

# The psychosocial effects of the Li-Fraumeni Education and Early Detection (LEAD) program on individuals with Li-Fraumeni syndrome

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**Purpose:** In the past 5 years, new screening protocols have been developed that provide improved cancer screening options for individuals with Li-Fraumeni syndrome (LFS). Very little has been published on the psychosocial impact of these screening protocols. The goals of this study were to determine how participation in screening impacts individuals psychosocially, to examine the benefits and drawbacks of screening, and to evaluate possible barriers to continued screening.

**Methods:** We performed a qualitative study consisting of semistructured phone interviews conducted from December 2015 to February 2016 with 20 individuals attending the LFS screening program at MD Anderson Cancer Center.

**Results:** Data analysis showed that benefits of screening include early detection, peace of mind, centralized screening, knowledge

providing power, and screening making LFS seem more livable. Perceived drawbacks included logistical issues, difficulty navigating the system, screening being draining, and significant negative emotional reactions such as anxiety, fear, and skepticism. Regardless of the emotions that were present, 100% of participants planned on continuing screening in the program.

**Conclusion:** Our data indicate that the perceived benefits of screening outweigh the drawbacks of screening. Individuals in this screening program appeared to have improved psychosocial well-being because of their access to the screening program.

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**Key Words:** comprehensive screening; Li-Fraumeni syndrome; LEAD program; psychosocial effects; screening barriers

## INTRODUCTION

Li-Fraumeni syndrome (LFS) is a rare hereditary cancer predisposition syndrome that is caused by mutations in the *TP53* gene.<sup>1,2</sup> Classically, this cancer syndrome has been associated with sarcomas, premenopausal breast cancer, brain cancer, adrenocortical carcinomas, and leukemia.<sup>2</sup> However, in recent years, more cancer types have been found to be associated with LFS, including colon, pancreatic, stomach, kidney, endometrial, ovarian, prostate, lung, and skin cancers.<sup>3</sup> Overall, by the age of 31, there is a 50% risk of developing cancer, with this risk nearing 100% by the age of 70.<sup>4</sup> Close to 50% of individuals who have one cancer diagnosis will develop another cancer within 10 years.<sup>4</sup> Moreover, young children may also be affected by cancers.<sup>5</sup>

The risk and occurrence of these multiple cancers create not only a large physical burden but also a psychosocial burden. For individuals going through the genetic testing process for LFS, 23% had clinically relevant distress.<sup>7</sup> Such distress has

been attributed to higher levels of cancer worry and greater perceived risks.<sup>8</sup> In addition, because 80–93% of individuals with LFS inherited it,<sup>9,10</sup> the prevalent cancer history in the family can also lead to an increase in overall distress.<sup>8</sup> Individuals with multiple cancers in their family due to LFS have been found to be “psychologically fragile” and they fear passing on “doom and death” to their children.<sup>11</sup> It has also been reported that individuals with LFS feel that their diagnosis is always on their mind and that their anxiety and distress can increase dramatically during a personal or family medical crisis.<sup>12</sup>

To address the large concern regarding these cancer risks, an important step is to participate in a cancer screening program. The available screening methods for LFS patients dramatically changed in 2011, when a study performed by Villani et al.<sup>13</sup> showed significant survival benefits for individuals following a new comprehensive screening protocol that combines ultrasound, urinalysis, blood tests, breast mammograms, colonoscopies, annual brain magnetic resonance imaging (MRI)

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examinations, and rapid whole-body MRI (WB-MRI) examinations. Using this screening regimen, cancers were detected early in asymptomatic individuals, and after 5 years the survival rate of the screening group was 88.8%. Conversely, individuals who chose not to undergo screening had a 5-year survival rate of 59.6%.<sup>13,14</sup> To provide support for using WB-MRI for children with LFS, a study using WB-MRI for children with hereditary cancer syndromes found a sensitivity of 100% for detecting cancers.<sup>15</sup> These studies have allowed for new screening modalities to be offered to individuals with LFS. Before the study by Villani *et al.*<sup>13</sup> was published, guidelines produced by groups such as the National Comprehensive Cancer Network (NCCN) provided LFS patients with specific screening recommendations only for breast cancer and colon cancer.<sup>16</sup> However, with the new findings, the 2015 and 2016 NCCN guidelines adopted additional recommendations, including WB-MRI.<sup>17,18</sup> The expansion of these guidelines may potentially improve the clinical picture and prognosis of LFS.

