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ORIGINAL RESEARCH

Easing the Burden: Describing the Role of Social, Emotional and Spiritual Support in Research Families with Li-Fraumeni Syndrome

June A. Peters[1] · **Regina Kenen**[2] · **Renee Bremer**[1] · **Shannon Givens**[1] · **Sharon A. Savage**[1] · **Phuong L. Mai**[1]

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Abstract This study presents findings of a mixed-method descriptive exploration of the role of friends and spirituality/religiosity in easing the burden of families with the rare inherited disorder, Li-Fraumeni Syndrome (LFS). LFS is caused by germline mutations in the *TP53* gene and is associated with very high lifetime risk of developing one or more malignancies. During the first clinical visit we assessed several types of social support among a subset of study participants ($N = 66$) using an established interactive research tool called the Colored Eco-Genetic Relationship Map (CEGRM). We performed both quantitative and qualitative analyses of social relationships with LFS family members and close non-kin. Distress scores ($N = 59$) were mostly low normal, with some outliers. We found that reported friendships varied widely, that the friendships were often deep and enduring, and were important sources of informational, tangible, emotional and spiritual support. Confidantes tended to be best friends and/or spouses. Organized religion was important in selected families, typically from mainstream traditions. However, a number of people identified themselves as "spiritual" and reported spiritual and humanist explorations. Our results shed preliminary light on how some people in families with LFS cope in the face of tremendous medical, social and emotional challenges.

✉ June A. Peters
petersju@mail.nih.gov

[1] Clinical Genetics Branch (CGB), Division of Cancer Epidemiology and Genetics (DCEG), National Cancer Institute (NCI), NIH, DHHS, Rockville, MD, USA

[2] Department of Sociology and Anthropology, The College of New Jersey, Ewing, NJ, USA

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Background

LFS Background

Li-Fraumeni syndrome (LFS, OMIM#151,623) is a rare inherited cancer predisposition syndrome associated with a wide variety of childhood- and adult-onset cancers (Malkin 2011). The cancers can occur at any age from infancy through adolescence to young, middle, and late adulthood. The inheritance pattern is autosomal dominant and the penetrance very high (Mai, 2015, submitted). Many mutation carriers have multiple primary tumors of the same or different types (Hisada et al. 1998; Kamihara et al. 2014). Thus the burden of the illness is high for this condition.

Classic LFS is defined by the presence of all of the following criteria (Li et al. 1988; McBride et al. 2014): 1) A proband with a sarcoma diagnosed before age 45 years; 2) A first-degree relative (FDR) with any cancer before age 45 years; and 3) A first- or second degree relative with any cancer before age 45 years or a sarcoma at any age. The most frequently reported cancers in LFS include breast, soft tissues, brain, adrenal gland, bone, hematological, and colorectal (Petitjean et al. 2007) (R17, November 2013 version). There are less stringent clinical diagnostic criteria (Li-Fraumeni-like, or LFL) as well as various clinical criteria for testing (Birch et al. 2001; Birch et al. 1994; Bougeard et al. 2008; Chompret 2002; Eeles 1995; Nichols et al. 2001; Varley et al. 1997).

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Germline mutations in the *TP53* tumor suppressor gene were discovered as the main cause of LFS (Malkin et al. 1990) and are found in approximately 70 % of LFS (Varley 2003) and 30–40 % of LFL families (Birch et al. 1994). The emergence of next generation sequencing (NGS) clinical testing multi-gene panels has revealed that the LFS phenotype may be broader and more variable than originally thought. There is additional evidence, yet to be confirmed, that phenotype varies with the type of *TP53* alteration (Bougeard et al. 2015). More detailed information about LFS diagnosis, testing, and medical risk management can be found online in Gene Reviews (Schneider et al. 2013), Online Mendelian Inheritance in Man (OMIM 2015) National Comprehensive Cancer Network (NCCN 2015), and the National Cancer Institute PDQ (PDQ,NCIPIS 2015).

Prior Colored Eco-genetic Relationship Map (CEGRM) Studies in Hereditary Cancer Syndromes

Our group has considerable experience in measuring social exchanges among members of families with various hereditary cancer susceptibility syndromes. The concept of the CEGRM to obtain and display information about various domains of family ties and health communications was introduced over a decade ago (Kenen and Peters 2001). It has been revised and applied in families with Hereditary Breast-Ovarian Cancer (HBOC) and Familial Testicular Cancer (FTC) susceptibility syndromes since then (Kenen and Peters 2001; Koehly et al. 2009; Koehly et al. 2008; Peters et al. 2004; Peters et al. 2012; Peters et al. 2011a, Peters et al. 2011b).

Co-constructing a CEGRM actively involves both the participant and the investigator in transforming a genetic pedigree into a concise visual picture of the participant's social world by the participant adding friends, family, co-workers and co-members of groups such as religious affiliations to the genetic pedigree. Once the full social universe is identified, we then apply variously colored dots and stars to symbolize those with whom the participant has varying forms of social exchanges. An early CEGRM revision included the addition of religious/spiritual exchanges to the original three social exchange domains of information, tangible and emotional (Peters et al. 2006). The rationale was that there were some families in which religion was so important that the social assessment via CEGRM was inadequate without adding a category of religious support. The great advantage of a CEGRM is that the social milieu can be appreciated at a glance; one can perceive immediately from the numbers and distribution of colors, whether there are social supports or not, whether from family, friends or both, and where the color symbols are located and where they are absent. The CEGRM method of social assessment is novel in that it is highly interactive, with the study participant as actively participating as the investigator. Both the interactive process and the colorful graphic end result provide opportunities to promote the participant's insights into their own family dynamics and communications, address grief of multiple family losses, elicit family illness narratives, have an opportunity to uncover and gently re-shape family beliefs about inheritance, and appreciate one's social supports (Peters et al. 2006). A sample CEGRM is shown in Fig. 1.

