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**PATIENT ATTITUDES TOWARD GENETIC TESTING FOR INHERITED
PREDISPOSITIONS TO HEMATOLOGIC MALIGNANCIES**

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A

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by

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Abstract

Although inherited predispositions to hematologic malignancies have previously been considered extremely rare, approximately 12 causative genes have been implicated in the last decade. Since individuals diagnosed with leukemia have not historically been considered for evaluation of inherited predispositions, genetic testing is underperformed in this population. This study used focus group discussions to explore the attitudes, motivations, and barriers to genetic testing for 23 patients with leukemia. Participants generally exhibited a positive regard for the utility of genetic testing, and were primarily motivated by concern for their family and a sense of altruism toward all leukemia patients. While drawbacks and barriers were difficult for participants to identify, a few individuals cited concerns about confidentiality of genetic information and possible discrimination based on test results. Participants unanimously agreed that the skin punch biopsy required for genetic testing in leukemia patients would not deter their decision to be tested. The findings from this study are valuable for guiding genetic counseling that best meets the specific needs of leukemia patients, and future studies will analyze how these issues are perceived by a larger and more diverse population of individuals with leukemia.

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Introduction

Germline mutations causing predisposition to acute leukemia (AL) and myelodysplastic syndrome (MDS) have been underappreciated, especially among affected adults. Prior to 2003, there were no clearly defined genetic etiologies underlying acute myeloid leukemia (AML), MDS, and/or other types of leukemia outside of inherited bone marrow failure syndromes like Fanconi anemia (1, 2). However, within the last decade, more than 12 inherited predisposition genes have been identified in association with these malignancies (3, 4). Current data support that between 10-29% of individuals with leukemia referred for genetic testing have germline mutations predisposing to hematologic malignancies (5, 6). According to the 2017 Surveillance, Epidemiology and End Results (SEER) data, there are 21,380 new AML diagnoses and 5,970 new acute lymphoblastic leukemia (ALL) diagnoses in the United States annually. Additionally, there are an estimated 10,000 new cases of MDS in the United States each year (7).

Emerging data regarding hereditary predispositions to hematologic malignancies suggest that MDS, AML, and aplastic anemia (AA) have the highest hereditary component, while hereditary predispositions to B-cell ALL and chronic leukemias remain rare. Predisposition syndromes involving autosomal dominant mutations in the genes *RUNX1*, *ANKRD26*, and *ETV6* share a similar clinical phenotype, including thrombocytopenia, platelet dysfunction, and an increased risk to develop MDS and AML (8-10). Familial MDS/AML has also been associated with autosomal dominant mutations in *DDX41*, *GATA2*, *SRP72*, and *CEBPA* genes (11-14). Additionally, a 700 kilobase duplication in the region of 14q32.2 that encompasses the *ATG2B* and *GSKIP* genes has been linked to an increased risk for AML, but also to other malignancies, including chronic myelomonocytic leukemia (CMML) and chronic myeloid leukemia (CML) (15). The inherited bone marrow failure syndromes (IBMFS) Fanconi anemia and dyskeratosis

congenita, previously well-described in the pediatric population, have also emerged as causes of adult-onset MDS, AML, and AA, even in those who do not meet phenotypic criteria (2, 16, 17).

In addition to these genes that cause inherited susceptibility to MDS, AML, and AA, there are also several genes identified in association with familial B-cell ALL. The *PAX5* gene exhibits a dominant predisposition to B-cell ALL with incomplete penetrance (18). While commonly recognized as the gene implicated in Li-Fraumeni Syndrome (LFS), heterozygous germline mutations in *TP53* also cause B-cell ALL in 5% of individuals affected with LFS (19). Additionally, the *SH2B3* gene has been implicated as an autosomal recessive predisposition locus for B-cell ALL (20).