Based on the significant survival benefit demonstrated by Villani *et al.*,<sup>13</sup> in 2013 MD Anderson Cancer Center initiated a similar screening program through its Cancer Prevention Center, called the Li-Fraumeni Education and Early Detection (LEAD) program. The goal of this program is to provide screening and education to individuals with LFS in an effort to improve their survival and medical management. For specific screening guidelines offered by the LEAD program, please refer to the **Supplementary Materials** online.

Although the main goal of the LEAD program is to increase survival for patients with LFS, the psychosocial impact of undergoing this novel comprehensive screening is largely unknown. Previous research on screening for LFS, prior to the introduction of comprehensive screening, showed that individuals felt that screening provided early detection and a sense of control and security.<sup>19</sup> However, one case study showed that an individual in a comprehensive screening program reported “exhaustion” with the amount of screening and number of cancer diagnoses she received.<sup>20</sup> To date, no other psychosocial studies have examined these effects across more extensive LFS populations. The aims of this study were to identify the psychosocial impact of LFS comprehensive screening options on individuals with LFS and determine whether psychosocial factors may influence screening adherence.

## MATERIALS AND METHODS

This study was approved by the institutional review boards at the University of Texas Health Science Center at Houston (HSC-MS-15-0410) and the University of Texas MD Anderson Cancer Center (BS99-038).

### Participants

Individuals were eligible for this study if they were 18 years or older, English-speaking, had a germ-line *TP53* mutation, and had completed at least one LFS screening visit in the LEAD program at MD Anderson Cancer Center. A total of 34 participants were initially eligible for this study.

### Study design

Potential participants received a study invitation followed by a phone call from study personnel to determine interest in participating. After giving informed consent, participants completed semistructured interviews by phone or in person that included questions regarding their experience with LFS screening. Interview questions addressed emotional reactions to screening and test results, satisfaction and perceived efficacy of screening, drawbacks of the screening process, future screening intentions, and financial and logistical implications of screening. Interviews were audiotaped and transcribed using Adept Word Management professional transcription services.

### Analysis

Qualitative analysis was guided by the grounded theory approach using ATLAS-ti software (ATLAS.ti Scientific Software Development GmbH, Berlin, Germany).<sup>21</sup> Each transcript was coded and analyzed to determine overarching themes. A preliminary codebook was created by the primary author (J.R.) and reviewed with a second coder (R.Y.). The primary and second coders reviewed and coded five transcripts until an inter-coder reliability of more than 80% was reached. Coding discrepancies were discussed until a consensus was reached. The primary author coded the remaining transcripts. Codes were grouped into the following categories: benefits and drawbacks of participating in LFS screening and plans for future participation.

## RESULTS

A total of 34 individuals met the eligibility criteria for our study. Of these, 10 (29%) did not respond or could not be reached, 4 (12%) declined participation, and 20 (59%) consented and were interviewed. Interviews were ceased when there was saturation of new themes. The final sample included 16 women and 4 men, which matched the gender distribution of the eligible population. Most participants had at least one previous cancer diagnosis. At the time of the interview, 5 individuals had previous incidental findings on WB-MRI or brain MRI that required follow-up imaging or biopsy. Prior to screening, all participants discussed the program with a health-care provider to learn more about the perceived physical benefits and limitations of screening: 11 met with a genetic counselor, 7 met with a nurse practitioner, and 2 met with a physician.

Because of the screening protocol's flexibility, participants were at different stages in their screening process at the time of their interview. Some participants had multiple WB-MRI examinations, others had one, and four had not yet undergone WB-MRI examination. Of those four, all underwent brain MRI examinations and three have undergone WB-MRI examinations since the interview period. Although the availability of WB-MRI is a key feature of the LEAD program and may affect the participant's responses in our interview, there were no detectable differences in responses between the groups. Those without WB-MRI information were able to comment on other screenings they had received, such as the brain MRI.

