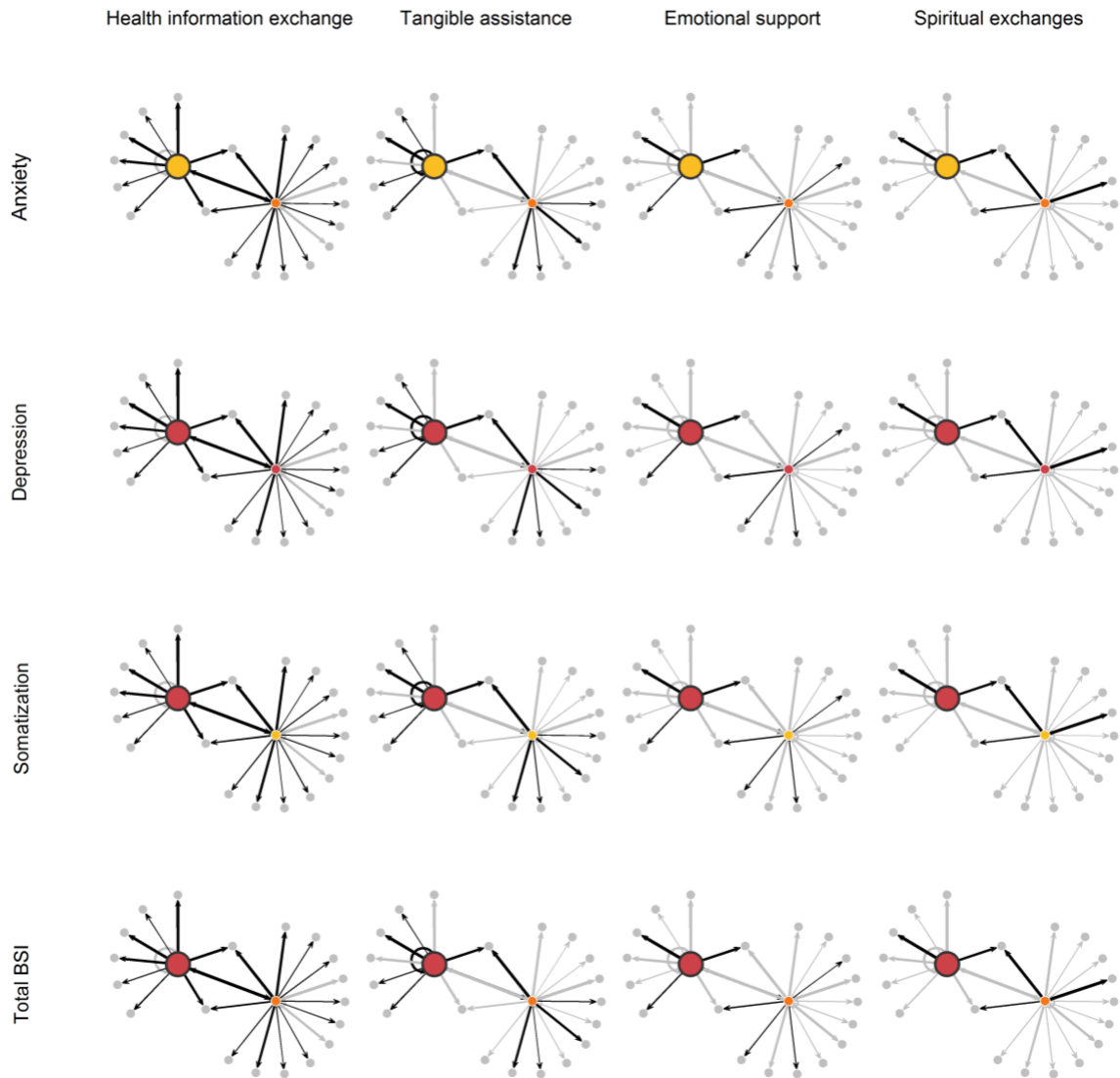
\_\_ **Changes over time:** You've told me a bit about how different types of support have been exchanged differently among members of your social network over time. I'd like us to take a look at all the CEGRMs we've created together, from all of your visits, and see if you have any other impressions about how things have changed or what things have stayed the same. What do these changes mean to you?

# Appendix G: Social Network Visualizations for LFS Couples

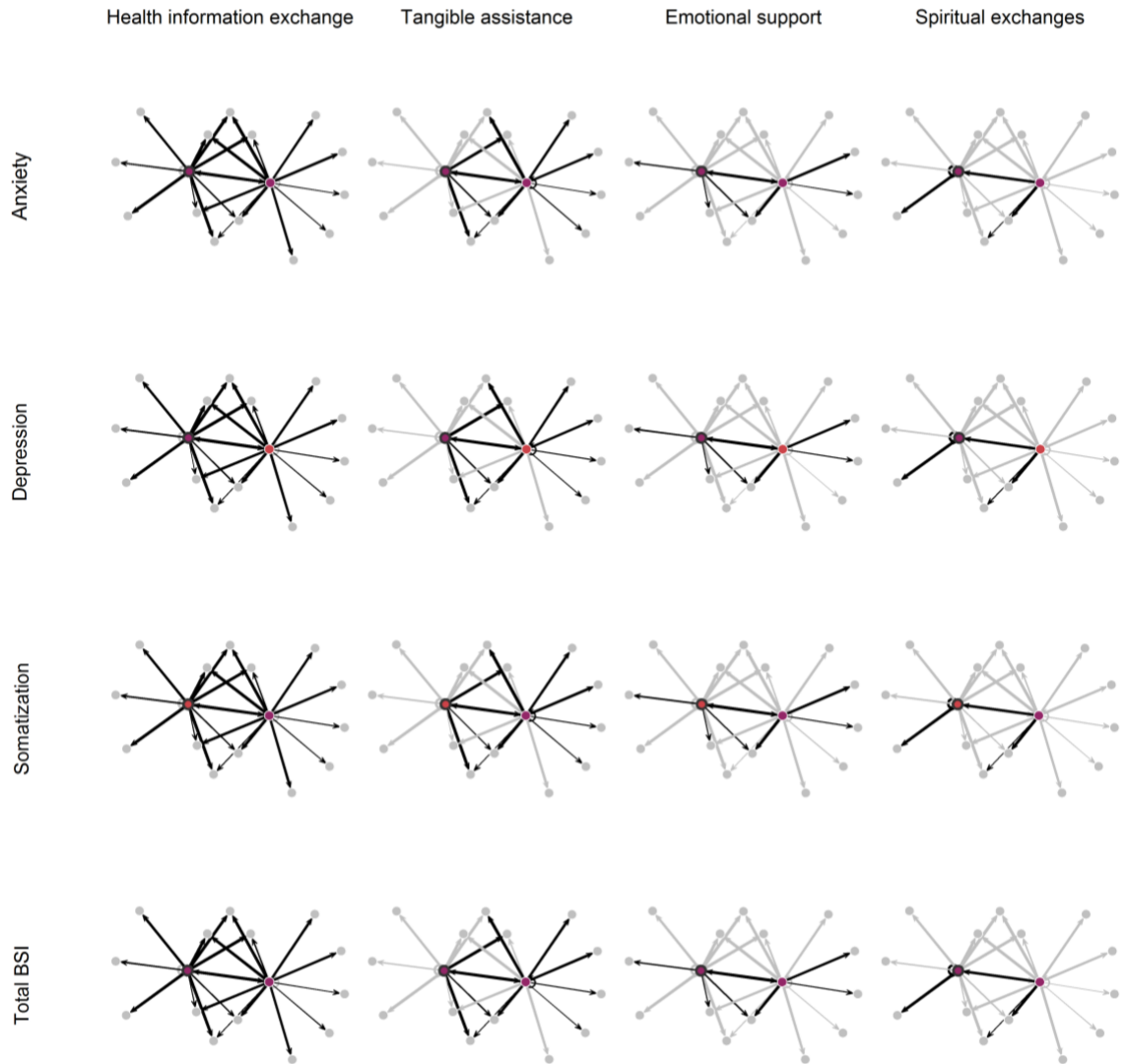
## Family 1



## Family 2

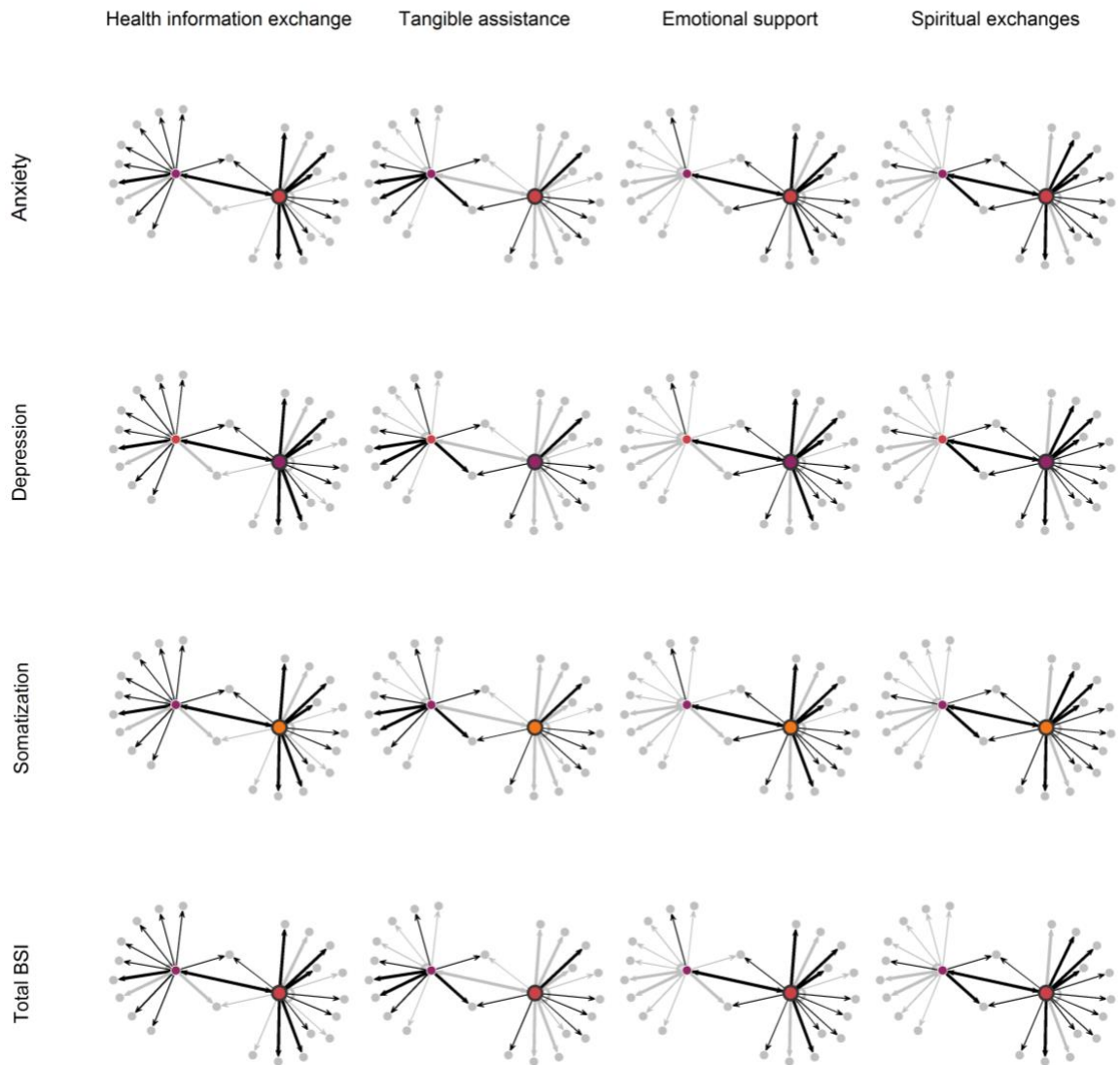


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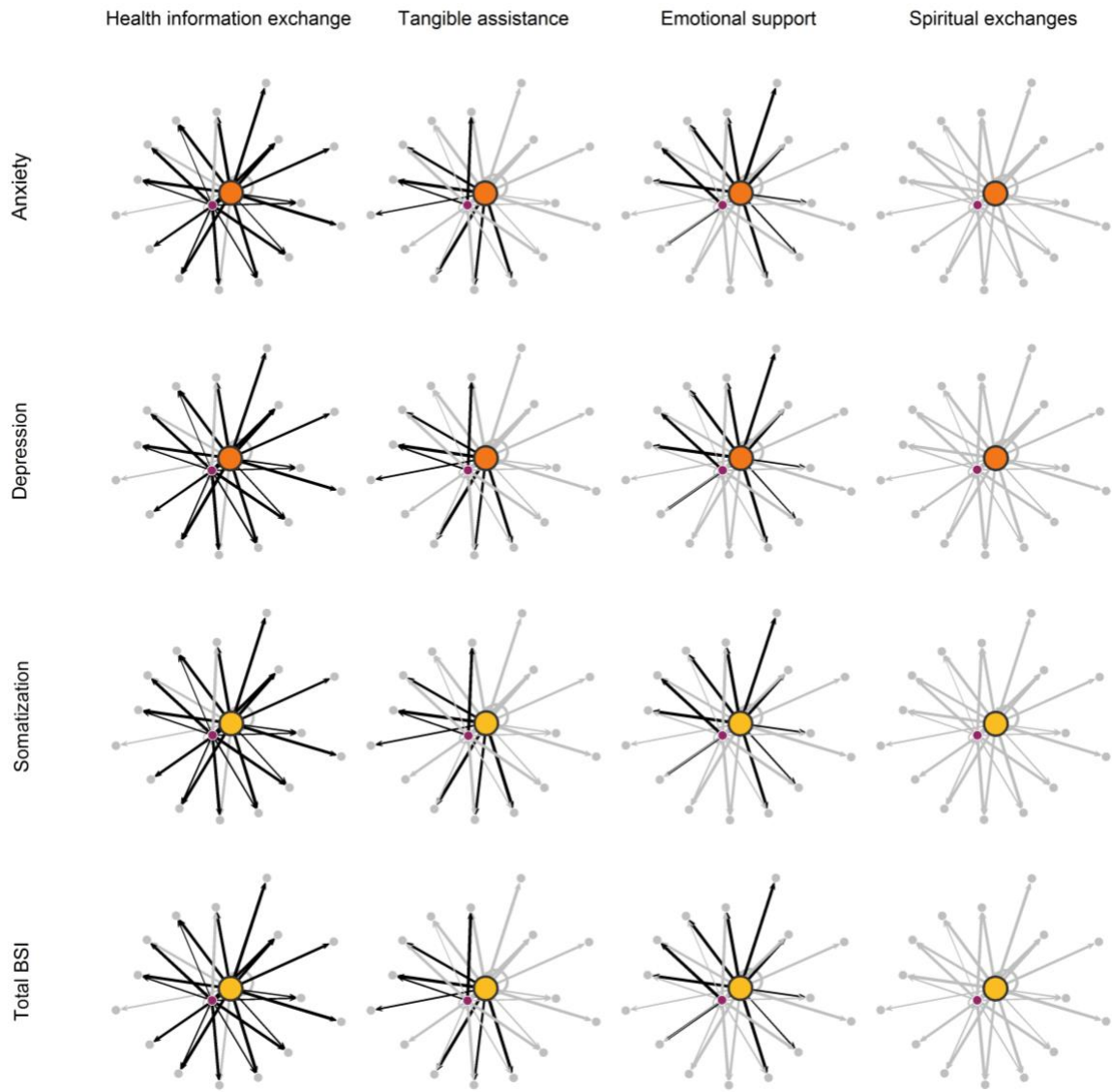




