Willingness to participate in a trial comparing standard genetic counseling versus genetic counseling with personalized cancer risk estimates in patients with Li-Fraumeni Syndrome

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Background

- Li-Fraumeni Syndrome (LFS) is associated with germline pathogenic variants/likely pathogenic variants (PV/LPV) in *TP53* and elevated lifetime risks of multiple cancers[1].
- Genetic counseling (GC) provides risk assessment prior to genetic testing and guidance amidst diagnosis.
- Standard GC for individuals with LFS involves generalized lifetime cancer risk estimates.
- Personalized GC would provide statistically individualized risks tailored based on personal and family history.
- The LFSPRO statistical model was developed and validated by our research team to[2]:
    1. Calculate pre-test risk prediction of a *TP53* PV
    2. Estimate cancer risks for individuals with LFS

Study Aim

- Understand patients' willingness to participate in a hypothetical randomized trial comparing standard GC practice to personalized GC via a risk model in development known as LFSPRO

Methods

- Eligibility Criteria:
    - English-speaking
    - 15 years of age or older
    - Parent/guardian of those under age 15
    - Underwent GC for *TP53* genetic testing and/or tested positive for a PV/LPV in *TP53*
- Invited by secure email to complete questionnaire

Questionnaire Details
- Demographic and clinical characteristic details
- Likert scale responses regarding hypothetical trial participation
- Perceived benefits and barriers to research participation

Statistical Analysis
- Descriptive summary statistics for survey responses
- Qualitative analysis for open ended (ATLAS.ti Scientific Software Development GMbH, Berlin).

Methods (cont.)

- Hypothetical clinical trial presented with two types of post-disclosure GC:

Approach One
- Standard GC
    - Generic risk prediction
    - Routine surveillance recommendations

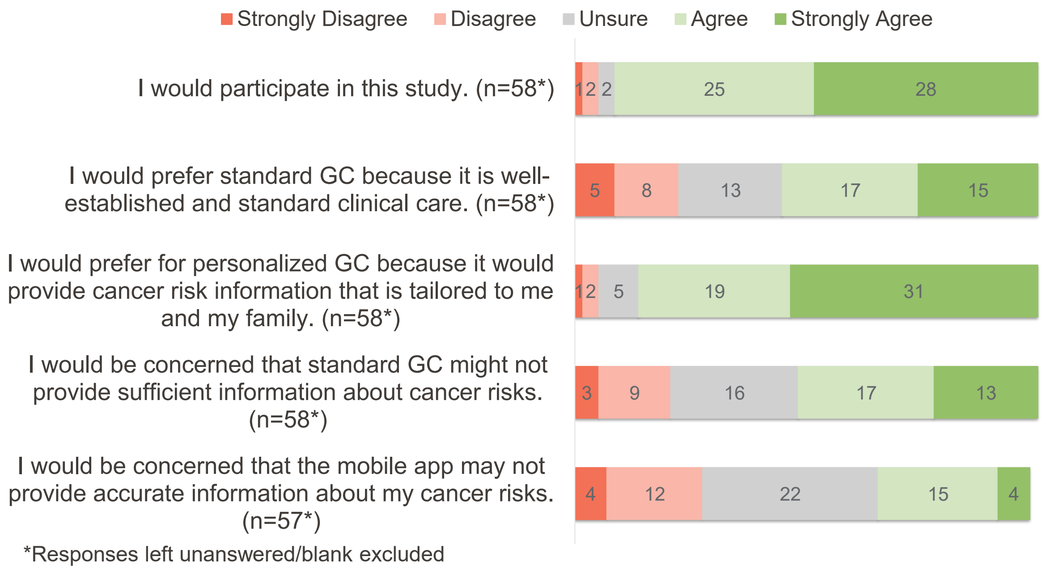
Approach Two
- Personalized GC
    - Informed by LFSPRO data (mobile app)
    - Individual cancer risks

Results

Response rate was 17.9% (65/364). 22% (14/65) identified their gender as female, 3.1% (2/65) as male and 75.4% (49/65) did not answer. 21.5% (14/65) identified their race/ethnicity as white, non-Hispanic and 3.1% as Black, and 75.4% (49/65) did not answer.

Most participants, 91.4% (53/58), strongly agreed or agreed to participate in the hypothetical. 75.4% (43/57) reported they would not be uncomfortable being randomly assigned to either study group (Standard GC vs. Personalized GC). The preferences and concerns to participate in the varying approaches are summarized in Figure 1.

Figure 1. Participation Responses



*Responses left unanswered/blank excluded

Results

Open response themes for trial participation are outlined in Figure 2.

Figure 2. Themes Associated with Trial Participation

Reasons for participation (n=46)
1. Desire to help others (20/46)
2. Want additional information to help their own health management (18/46)
3. Want to improve research and knowledge about LFS (16/46)
4. Want to help their own family (15/46)
Reasons against participation (n=23)
1. Logistics (11/23)
2. Concern for accuracy (5/23)
3. General risks are "good enough" (4/23)
4. Concern for personal information to be used (3/23)
5. Emotional toll (3/23)
6. Preference for personal conversation over apps (2/23)

Conclusion

Despite the low response rate, individuals in this study report interest and willingness to participate in a hypothetical randomized trial comparing standard GC and personalized GC. Most individuals would prefer personalized GC and risk assessment. The interest in a personalized risk assessment application in this population is high. Future studies to demonstrate the clinical utility of such an application are the next steps.

References

1) Li, F.P., et al., *A cancer family syndrome in twenty-four kindreds.* Cancer Res, 1988. 48(18): p. 5358-62.
2) Nguyen, N.H., et al., *LFSPROShiny: An Interactive R/Shiny App for Prediction and Visualization of Cancer Risks in Families With Deleterious Germline TP53 Mutations.* JCO Clin Cancer Inform, 2024. **8**: p. e2300167.

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