**Table 1** Participant ( $N = 20$ ) demographic characteristics at the time of study

Characteristic	n	%
Mean age (range), years	39.1 (18–61)	
18–25	3	15%
26–33	4	20%
34–41	5	25%
42–49	3	15%
50–57	2	10%
58–64	3	15%
<i>Ethnicity</i>		
Caucasian	12	60%
Hispanic	4	20%
African American	2	10%
Other	2	10%
<i>Gender</i>		
Female	16	80%
Male	4	20%
<i>Screening history</i>		
Previous WB-MRI	16	80%
Previous brain MRI only	4	20%
<i>Personal cancer history</i>		
Previous cancer diagnosis	17	85%
Mean number of cancers (range)	2 (0–6)	
<i>Reproductive history</i>		
Number with children	11	55%
Mean number of children (range)	1.1(1–3)	
<i>Incidental findings that required further imaging/biopsy</i>	5	

Demographic characteristics and screening history are shown in **Table 1**.

#### Perceived benefits of participation in the LEAD Program

**Early detection.** Participants indicated that early detection of cancer is a benefit of screening; they perceived that if cancer were to develop, it would be caught early and with a better outcome. Some reported that early detection was the sole reason they participated in screening. When considering what would happen if the program did not exist, one participant said, “Early detection is key to...fighting off cancer. So I don’t know how you’d do it without screening.”

**Peace of mind.** Individuals said that having access to screening has provided peace of mind, which they attributed to worrying less about their cancer risk and knowing their current health status. Specifically, one person explained that individuals with LFS worry that every illness they have is a sign of cancer and that screening has helped mitigate those feelings: “The screenings—when they told me...you’re good. Everything’s fine. Later on, if I get a flu or something, I’m fine because I already know my screenings are good.” When asked how screening affects their feelings about their LFS

**Table 2** Number of participant responses per perceived benefit category

Benefit	n	%
Early detection	13	65%
Peace of mind	12	60%
Centralized screening	10	50%
Knowledge is power	16	80%
LFS is more livable	16	80%

cancer risk, one person said, “It’s lessened my feelings about feeling worried about future cancer. I’d be naive to think that it couldn’t happen to me again, because I know darn good and well it could. But...the goal is to catch things early before it’s too late.”

**Centralized screening.** Participants said they valued having screenings centralized in one location. Prior to an organized screening program, many noted that LFS is “so rare, most doctors haven’t heard of it.” They indicated how difficult it was to organize screening for multiple cancers on their own: “It was just you or going [to] each department [independently]. It was a little bit overwhelming.” These individuals said that a centralized screening program provides a means of keeping track of all their screenings and assurance that the screening protocol is being followed.

Respondents also valued having health-care providers who were knowledgeable about LFS and could advocate for the need for screening. They noted the burden of having to explain LFS to health-care providers who often were not knowledgeable about the syndrome as well as the need to act as their own advocate in regard to LFS-related care. A participant said that the screening program enabled affected persons to “sit in the back seat, instead of always in the driver’s seat.”

**Knowledge is power.** The vast majority of participants also conveyed that the information gained from screening is beneficial. For some, the information regarding their current health status was most important, whereas others thought that “being a little bit more educated about...what you put in your body and what you expose yourself to” was important information gained. Regardless of which information each participant felt was most powerful, many said that if they did not have access to the LEAD program, they would be losing vital information. As one woman explained, “I would feel like I’d be in the dark, like I wouldn’t know anything.”

**LFS is more livable.** It was reported that screening makes LFS feel more “livable.” Prior to participation in the LEAD program, a diagnosis of LFS led patients to feel as though they were being told, in one participant’s words, “You have this horrible disease and you’re going to die of cancer.” However, with the program and its screening protocol, there is hope that LFS will be easier