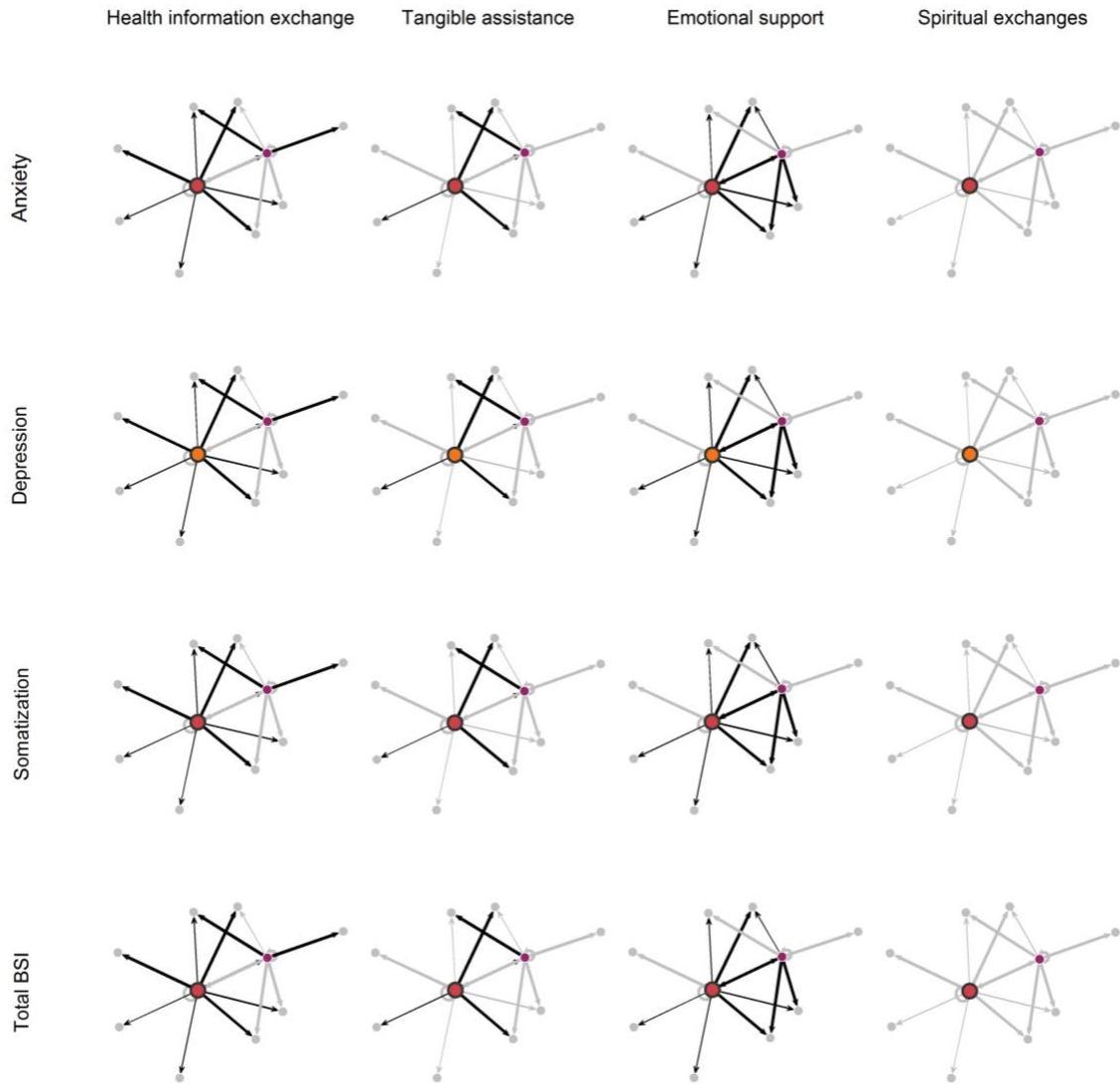
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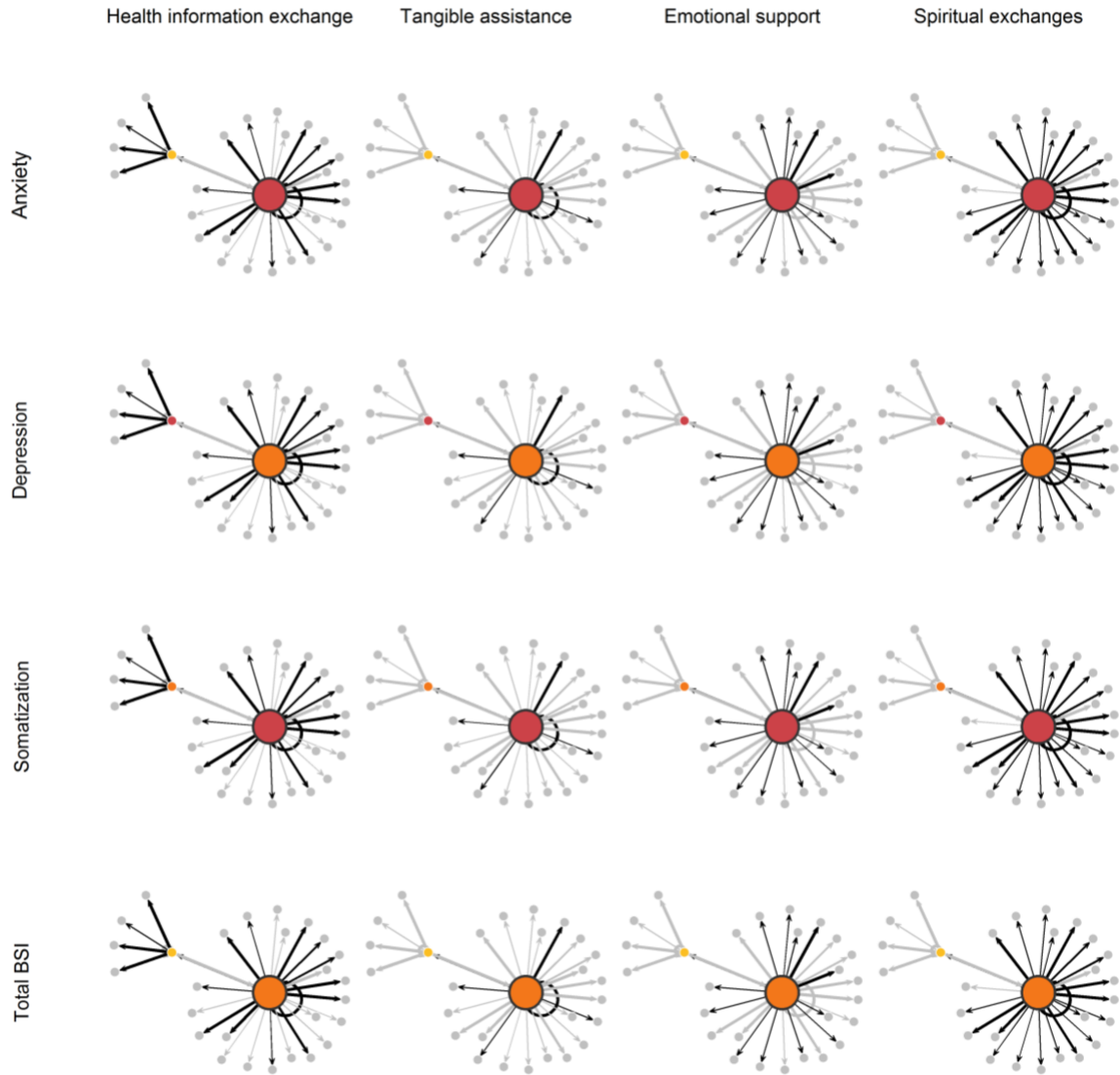
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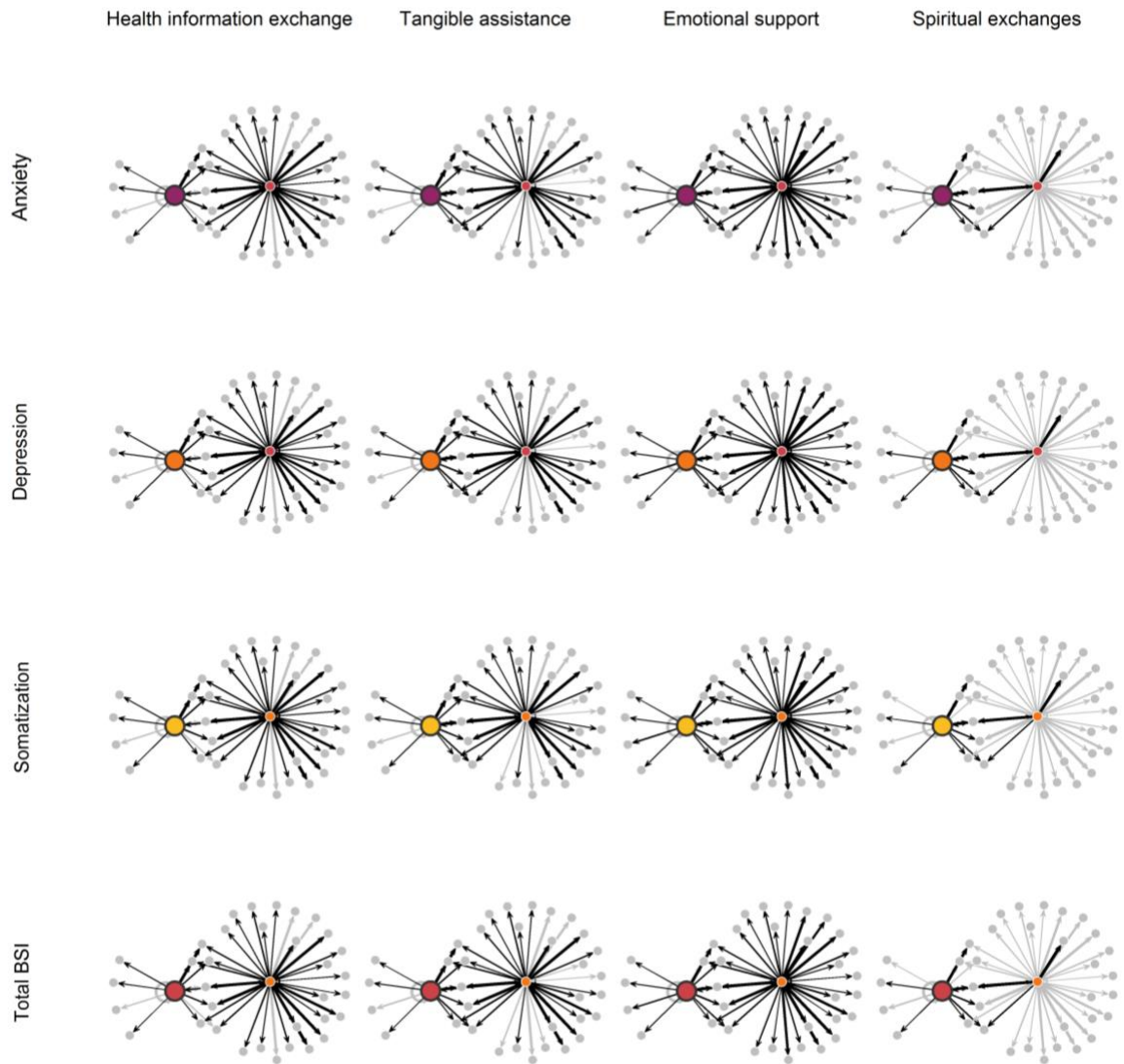
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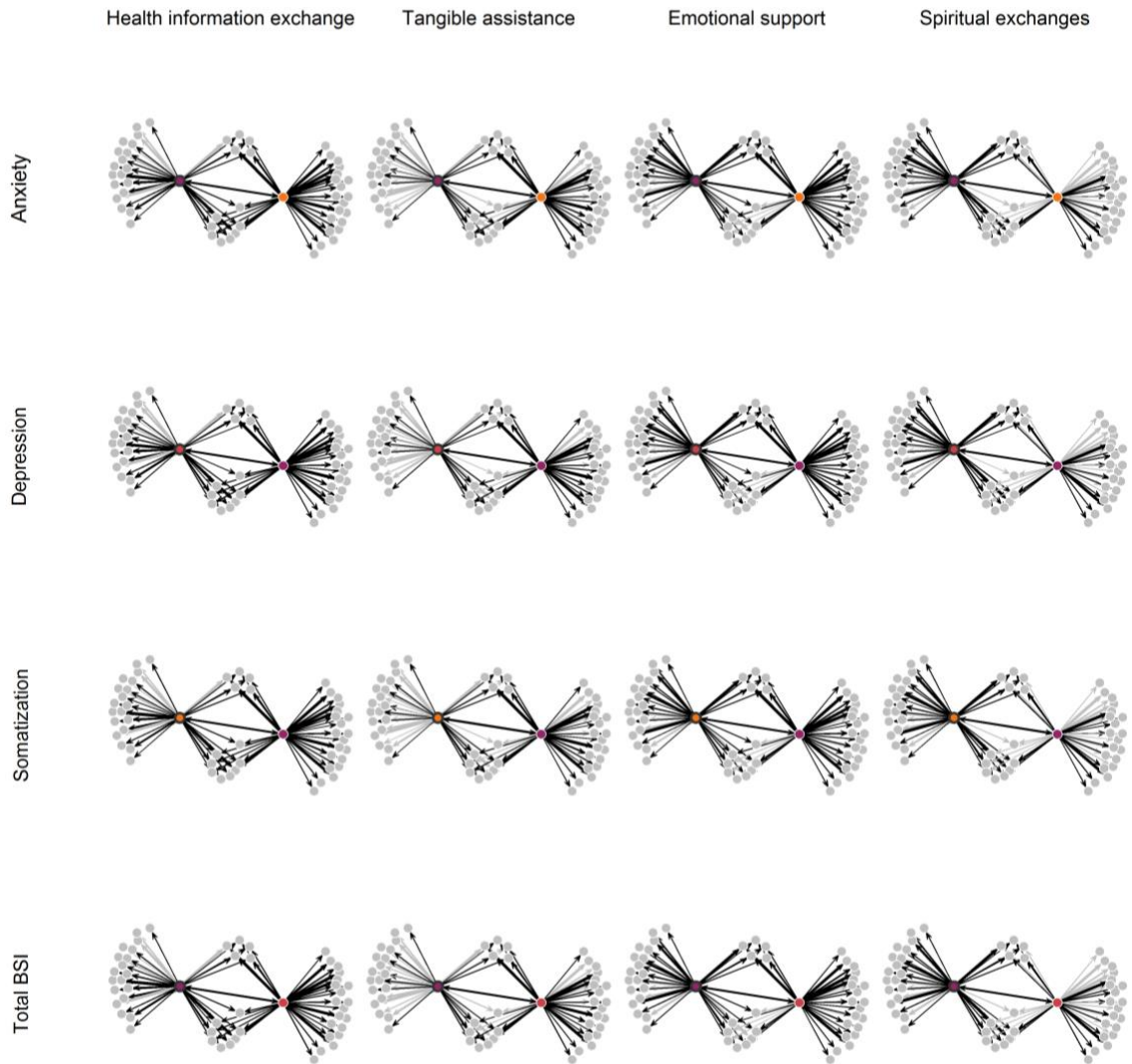
# Family 7