Genetic testing for inherited predispositions to leukemia has several imperative implications for the clinical care of affected individuals. If a germline mutation is identified, this information can be used to guide treatment and surveillance plans, aid in donor selection for hematopoietic stem cell transplantation (SCT), and evaluate risks for certain comorbidities and treatment-related complications. For example, as several predisposition syndromes are associated with increased toxicity when treated with standard doses of chemotherapy or radiation for SCT conditioning, identification of at-risk patients can allow clinicians to provide tailored, reduced-intensity conditioning regimens (21-23). Moreover, although HLA-matched siblings are often regarded as ideal donors for allogeneic SCT, genetic testing helps prevent the selection of a related donor who carries the same germline mutation as the patient, which can potentially result in graft failure, donor-derived leukemia, and severe graft-versus-host disease (24, 25). Detection of a familial mutation also has key implications for unaffected relatives. Predictive genetic testing can aid in identifying individuals who may be at increased risk to develop leukemia in their lifetimes. While there are currently no means to prevent leukemia, identification of at-risk relatives may allow for those individuals to obtain surveillance

bloodwork and/or bone marrow evaluation for emerging clonal disease or hematologic malignancies (4). Additionally, identifying families with hereditary syndromes can also help connect them with valuable resources for family counseling, psychosocial support, and family planning.

As availability and awareness of genetic testing for inherited predispositions to leukemia increases, much remains unknown about the behavioral and psychosocial aspects of genetic counseling and testing in this patient population. Unlike solid tumor patient populations such as breast and colorectal cancer, leukemia patients are entirely unexplored regarding their knowledge, attitudes, and perceived motivations and barriers to genetic testing. After genetic testing for predispositions to breast and colorectal cancer first became available in the early 1990s, numerous studies sought to assess attitudes towards and perceptions about genetic testing in these two distinct populations (26-29). Common themes elicited during these studies included feelings of guilt for passing cancer susceptibility on to children, relief from uncertainty after learning one's genetic information, concern for cancer risks in family members, fear of discrimination based on genetic information, and concern for psychological distress after a positive result. Many of these studies also sought to identify differences in genetic testing uptake based on perceived benefits, drawbacks, and one's own cancer risk (28-36). Unlike solid tumor patients where genetic testing can be performed on a blood or saliva sample, genetic testing for individuals with leukemia requires a non-hematopoietic specimen. In these individuals, peripheral blood is contaminated by the hematologic malignancy which contains somatic mutations and chromosomal abnormalities that can confound genetic test results. As such, cultured skin fibroblasts are the gold standard for germline analysis and are obtained through a skin punch biopsy procedure. This presents a potential barrier to genetic testing that is unique to the leukemia patient population and has yet to be explored.

This study seeks to elicit leukemia patients' attitudes, motivations, and barriers to genetic testing through the use of focus group discussions. Focus groups are a well-established qualitative research methodology that can be used to identify perceptions among subpopulations about certain experiences such as genetic testing (37). They are ideal for eliciting individuals' attitudes and beliefs in order to design appropriate interventions for the subpopulation of interest (38). Focus groups have been shown to serve as a fundamental tool in generating themes surrounding attitudes towards genetic testing as well as generating focused hypotheses for further study in these populations (28, 29, 32, 35, 39-41). A deeper understanding of the attitudes, motivations, and barriers to genetic testing in the leukemia patient population will impact patient care by allowing clinicians to address the specific concerns and needs of this unique population.

Methods

Participants and Recruitment

Individuals were eligible to participate in a focus group if they were 18 years or older, English-speaking, and had a current or previous diagnosis of any type of leukemia. Potential participants were identified by screening the daily clinic census for the Leukemia Center at The University of Texas M.D. Anderson Cancer Center (MDACC) in Houston, Texas. Individuals who were at the clinic on the day of a scheduled focus group were randomly selected and contacted by phone to recruit for focus group participation the week before the scheduled meeting.

Procedures and Setting

Institutional review board approval was obtained. Verbal informed consent was obtained from all study participants by the principal investigator (TB). Each focus group had a minimum of 2 and a maximum of 5 participants. Focus groups were conducted between November 2017 and February 2018. Each discussion generally lasted 20 to 45 minutes and was facilitated by the principal investigator (TB). A second investigator (SB) was present at each focus group to record notes about the discussion and nonverbal cues from the participants.

