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

Hi,

Thank you very much for putting together this paper!

I originally had a longer comment, but I thought that it was hard to read. So, in a sense, I am glad that it got flagged so that I could focus on posting a shorter comment in this system.

For context and details, you can see something similar to that earlier version here. For example, the FDA MedWatch report that I submitted for my Nebula lcWGS results (before they were discontinued) is registered in the MAUDE database under MW5093887.

However, I think these are the most important questions to ask:

1) I have concerns about the consumer lcWGS that I have received, such that I would be concerned about use for medical applications. However, I thought results like **Figure 4 and Table S4/S5** in this paper might match my experiences, while also giving a reason not to unfairly discount any result labeled as "lcWGS".

In other words, do you think some of the problems that I encountered were an issue of **how "low" the coverage sequencing is (such as 0.1x-0.5x, versus 4-6x)**?

Also, do you think the **~0.5x** sequencing is a fair representation of what you see currently available to consumers, across various companies?

2) For your comparisons, do you always **include imputations** (both lcWGS and SNP chip)?

In other words, for medically actionable results, I might group **imputed** SNP chip *or* lcWGS in one category, and **directly measured** SNP chip genotypes (perhaps for tested populations) in another category.

So, I think there are at least some situations where I would prefer a SNP chip with measured genotypes (without any imputations) over ~0.5x lcWGS. Do you think this is fair?

Thank you again for your contributions to the field!

Sincerely,

Charles