**Table 3** Perceived benefits of screening

Themes	Participant responses
Early detection	"I think the biggest thing was I knew it was going to help catch things early, and I felt that was—with the way cancer treatment is now, it's all about catching things before they've progressed."
Peace of mind	"The program definitely gives me more peace of mind. Like I know I still have a significantly higher chance of getting cancer than the most average person. But I have more confidence that if I do, it will be more manageable." "I just feel more confident. I feel I have more peace of mind and even for my child. I feel like it's very good for her, and she knows it now."
Centralized screening	"Just the overall screening and not having to take care of it yourself. It's allowed me to step back from being my own doctor. I didn't go to med school, I don't know things, and people with Li-Fraumeni should not have to know as much as they do because it makes it hard to just live life. So I try and leave that to other people, and the screening has allowed me to really step back and just enjoy being me." "Just literally having it all under one roof, and having one person who really knows—what'd y'all call it? The syndrome? The disease? Someone who knows all about it."
Knowledge is power	"The only way to know is to screen. And that is the most beneficial. That's the reason I do it." "So, this to me is knowledge is power. You know, the more I know, the better off I am."
LFS is more livable	"I have much more confidence that if I continue doing this, that it's more likely for me to live a long and healthy life".

to cope with, as this woman said, "Just knowing that it's not a death sentence...and that it is livable for a lot of people."

The number of respondents for each theme is shown in **Table 2**. Further examples of the perceived benefits are listed in **Table 3**.

#### Perceived drawbacks of participation in the LEAD Program

**Logistical issues.** Several logistical issues were seen as drawbacks of the screening process. For some, the time commitment was burdensome. Individuals described having to travel across the country multiple times per year for appointments. This time commitment proved to be not only burdensome but also expensive. As one person said, "I'm not capable of driving all that way. So, I have to fly, which means scheduling and money and...we're on a fixed income, so it's a burden. But I'm doing what I can to stay alive."

The biggest logistical issue, however, involved insurance and whether it would cover the recommended screening. Nine participants noted that they have concerns about insurance coverage. One individual's insurance recently denied the WB-MRI, triggering a significant emotional reaction: "I got sick from it. I was depressed. I got really sick." Another group of eight individuals had not had insurance difficulties but feared them in the future. The remaining three individuals did not feel that insurance coverage was a concern.

**Organization and navigation within the program.** Participants felt that the organization of the program needed improvement. The lack of organization was in relation to communication errors within the LEAD program, scheduling problems, and lack of knowledge about the program by other health-care providers. However, many noted considerable improvements in the organization of the program over time.

Other individuals said that trying to navigate the program (e.g., finding the location or knowing whom to call with questions) was difficult and posed a barrier to screening. One individual expressed concern about other participants' ability to navigate the system: "I know other people in this—they're

going to give up and quit." Although there are challenges to navigating through the program, one woman said, "I think your first time there, it's a little confusing at times...But I think the second time is a lot easier."

**Draining.** The screening process was described as being both physically and emotionally draining. From a physical standpoint, many of the screening techniques, particularly the WB-MRI, were time-consuming. One person explained how they felt during the WB-MRI: "I want to get out...I'm just stiff...I'll fall asleep. And once I get up, I'm like, man. I'm still here."

Others noted that, from an emotional standpoint, "there are still times you just get tired of it and you just...don't want to do it anymore." Sometimes screenings brought up old memories, as reported by one individual: "If you had something detrimental happen or take a trip down memory lane—it might get you in the gut a little bit."

**Negative emotions.** The vast majority of participants expressed negative emotions throughout the screening process, with three emotions being most prevalent: anxiety, fear, and skepticism. The most frequently reported negative emotion was anxiety, referred to by a few people as "scan-xiety." The "scan-xiety" stems from the uncertainty about what will be found during screenings. For some, this anxiety is so severe that they report taking medication to control it. Some experience anxiety prior to screening; others say that waiting for the results is the worst part, "worse than when they actually give you the results...it makes you crazy." Although the anxiety associated with the initial screening process can be intense, approximately half said they felt that their anxiety decreased with additional screenings.

Half of the participants also described fears related to screening, which was often related to claustrophobia during the MRI examinations; one person said, "I have to be strapped down." Another cause of fear was inconclusive or benign findings on the screening examinations; one person said, "I was so scared, and I thought I had breast cancer. But no, it was just...fat."

A small proportion of the participants also expressed skepticism regarding whether the screening results or the doctors themselves would be correct. When asked about receiving a normal screening result, one participant replied, "I feel relieved, but I feel like 'are they sure?' I need to read it myself, like I'm going to find something they didn't."

Although there were significant negative emotions for many individuals, some indicated a lack of negative emotions related to screening. These people said they felt like a "rare breed" because of their lack of screening-related emotions. Some said that without screening they would have "panic attacks," for example, "If I get a cough, I think I have throat cancer. Or if my head is hurting or my eyes are hurting, something's going on with me. Something's back."