The facilitator provided a description of the study, measures used to protect confidentiality, and instructions for effective focus group participation (Supplemental Document 1). Participants completed an anonymous demographics survey. A brief introduction was given on cancer genetics and genetic testing for hereditary leukemia. The facilitator utilized a script to guide the discussion. Open-ended questions were asked to assess attitudes toward, motivations for, and barriers to genetic testing for hereditary leukemia (Supplemental Document 1).

Data Analysis

All discussions were recorded and transcribed verbatim by a transcription service. The transcripts were then independently coded by two study investigators (TB, SB) to identify themes. A total of 173 thematic codes were used to code each transcript. The independently coded transcripts were subsequently compared using line by line analysis and found to have an inter-rater reliability (IRR) of 99.4%. Coding and analysis of themes was conducted through the qualitative data analysis and research software program, ATLAS.ti. Descriptive statistics were utilized to describe participant demographics.

Results

Participant Characteristics

Table 1 summarizes the demographic characteristics of the focus group participants. The sample included 6 women and 17 men with an average age of 63 years (range 30-84 years). The majority of participants self-reported as White/Non-Hispanic (78%), followed by 9% African-American, 9% Hispanic, and 4% Asian. Most participants (39%) had a diagnosis of chronic lymphocytic leukemia (CLL), followed by 22% with AML, 13% with CML, 13% with MDS, and 9% with ALL. One individual (4%) reported a diagnosis of essential thrombocytosis (ET). The majority of participants had at least a bachelor's degree (57%) and a household income greater than \$100,000 USD per year (39%). Additionally, most participants reported no family history of leukemia (87%) and had not had genetic counseling or genetic testing (91%) for non-hematologic cancer.

Table 1: Demographic Characteristics (n=23)

Variable	No. of participants (%)
Mean age (years) (range)	63 (30-84)
Gender	
Female	6 (26)
Male	17 (74)
Race/Ethnicity	
White	18 (78)
Hispanic	2 (9)
African American	2 (9)
Asian	1 (4)
Education	
High school or GED	4 (17)
Some college	5 (22)
Associate's degree	1 (4)
Bachelor's degree	8 (35)
Doctorate or post-graduate	5 (22)

Household income	
Not disclosed	2 (9)
<\$20,000	2 (9)
\$20,000 – 49,999	3 (13)
\$50,000 – 74,999	4 (17)
\$74,000 – 99,999	3 (13)
>\$100,000	9 (39)
Leukemia diagnosis	
AML	4 (17)
ALL	2 (9)
MDS	3 (13)
CML	3 (13)
CLL	9 (39)
Other	2 (9)
Family history of leukemia	
No	20 (87)
Yes	3 (13)
Previous genetic counseling for non-hematologic cancer	
No	21 (91)
Yes	2 (9)
Previous genetic testing for non-hematologic cancer	
No	21 (91)
Yes	2 (9)

AML: acute myeloid leukemia; ALL: acute lymphoblastic leukemia; MDS: myelodysplastic syndrome; CML: chronic myeloid leukemia; CLL: chronic lymphoblastic leukemia.

Motivations for Genetic Testing

At each focus group, participants were provided a short explanation of genetic counseling and genetic testing for hereditary predispositions to hematologic malignancy, including a description of genes, patterns that would suggest an inherited predisposition, and the genetic testing process (Supplemental Document 1). Focus group participants were then asked a series of questions to elicit how they would feel if they were offered genetic testing and what they perceived as their primary motivations for genetic testing.