# Family 8

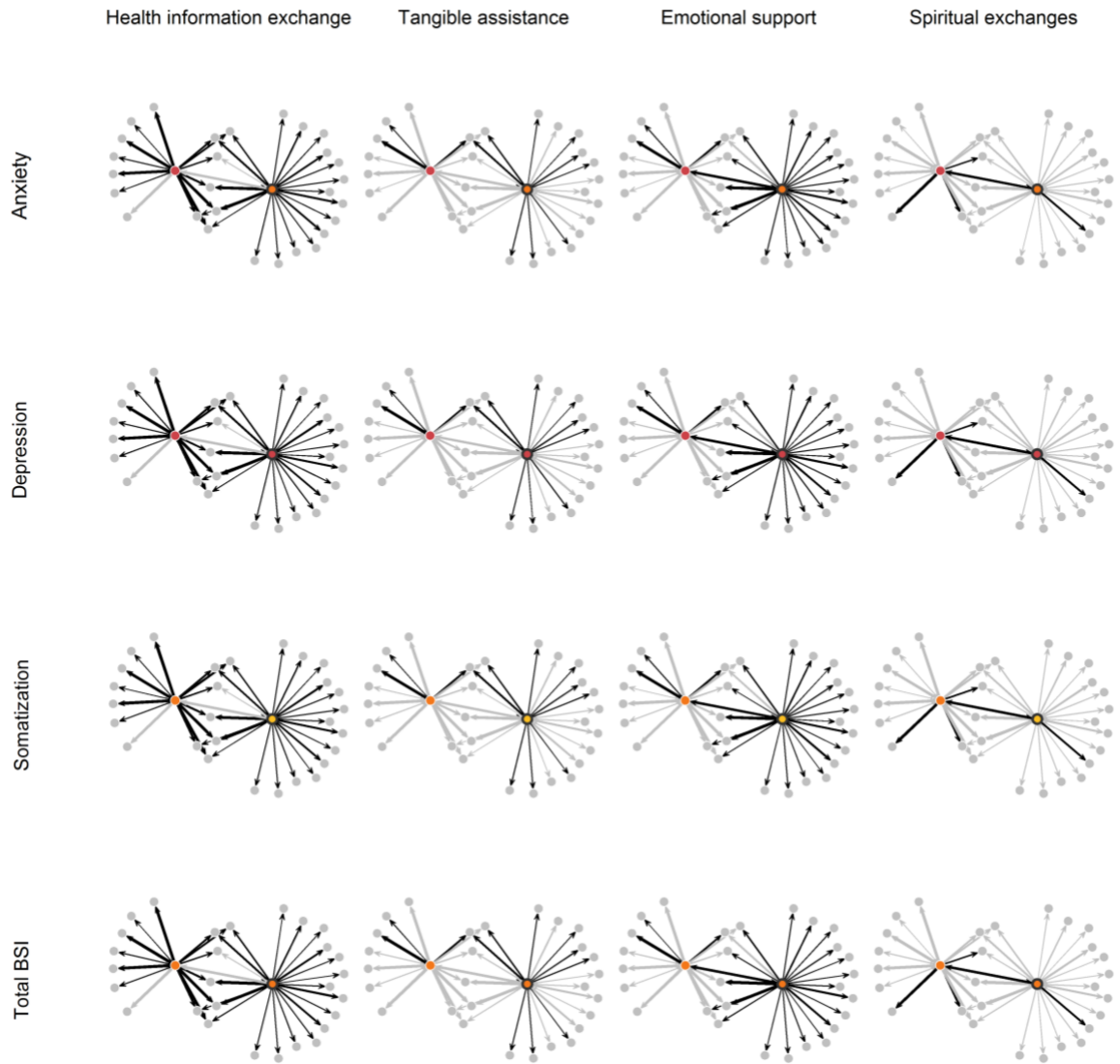


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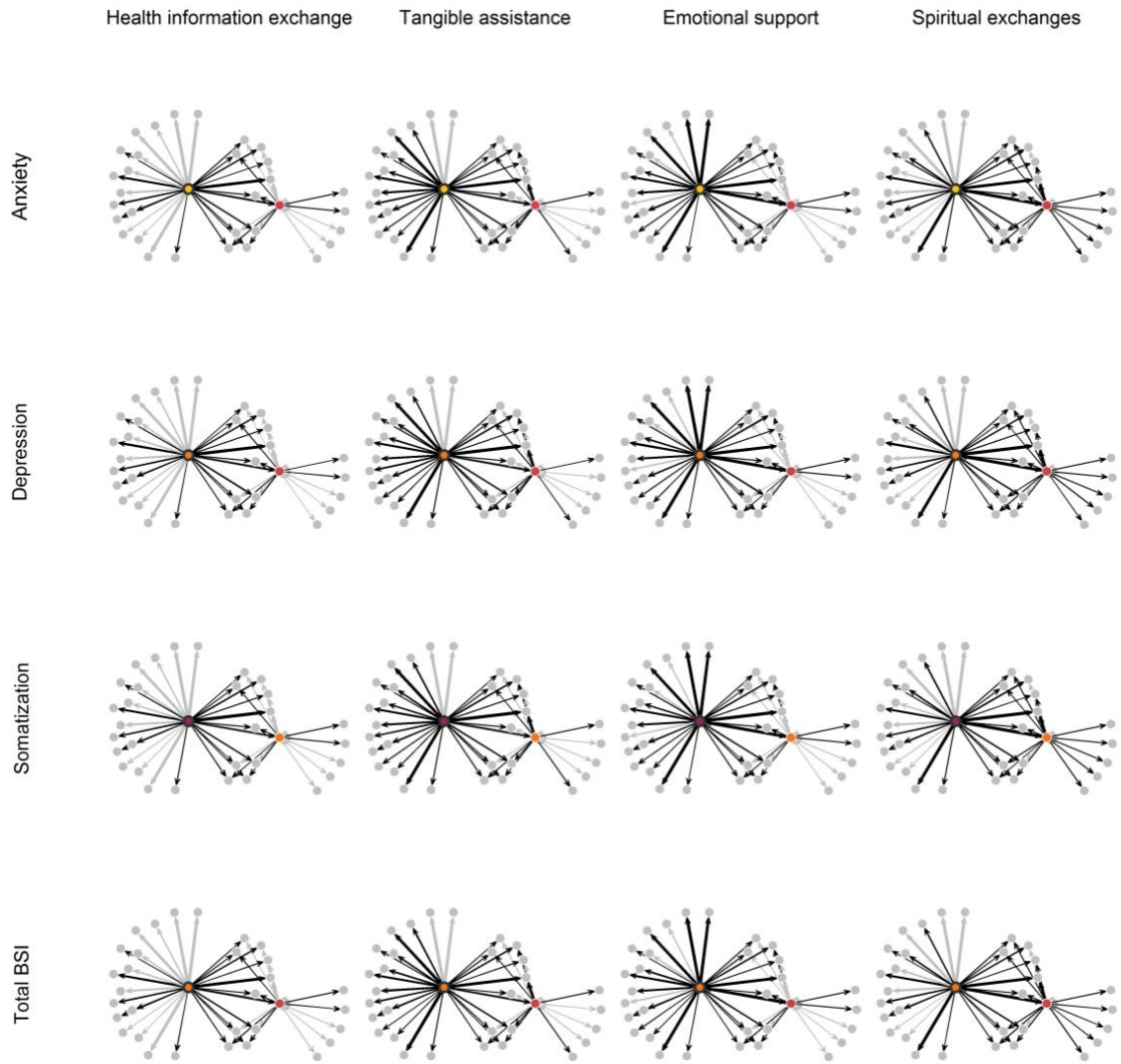




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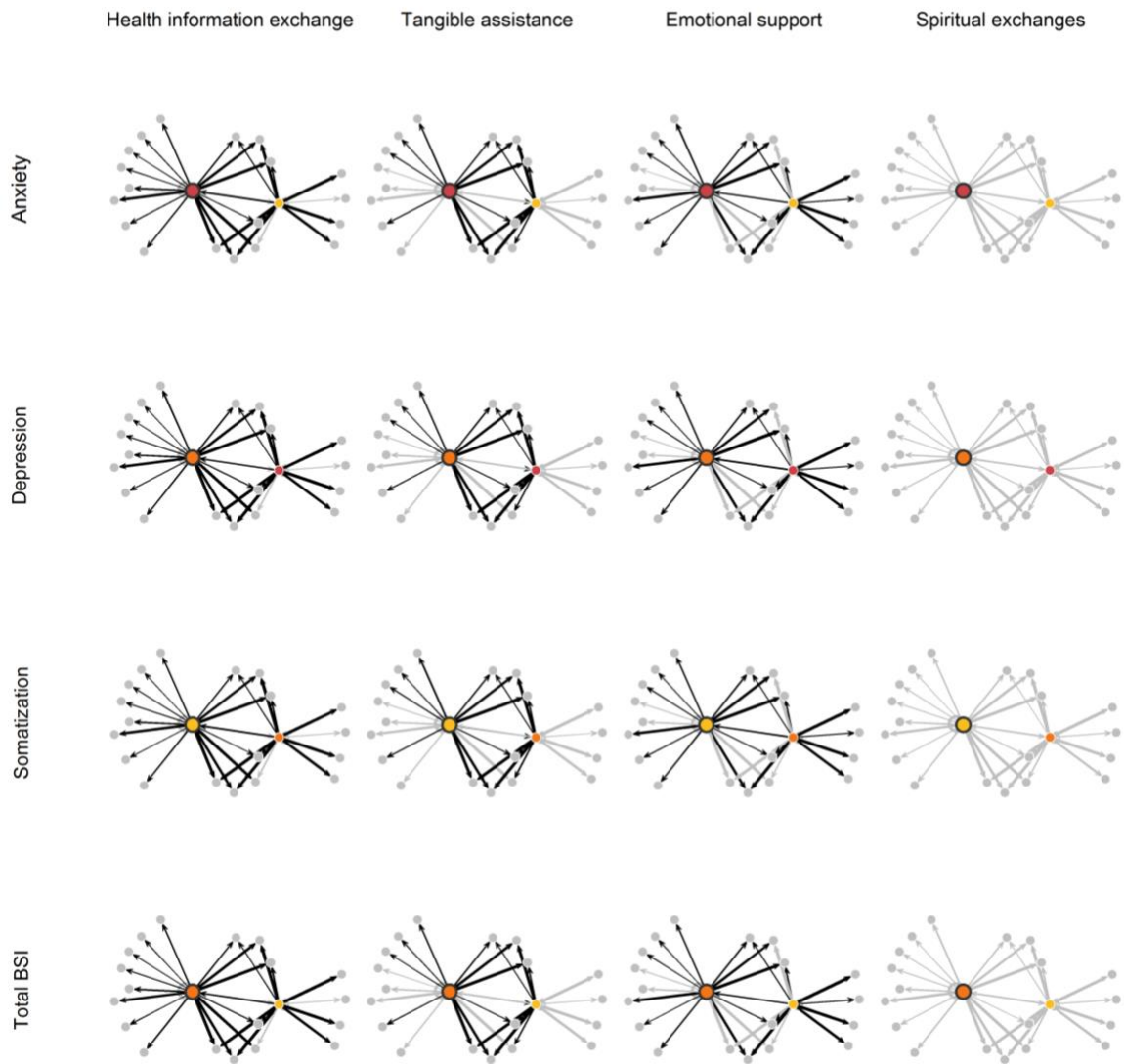