Psycho-social Aspects of LFS - Key Prior Studies

Studies of the psychosocial aspects of LFS are sparse and were often performed prior to the widespread clinical use of *TP53* mutation testing. The early LFS psychosocial studies focused on several areas which have relevance to our study population: 1) characteristics of patients who elect to have testing; 2) genetic testing of children; 3) perceptions and beliefs about LFS; 4) emotional impact of LFS; and 5) relational impact of LFS (Patenaude et al. 1996).

There have been several debates about genetic testing of children in LFS families at a time when prevention or screening interventions were not available, which raised many ethical, legal, and social concerns among clinicians, policy makers and professional societies (Evans et al. 2010; Evans 1992; Wilfond and AAP Bioethics Committee 2001). However, scientific and clinical advances have improved and people seem more willing to test themselves and their children (Clayton et al. 2014; Evans et al. 2010; Lammens et al. 2010a; Tercyak et al. 2011; Wade et al. 2010). As a result of this trend, we have a number of mutation-positive minors included in our study.

Self-perceived beliefs about etiology and about medical care are often powerful and may influence health behaviors (Patenaude 2005; Peterson et al. 2008). Screening for multiple cancers may affect people's psychological well-being differently (Lammens et al. 2010b; Oppenheim et al. 2001).

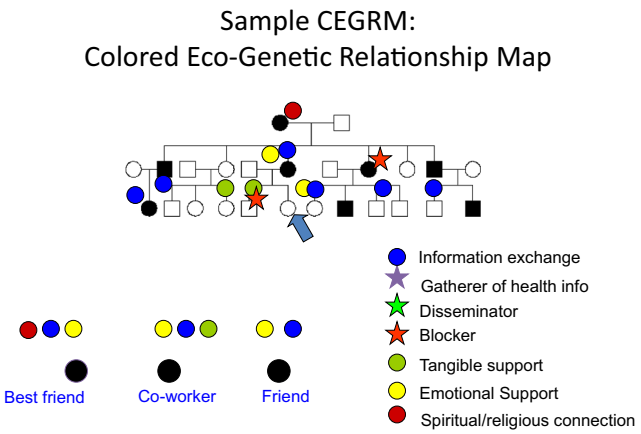

Fig. 1 Hypothetical CEGRM for Jane

Finally, concerning the relational impact of LFS, a topic most closely related to the present study, a recent study of spousal dyads found that levels of distress and worries of the participants and their partners/spouses were significantly correlated (Lammens et al. 2011). Younger age and a lack of social support were also associated significantly with heightened levels of distress and worries in these couples.

Social Ties: Family, Friendships And Confidantes

Social relationships are important to life enjoyment and to mental and physical health and well-being. Social support refers to the emotionally sustaining qualities of relationships, such as a sense that one is loved, cared for, and listened to (Umberson and Montez 2010). Social support and relationships are related to mental and physical health and personal sense of control of one's health (Cohen et al. 2007; Uchino et al. 1995; Uchino et al. 2014). It is not unusual for an individual in a family with LFS to have lost a parent and/or other close relatives. This can result in a significant social as well as emotional loss due to few living relatives on one side of the family. Social networks are the connections among people in one's social world; we have published several papers on the social networks of women in HBOC families, showing that females, those with a previous cancer diagnosis, and emotional support providers were often those who gathered and disseminate information (Koehly et al. 2009; Koehly et al. 2008).

Social Ties: Religion/Spirituality

Religion and spirituality are rarely investigated in studies of hereditary cancer predisposition. In a study of women referred for *BRCA1/2* genetic testing, level of spiritual faith was shown to be associated with the decision to pursue genetic testing, particularly among those who perceived themselves to be at low risk of developing breast cancer again (Schwartz et al. 2000). Religion refers to the belief in and worship of a superhuman controlling power, especially in a personal God or gods; often involves particular ceremonies, rules of behavior; and constitutes a particular system of faith, attitudes, practices and devotions as exemplified by the world's great religions (e.g., Judaism, various forms of Christianity, Islam, Hinduism, and Buddhism) (OxfordDictionaries 2015). A religious community generally shares beliefs and practices which express the communal culture and values through myth, doctrine, and ritual. Worship and prayer are probably the most common element of religion. Moral conduct based on sacred texts and participation in religious institutions also constitute elements of religious life (Hill et al. 2000).

Historically, the words *religious* and *spiritual* have been used synonymously, however, the word *spiritual* gradually came to be associated with the private realm of thought and experience while the word *religious* came to be connected with the public realm of membership in a religious institution with official denominational doctrines (Durkheim 1915). While some people highlight the internal experience (e.g., peacefulness), others emphasize the relational aspects of spirituality (e.g., a transcendent relationship with that which one holds sacred and sometimes with one's community of spiritual friends).

"When faced with a crisis, why do some people turn to religion to help them cope, while others turn away? Is religion a help or a hindrance in times of stress?" (Pargament 1997)(cover). Given all we know about the medical, emotional and existential manifestations of LFS, we hypothesized that some families with LFS might seek succor from religion.

Purpose of the Study

In this study, we investigate the role of social, spiritual and emotional support for families with LFS through use of the CEGRM and a standardized measure of emotional distress (BSI-18). Specifically, our aim was to explore whether/how spouses, family, friends and spirituality/religiosity helped ease the burden of this genetic condition. In this manuscript, we concentrate on the involvement of friends and confidantes, particularly those who provided emotional and/or spiritual/religious support.