Concern for Children and Family Members

The questions elicited a strong theme of concern for children as well as concern for extended family, which consistently emerged in every focus group. These two responses were the most frequently coded themes, together appearing 69 times out of 754 total coded responses (9.2%). Participants expressed concerns regarding the risk of passing a predisposition to leukemia on to their children, as well as the risk for other relatives to receive a leukemia diagnosis. For instance, one woman shared, “I have two daughters, and I would want to know if what I have, I could have passed on to them.” Participants conveyed a desire for their children and other relatives to obtain genetic testing to assess their risk status. One participant stated, “I think that if I was tested, I would hope that eventually too my kids would be tested. I think that the earlier that you can catch any illness or any disease, the better off you are.” Several individuals shared that they would never want to see their loved ones go through such a devastating diagnosis. “I would want to see if there is something lying there that could go to my niece or nephews or if it could even go to my sister, and if we could prevent it, I would definitely... I don’t want [my sister] to go through what I went through last year by any means.” As such, they were often motivated by the hope that obtaining genetic information could empower their families with an awareness of their cancer risk and allow them to take measures to detect leukemia early or preferably avoid the disease altogether:

“I would definitely want them to have a heads up. I mean some things can't be prevented, but if there is any preventative steps that could be taken, then I would really like my family members to know.”

“My wife has a predisposition for breast cancer on her mother’s side of the family. So, she knows that, so then she takes extra precautions to be safer. So, I mean if I could do that for my family, I would love to.”

Altruism

Participants also expressed altruism, or a desire to obtain genetic testing to contribute to research and benefit all future leukemia patients, as a motivation for undergoing genetic testing. This theme appeared 20 times out of 754 total coded responses (2.7%). For example, one individual shared, “I would definitely do it. Just if I can help any person, that makes it worthwhile for me.” Multiple participants expressed a desire that their participation in genetic testing would contribute to the growing body of knowledge about the etiology of leukemia as well as the development of new treatments and potential cures. For instance, these two individuals who shared the following:

“I think that that’s actually the way that cancer treatment is going to [get] better is through genetic testing.”

“I mean if there is further research down the road that you can be a participant in that may help someone else, even if it’s not even with your immediate family. If it could help somebody else’s family, I mean it’s well worth it.”

Participants were especially communicative of a willingness to do anything to help prevent future patients, not just their relatives, from enduring similar hardship in their lives due to a leukemia diagnosis. Many expressed a sentiment similar to this participant who stated, “You know, if I can participate in some way that paves the road for somebody else to have an easier life, then I’m all for it.” Overall, a strong desire to improve circumstances and leukemia

treatments for future generations, including both related and unrelated individuals, was a common theme in most focus group discussions.

Curiosity Regarding Personal Genetic Health Information

Although not raised as frequently as the above themes, several participants reported motivation for genetic testing in order to learn about their risks for future cancer diagnoses (two individuals), to identify the cause of their leukemia (three individuals), or to satisfy a general curiosity about their genetic information (three individuals). For example, one gentleman explained that he wanted testing “to see if I have a tendency for other cancers [...] Any other cancers lurking about and hiding, waiting to pop up.” A few participants expressed that their motivation would increase if there was clear clinical actionability, either for their current treatment or the prevention of future diagnoses: “The only part about that that makes any sense to me is if there is something to be done as a result of knowing in advance that you’re predisposed.” Regardless of their personal motivations, all 23 participants (100%) expressed a positive intent to have genetic testing. Some individuals felt eager to pursue testing right away, including one participant who stated, “Where is the line? Do you want me to sit down [for the test] right now?”

Drawbacks and Barriers

Participants were also asked to identify potential barriers or drawbacks to genetic testing, including issues they could imagine for themselves as well as for others. In all seven focus groups, participants consistently struggled to identify drawbacks or barriers to genetic testing, providing responses such as “there’s nothing that I can think of” and “I’m not concerned about it.” The limited drawbacks they identified included issues regarding confidentiality of the data and discrimination. Participants voiced general concerns surrounding negative impacts to

insurance coverage, increased premium costs, and ineligibility for health and life insurance. One gentleman shared his concern, stating: “There is also still the open question of what insurance is going to be allowed to do with the information, and that we don’t know.” A few individuals expressed worries about the potential lack of privacy and security of genetic testing results in the medical record, while only one individual mentioned uncertainty about employment discrimination:

“We don’t know if it can be used for employment decisions. We don’t know if it’s going to make people less eligible for insurance, and we certainly don’t know about security of that information. So all of those things to me create concerns.”

“I think that everyone is kind of worried about is the privacy of any information that is passed between you and your doctor.”