The number of respondents for each category is shown in **Table 4**. Further examples of the perceived drawbacks are listed in **Table 5**.

### Plans for future screening

All of the participants said that they would like to continue screening within the LEAD program. Reasons given for why they would like to continue included "I think it would be foolish of me not to" and "I want to stay alive."

**Table 4** Number of participant responses per perceived drawback category

Drawback	N	%
Logistical issues	17	85%
Insurance concerns currently	9	45%
Insurance concerns for the future	8	40%
Organization and navigation within the program	9	45%
Draining	10	50%
Negative emotions	18	90%
Anxiety	14	70%
Fear	10	50%
Skepticism	4	20%

**Table 5** Perceived drawbacks of screening

Themes	Participant responses
Logistical issues	<p>"But some people may have to pay way more than that, so I think cost is really, really prohibitive for some people being able to do all the screenings—just because it's—imaging is expensive."</p> <p>"I mean the time because it's a field trip every time you go to Anderson."</p>
Organization and navigation within the program	<p>"My insurance doesn't cover my whole-body MRI. So I haven't had one of those yet."</p> <p>"It seemed a little bit disorganized at first, but I think it was just—maybe I was one of the first patients that was in it. But I think that has gotten better."</p> <p>"I think the harder thing for me is knowing who to get in touch with to figure things out. That's a little confusing, I will say. Because I know some people do just some things in their local area and then some things out. I wish there was a social worker at my full program that I could kind of contact to ask questions."</p>
Draining	<p>"They can be kind of draining, in terms of like energy and emotionally sometimes. Just you know, knowing that you have the condition and that you have to go do it."</p>
Negative emotions	<p>"It was just the anxiety that you go through every time you've got to go do your screening. It's just like, 'Oh, my God. What are they going to find now?'</p> <p>"I think that a lot of the anxiety has subsided and kind of the nervousness and the fear of the unknown has subsided. And now they're familiar and I know the drill."</p> <p>"I take a Xanax in the morning, just because—you know—being in enclosed spaces really bothers me"</p>

A few individuals reported that a family member had quit screening in the LEAD program for reasons including being physically and emotionally tired of the screening process, moving away from MD Anderson, and lack of communication from the program.

We asked each participant what potential barriers might prevent them from continuing screening. Most cited loss of insurance coverage as the largest barrier. Another barrier was moving to new locations where they might not have direct access to screening, a concern noted particularly by young individuals, who might decide to move away for college or work. One young adult explained, "If I ever want to transfer out of state...that kind of scares me, because I'm like, 'What am I supposed to do?' All my testing and everything is here."

### DISCUSSION

This study, to the authors' knowledge, is the first multiparicipant study examining the psychosocial effects of a comprehensive LFS screening program. Consistent with a previous study involving screening prior to the comprehensive protocol, we found that LFS screening provides patients with a sense of security, and the largest perceived benefit was early detection of cancers.<sup>19</sup> However, our findings contradicted those of a previous case study whose authors expressed concern that comprehensive screening may lead to testing fatigue and may put a significant emotional strain on patients.<sup>20</sup> Although some of our participants' responses support such concerns, our study showed that the benefits gained from screening significantly outweigh the perceived drawbacks, as shown by the fact that 100% of patients said they planned to continue screening within the LEAD program. Although screening increased some negative emotions, such as "scan-xiety," fear associated with screening, and skepticism about the tests and doctors, some negative emotions were actually eliminated because of screening. Participants felt less worried about their personal and family cancer risks, were less fearful about LFS, and became less focused on their mortality.

They also indicated that access to the LEAD program makes LFS seem less overwhelming and more livable.

The information we gained in this study contrasts with the findings by Gopie *et al*,<sup>22</sup> who found increased distress and lower quality of life in individuals undergoing screening for hereditary cancer syndromes. The LFS patients in that study underwent screening prior to 2012 that consisted of breast MRI and targeted screening dependent on family history, which is in contrast to the comprehensive screening in the LEAD program. Prior to comprehensive screening, there may have been significant distress and lower quality of life for individuals with LFS. In our study, however, although not measured directly, we heard from patients that participating in comprehensive screening actually lowered their distress and improved quality of life. This shows that comprehensive screening programs are important to patients' well-being.