Methods

Participants

The National Cancer Institute's IRB-approved LFS study (11-C-0255, ClinicalTrials.gov; Identifier NCT01443468; www.lfs.cancer.gov) opened to accrual in 2011. Individuals with LFS and their families are enrolled for the purpose of molecular, clinical, psychological and social research. Study inclusion eligibility included LFS or Birch LFL clinical diagnosis, documented *TP53* mutation, 3 or more LFS-related primary tumors, adrenal cortical carcinoma (ACC) or choroid plexus carcinoma diagnosed at any age. We invited some families with unknown mutation status for genetic testing at the beginning of the study, but the majority of study participants were mutation-positive participants. We excluded those with active cancer and within 6 months of treatment completion. Screening participants were seen for a clinical visit during which a cancer screening regimen for mutation carriers and the psychosocial interactions occurred. Some of the participants attending clinic were accompanied by family members (non-bloodline, mutation non-carrier bloodline relatives or spouses). All individuals older than age 12 years attending clinic were invited to participate in the co-construction of a CEGRM.

Design

We used a cross-sectional, mixed-method approach to collecting and analyzing data from questionnaires and CEGRM interviews. We collected four types of data used in this analysis: 1) baseline CEGRM co-constructed at the first clinical visit and accompanying interview interaction notes; 2) written transcriptions of audio-recorded, semi-structured CEGRM interviews; 3) quantitative assessment of participants' level of distress using the BSI-18, a standardized psychometric instrument; and 4) demographic data from Individual Information Questionnaires (IIQ) completed at the time of enrollment.

Instrumentation and Procedures

CEGRMs We collected qualitative and quantitative data regarding the roles of support. The CEGRMs were co-constructed by investigator and participant in accordance with methods described elsewhere (Kenen and Peters 2001; Peters et al. 2006). Participant-designated confidantes and groups are noted on the CEGRM image and in handwritten interview notes.

The CEGRMs were conducted in a private clinic room in the NIH Clinical Center outpatient clinic with the lead investigator or other trained co-investigator/co-author. Each CEGRM interview lasted on average 30–45 min (range 18–85) and was conducted with individual family members separately. The interviews were audio-recorded and transcribed verbatim. The interview in embedded in the CEGRM process, resulting in two interconnected sources of data–the transcribed interview and the CEGRM image.

Measure of Distress The Brief Symptom Inventory-18 (BSI-18) is the short form of a psychometrically validated self-report instrument that is used to measure psychological distress within the past 7 days, which includes 3 subscales measuring depression, anxiety, and somatization, and a summary Global Symptom Inventory (GSI) (Derogatis 2001). There are 18 items (6 in each of the 3 sub-scales) each with a 5-point rating scale from 1 to 5. The BSI-18 raw scores are converted and reported as standardized T-scores with a mean of 50 and standard deviation of 10, with higher score indicating more distress. The BSI-18 has been judged reliable and used in multiple health studies and in our own prior research and is sensitive to relatively recent changes in mood that may accompany difficult recent events in self or others. We administered the BSI-18 to all participants older than the age of 18 at the start of the clinical visit.

Demographics Demographic data including age, gender, cancer history, marital status, and education were obtained from the Individual Information Questionnaires (IIQ) that all participants completed at the time of enrollment.

Quantitative Descriptive Data Analysis

We generated descriptive statistics, simple independent sample t-tests for group differences, and Pearson correlations as appropriate. For the social support variables, we counted the numbers of Friends, Confidantes, and Social Groups as well as the number of types of supports. Types of support included: 1) Health Information, 2) Tangible, 3) Emotional, and 4) Religious/Spiritual support. We conceived three summary social domains: 1) breadth of support, 2) types of support, and 3) depth of support. Breadth of support was calculated by counting the total numbers of Friends, Confidantes, and Social Groups reported. Confidantes can be spouse, friend/non-kin, or relative. Social groups can be religious community, recreational team/group, social media, or informal. We classified depth of support by summing the total of the 4 types of support listed above (ranging from 0 to 4) noted for each relationship. A relationship that had a total of 3 or 4 different types of support noted was considered as "deeper" than one providing 0 or 1 types of support.

For analysis, variables were continuous but were grouped for display. We calculated correlations between BSI-18 score and gender, age, cancer affected status, mutation status and the social variables from the CEGRM (breadth of support and types of support). Correlations between BSI-18 score and the breadth of support, types of support, and depth of support were conducted for the entire cohort and stratified by gender, mutation status, cancer status, and for the non-carriers. All analyses were carried out using the software SPSS Statistics 21.

Qualitative Analysis

We analyzed the qualitative data, including the CEGRM interview transcriptions and CEGRM interaction notes, using a targeted, iterative, inductive reasoning approach (Tong et al. 2007). Initially, the first two authors (JP and RK) independently read and re-read the transcripts in conjunction with CEGRM handwritten notes and the graphic end product CEGRM, in order to identify themes of friendship and religion/spirituality. Authors used memo-ing techniques to track and document identification of themes and exemplary quotes. Then the investigators presented identified themes to each other and finally to the full research team. When there was a disagreement in interpretation, the investigators discussed the issues of disagreement and went back to the source material to ascertain the meanings they attached to the precise wording used and eventually came to an agreement.