Two participants suggested drawbacks unrelated to the issues of confidentiality and discrimination. One gentleman deliberated whether his family would feel burdened or worried by positive results, saying, “The question is, would they worry about [positive results] all of the time? I mean we know that there are people that do that.” Another woman expressed worry about her genetic testing results being shared with anyone “who has any effect over whether [I] get treatment or how it’s treated or whether you’re a candidate or not.”

Participant responses when asked to identify potential barriers to genetic testing were also much less robust. Most responses in this category were only voiced by one or two participants. Two individuals shared that they felt less interested in genetic testing simply due to their older age. They felt that knowledge of their genetic information would have less utility for them at this stage in their life. One gentleman elaborated that although his older age currently acted as a deterrent, he may have been more interested in testing at a younger age for family

planning purposes: “If I was younger and planning a family, you know. I would definitely count that as a good reason. But since I’m almost elderly, it doesn’t matter.” Conversely, a participant in another focus group explained that younger age would have been a deterrent for him based on employment and insurance discrimination concerns, whereas his older age concerned him less and would not deter him from pursuing genetic testing. Another male participant felt that his perceived barriers would be particularly influenced by his children. After sharing that his decision to be tested would be based on whether his two children wanted him to have testing, he explained, “If my kids didn’t want me to do it because they didn’t want the data to be in the system, that certainly could deter me... If one of them wants to know and the other one doesn’t, then we’ll have to figure that one out too. If one of them is worried about the security of data and the other one isn’t, we’ll have one of those little family meetings.”

Several other potential barriers were proposed only once by various individuals. These included the potential inconvenience of testing, uncertainty about benefits, and limited clinical actionability. For instance, one gentleman explained, “Basically, you want to know if there is something that you can do about it. If there is nothing that you can do about it, I’m probably not that interested in knowing.” Another individual proposed that some people may desire to not be informed about their genetic information, preferring to leave their situation to fate: “Some people just don’t want to know. I think they kind of live blindly. I’m not that person, but I mean I’m sure that there are people that would rather just say whatever happens, happens.”

The most prominent response when participants were questioned about barriers and drawbacks to genetic testing was that there simply were none. In fact, 12 participants explicitly stated that they could not identify any deterrents at all, sharing thoughts such as, “I don’t think that there would be a real reason why you shouldn’t [pursue genetic testing].”

Table 2: Thematic Codes (total responses = 754)

Theme	Frequency (%)
<i>Motivations</i>	
Concern for children	43 (5.7)
Concern for family	26 (3.5)
Altruism for all leukemia patients	20 (2.7)
Prevention and early detection	19 (2.5)
Desire for genetic awareness in relatives	13 (1.7)
<i>Drawbacks and Barriers</i>	
Concerns about privacy/security	13 (1.7)
Negative impacts to insurance coverage	12 (1.6)
Less interest in testing due to older age	4 (0.5)
Children not wanting testing or results	4 (0.5)
Burden on relatives due to test results	3 (0.4)

These are the top five most frequent themes for the categories of *Motivations* and *Drawbacks and Barriers*. Note the frequency differences between the two categories.

Perceptions Regarding Skin Biopsy

Focus group participants unanimously agreed that the skin biopsy procedure would not be a deterrent to genetic testing. Each time they were directly questioned about having a skin biopsy for genetic testing, participants would often laugh and explain that they have experienced far more painful and difficult procedures as part of their leukemia treatment:

“I don’t have any problem. I’ve gone through 12 bone marrow biopsies. As many times as I’ve been stuck, you know. So, I mean it doesn’t matter.”

“I get a bone marrow biopsy every other time here. I mean I could probably do the skin thing myself (laughing). Just tell me how many square inches you want, and I’ll give it to you.”

Some participants openly disclosed that they had previous experience with a skin biopsy.

However, regardless of whether or not they had previous experience with the procedure, their view that it would not impact their testing decision remained the same.

Overall, motivations for genetic testing were among the most robustly developed themes throughout all seven focus groups. This is in contrast to themes related to drawbacks and barriers, which participants overtly expressed were difficult to identify. Accordingly, drawbacks and barriers appeared less frequently and were less pervasive throughout the focus group discussion transcripts.

