Reviewer Report

Title: Korea4K: whole genome sequences of 4,157 Koreans with 107 phenotypes derived from extensive health check-ups

Version: Revision 1 **Date:** 12/31/2023

Reviewer name: Pui-Yan Kwok

Reviewer Comments to Author:

The authors made attempts to address the issues raised previously but did not do so adequately.
1. Using the same GWAS cutoff of P <5E-8 and adding the FDR correction (Benjamini-Hochberg) does not solve the problem of multiple testing using whole genome sequencing data (where there are orders of magnitude more variants than those on typical SNP arrays) for the study. With clinical data available for only 2,262 samples, each phenotype under study will have a very small number of individuals, making the result of 2,314 variants from 30 clinical traits with significant association highly suspect. The authors should consult statisticians with experience using whole genome sequencing data for association studies to come up with a better statistical study design.
2. The authors acknowledge that using the newer reference will be a good approach but will not do so because the "T2T reference lacks enough annotation data" is not an adequate response. The point is to have the best variant calls for the Korea4K data, annotation is irrelevant until variants with significant association are identified. Claiming that they will do so in future versions of the project diminishes the significance of the current manuscript.

Methods

Are the methods appropriate to the aims of the study, are they well described, and are necessary controls included? Choose an item.

Conclusions

Are the conclusions adequately supported by the data shown? Choose an item.

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Statistics

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