Results

Characteristics of the Study Participants

This is the first report of CEGRM use in families with LFS. We evaluated the first group of baseline CEGRMs we co-constructed with participants in the LFS study from 2011 to August 2014. Sixty-six participants completed baseline CEGRMS and 59 also completed a BSI-18, including male and female family probands, their close relatives, spouses, children and occasionally "others" such as in-laws, ex-in-laws, second and third degree relatives. All were of European ancestry; only 4 participants from the same family reported Hispanic/Latino origins. About two-thirds of participants were female. Most adults were or had been married and were well-educated. At the time of the CEGRM and BSI-18, 42 (63 %) knew they had a *TP53* mutation, 5 (8 %) tested negative for the mutation identified in the family, 12 people attended clinic with their parents or spouses for genetic counseling and testing, and 12 were spouses or from the non-carrier side of the family. Detailed study participant demographic characteristics are summarized in Table 1.

Social Variables via CEGRM

The social variables are summarized in Tables 2, 3, and 4. Table 2 lists the numbers of friends, confidantes and groups as well as the types of confidantes and groups. The majority of participants reported having more than 3 friends; 12 % of the participants reported having more than 3 confidantes. Most of the confidantes were friends (41 %) and spouses (20 %). Almost 50 % reported not having a defined social group that provided support. Among those 34 reporting interacting with a specific social group, the most commonly reported group was religious community (29 %).

Table 3 lists the mean, median and modal frequencies of the number of supports per participant for each of the four types of social supports elicited from the CEGRM (i.e.,1) health information; 2) tangible; 3) emotional; 4) spiritual supports). The most commonly reported supportive interactions involved exchange of health information.

Table 4 summarizes the frequencies of multi-dimensional supports which we used as an indication of the depth of reported relationships (i.e.., the number of friends offering 4, 3, 2, 1, or 0 specific types of social supports). Overall, most participants had 1–6 friends providing between 1 and 3 types of support. In other words, it was most common for people to report having a handful of good friends with mutually supportive relationships in at least several realms.

We found that men and women differed in the number of supportive confidantes and groups that they reported. More specifically, women reported statistically more confidantes than men [approximately 2 confidantes/woman and 1 confidante apiece for men (p = 0.025)]. There was a trend

Table 1 Demographics

Feature	Category	Number	Percent
Sex	Male	27	41 %
	Female	39	59 %
Marital Status	Married	41	62 %
	Single	6	9 %
	Divorced/Separated	8	12 %
Age	Teens	9	14 %
	20–39	26	39 %
	40–59	25	38 %
	60+	6	9 %
Mutation Status	Positive	42	63 %
	Negative	5	8 %
	Unknown or Unnecessary	19	29 %
Cancer Status	Affected	28	42 %
	Unaffected	38	58 %
Education	Graduate school/professional	21	32 %
	College	26	39 %
	HS/trade/	7	10 %
	Currently in school	5	8 %

Table 2 Social variables

Feature	Category	Number	Percent
Number of Friends	None	2	3 %
	1–3	20	30 %
	4–6	27	41 %
	7+	15	23 %
Number of Confidantes	None	8	12 %
	1–3	49	71 %
	4–6	7	9 %
	7+	2	3 %
Types of Confidantes	Spouse	13	20 %
	Friend	27	41 %
	Relative	9	14 %
	Multiple types	6	9 %
	Other	2	3 %
Number of Groups	None	31	48 %
	1–3	31	47 %
	4–6	3	5 %
Types of Groups	Religious community	10	29 % of 34 with groups
	Recreational team/group	7	21 %
	Social Media	6	18 %
	Informal	3	9 %
	Multiple	8	23 %

Table 3 Types of social supports of each type per individual participant

Type of Support	Mean	Median	Mode	Range
1- Informational	9.5 per participant	9.0 per participant	Multiple, 5, 8, 9	2–28
2- Tangible	6.4	6	3	0–21
3- Emotional	6.7	6	3	0–26
4- Spiritual	4.7	4	0	0–20

approaching significance for women to belong to more groups than men (1.1 groups/woman vs. 0.6/man, $p = 0.056$). Conversely, men reported more friends with 0 specific types of support than women (women had almost no friends offering no supports vs. men with an average of 1.3 friends offering no specific types of supports, $p = 0.006$). Age was positively correlated with having friends offering no specific types of social support ($r = 0.28$, $p = 0.02$); that is, some older male participants had more friends with 0 reported types of social exchanges (i.e. fewer deep connections).

Anxiety, Somatization, Depression and Global Distress via BSI-18

Fifty-nine adult participants completed the BSI-18 at the time of the clinical visit. Table 5 shows results which demonstrate that LFS study participants, as a group, reported low global emotional distress, in fact, many scores were in the low normal range below the T-score median of 50.

The results showed that there were no significant differences in distress between men and women, being affected or unaffected with cancer, or being a mutation carrier. Further, there were no significant group differences in BSI-18 measures of distress by the number or depth of friends, confidantes, groups, types of social supports. The only statistically significant group differences on t-tests were:

BSI-18 ***Somatization*** scores ranged from 39 to 75 with a mean of 46 and median of 40.

There was, among 36 Parents of *TP53*+ offspring, a negative correlation of somatization with having three support types in total family and friends ($r = -0.90$, $p = 0.016$, $n = 36$), that is, less somatization with more supports. The parents were a mixed group of cancer affected and unaffected, mutation positive and mutation negative individuals. None of the other frequencies of supports was significant.