Discussion

This study sought to identify the attitudes, motivations, and barriers to genetic testing for hereditary hematologic malignancies in the leukemia patient population. The majority of focus group participants were white males over the age of 50 with a high education level and an annual income of \$75,000 USD or more. Moreover, most participants had chronic leukemia. The focus group discussions highlighted that leukemia patients were able to readily identify motivations for genetic testing, which most often included concern for children and family as well as altruism for all leukemia patients. On the other hand, they struggled to identify drawbacks and barriers and, as a result, these themes were less developed.

For most participants, the information provided during the introduction to the focus group discussion was the first time they were made aware of the hereditary component to leukemia. In fact, four participants distinctly recalled asking their healthcare provider about a hereditary component to their diagnosis and being told that such information was still not known. Despite a lack of previous knowledge about genetic predispositions to leukemia, participants were able to recognize the impact that their personal genetic information could have on their lives and families.

Overall, a positive regard for genetic testing was ubiquitous throughout all seven focus groups. Participants frequently articulated a view that testing is beneficial because it has the potential to help their children and extended relatives as well as other leukemia patients. They largely agreed that the information provided by testing results can have important implications for their family, especially if the results are positive. Participants recognized that genetic testing could be used as a tool to identify at-risk relatives and expressed that they would inform their family members if a mutation was detected. In general, a desire to identify a genetic predisposition and promote genetic awareness among relatives was commonly expressed. They

conveyed hope that these proactive measures could help prevent disease or lead to earlier diagnosis in their loved ones. It is interesting to note that the thematic code for concern for family frequently co-occurred with the codes for prevention and early detection in the discussion transcripts. These themes commonly emerged together even though the information provided during the focus group introduction did not allude to the possibility of prevention or early detection in relatives. Additionally, while a few participants shared that they felt autonomy was important for each relative's personal genetic testing decision, several discussed that they would actively encourage their family members to be tested. These findings are consistent with focus group studies in the solid tumor patient populations (28, 29, 32, 35).

Genetic testing was also commonly viewed as an important tool for gaining knowledge about the etiology of leukemia and contributing to the advancement of leukemia research. This was underscored by a strong sense of altruism for all leukemia patients, both present and future. Many individuals shared stories about the devastating effects of their disease, and these experiences seemed to drive their motivation to obtain genetic testing with the hope to prevent leukemia or at the very least improve diagnostic and treatment techniques for future generations. There was often a sense of agreement among participants that they would not wish a leukemia diagnosis on anyone, whether they were family members, friends, or strangers. Accordingly, several individuals expressed great willingness to contribute to leukemia research through genetic testing. Interestingly, a strong sense of altruism has also been reported among focus group participants in the breast cancer population, but not readily observed in focus groups among patients with colorectal cancer (28, 32).

While the above themes were robustly developed, there were several motivations that were expressed with less regularity. These motivations were all issues that focused more on the self than other people. This included issues such as a desire to pinpoint a cause for one's

leukemia and to learn about one's risk for other cancer diagnoses. A valuable observation here is that participants tended to communicate these self-oriented motivations with much less frequency than motivations oriented towards helping relatives and future leukemia patients.

Throughout all seven discussions, there was a generalized inability to recognize drawbacks and barriers to genetic testing. While some participants were able to voice limited concerns, the frequency and depth of these responses were less robust than the perceived motivations for genetic testing in our analysis. One of the only issues proposed by more than one or two participants was a concern for the confidentiality of genetic testing data and discrimination based on positive test results. While this theme has also been identified in similar investigations with the breast and colorectal cancer populations, it is a more predominant and well-developed theme in these studies (28, 29, 32). Interestingly, a focus group study conducted by Ramsey et al. also reported participants who experienced similar difficulty with imagining potential drawbacks and barriers. However, when later presented with specific information regarding the risks and implications of genetic testing, some participants viewed these as drawbacks or barriers and felt more reluctant to have testing (35). Future studies in the leukemia population should assess how patients feel about the risks and implications of genetic testing after being given more specific information on this subject. Such an approach was not utilized in this study, as the investigators wished to ascertain which issues would arise organically without introducing ideas. Outside of the subject areas of confidentiality and discrimination, participants were unsuccessful in consistently identifying other drawbacks or barriers. For example, only one gentleman in the present study discussed possible burden or distress on relatives due to positive genetic testing results, while previous studies in solid tumor populations have identified this as a more common concern (28, 29, 32). Other drawbacks and barriers seen in previous studies which were not raised by participants in this study include topics such as the cost of

