I received an e-mail on 6/18/2020 indicating that there was a “new” 0.4x low coverage Whole Genome Sequencing (lcWGS) option available from Nebula. I didn’t think this was true, since I had an earlier lcWGS from Nebula. However, there was a period of time after my previous FDA MedWatch report (**MW5093887**) that the lcWGS data was not available from Nebula.

So, I ordered another lcWGS sample.

This time, the coverage was approximately 2.5x higher, and my APOE genotype was called correctly. I would guess this could be random variation in small libraries, but I am not 100% certain that the average coverage was not increased in the re-release.

Even if you only focus on my newer sample, you can see the table with percentiles for my new samples. So, I am not sure if some of the reports should be considered “medical”.

For example, in my 23andMe report, non-genetic factors contribute more than genetic factors to my risk for Type 2 Diabetes (such as BMI, etc.). Possibly similarly, my “critical” COVID-19 risk was average, but I thought age was one of the strongest risk factors (and I would therefore consider myself lower risk). If being used to make medical decisions, then I think that would need to be made clear. Plus, if you use my earlier lcWGS sample, my percentage for “critical” COVID-19 risk changes from 49th to 29th. So, I would say there is also an issue with using lcWGS for the Polygenic Risk Score analysis, which might be an even bigger problem than non-genetic risk factors in this specific example.

In general, you can see the new results and a comparison to earlier results here:

https://github.com/cwarden45/DTC\_Scripts/tree/master/Nebula/Sample2

For example, the Pearson correlation coefficient between the PRS percentiles for the 2 replicates is 0.8. However, some differences were very large: for example, for the “*Bone mineral density (Kemp, 2017)*” PRS, the largest percentile difference being 2% for one replicate and 99% for the other. I double-checked to confirm that this was not a typo on my end (for the PRS with the difference in percentiles of 97% for the 2 replicates).

To be fair, Nebula describes the “Basic” lcWGS coverage as “Medium” accuracy, and the regular WGS coverage as “High” accuracy. However, I was not sure how clear this was made to customers, or how others intended to use the results.