The BSI-18 ***Depression*** mean score was also 46 with a range from 40 to 74. Age was positively correlated with

Table 4 Depth of social support: frequencies of multi-dimensional supports

Support density = How many types of support from same person	Number of friends giving 4, 3, 2, 1, or 0 types of support	*Number*	*Percent*
4 types support	No one with 4 types of supports	44	67 %
	1–3 people giving 4 types of supports	18	28 %
	4–6 people giving 4 types of supports	1	2 %
	7+ people giving 4 types of supports	1	2 %
3 types	No one with 3 types of supports	22	33 %
	1–3 people giving 3 types of supports	35	43 %
	4–6 people giving 3 types of supports	6	9 %
	7+ people giving 3 types of supports	1	2 %
2	No one giving 2 types of supports	16	25 %
	1–3 people giving 2 types of supports	39	61 %
	4–6 people giving 2 types of supports	8	13 %
	7+ people giving 2 types of supports	1	2 %
1	No one giving 1 type of support	26	39 %
	1–3 people giving 1 types of supports	36	54 %
	4–6 people giving 1 types of supports	1	2 %
	7+ people giving 1 types of supports	1	2 %
0	No one giving 0 types of supports	46	70 %
	1–3 people giving 0 types of supports	16	24 %
	4–6 people giving 0 types of supports	4	6 %
	7+ people giving 0 types of supports	0	0 %

Table 5 BSI-18 emotional distress scores

	Mean	Median	Mode	Standard deviation	Range
Somatization	45.8	40	40	8.6	39–75
Depression	46.4	42	40	7.8	40–74
Anxiety	48.4	47	36	9.5	36–74
Global distress (summary score)	45.9	46	34	10.0	31–75

depression ($r = 0.25$, $p = 0.05$, $n = 59$), that is, older participants reported more depressed symptoms.

The BSI-18 ***Anxiety*** mean was 48 and the median 47, with scores ranging from 36 to 74. Anxiety was higher for mutation negative vs. mutation positive participants ($p = 0.029$). In 36 *TP53* mutation positive participants, there were nonsignificant trends of positive correlation of higher anxiety associated with reporting more friends providing all 4 types of support (religious, informational, tangible and emotional supports, $r = 0.32$, $p = 0.059$). In 9 spouses there was a negative correlation of Anxiety ($r = -0.759$, $p = 0.02$) with having friends offering no specific types of support. In 38 cancer unaffected participants there was a negative correlation of Anxiety with friends reportedly offering no specific supports ($r = -0.679$, $p = 0.02$).

Finally, the BSI-18 ***Global Symptom Index*** (*Distress*) *score* is a composite of the 3 sub-scales had both mean and median of 46. Among all cases (N = 59) with BSI results and CEGRMs, we found little statistically significant correlation between Global Distress and sex, cancer, mutation status, number of friends (except 0), confidantes, groups, emotional supports, religious supports. In 9 spouses there was a negative correlation of Global Distress ($r = -0.735$, $p = 0.024$) with having friends offering no specific types of support. In cancer-unaffected participants, there was negative correlation of Global Distress ($r = -634$, $p = 0.036$) with friends offering no specific support. There were no correlations with any other variables in participant sub-groups of: (1) participants affected with cancer, (2) mutation negative individuals, (3) men, (4) women.

Exceptional Cases of High or Low Distress

There were a few participants with *high BSI-18 scores of 60+*, *greater* than 1 standard deviation above the mean of 50: 7 high Anxiety scores; 4 high Depression, 6 high Somatization; and 5 high Global Distress. We found 3–4 people who were high across the board with the others high in only certain domains (e.g., anxiety or somatization).

Those with high BSI-18 results often told of multiple crises in their lives, such as multiple and recent family losses, traumas, recent LFS diagnosis, miscarriages, getting laid off from steady work, loss of purpose and identity due to retirement and disability, loss of friends, moving, identity theft, and "tired of burying people." For example, one 47 year old unaffected man explained that in his family "A lot is left unspoken; we just bottle it up until we explode." Some of those ($n = 5$) with high global distress scores reported 2–3 types of support, one distressed participant noted many religious connections as well.

At the other end of the spectrum, there were also a number of people with very low (<40) BSI-18 distress scores. These include reports of 18 low Anxiety scores. 15 low Somatization and 16 low GSI. There were no low Depression scores. All of those with low somatization scores were women, whereas half of those reporting very low anxiety were women, and half of low anxiety participants were men. One family was interesting in that one cancer-unaffected, mutation-negative brother had a very high anxiety score whereas his cancer- unaffected brother, also mutation-negative, a very low score. The first was more aware of or willing to share his anxious feelings about the LFS condition in his family whereas the other brother told us that he was more inclined to escape his multiple life losses and other stressors with "piddling around the house" and watching downloaded videos.

Role of Social and Emotional Support: Qualitative Themes: Friendships

In contemporary American society personal friends are becoming increasingly important since close relatives may no longer live nearby and computer technology has broadened a person's social networks to include "voluntary kin" (Braithwaite et al. 2010). In families with LFS, there seems to be a similar emphasis on the importance of friends along with family. While the number of friends varied greatly across participants (ranging between 0 and 15), most of the friends were counted on for support on two or three of the types of support, primarily tangible, informational and emotional, indicating a greater depth of friendship. As one young female cancer survivor with LFS said, "LFS encompasses everything. It's not just physical. In fact, it's probably more emotional."

Some friends appear to have the license to speak frankly to their LFS friend in the middle of a life-threatening crisis. One middle-aged participant with multiple primary tumors said, "When they gave me the prognosis of 8–10 months to live… I moaned and groaned for a while, you know. Finally my friend said, 'Get up off your butt and do something.' So we went on a bucket-list trip together."

Sometimes the lines between family and friends blur into a hybrid: A young female participant told us, "My cousin is 20 years older but she's the one who lives here. We are going

to visit tomorrow. We just started having a new relationship on an adult level, like a friend."