# Family 11





## Family 12



# Family 13

Health information exchange

Tangible assistance

Emotional support

Spiritual exchanges

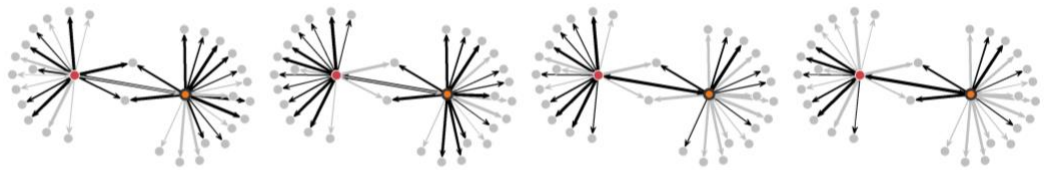
Anxiety



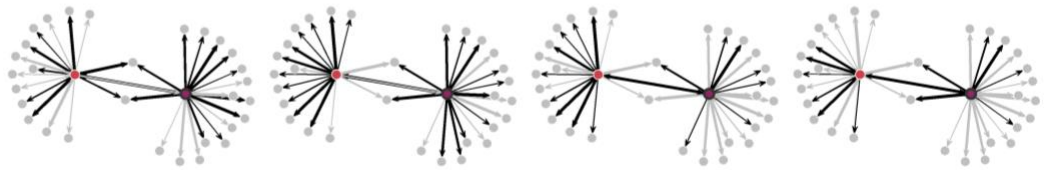
Depression



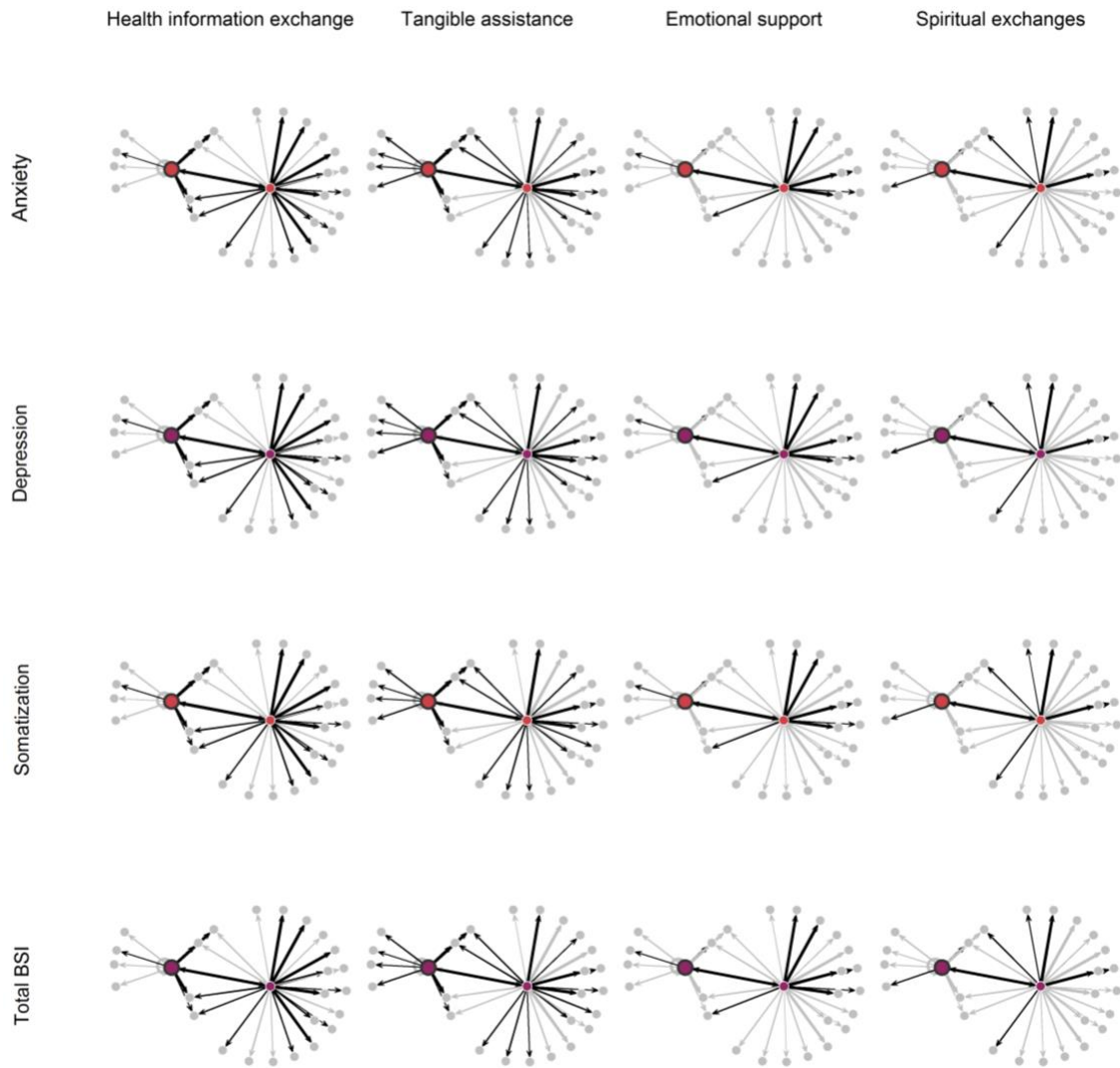
Somatization



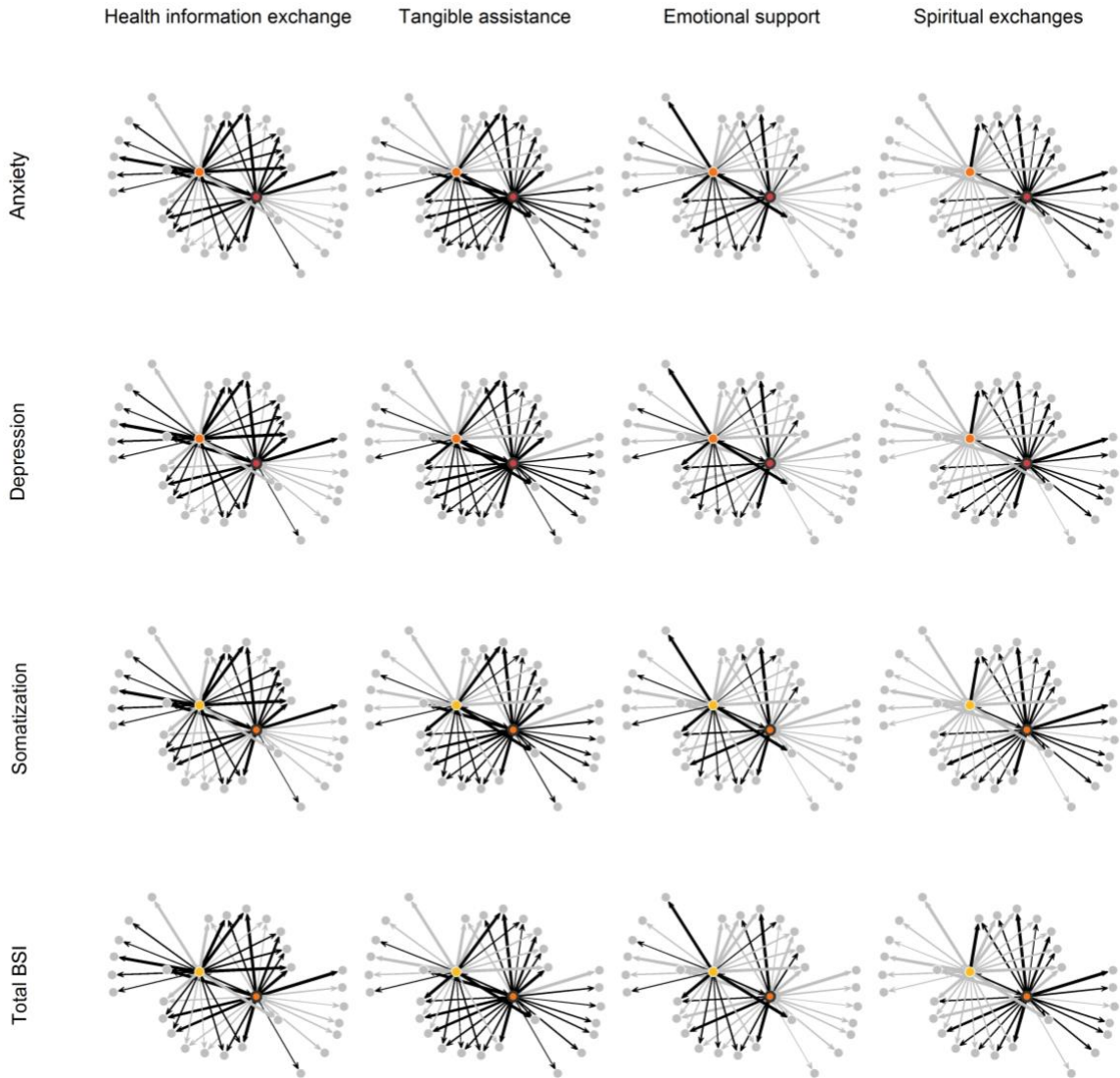
Total BSI



# Family 14



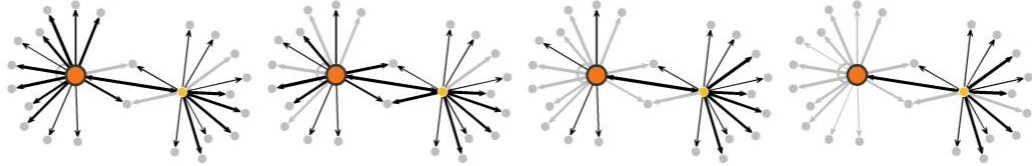
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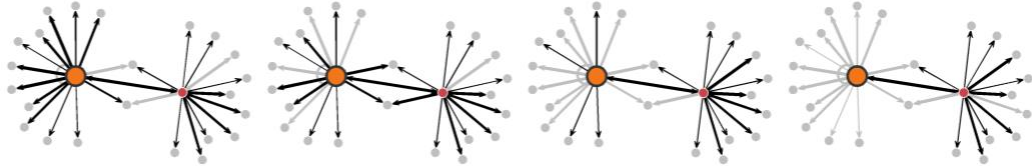
Family 16

Health information exchange      Tangible assistance      Emotional support      Spiritual exchanges

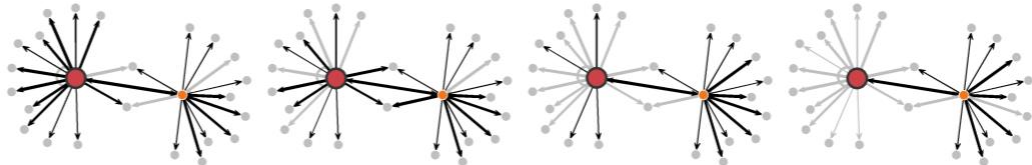
Anxiety



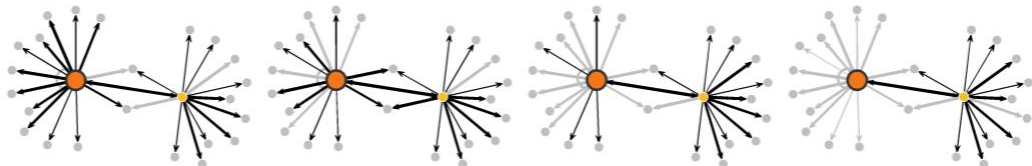
Depression



Somatization



Total BSI



# Family 17

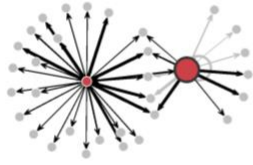
Health information exchange

Tangible assistance

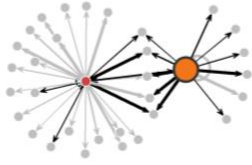
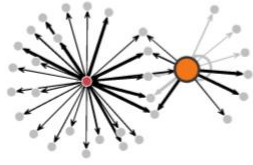
Emotional support

Spiritual exchanges

Anxiety



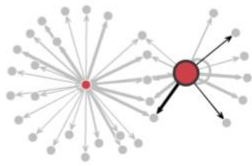
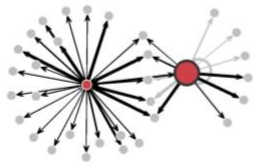
Depression



