Author's response to reviews

Title: Patient experiences living with pancreatic cancer risk

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Author's response to reviews: see over
We thank the reviewers for their detailed comments. We have addressed each point within the manuscript. Changes within the text are indicated in bold text. Responses to each comment are detailed below and include the page number and line where the change was made. The bolded text is the change that was made in the manuscript. The entire manuscript has been reviewed for grammar and punctuation and edits have been made throughout for clarification and consistency.

Reviewer 1

Major Compulsory Revisions

1. **Description of recruitment and eligibility criteria:** The methods section has been updated on pages 5-6 lines 17-4 to describe recruitment strategies and sample characteristics. Participants were recruited from the Gastrointestinal Cancer Genetics and Prevention Program either in person at a scheduled clinic visit or over the telephone by clinical staff that were part of the research team. Eligible participants were over the age of 21 and did not have a PancCa diagnosis. Participants all had personal, genetic, or familial factors that implicated elevated PancCa risk, as verified by medical record review. Specifically, all participants came from a unique family in which two or more members had a diagnosis of PancCa, and were first degree relatives of one of the affected cases, or the participant had a known hereditary cancer syndrome (based on germline genetic testing demonstrating a pathogenic mutation) that is associated with elevated pancreatic cancer risk plus any family history of PancCa. Written informed consent was completed prior to each interview.

   Additionally, the sample has been described in greater detail in the results on page 7 lines 15-23 in addition to the already present table. Limited personal information has been shared in the manuscript to protect the identity of the sample, which is a small and select group of individuals.

   **Forty eligible patients were approached to participate in the study, 16 were lost to follow-up and 5 declined. Nineteen participants (9 male and 10 female) consented to the study and were interviewed, with interviews lasting 60 to 120 minutes. Table 1 describes the study sample; including information pertaining to personal, genetic, and family history. The sample had a median of 3 (range 2-6) affected individuals within the family. Cancers of the breast, ovaries, colon, prostate, stomach and melanoma also were mentioned as occurring within the families; breast and ovarian were most common.**

2. **Qualifications of interviewer:** This has been briefly addressed under study and process on page 6 lines 8-9. The first author, Dr. Underhill, completed all interviews and has been an author on 6 manuscripts presenting the results of qualitative research, 4 of which she is first author. Additionally, she has extensive doctoral training in qualitative methods and post-doctoral experience and training. Dr. Berry, second author on the manuscript, is also an expert in qualitative methods and assisted with the study process and manuscript presentation.

   **Data were collected through a single one-on-one, in person interview conducted by the first author (MU) who is trained and experienced in qualitative methods.**
3. In the Interview guide additional description of the interview guide is warranted with regard to topics beyond the initial experience of learning at-risk status: This has been addressed under study and process on page 6 lines 9-18.

The semi-structured interviews began by asking participants to “Think back to when you first learned that you were at increased risk for PancCa and describe that experience.” The interviewer prompted discussion of the following topics if the participant did not discuss the topic independently: 1). What does PancCa risk mean to you?; 2) What information is important for you to know about PancCa risk?; 3) How do you feel about PancCa screening and what, if any, screenings have you had?; and 4) What advice would you give someone else living with PancCa risk.? All participants were asked to discuss any additional relevant information not covered in the questions at the conclusion of the interview.

4. More information regarding results verification by expert team consensus is required as this is unusual for qualitative research: We agree with Reviewer 1 that the patient experience was the primary goal of the study and results – these were not altered in any way. Our statement of the verification of results by expert team consensus referred to the data analysis phase, and specifically the decision about when there was saturation of themes in the patient experience and if the emerging themes were consistent with existing literature and clinical experience. This has been clarified under analysis on page 7 lines 7-11.

New participants were enrolled and data collected until saturation of themes, or redundancy in data, occurred [22]. After data were analyzed, results were verified through comparison to existing literature and by consensus of the research team that consisted of clinicians and researchers.

