https://pubpeer.com/publications/D780DD5C4D665BBC415F45C707D0C4

Hi,

Thank you very much for communicating details about your research!

Because the journal doesn't have a comment system, I wanted to add a comment in this system.

First, here a comment on the earlier preprint:

https://www.biorxiv.org/content/10.1101/2020.04.29.068452v2#disgus thread

So, I will try not to over-emphasize the question of *directly measured* genotypes versus Minimac4 imputed genotypes, since I asked that before.

I also have a comment on another recent paper (other authors describing lcWGS versus genotyping arrays):

https://www.cell.com/ajhg/fulltext/S0002-9297(21)00096-3#comments-heading

The questions posted in that comment are a little different (although some overlap the preprint version of this paper). If anybody cannot access the AJHG comment, I also have a draft posted here.

The <u>Martin et al. 2021</u> paper mentions Gencove worked relatively better at lower coverage, and BEAGLE worked relatively better at the 4-6x WGS (with that being the highest imputed accuracy reported in Table S4 or Table S5).

So, I believe these would be the questions with updated information:

- a) Since the preprint post, I have added at least 1 extra example of a lcWGS imputation having noticeable problems at 0.1x-0.5x. While hard to tell the exact genomic coverage (filtering adapters and non-genomic sequence) without the raw data, I am guessing the cat lcWGS may be roughly 0.2x-0.3x. I think might be roughly similar to the leftmost point in *Figure 1*.
 - My impression from the Martin et al. 2021 paper was that some my ~0.5x lcWGS results (for myself and for my cat) might have been improved with **higher coverage lcWGS**. Do you think that is a fair assessment?
- b) In the Martin et al. 2021 paper, the GSA had the lowest performance among all of the arrays. For example, in that paper, I would expect the Omni 2.5 array to outperform 0.5x to 2x lcWGS (with either Gencove or BEAGLE). I believe was also noted in the earlier preprint comment, although that was in reference to the EUR and ASW interactive plots from the GLIMPSE paper.

So, you do specifically mention the GSA array in the abstract, but I do not believe the title is universally true (even if you look at SNP chip genotypes that I believe include imputations).

Is there anything that I might have misunderstood?

Best Wishes,

Charles