Somatization

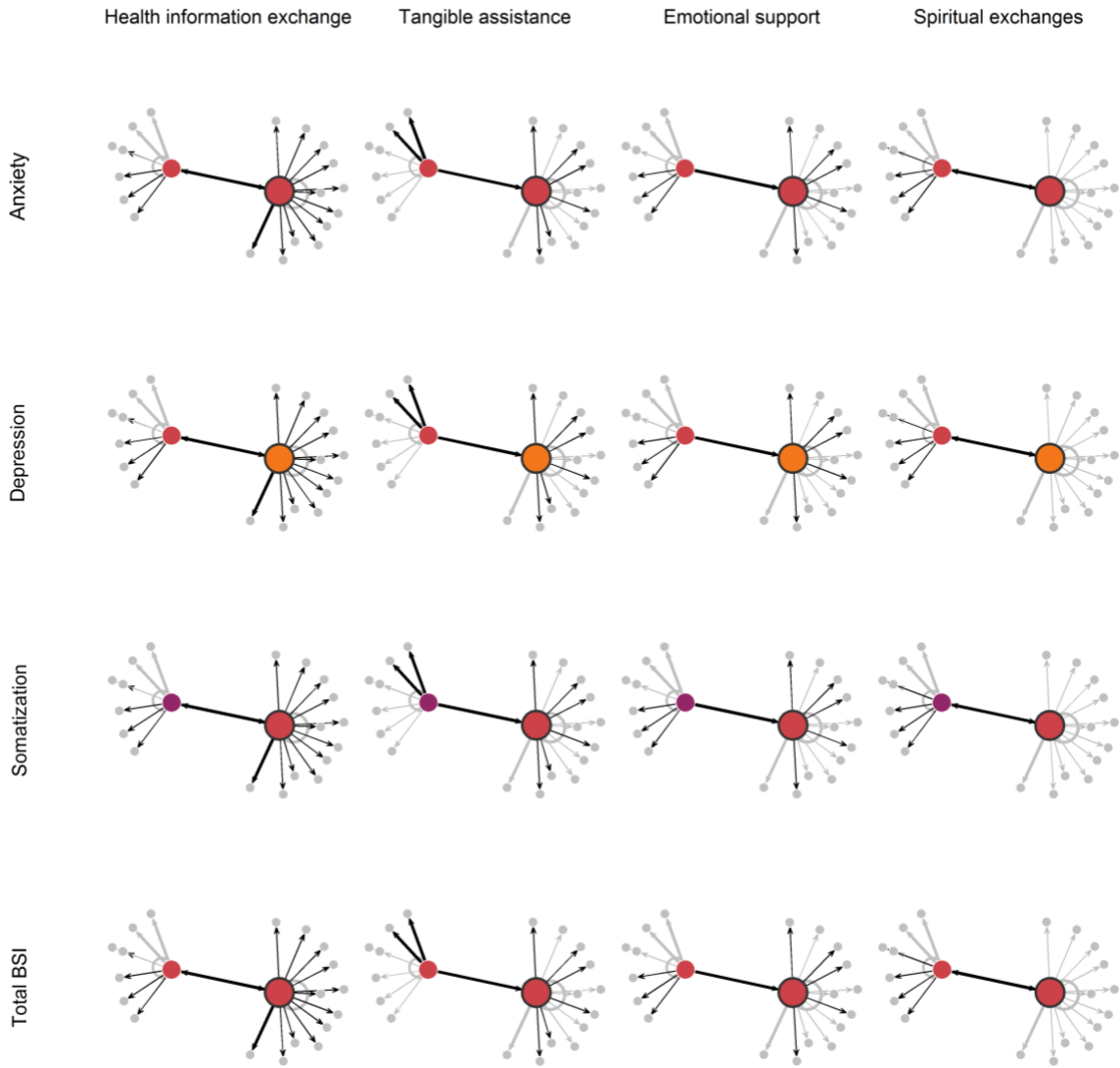


Total BSI

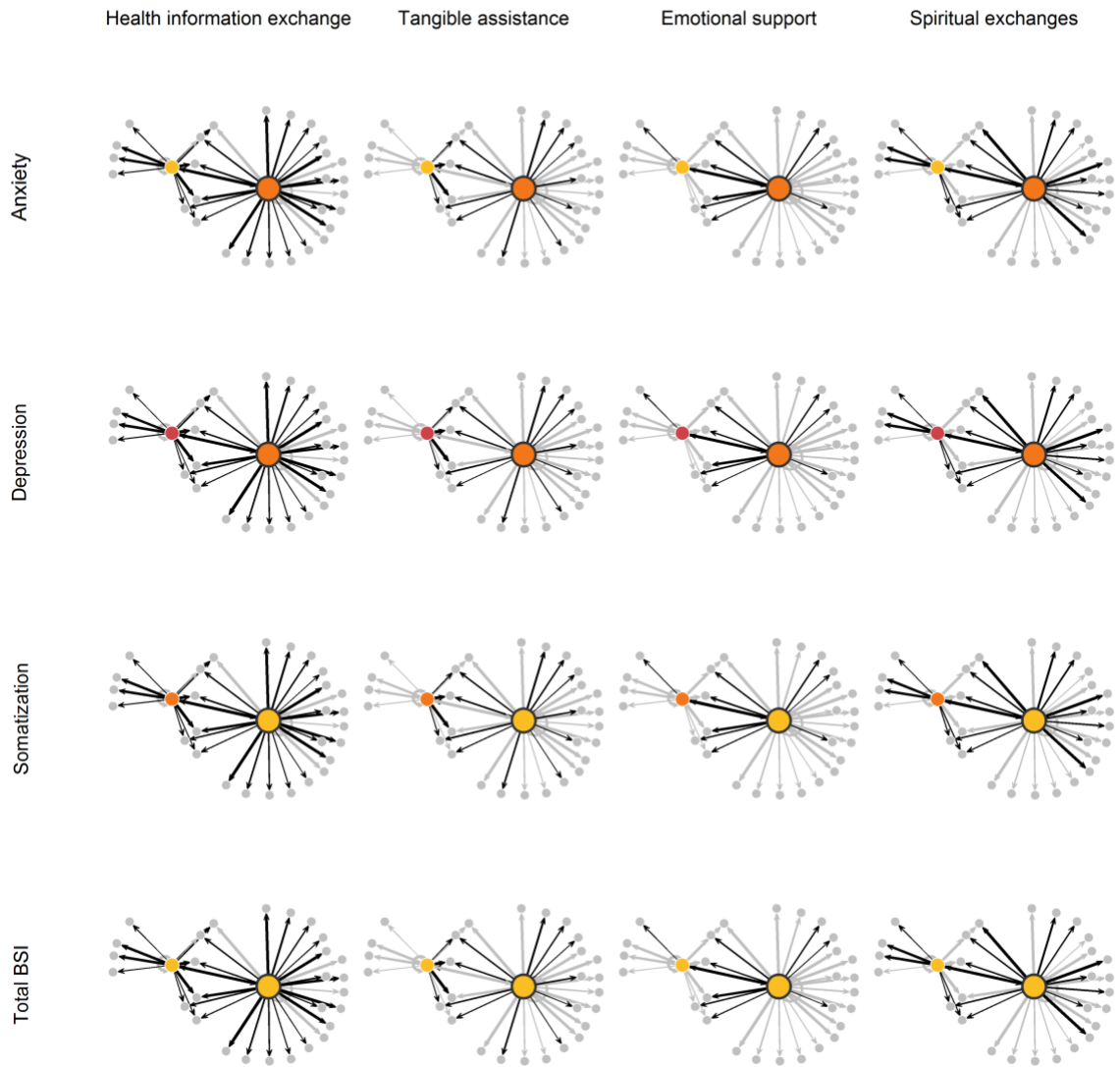




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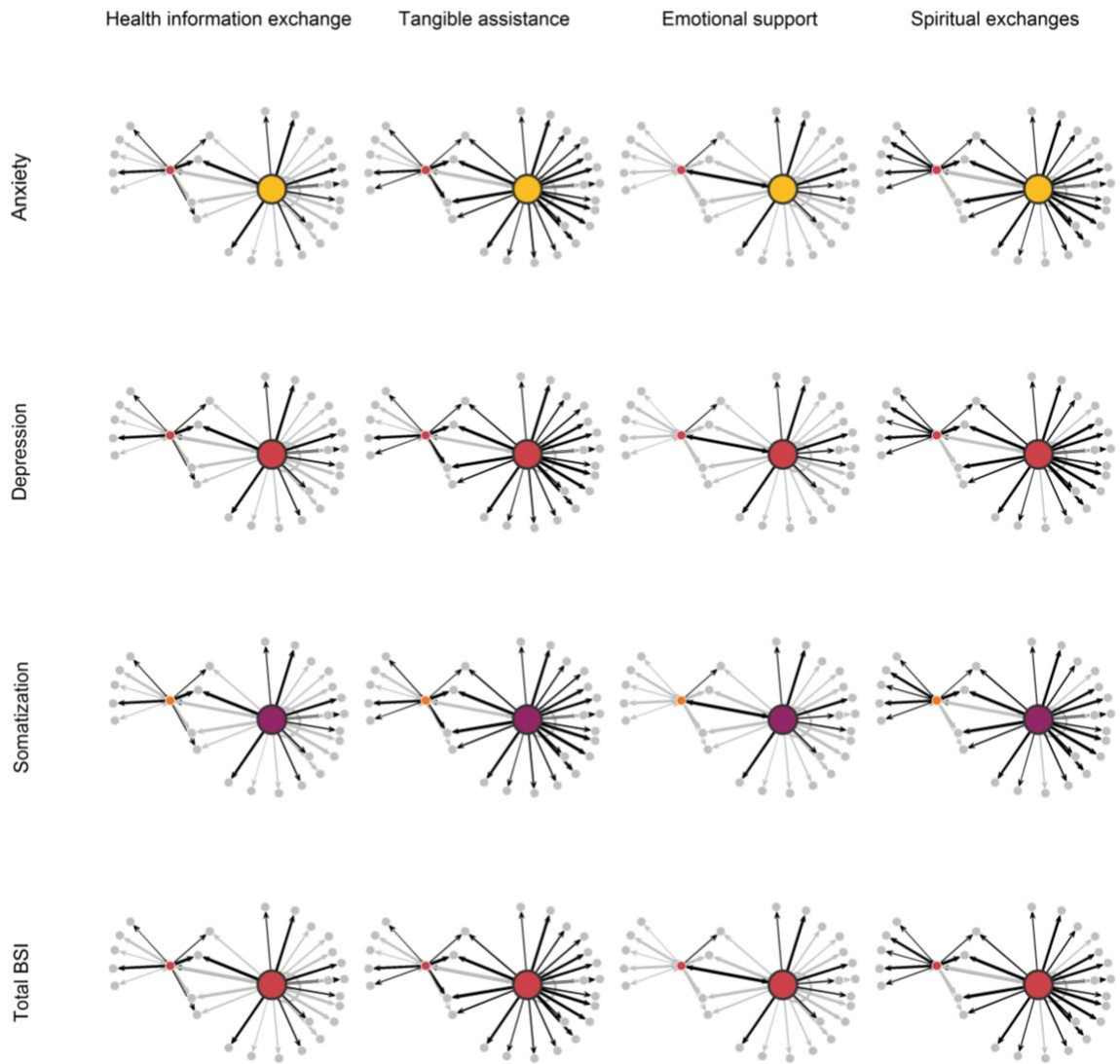


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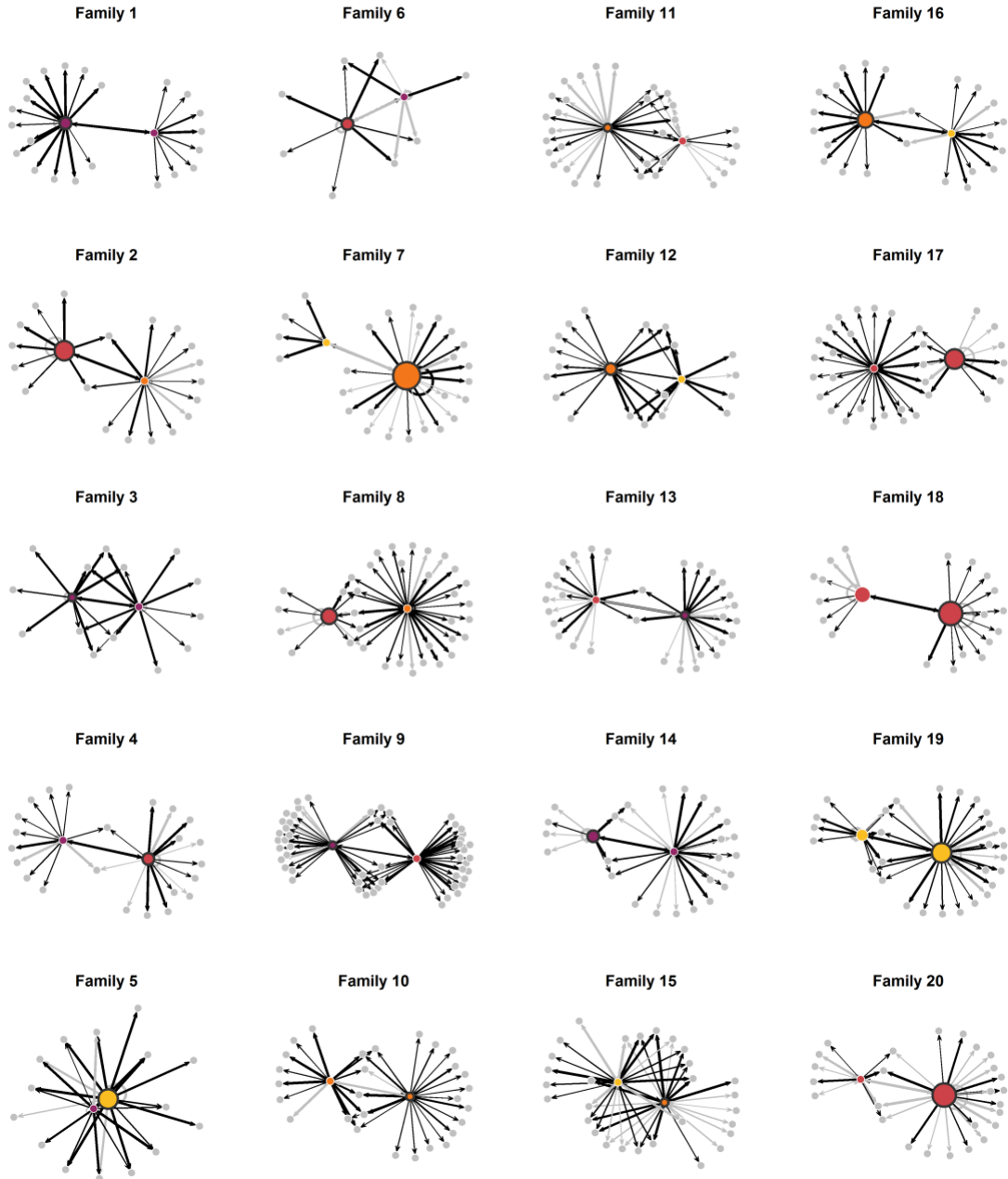
## Family 20