genetic testing, feelings of guilt after learning that cancer susceptibility has been passed to children, and the potential for psychologic distress in oneself or one's relatives (28, 29, 32).

A unique and important finding of this study was the participants' universal acceptance of the skin biopsy procedure that is necessary for genetic testing in the leukemia patient population. One hundred percent of participants agreed that this procedure would not impact their decision to be tested. Although reason would suggest that a skin biopsy could be a significant deterrent to testing in other patient populations, the participants in this study were adamant that it would pale in comparison to other procedures that are part of their routine care, especially bone marrow biopsies. Of note, participants with no previous experience with skin biopsies did ask several questions about the logistics of the procedure, including where on the body is the skin taken from, how large of a skin sample is retrieved, and whether the test can be conducted when the patient has low platelet counts. Still, participants unanimously voiced a willingness to undergo the procedure. This suggests that as long as the patient's questions about the procedure are addressed, skin biopsy is not likely to be a deterrent to genetic testing in this patient population.

Participants raised a number of appropriate questions throughout the focus group discussions. The majority of their questions pertained to logistics of the skin biopsy procedure, as noted above. Outside of this topic, several other types of questions were raised by only one or two individuals. These included inquiries about the reliability and validity of genetic test results, how long testing has been available, and what clinics offer testing. One participant also asked about the penetrance of hereditary hematologic malignancy syndromes while two others inquired about preventative options and/or next steps after positive predictive testing in their children. Another individual wondered whether someone with a bone marrow transplant can have genetic testing. While the majority of these questions were posed only once and did not

present as an overarching theme, all of them were pertinent to genetic testing for leukemia patients and illustrate the types of questions that could be asked by these individuals in a typical genetic counseling session.

To our knowledge, this represents the first study to explore the attitudes, motivations, and barriers to genetic testing for inherited hematologic malignancies among patients with leukemia. One of the primary limitations of this study was the relative homogeneity of the focus group participants in terms of age, gender, race/ethnicity, education, and income. While the socioeconomic background of our participants is representative of the patient population undergoing treatment at M.D. Anderson, this sample is not representative of all leukemia patients. Further research is needed to assess whether these views are reflective of a larger sample of leukemia patients from more diverse backgrounds. Additionally, the conclusions drawn from this study are subject to a selection bias. Participants' willingness to attend the focus group suggests a desire to participate in research, which would provide an inclination for these individuals to express positive regard and intent for genetic testing as well as an altruistic outlook. Another limitation of this study was the size of some of the focus groups. Most of the discussions included three to five participants, but one discussion had only two participants. While the ideal focus group size has not been established, experts suggest that it is practical to have 4-12 participants per group (38). Lastly, most participants (91%) had no previous experience with a genetic counselor. As such, these individuals were only able to discuss topics that they could imagine on their own, which may have limited the findings of this study.

Conclusions

In summary, our focus group discussions revealed that participants held a positive regard for genetic testing, and were primarily motivated by concern for their family and a sense of altruism. While drawbacks and barriers were more difficult for participants to identify, a few individuals cited concerns about confidentiality of genetic information and discrimination based on test results. Participants also unanimously agreed that the skin punch biopsy required for genetic testing in leukemia patients would not deter their decision to be tested. As focus groups studies are utilized to identify and describe issues of importance specific to the participants, the conclusions drawn from this study cannot be used alone to extrapolate to the entire population of interest. Future studies on this subject should analyze how these motivations and barriers to genetic testing are perceived by a larger and more demographically diverse sample of leukemia patients.