Screening through the LEAD program has also reassured patients about their current health status. Many of the participants said that prior to the screening program, they worried that every bruise, headache, or illness was a sign of cancer. Now, they rely on their normal screening results as reassurance that such conditions are not indicative of cancer. This has allowed people with LFS to live without constant worries about cancer and to focus more on everyday life.

### Implications

Our findings can be used not only to help grow the LEAD program but also to guide centers around the world that are implementing improved screening for LFS. Some participants stated that they have family members who cannot access appropriate screening because there are no screening programs in their area. These testimonies support the need for easier access to screening programs worldwide. Currently, other groups are utilizing screening protocols similar to those of the LEAD clinic, including the University of Utah; the National Cancer Institute; the National Institutes of Health; the Dana-Farber Cancer Institute; the Gustave Roussy Institute in Paris; the Institute of Cancer Research in Surrey, United Kingdom; and the Australasian Sarcoma Study Group in Victoria, Australia (contact information is available from the authors). It will be important to compare data from these sites to continue to learn how to develop successful screening programs.

Despite the benefits of screening, there are still notable drawbacks that limit participation. In particular, significant negative emotions may be associated with the screening process. All health-care providers who interact with these individuals should be aware of these potential emotions and be able to provide appropriate referrals if necessary.

Finally, many individuals interviewed desired improvements to insurance coverage. Some stated that screening is the only thing keeping them alive, and when screening was not covered by insurance, they experienced significant negative emotional reactions. While insurance coverage may be out of the hands of health-care providers, we hope that by providing more research-based evidence showing that screening is necessary

for patients' physical and emotional well-being, the insurance companies will be more amenable to covering screening and lack of coverage will no longer be a barrier for patients.

### Study limitations

One of the limitations of this study is its small sample size. Because this condition is rare, there is little opportunity to observe a large LFS population at a single cancer center. However, we obtained a 59% response rate from the eligible participants and an 83% response rate from those we reached, and we reached saturation in terms of identifying new themes in the interviews. Therefore, we feel that having a larger sample size would not change our findings significantly.

Another limitation of the study is that many of the participants had undergone their most recent screening weeks or months prior to our interview. This interval may have affected their memory of the emotions surrounding that screening experience. Also, it is important to note that most individuals had received normal screening results at their last visit, which may have led to a more positive memory of their experience. However, the one individual in whom cancer was found at the last screening visit did not express negative feelings about the screening process.

Bias may have been introduced when the participants met with a health-care provider to discuss the potential physical benefits and limitations of screening prior to beginning the program. Most individuals were probably told that the reason this program exists is to help detect cancers and improve survival. These conversations make it difficult to determine whether participants independently identified these as benefits of screening or whether the conversations with health-care providers prompted these responses.

Importantly, because this study was performed at one point in time rather than over many years, it cannot be known whether these patients would eventually develop testing fatigue. Participants in our study all expressed the desire to continue screening; however, if they were followed for a longer period, we might learn more about the risk for study fatigue in the long term. Interestingly, there was no difference in responses between those who had participated in the screening program for a few years and those who had recently joined the program.

Finally, four individuals declined to participate in our study and so their unique perspectives were not captured. These individuals might have had negative experiences that they did not feel comfortable sharing with people at the institution where they receive their care. They may also be less likely to participate in screening in the future, in which case we would not have an accurate representation of their perspective.

### Future directions

Although our study investigated individuals' experiences with LFS and the LEAD program, many noted a large familial impact as well. It appears that family members are affected by both the patients' diagnosis of LFS and their participation in screening. Further research should investigate the impact of screening on the family

because familial support is important to many cancer patients.<sup>12,23</sup> Relatedly, many participants have children enrolled in the pediatric LEAD program. It would be beneficial to interview these children to learn about the psychosocial impact of screening on children.

Finally, it would be valuable to talk with individuals who either quit or declined initial participation in screening. These individuals were not captured in our study, and understanding their motivations could help improve the program to include as many high-risk LFS individuals as possible.

## SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at <http://www.nature.com/gim>

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## DISCLOSURE

The authors declare no conflict of interest.

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