# Appendix H: Social Network Visualizations by Support Type

## BSI Global Scores

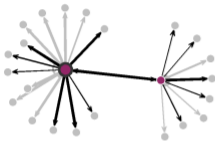
### Health information exchange



# BSI Global Scores

## Emotional support

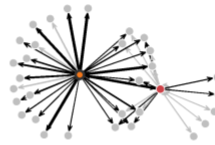
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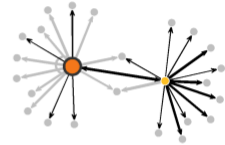
Family 6



Family 11



Family 16



Family 2



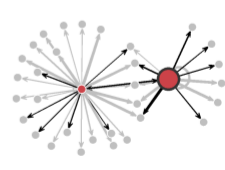
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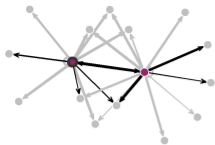
Family 12



Family 17



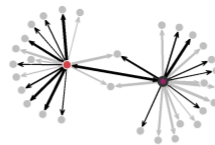
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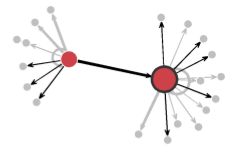
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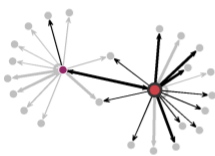
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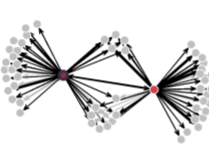
Family 18



Family 4



Family 9



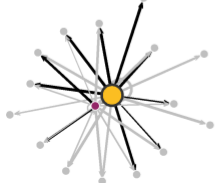
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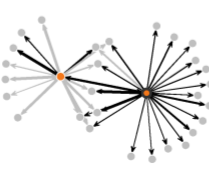
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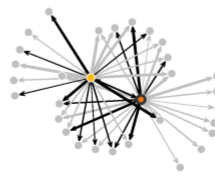
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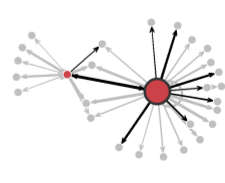
Family 10



Family 15



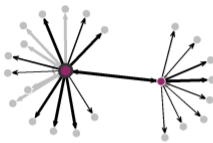
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# BSI Global Scores

## Tangible assistance

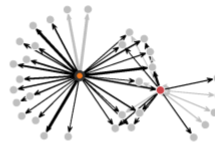
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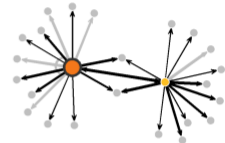
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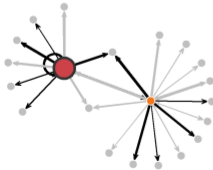
Family 11



Family 16



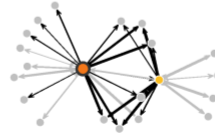
Family 2



Family 7



Family 12



Family 17



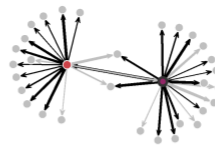
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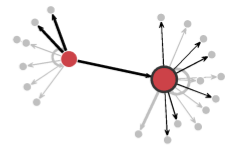
Family 8



Family 13



Family 18



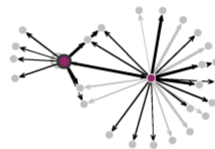
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Family 9



Family 14



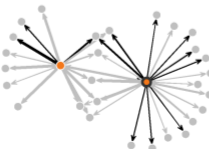
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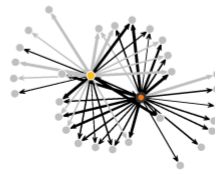
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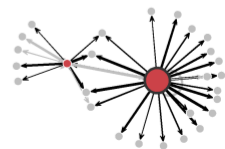
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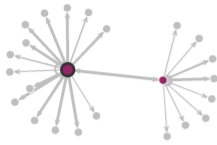
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# BSI Global Scores

## Spiritual exchange

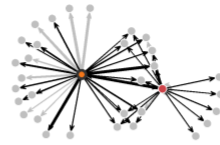
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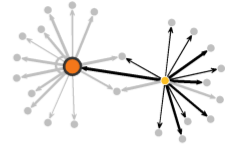
Family 6



Family 11



Family 16



Family 2



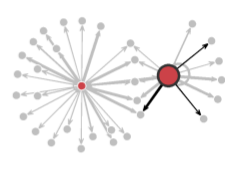
Family 7



Family 12



Family 17



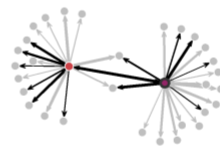
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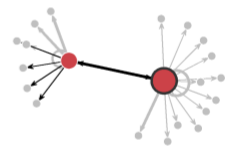
Family 8



Family 13



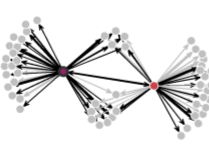
Family 18



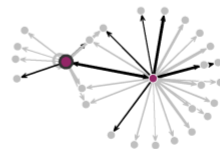
Family 4



Family 9



Family 14



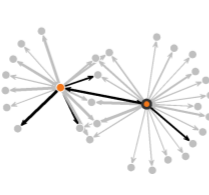
Family 19



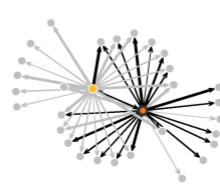
Family 5



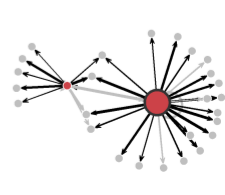
Family 10



Family 15

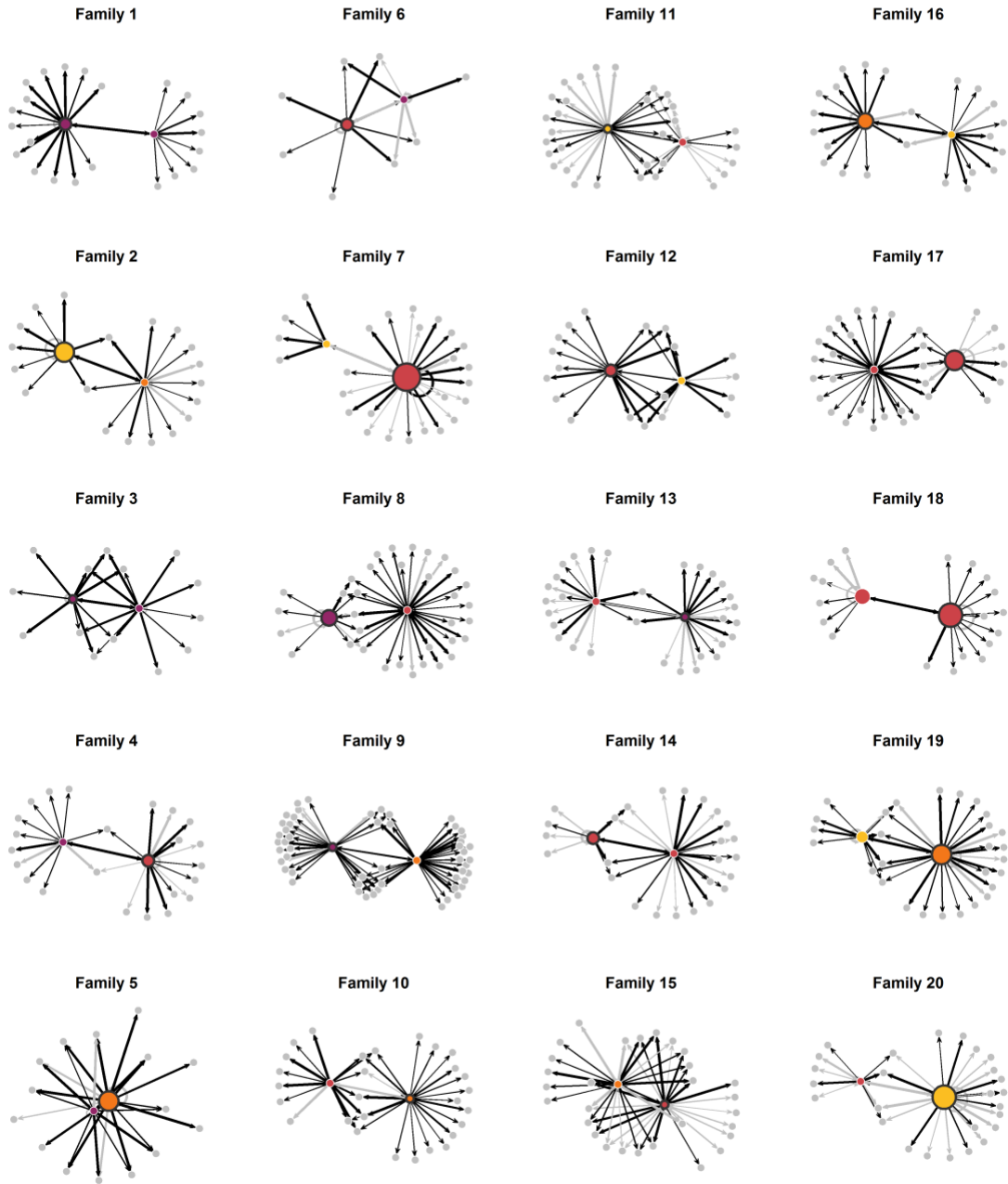


Family 20



# BSI Anxiety Scores

## Health information exchange



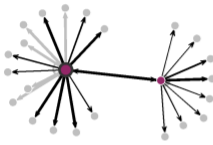




# BSI Anxiety Scores

## Tangible assistance

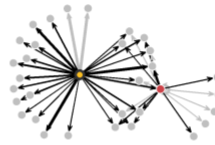
Family 1



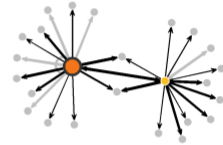
Family 6



Family 11



Family 16



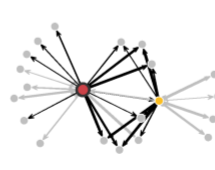
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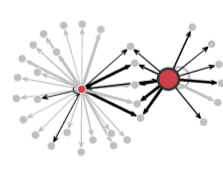
Family 7