One male spouse spoke about the difference in speaking to friends and to family: "With family dynamics, if you actually start talking about things that are real, it's uncomfortable. It's the opposite with my friend where I can be very vulnerable and talk about hard things. I can share my feelings and thoughts and get support and share my struggles or whatever."

Confidantes were important to study participants regardless of their sex, age, mutation-status and cancer experiences. Many women picked their best friend as confidante. Even among married women, the wife frequently picked her best woman friend as confidante rather than her husband, while the husband chose his wife more often than a male best friend. One young survivor said of her friend, "She is my everything… my soul-mate."

Despite the importance of friendship to most of the members of families with LFS, a few were dismayed by the reactions of people toward the problems that they face. For example, a middle-aged spouse of a participant who had survived several LFS-related cancers said, "People do not understand. A lot of this stuff is so hard. It's amazing when I talk to people who are very well-educated, their knowledge is very limited, just in general, about cancer, types of cancer, cancer treatment. You know, they do not even know the difference between radiation and chemotherapy. Either they do not want to know, or they are just naïve, or they have not been exposed."

Religion and Spirituality

People in the study had a wide range of religious and spiritual social connections, ranging from 0 to 20 with a mean of about 4–5, and a wide range of religious traditions were represented including Christian, Muslim, New Age, Roman Catholic, Ashkenazi Jewish, and Buddhist. Almost one third reported no religious or spiritual contacts. Those having many religious or spiritual connections felt them deeply and their shared beliefs played a large part in their lives. This was particularly true of those affiliated with mainstream religious groups that had a formal structure of social activities where attendees could make friends. Often their friendship community revolved around their religious institution.

Many of the more religious participants cited a variety of religious activities such as attending a place of worship, prayer group, socializing, reading, studying, introspection and meditation. Some sought out a clergy leader rather than a therapist in hard times, e.g., one affected woman talked to her pastor about her divorce because she found it hard to break her marriage vows when separation became necessary. A few of the Jewish participants remarked that they felt very connected to Jewish life, culture and traditions, including the high value of family. As one mother said, "Being Jewish is an important part of life; it is our life." Feeling close affiliation to one's religious/cultural group was usually in addition to other dimensions (e.g., emotional) of close relationships across the various religious traditions. For example, one middle-aged woman with multiple types of cancer said: "How do I explain my Bible Group? We go to study the Bible, but we are really there to help each other. And there are many times that all we do is pray, and pray specifically for someone or one of our members or whatever."

Some people described themselves or relatives becoming religious in response to the cancers. The cancer becomes a catalyst in changing their beliefs and practices. As one male spouse said, "My wife and relatives enjoy church- that all came about when my sister died. They were going to church with her right before she died. They have always gone since." Others have always been very clear about their religion playing a part in their coping: "I know that I am dying. God keeps me going. I feel like God leads me in how I need to go, to the next step I need to take." In contrast, another young affected female participant had a bit of fatalism about religion and life: "I live by the 'Laws of Attraction' - If you think about it, it will happen."

We found from our participants that being religious does not always run a straight course across one's lifetime; one can be very religious as a child and not as an adult, or vice versa. Life experiences can push one toward religion or away from it, or both at different times. For example, a middle aged woman became a Christian after having cancer at an early age; then she became very angry at God because she had to give up her life plans. However, this alienation did not last. When she subsequently developed another tumor, she returned to her faith and God, saying "I think about death all the time since I now have a young child, but now I have peace. Even if I die, I am not scared. This is my spiritual journey."

The participants who described how spirituality rather than religion per se was a vital part of their life were more of an amorphous group. They did not adhere to one spiritual dogma, but often created their own definition of spirituality and what it meant to them. One man said: "Spiritual absolutely! But non-religious … We have common beliefs about the purpose of life. We see my deceased relative in a lot of different parts of nature, and definitely believe in a supreme being." Echoing this theme, another male spouse of a woman with LFS was brought up in a formal religion, but he was no longer practicing it. Instead, he found spirituality in nature, "If I wanted to have some deep thoughts or internal reflection, I might get outdoors and go on a hike into some of the beauty in remote areas…It's really connecting with Mother Nature."

Discussion

We found the families with LFS in our study to be remarkably "matter of fact" during the CEGRM process and throughout the entire clinical interaction. Could this be a function of who

participates in research? Before the study began we had speculated that our participants might be very distressed and withdrawn due to the many physical, emotional and social challenges associated with LFS. We found the opposite for the most part; specifically, most participants reported few psychosocial symptoms and appeared well connected and resilient. Members of families with LFS included in this report seem to have learned to adapt and cope with serious illness, uncertainty, loss, and negotiating the medical and informational systems in their own ways, often with some help from their family and friends.

The minority who reported high psychological distress also coped with multiple adverse conditions in their lives (e.g., early life losses, retirement, unemployment, miscarriage). It is likely that these life factors, in addition to living in a family with LFS, compounded their distressed psychological state. Many of those with high distress seemed to have experienced "the straw that broke the camel's back." They talked more about these life difficulties as affecting their sense of well-being than they did about LFS *per se*. For many participants, LFS appears to remain in the back of their minds until a medical crisis or cancer screening visit brings it front and center.

The important role that friends played in our study group appears to reflect a change in our larger society (Allan 2008). In some respects, it is not that family is not important or that there exists a friend vs. family dichotomy, but rather that the everyday definition of family has changed. In some situations, the role of "volunteer kin" (non-blood relatives) has emerged as more of a source of social support than relatives (Braithwaite et al. 2010). We wondered whether, in families with LFS, it is possible that friends and non-relatives may be a preferred confidante since friends may not have to face the worry associated with having a hereditary risk themselves, enabling affected individuals to be more open about their needs.