As genetic testing for inherited hematologic malignancies becomes progressively more available, it will provide important information for the treatment of an increasing number of leukemia patients. The knowledge gained from this study and future studies will be paramount in providing genetic counseling that meets the needs of leukemia patients. Our current data suggest that this population may not be significantly dissimilar from solid tumor populations. Although leukemia patients seen in the genetic counseling setting may be able to readily recognize benefits to testing, they likely need education regarding the risks and implications of testing, as these issues could be perceived as potential drawbacks or barriers. Additionally, while the skin biopsy may not be a deterrent to testing for patients with leukemia, they may raise logistical questions about the procedure that could impact their decision undergo genetic testing.

Appendix

Supplemental Document 1: Focus Group Discussion Guide

Introduction:

Thank you for agreeing to participate in today's focus group discussion. The purpose of this informal discussion is to learn more about your opinions and feelings about genetic testing for leukemia. Please feel free to share as much or as little as you would like. There are no right or wrong answers, so please answer by giving information that best describes your opinions and thoughts.

I would like to remind everyone that everything you say here today is completely confidential. We will be recording the discussion so we may capture your thoughts exactly as you say them. However, we will not be using any names during the discussion. Please be sure to speak loudly so that the recorder can capture your thoughts.

In order to get the discussion started, I want to give you some background information on genetic testing for leukemia. This is a very new field that many people have not heard about yet. We will start with a brief science lesson. Our bodies are made of billions of cells and inside each of these cells is DNA, which contains the genetic instructions that tell our body how to grow and develop. DNA is made up of thousands of genes. Each gene contains specific instructions that help the body perform a specific job. For example, some genes determine eye or hair color. Other genes contain instructions to help our body fight off cancer. When there is a change in a gene, called a mutation, this can cause the instructions in that gene to be incorrect. Without the correct instructions, a gene that helps the body fight off cancer may not do its job properly. When this happens, that person has a higher chance to develop certain cancers in their lifetime. You may have previously heard about something very similar to this with breast cancer

and the BRCA gene. Since genetic information is passed from parents to children, we often find that mutations in genes like BRCA run in families.

Multiple gene mutations have recently been found to cause different types of leukemia to run in families. Genetic testing has become available for these genes. This testing allows us to take a close look at a person's genes to see if someone has a mutation that causes an increased chance for them to develop leukemia. Typically, genetic testing is done by collecting a blood or saliva sample and sending that sample to the lab. Since leukemia is a cancer that occurs in the blood, there are cancer cells in the blood that can confuse the genetic testing results. As a result, genetic testing must be done through a skin biopsy for people with leukemia. A skin biopsy is the same process as having a mole removed by a dermatologist and involves numbing the skin and taking a small piece, smaller than the size of a pencil eraser, which is then sent to the lab for genetic testing. As I mentioned earlier, our discussion today is meant to learn more about your thoughts surrounding genetic testing for genes that cause increased risks for leukemia. We hope to use your thoughts and feedback in order to improve the care of leukemia patients who may have genetic testing in the future. Let's begin.

Questions:

- 1) After learning that leukemia can run in families, what does that make you think about?

Probe: How does that make you feel?

Probe: Is this the first time you have heard that leukemia can be hereditary?

- 2) Using your own words, describe how you would feel if you were offered genetic testing to see if your diagnosis of leukemia had a genetic cause, or if leukemia runs in your family.

Probe: Imagine you had genetic testing and your results were positive for a genetic mutation. How would that make you feel?

Probe: Imagine you had genetic testing and your results were negative. How would that make you feel?

- 3) Describe what, if anything, may prevent you from wanting to have genetic testing.
- 4) Even if they may not apply to you personally, describe any other possible drawbacks you could imagine to genetic testing.
- 5) If you did want to have genetic testing, why would you want to have it?
- 6) Even if they may not apply to you personally, describe any other potential benefits you could imagine to genetic testing.
- 7) If applicable, describe how your opinions have changed as you have discussed potential drawbacks and benefits with the other participants today.
- 8) After learning that genetic testing for leukemia patients requires a skin biopsy, how does that make you feel?

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