5. Results Theme 2: There are three perspectives described in the text in terms of the subtheme “Changing approaches to health” ie, living more healthfully, live in the moment, questioning whether changes would truly make a difference, but the data example in Table 2 only reflects living more healthfully.; could the authors add to the table additional quotes to reflect the other two perspectives?

Exemplar quotations have been added to Table 2. A difference between respondent characteristics has been elaborated upon in the text on page 11 lines 5-10.

One participant described alcohol consumption as a potential risk factor for PancCa, but described enjoying alcohol and stated “...it’s not as if I put down the wine.” Living each day to the fullest were mentioned by those who have had illness in the past, including a cancer diagnosis. Those individuals who had not had a personal diagnosis of cancer spoke more often about modifying risk factors to avoid cancer.

6. Results The idea of "Doing something" appears as a subtheme under themes 2 and 3. It seems that undergoing screening (theme 3) is a subset of them 2 (seeing a way to control cancer risk). A clearer distinction needs to be brought forth about how distinctions were made between doing something to avoid cancer and doing something to catch cancer early. The text and table has been updated on page 11 lines 11-22 to make a better distinction and theme title wording has been updated to "Avoiding a similar familial cancer experience".

Avoiding a similar familial cancer experience. Participants described a need to take action related to their knowledge of PancCa risk which is what led them to seek care at the cancer center. The goal discussed by participants was to avoid a cancer death experience as seen within the family. There were not stories of survivorship within the participant's families and all had witnessed one or more loved ones die of the disease. PancCa had meant pain and suffering.
One participant felt so strongly that seeking specialty care was important and despite a limited budget, coming to the cancer center was a priority. Taking part in research was another strategy that participants described to avoiding a similar experience as in the past and helping other family members avoid this same cancer death. As one woman described “...this [research participation] isn’t really for me. It is for my children and my grandchild.”

Additional edits were made to this aim for clarification on page 10 lines 9-15

Wanting to be taken care of. Participants felt “taken care of” by PancCa expert clinicians and “grateful” for the opportunity to be cared for in a way that deceased family members had not experienced. Participants aimed to avoid similar experiences of a PancCa related death, and felt that access to specialists offered more “control” for both early detection and prevention. Participants discussed that having access to specialists was not a resource available to their family members in the past and therefore they were grateful for the resources.

7. Limitations: The limitations section has been updated on page 18 lines 9-14.
   We acknowledge that the experiences of individuals taking part in a high risk cancer prevention program may be different from experiences in other clinical settings. Most work with this population is currently being done in academic medical centers and therefore this study is just a first step in describing the needs of this population. Future work will need to expand recruitment to outside of the academic setting.

8. Range of time since death of the most recently deceased relative: These data were not specifically collected. However, after going back through the medical record and the interview transcripts, timeframes since death were able to be extracted for 15 of the participants. A paragraph describing these findings was added to Theme 1 under grieving on pages 8-9 lines 24-2. Most participants who specified a timeframe, though vividly describing their experiences, lost loved ones to pancreatic cancer years, and even decades, prior.

   Of the 15 participants who described a timeframe for witnessing PancCa in the family, only 2 had experiences within the past year. All others told detailed stories of lost loved ones from years, even decades, prior. The four individuals who did not describe a timeframe for witnessing PancCa in the family, shared stories in the past tense, not the present.

   Additional edits have been made throughout the results section for clarification.

   Minor Essential Revisions
   All comments have been addressed. The three major themes have been annotated, the sentence in the results section has been moved to the methods section (page 5). All participants were from unique families and this is now stated under sample on page 5 line 23.

   Discretionary Revisions
   1. Yes, only one individual chose to not undergo screening. The participant quoted did choose screening but was questioning the efficacy. A sentence to clarify this has been added on page 12 lines 20-21.
While this participant chose to undergo screening at the time of the interview, he questioned the uncertainty of what would be done with the information from the screening outcome.

