Author’s response to reviews

Title: Genetic counselling and personalised risk assessment in the Australian pancreatic cancer screening program

Authors:
Tanya Dwarte (t.dwarte@garvan.com.au)
Skye Mckay (skye.mckay@uts.edu.au)
Amber Johns (a.johns@garvan.org.au)
Katherine Tucker (kathy.tucker@health.nsw.gov.au)
Allan Spigelman (allan.spigelman@svha.org.au)
David Williams (dwilliams@stvincents.com.au)
ALINA STOITA (alinastoita@yahoo.com.au;alina.stoita@svha.org.au)

Version: 1 Date: 10 Oct 2019

Author’s response to reviews:

In response to Reviewer 1, we have the following comments:

Thank you for your positive assessment of our paper.

1. Request for confidence intervals: We have included the confidence intervals in table 3 as requested. PancPRO reports single values for 5-year/lifetime pancreas cancer risks and probability of a pancreas cancer susceptibility gene. We indicate the range in participant risk-estimates by showing the lowest and highest values within each family history subgroup.

2. Justification for pancreatic cancer surveillance: We have addressed that population screening is not feasible nor recommended (line 79-81), though may be of benefit for high-risk populations in research setting. We have added the results of a systematic review on benefits of PC screening in HRI and the results of recently study on long term surveillance (16 years) surveillance (lines 86-93 of the introduction). Although we recognize the importance of this issue, this was not the focus of the current manuscript, and we plan to prepare a follow-up manuscript addressing the clinical outcomes of our participants undergoing surveillance and further analysis of international data covering these aspects.

3. Shorten/two papers: We agree this is a big topic to be cover in detail in one original article. Genetic counselling, genetic testing and risk assessment are all covered by genetic cancer services in one session hence we felt that all information should be presented succinct in one paper. We have shortened the manuscript to make it more concise and focused on the essential points as indicated by track
changes without significantly compromising readability and content.
4. Addressing mismatch around patient expectations and reality in genetic counselling: Although genetic counselling is a study prerequisite, participants are referred to external genetic counselling services (their closest/preferred FCC). We address the range in timing of counselling (on/off protocol and year of recruitment) and that multiple services/counsellors performed genetic counselling in the limitations of the study, contributing to variation in counseling provision. We have added in the conclusion that genetic counselling guidelines will be updated to reflect this study data to aid FCCs to further explore perceived risk, estimated risk, and current evidence for the clinical benefit of screening during genetic counselling (line 508). We view this manuscript as essential preliminary data to inform FCCs of participant feedback and areas of improvement. Disclosure of PancPRO risk estimates to participants/FCCs is also being considered but is expected to be used based on clinical discretion, and uncertainty regarding accuracy of the estimate will need to be acknowledged until the validity of PancPRO is established in other studies.
5. More structured reasons for declining participation: We have addressed this more clearly in the discussion (line 337-359). Majority were “passive decliners” meaning they did not return their recruitment paperwork and were lost to follow-up. The clinical research coordinator made only two repeat contact attempts. Unfortunately, it was not possible to obtain further information from passive decliners to indicate why they chose not to proceed with screening, though we noted that this would have been valuable (line 460).

In response to reviewer 2, we have the following comments:
1. Thank you for your positive evaluation of our paper. We have reviewed the lines indicated in the manuscript and accepted the previously entered track changes.

In addition to these changes, we also wish to highlight corrections to Fig. 2 which were identified as some participants were counted twice.

Thank you for considering the revised manuscript for publication.