As in other hereditary conditions, our results reinforce our belief that LFS is truly a "family condition" in which the emotional and social effects extend far beyond the individual with a mutation. Everyone in the family must deal with the LFS diagnosis and its sequelae. Surprisingly, in our study, reports of anxiety symptoms were higher for non-mutation carriers than for those carrying *TP53* mutations, further reinforcing the diffuse effects of LFS. We saw that cancer diagnosis did not differentiate study participants with respect to reported distress or social milieu. Rather, participants in this study, regardless of demographic or emotional characteristics, were similar in terms of friends, confidantes and spiritual communities becoming like extended family. Our finding adds to the prior literature in which carriers were not significantly more distressed than non-carriers or than those with a 50 % risk who did not undergo genetic testing (Lammens et al. 2010a). Those with a lack of social support were more likely to report clinically relevant levels of distress. In the prior study, a substantial proportion of individuals, irrespective of their carrier status, exhibited clinically relevant levels of distress that warranted psychological support. We did not find this same level of distress in our study. This difference could represent changes in mood and coping styles due to recent advances in risk management options or due to study population or methodological differences, but further research is needed to explore these hypotheses.

Religion/spiritual supports were endorsed by about two-thirds of participants, with one-third designating no spiritual or religious social exchanges. This is consistent with a recent findings that the number of Americans who do not identify with any religion continues to grow, about one fifth of the US public and one third of adults under 30 are currently religiously unaffiliated Nones" on the Rise (2012). However, this same study found that many of these unaffiliated adults are religious or spiritual in some way, in that they believe in God, feel connected with nature, and seek meaning and peace in their lives. Reportedly, "Spiritual but not religious" (SBNR) has become a popular identity moniker (Oppenheimer 2014).

Friends and spirituality/religiosity could have several functions in helping families with LFS stay afloat. Perhaps they supply ballast to keep one's mood from sinking too low. There is also a sense of normalcy, including the retention of a normal life identity with the reinforcement of having good friends and community. Balance between crises and smooth sailing may be mediated by good friends, confidantes and spiritual community. These speculations deserve further attention such as the cancer-specific report of religion and spirituality among prostate cancer survivors (Bowie et al. 2004).

Social networks often fill complex roles in a person's life, potentially positive or negative. For example, interaction with others can foster or impede adjustment (Stanton et al. 2007). Social interactions involve obligations as well as supports and sometimes the supports are not in the desired domain. We wondered if participants reporting friends with zero types of support might represent people being kept at arms' length to avoid incurring social and emotional obligations or, alternatively, in order to "use" friends as a respite from their situation? Or, might it be a mutual reluctance to share due to friends feeling at a loss as to how to be supportive?

Similarly, religious coping can have positive and negative aspects as we saw with the participant who was very religious in early life, then disillusioned with the multiple health problems and then reconciled. As Pergament and colleagues found from their research on 3 groups coping with different types of stressors, "The positive pattern consisted of religious forgiveness, seeking spiritual support, collaborative religious coping, spiritual connection, religious purification, and benevolent religious reappraisal. The negative pattern was defined by spiritual discontent, punishing God reappraisals, interpersonal religious discontent, demonic reappraisal, and reappraisal of God's powers" (Pargament et al. 1998, p. 710). In our study,

we found that people described making more use of the positive than the negative religious coping methods. For example, they would say something like "God leads me to the next step" more often rather than expressing discontent and resentment at their lot in life.

Those participants who indicated that certain friends and relatives provided religious/spiritual connections generally also endorsed friends and relatives for a variety of other types of support, e.g., informational, tangible and emotional. It is possible that the combination of friendship and spiritual connection provided them with additional assets to fight LFS and distress, a version of the "communal coping" that we found among sisters in families with Hereditary Breast-Ovarian Cancer susceptibility (Koehly et al. 2008).

Study Strengths and Limitations

Our sample size of 66 participants is both a study strength and limitation. This is a good sample size for a study of a rare hereditary condition at a single research center. We obtained detailed medical and family histories, and used standardized as well as study-specific psychosocial measures, interviewers, and transcribed interviews. We included mutation positive and negative participants, those with and without prior cancer diagnoses, spouses and other supports. We were able to refer to written transcripts and audio recordings to provide samples of participants' views in their own words.

However, this study is only a preliminary glimpse of selected emotional and social aspects of some members from families with LFS who have volunteered for our study. While larger than some psychosocial studies of LFS, this study is limited by relatively small sample size which limits the power for achieving statistical significance in our quantitative analyses. In addition, we conducted a number of univariate statistical analyses which, although considered acceptable for an exploratory, increases the likelihood that some significant findings are due to chance. It is possible that larger studies that employ multiple variable analyses might reveal different patterns and insights. Our data are based on subjective self-reports, potentially subject to implicit or explicit biases. Our study participants are highly motivated and able to participate in state of the art clinical research and may represent selection bias and unknown external validity for non-research families. Cross sectional design always limits interpretation of the data, however, we will have additional opportunities to assess some of the participants when they return for yearly screening visits.

Practice Implications

Given preliminary information about the importance of social context in coping with hereditary cancer susceptibility conditions, we recommend that all health professionals seeing patients with LFS consider expanding their discussions about management of risk to include the 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. Relatives and spouses should also be included in the discussions as appropriate, feasible, and desired. Genetic counseling training programs could incorporate training in systems-based counseling approaches as well as in research methods that incorporate social factors. Likewise, incorporating spiritual components of psychosocial assessment may help identify individuals for whom the inclusion of a religious aspect might be important in risk management discussion.

