

## Reviewer Report

**Title: PRSice-2: Polygenic Risk Score software for biobank-scale data**

**Version: Revision 1**      **Date: 3/25/2019**

**Reviewer name: Daniel Belsky**

### Reviewer Comments to Author:

The authors have addressed my comments.

I have to say I am surprised by the results of the simulation analysis that finds polygenic scores computed using the PRSice2 and LassoSum methods are substantially more predictive of their target phenotypes as compared to the LDpred method. I think I understand why LassoSum should perform better than the other methods. It's based on multivariate regressions rather than a series of univariate regressions. But I am unclear how PRSice2 is deriving its advantage over LDpred. Some explanation of this finding through discussion of the differences between these tools would help clarify the result.

### Level of Interest

Please indicate how interesting you found the manuscript: Choose an item.

### Quality of Written English

Please indicate the quality of language in the manuscript: Choose an item.

### Declaration of Competing Interests

Please complete a declaration of competing interests, considering the following questions:

- Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
- Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
- Do you hold or are you currently applying for any patents relating to the content of the manuscript?
- Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?
- Do you have any other financial competing interests?
- Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (<http://creativecommons.org/licenses/by/4.0/>). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal

To further support our reviewers, we have joined with Publons, where you can gain additional credit to further highlight your hard work (see: <https://publons.com/journal/530/gigascience>). On publication of this paper, your review will be automatically added to Publons, you can then choose whether or not to claim your Publons credit. I understand this statement.

Yes Choose an item.