Family 12



Family 17



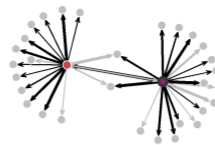
Family 3



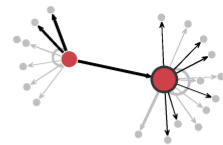
Family 8



Family 13



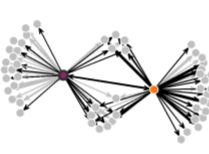
Family 18



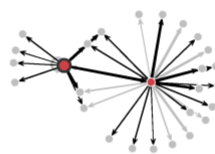
Family 4



Family 9



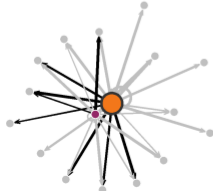
Family 14



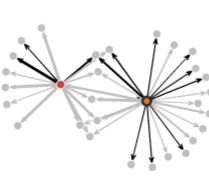
Family 19



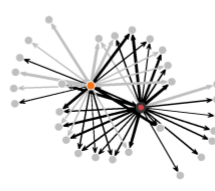
Family 5



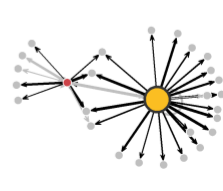
Family 10



Family 15



Family 20

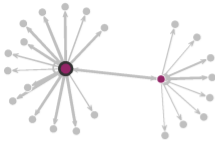




# BSI Anxiety Scores

## Spiritual exchange

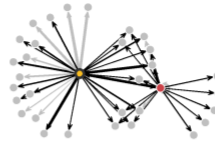
Family 1



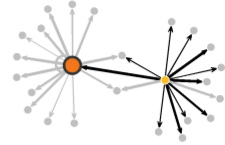
Family 6



Family 11



Family 16



Family 2



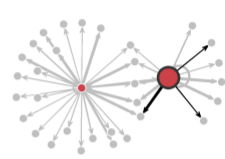
Family 7



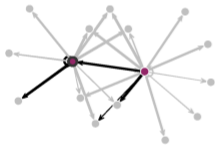
Family 12



Family 17



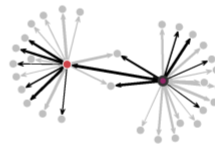
Family 3



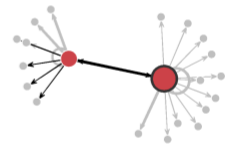
Family 8



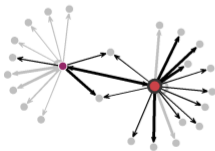
Family 13



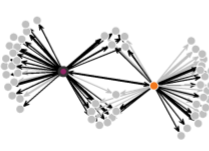
Family 18



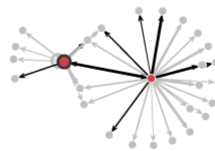
Family 4



Family 9



Family 14



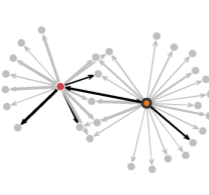
Family 19



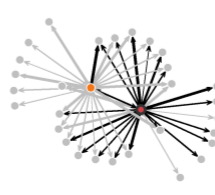
Family 5



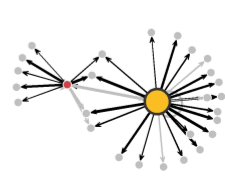
Family 10



Family 15

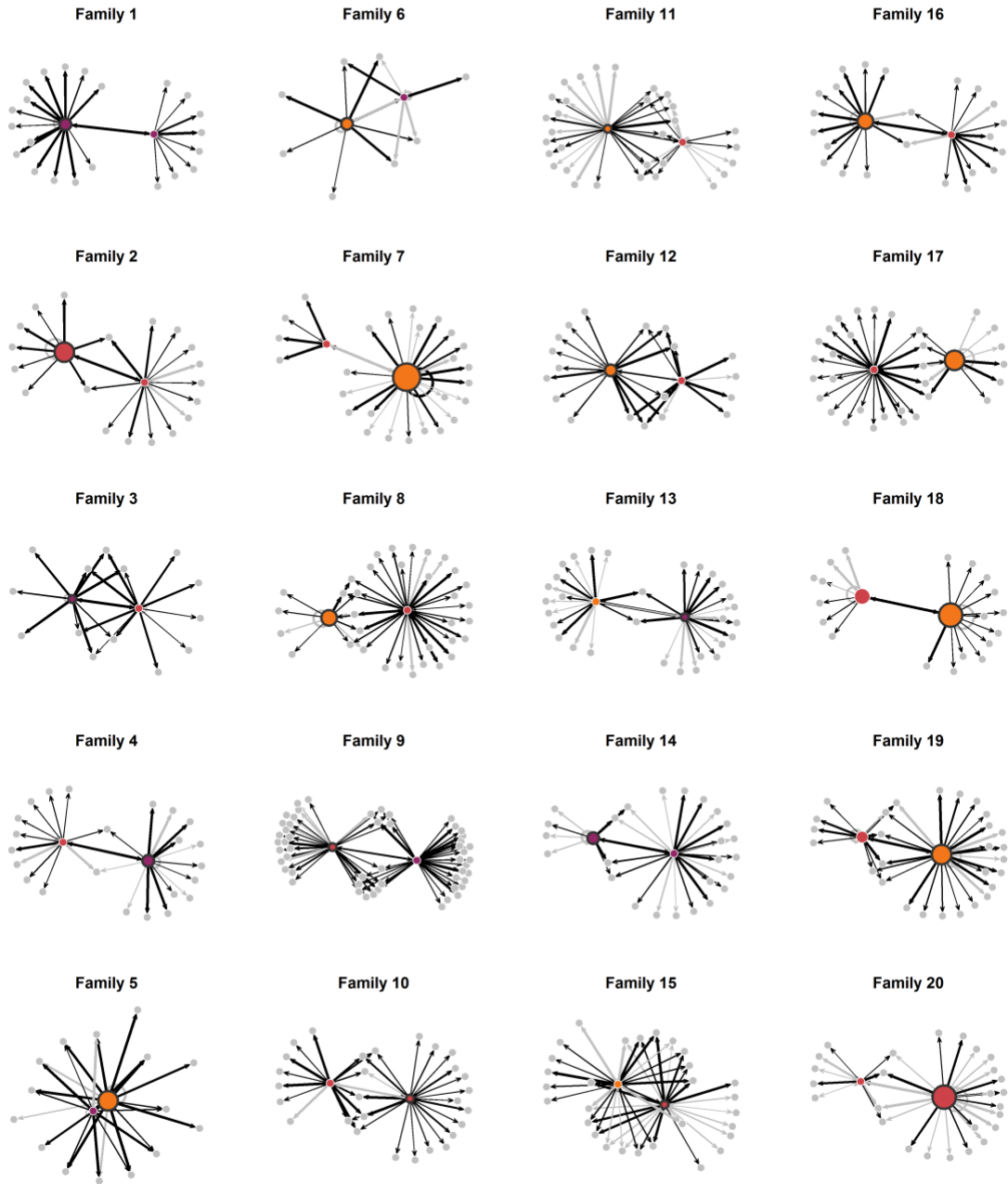


Family 20



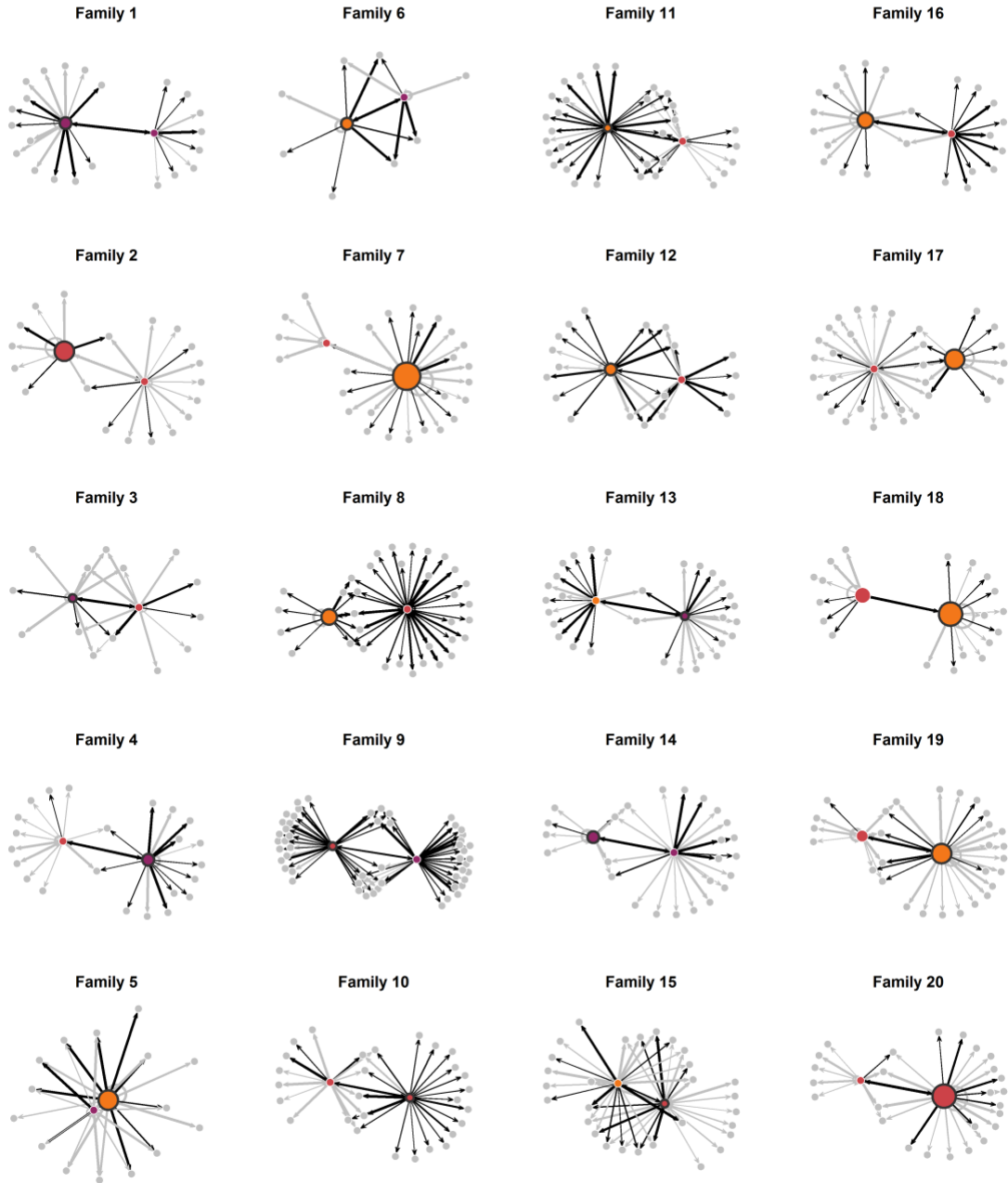
# BSI Depression Scores

## Health information exchange



# BSI Depression Scores

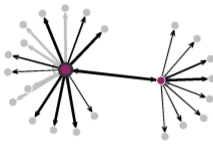
## Emotional support



# BSI Depression Scores

## Tangible assistance

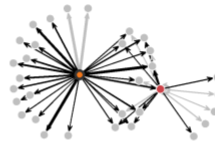
Family 1



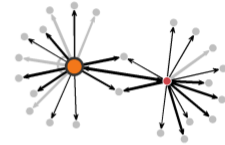
Family 6



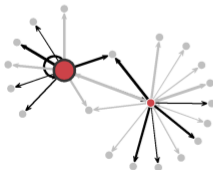
Family 11



Family 16



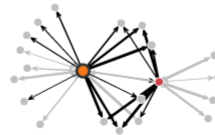
Family 2