A number of professional organizations and accrediting bodies have recognized the importance of regular assessment of religion and spirituality in patient care and the National Comprehensive Cancer Network identifies spiritual or religious concerns as a specific source of distress in cancer patients (Salsman et al. 2015a). As Quillin et al. (2006) have observed, there is a growing interest in assessing and integrating patients' spiritual beliefs as part of genetic counseling care. Perhaps the NSGC and ABGC will expand conceptualization of this realm of clinical care in practice guidelines and core competencies.

Research Recommendations

We believe that our preliminary results presented herein warrant additional research in several areas. A potential area of further research relates to studying the effects of the increasing knowledge about LFS, genetic testing availability and modern screening tools that may give individuals in families with LFS more of a sense of meaning and control over LFS. Along with medical and scientific advances, there has been the development of social and educational resources for families with LFS that were not present a decade ago, such as online LFS support organizations, blogs, and joint meetings of families, researchers and clinicians (Mai et al. 2012). Disease-specific support groups may constitute another type of "family-of-choice" with shared risks, ordeals and triumphs but with less vulnerability than daily face-to-face social interactions. We speculate that these developments may allow families with LFS to consider living with the condition as the "new normal" thus alleviating the anxiety and depression usually associated with a life threatening disease and providing families with a sense of hope.

Another area deserving attention is psychosocial adjustment to cancer in children, adolescents, young adults and adults in the family. A review of a few studies of childhood cancer survivors shows inconsistent findings regarding participants' psychosocial adjustment; clearly more data are needed (O'Leary et al. 2007). Another area of potentially important research would be our observation of the low reported distress

scores. Several groups have observed that some persons with cancer reported slightly lower amounts of psychosocial distress, though the underlying reasons have not been elucidated (Phipps 2007; Zeltzer et al. 2008). It would be useful to explore this observation further in families with LFS to investigate possible explanations such as those previously suggested (e.g., post-traumatic growth, psychological resilience, stress inoculation and adaptation, and biased reporting style by some survivors who may tend to deny difficulties and over-estimate positive health). Likewise, we would like to better understand the sources of anxiety reported by our mutation-negative participants (i.e., mostly unaffected relatives and spouses who may also be caretakers). It would also be useful to utilize positive psychology and resilience theory and models to direct future research (Phipps 2007).

Ideally, the observations in our research should be extended to larger and more diverse groups of study participants, perhaps via national and international research consortia such as the LiFE Consortium (Consortia, 2010). We and others have studies under way to more thoroughly examine psychological profiles of members in families with LFS via batteries of standardized psychosocial testing and social media use of study participants beyond those with whom we interacted in clinic. Topics such as spirituality and the role of friends and confidantes in coping with chronic condition also deserve more attention.

Similarly, there has long been known a positive relation between religion/spirituality and better health in general population and patient populations. Several studies have found a potential link between religious activity and longevity, overall health status, and the ability to recover from an adverse health event (Koenig et al. 2000; Mulligan et al. 2005). A new set of meta-analyses of religion/spirituality associations with physical, mental and social health has recently been published (Jim et al. 2015; Salsman et al. 2015b; Sherman et al. 2015). In this coordinated effort the authors identify interconnected religion/spiritual domains including affective, behavioral, cognitive and other/social (Salsman et al. 2015b). The meta-analyses' conclusions suggest that greater religion/spirituality is associated with better patient-reported physical health, and modestly associated with mental health and capacity to maintain satisfying social roles and relationships in the context of cancer. In an accompanying commentary by all of these authors, the most important dimension of religion/spirituality on health was emotional, a finding compatible with our results (Park et al. 2015).

The issue of physiological effects of religious/spiritual and other social connections has received little attention in hereditary cancer syndromes. A review of an ample and growing literature suggests that relationships affect health directly and indirectly; supportive relationships offer positive benefits, whereas negative relationships are associated with immune, endocrine, cardiovascular, mortality, unhealthy behaviors and other untoward effects (Umberson et al. 1996). More specifically, there is beginning to be a body of literature linking emotional states and social variables such as stress and social relationships with physiological markers such as telomere length (Epel 2009; Epel et al. 2004) and inflammation (Fagundes et al. 2011; Fagundes et al. 2013; Kiecolt-Glaser 1999). Conversely, there may be bio-psycho-social markers of heightened resilience and adaptation. It would be worthwhile to include some of these physiologic measures in studies of families with LFS.

Conclusion

The results demonstrate that families with LFS reported friendships that varied widely, but that friendships were often deep and enduring and were viewed as important sources of information, and tangible, emotional and spiritual support. For many participants, designated confidantes were usually best friends or spouses. Furthermore, for some people, organized religion or spirituality was a very important source of social and emotional support, but often in varying ways across their experiences and lifetime. Based on our preliminary findings, most participants in families with LFS in our study seem to be coping well during quiescent periods between diagnoses, drawing on a range of emotional and social supports. A minority of participants gave hints of not coping well, most of whom reported being overwhelmed by multiple simultaneous stressors. Personal relationships and social networks seem important in emotionally coping with the condition; family, friends, spouses, and confidantes are especially important to most participants. A significant subset find solace and support from their religious or spiritual communities. We hypothesize that the roles of various types of social support that families with LFS report are likely to translate to other hereditary cancer syndromes and chronic diseases.

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Compliance with ethical standards

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Conflicts of Interest June A. Peters, Regina Kenen, Renee Bremer, Shannon Givens, Sharon A. Savage and Phuong L. Mai declare that they have no conflict of interest.

Human Studies and Informed Consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from all patients for being included in the study.

Animal Studies No animal studies were carried out by the authors for this article.

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