**Author’s response to reviews**

**Title:** Pediatric Reporting of Genomic Results Study (PROGRESS): A mixed-methods, longitudinal, observational cohort study protocol to explore disclosure of actionable adult- and pediatric-onset genomic variants to minors and their parents

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Ana Donnelly, PhD
Manuscript Editor
BMC Pediatrics

Dr. Ana Donnelly,

Thank you for provisionally recommending the manuscript entitled “Pediatric Reporting of Genomic Results Study (PROGRESS): A mixed-methods, longitudinal, observational cohort study protocol to explore disclosure of actionable adult- and pediatric-onset genomic variants to minors and their parents” (BPED-D-20-00291). Responses to your comments are summarized below, with corresponding revisions in the revised manuscript.

We hope these responses sufficiently address your comments reviewers’ and would be happy to address any additional concerns you may have.

Sincerely,

Juliann M. Savatt, MS, LGC

Editor Comments:

1. Please include the words Study Protocol in the title so readers can identify the manuscript as a Study Protocol. Suggestion: Reporting of Genomic Results Study (PROGRESS): A mixed-methods, longitudinal, observational cohort study protocol to explore disclosure of actionable adult- and pediatric-onset genomic variants to minors and their parents.

   We have edited the title accordingly.

2. Methods/Design - Please include the study design in this section - the design is described in the title but it is not described in the Methods.

   The description of the study design, “a mixed-methods, longitudinal, observational cohort study,” has been added to the methods section on page 9, line 5.
3. Sample size calculation - Please provide the references used to reach the planned Sample Size and provide Power calculation for the sample size presented.

   The rate of pathogenic/likely pathogenic variants in the 60 genes of interest in MyCode participants (2.3%) is derived from the current results return experience in adult MyCode participants. We now reference the MyCode Results Reported website that summarizes this experience to date (page 12, line 23-24). The rate of consent for additional studies (65%) is based on unpublished data. We have highlighted that this value is based on internal data in the text (page 13, line 3).

   Power calculations have been moved from the data analysis section to the “sample size” section beginning on page 13, line 13. We have also added a detailed data analysis section to describe our methodology more completely.

4. Funding - Please include statement to the effect that the funding body has peer-reviewed the protocol as part of the grant award process.

   In our declarations, we have now stated, “The funding body peer-reviewed the protocol as part of the grant award process” (page 23, lines 8-9).

5. Please include a section 'Study status' under Methods/Design and detail the status of the study at the moment of submission.

   A “Study Status” section has been added on page 19, line 14. This section summarizes that 5212 pediatric participants have consented to MyCode and provided a sample for genomic analysis. Of those, 1878 have undergone exome sequencing as part of the DiscovEHR collaboration with Regeneron Genetics. Review of research sequence data has shown that seven should be sent for clinical confirmation of an expected pathogenic/likely pathogenic variant in and one of the 60 genes designated as actionable by MyCode. To date, seven parents of minors have been approached for the study none have consented to participate.

6. At this moment you can remove the IRB document and Funding proof from supplementary file.

   The IRB documentation and funding proof have been removed.