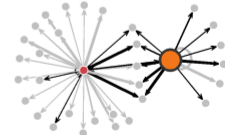
Family 7



Family 12



Family 17



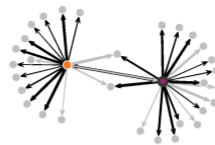
Family 3



Family 8



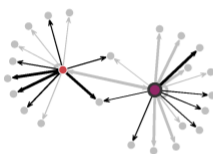
Family 13



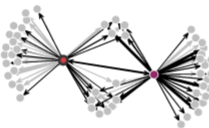
Family 18



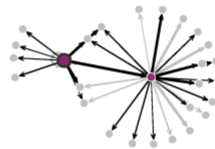
Family 4



Family 9



Family 14



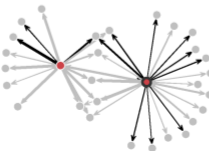
Family 19



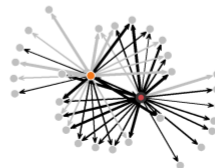
Family 5



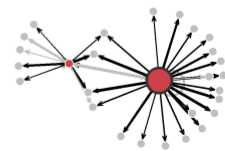
Family 10



Family 15



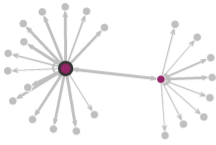
Family 20



# BSI Depression Scores

## Spiritual exchange

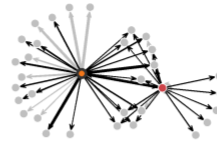
Family 1



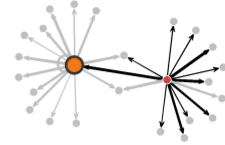
Family 6



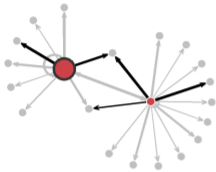
Family 11



Family 16



Family 2



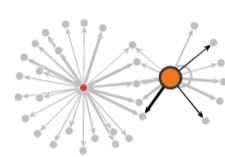
Family 7



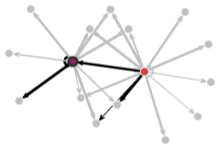
Family 12



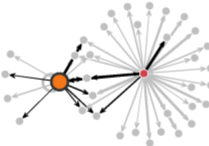
Family 17



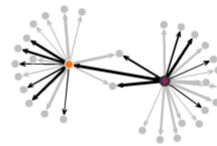
Family 3



Family 8



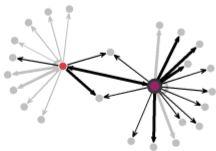
Family 13



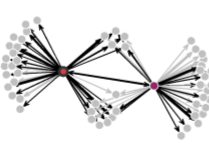
Family 18



Family 4



Family 9



Family 14



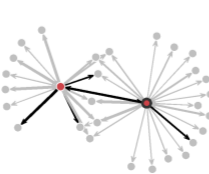
Family 19



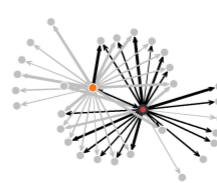
Family 5



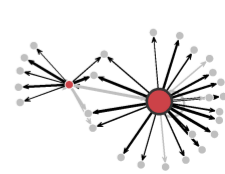
Family 10



Family 15

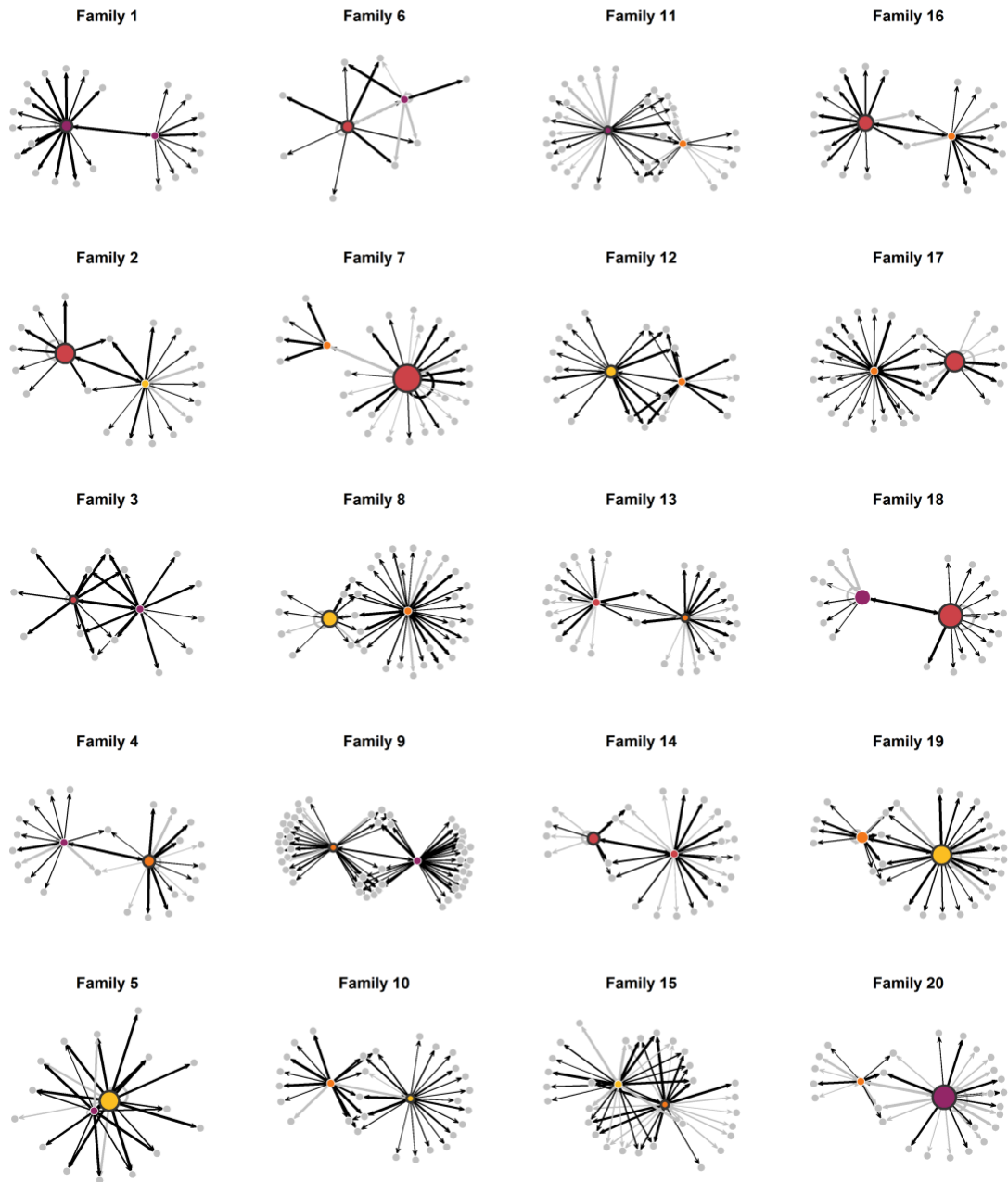


Family 20



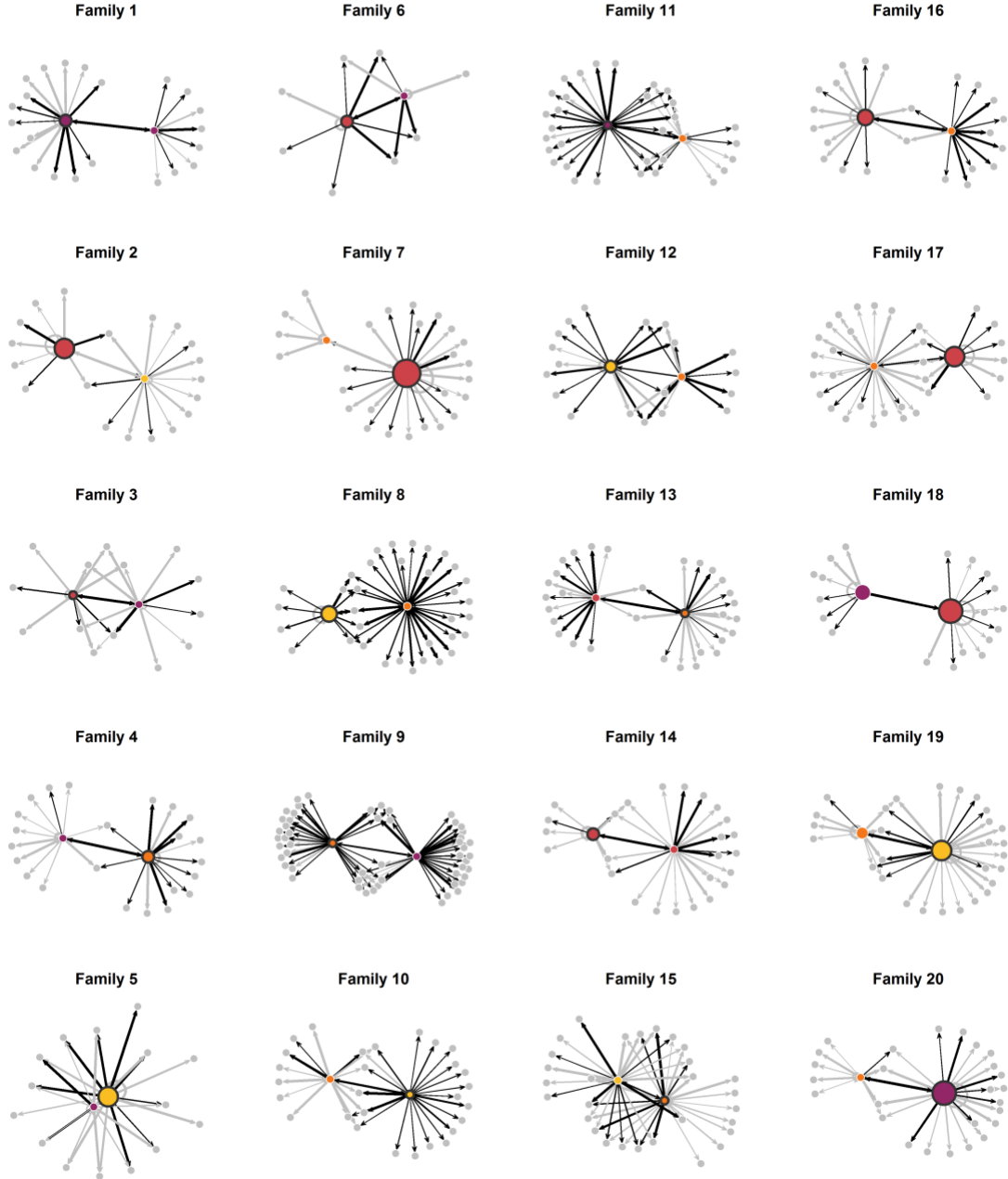
# BSI Somatization Scores

## Health information exchange



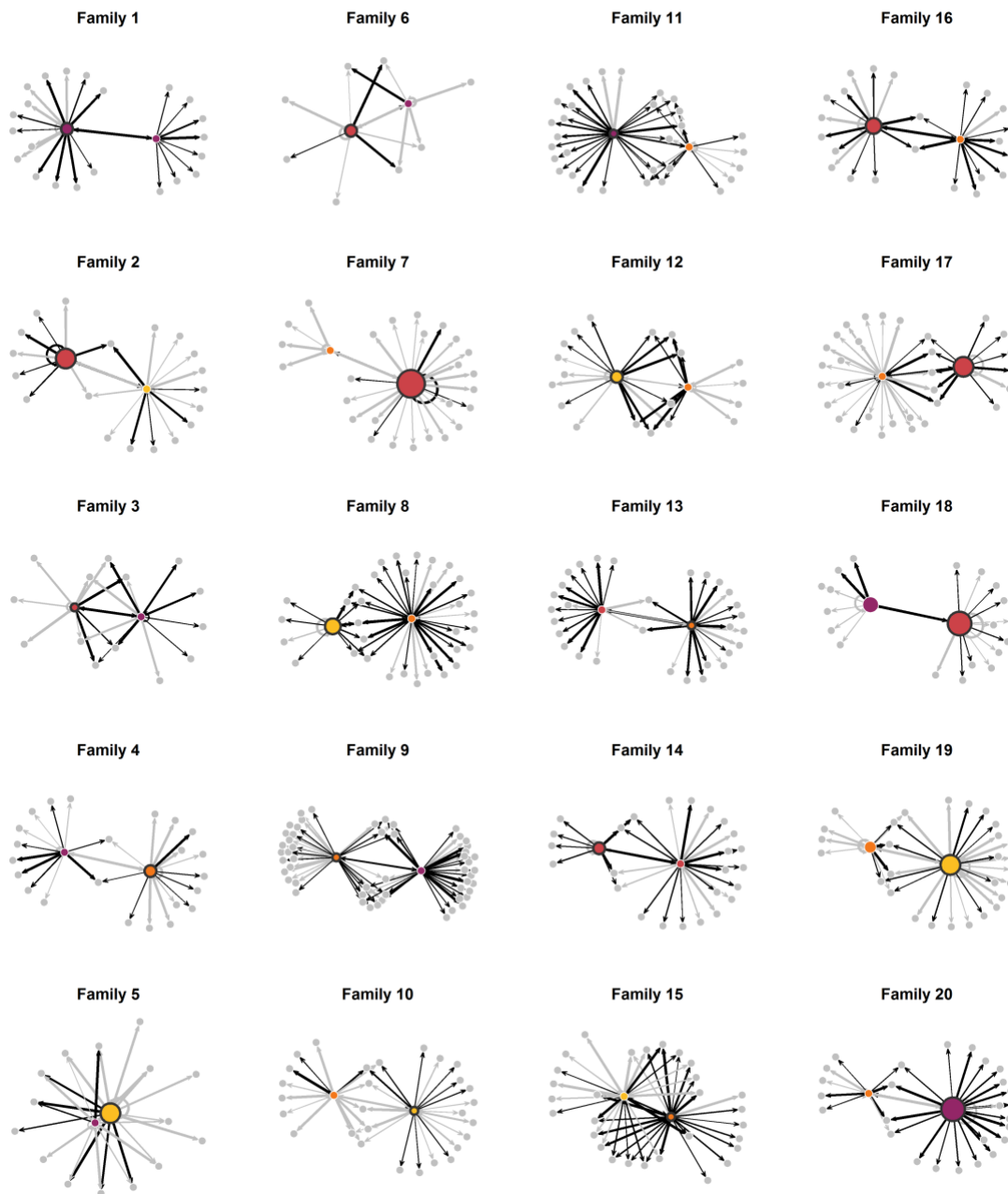
# BSI Somatization Scores

## Emotional support



# BSI Somatization Scores

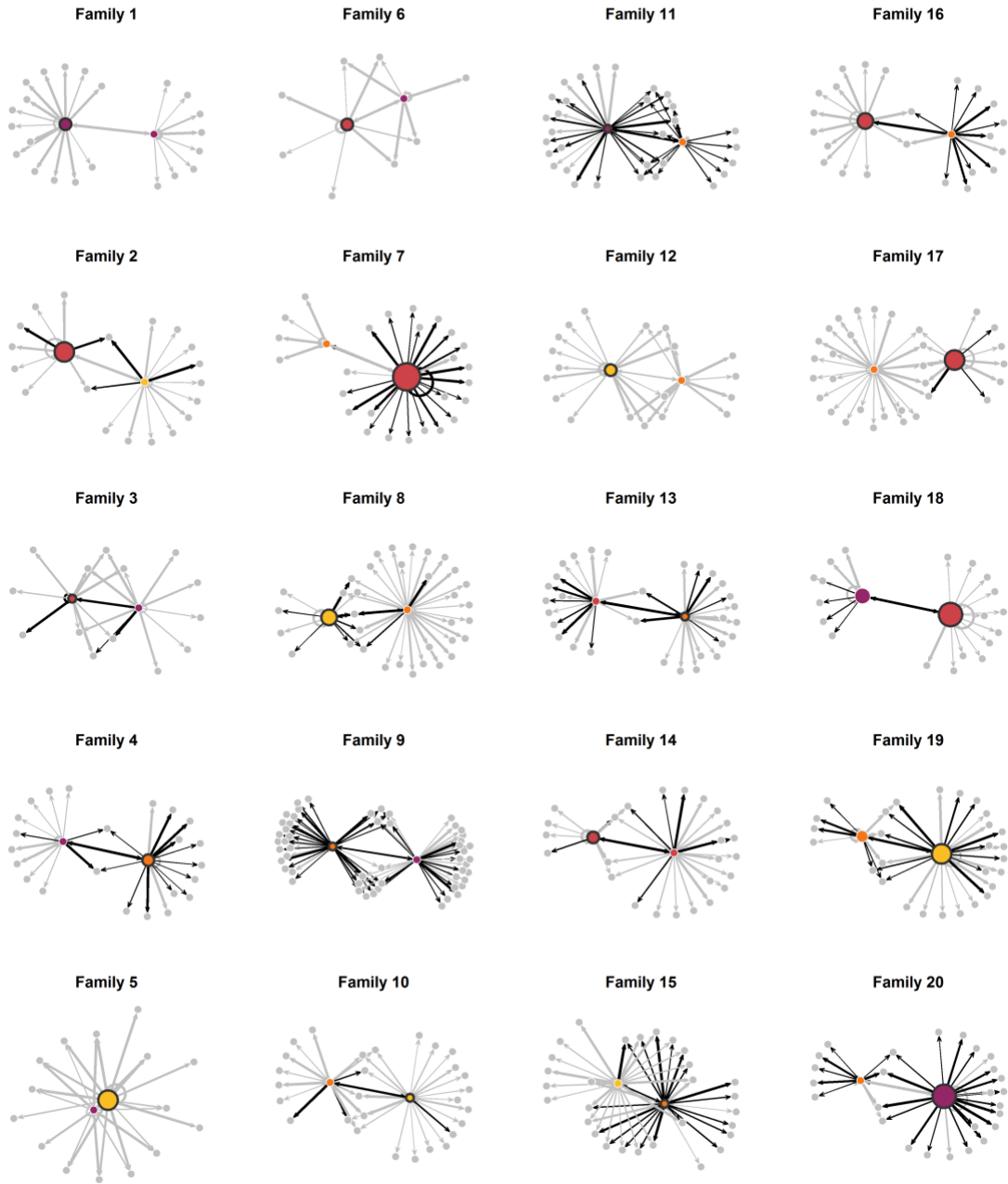
## Tangible assistance





# BSI Somatization Scores

## Spiritual exchange



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3
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