2. The discussion has been updated and the literature mentioned added to the text on page 17 lines 12-23.

These individuals living with familial PanCa risk were highly engaged in the health care system, and actively seeking self-care information. Lawson & Flocke (2009) describe this as a “teachable moment” where individuals have a significant life event, such as witnessing a family member die of cancer or learning of one’s own risk for cancer, where they are more likely to make a personal change[27]. Breitkopf and colleagues (2014) further validate this model in a sample of family members of persons with colo-rectal cancer and find that participants who are family members of individuals who have or had a diagnosis of colorectal cancer are willing to take part in a cancer prevention intervention [28]. Therefore, future research interventions targeting this population of caregivers of individuals with PancCa could have the potential to positively impact both medical and psychosocial outcomes.

Minor issues not for publication

All comments have been addressed in the manuscript and the manuscript has been reviewed by a copy editor for grammar and punctuation.

Reviewer 2

Major Compulsory Revisions

1. Description of recruitment and eligibility criteria: The methods section has been updated on pages 5-6 lines 17-4 to describe recruitment strategies and sample characteristics. Participants were recruited from the Gastrointestinal Cancer Genetics and Prevention Program either in person at a scheduled clinic visit or over the telephone by clinical staff that were part of the research team. Eligible participants were over the age of 21 and did not have a PancCa diagnosis. Participants all had personal, genetic, or familial factors that implicated elevated PancCa risk, as verified by medical record review. Specifically, all participants came from a unique family in which two or more members had a diagnosis of PancCa, and were first degree relatives of one of the affected cases, or the participant had a known hereditary cancer syndrome (based on germline genetic testing demonstrating a pathogenic mutation) that is associated with elevated pancreatic cancer risk plus any family history of PancCa. Written informed consent was completed prior to each interview.

2. Description data collection: This has been addressed under study and process on page 6 lines 9-18. The semi-structured interviews began by asking participants to “Think back to when you first learned that you were at increased risk for PancCa and describe that experience.” The interviewer prompted discussion of the following topics if the participant did not discuss the topic independently: 1) What does PancCa risk mean to you?; 2) What information is important for you to know about PancCa risk?; 3) How do you feel about PancCa screening and what, if any, screenings have you had?; and 4) What advice would you give someone else living with PancCa risk.? All participants were asked to discuss any additional relevant information not covered in the questions at the conclusion of the interview.

Additionally, we have added a statement about data collection on page 7 lines 7-11.
New participants were enrolled and data collected until saturation of themes, or redundancy in data, occurred [22]. After data were analyzed, results were verified through comparison to existing literature and by consensus of the research team that consisted of clinicians and researchers.

3. **Results:** Per comments from reviewer 1, the results have been updated and additional quotations added to the table. We have softened the language on page 8 line 3 about quotations. Additionally, we have clarified in the manuscript on page 12 lines 2-3 that screening meant endoscopic ultrasound and MRI.

4. **Organization of the Discussion:** The discussion has been restructured to reflect the study aims. We agree that the points brought up by the reviewer are important. However some of the points are outside of the scope of this single qualitative study. Therefore, we have structured the discussion in response to the study aims and have incorporated additional updates based on reviewer 1. The entire discussion has been restructured on pages 13-16. We have added additional literature.

5. **Conclusion:** The conclusion statement has been modified on page 18 lines 13-20.

Study results begin to describe the lived experience of individuals with PancCa risk. Through this research we have uncovered important variables to further understand, measure, and intervene upon in future research, such as fear, worry, and family experience. Distress related to risk was not described as ongoing, but occurred around specific and salient time points that brought risk to the forefront. Individuals with familial PancCa risk may have a unique experience compared to other hereditary cancer syndromes due to the high mortality of the disease and uncertainty related to prevention and early detection outcomes.

**Minor grammatical and stylistic errors**

All comments have been addressed. The manuscript has been reviewed by a copy editor for grammar and punctuation.