Author’s response to reviews

Title: The Prospective Lynch Syndrome Database reports enable evidence-based personal precision health care

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Response to referees

Referee 1

The submitted manuscript is very valuable and it is extremely important to continue PLSD activities. In my opinion this summarization done by author is well done, although I would like to suggest some improvements: 1. Tables 1 and 2 should present not only percentages by exact numbers. 2.

Response:

Both tables are copying calculated cumulative incidences by segregation analyses, cumulative incidences as described in the PLSD papers references, or survival by K-M algorithm, all of which returns fractions (percentages) only. Interpreting the question as asking for precision of the point estimates, the 95% confidence intervals for the point estimates are now copied into Table 1. Table 2 is demonstrating the products of cumulative incidences and survival estimates both having confidence intervals declared in the references from which the point estimates are copied, to arrive at point estimates for dying from cancer in the various organs. The intention is to demonstrate that CRC and gyn cancer no longer are the only major causes of death in LS. A discussion of the precision of the point estimates arrived at in Table 2 is outside the scope of the current paper. This will be addressed in future studies.

Basing on existing data it cannot be excluded that significant proportion of cancers can be however excluded by polypectomies. This is the question of numbers and time. Data obviously also suggest that large proportion of CRCs can be developed from non-polyposis lesions. Thus, more complex explanation of colorectal carcinogenesis should be at least considered.

Response:

Agreed. All contributors have been asked for details on adenomectomies, but the reports received to the PLSD ar so far not not complete enough for detailed analyses. The current paper is restricted to what of interest PLSD has reported, a discussion of what of interest we so far have
not managed to report is outside the current format and word count for the paper is already exceeding the editorial guidelines.

More profound analysis concerning ovarian cancer in Lynch Syndrome should be presented. I would like to the author to write more about ovarian cancer cases in PLSD.

Response: Agreed. We are currently putting together a detailed report on uptake of risk-reducing hysterectomy and oophorectomy, the following sentence is now added to the text: “An analysis of prophylactic hysterectomy and oophorectomy reported to the PLSD and current clinical guidelines for risk-reducing surgery in the collaborating centres are currently in progress.”

Referee 2

This is an excellent paper describing how "Prospective Lynch Syndrome Database" contributed to significant progress in scientific and medical on Lynch syndrome. I believe it will attract wide audience of the readers. This has chances to be frequently mentioned in subsequent studies devoted to various aspects of hereditary cancers.

Response:

Thanks.