

What's the Value of 23andMe's Genetic Risk Calculation for Diabetes?



By *Chuck Dinerstein* — March 18, 2019



Courtesy of Cedric Husler [1]

I was skeptical about the latest announcement by 23andMe surrounding the release of their new report describing to its subscribers their risk of Type 2 diabetes. The statement, last week has garnered some commentary within the medical community including a good discussion by an academic family practitioner in [The Conversation](#) [2]. From my point of view, there are two considerations, the “science” behind the report and the value to patients and physicians.

The science

The scientific basis for 23andMe’s reporting is as good as any to be found in a peer-reviewed journal. It is summarized in a [whitepaper](#) [3] which is not immediately identifiable on the website and searching for it let alone reading it may be more than many want to do. For those who have followed my reporting on Genome-Wide Association Studies (GWAS), this is their version.

For those of you late to the party, GWAS look at genetic variations of individuals with a specific phenotype, like people who wear eyeglasses or go to college or in this case have been told they have type 2 diabetes. By a variety of sophisticated statistical techniques, a group of genetic variations is identified that are more likely to be present in those phenotypical individuals. The genetic differences are found not in one gene, but many, in the range of 1000’s of genes. A polygenic score (PGS) is calculated that indicates to what degree your genetic variations match the genetic variations characterized for the phenotype.

As with all GWAS studies, the polygenic score reflects the humans studied; this is particularly important because 23andMe, like the UK Biobank, has samples predominantly from Europeans and the scoring is not readily transferable to African Americans, Asians or Hispanics. 23andMe

“calibrated” or adjusted the polygenic scoring for these other groups, but recognizes that only more genetic data from these groups will resolve the problem – and yes, their website indicates they have outreach programs to those communities.

How well does the test perform and what do the results mean?

With the polygenic scoring in hand, 23andMe had to determine a cutoff value for what they describe as “typical likelihood” or “increased likelihood.” Too low a cut-off and the number of false positives increases, creating needless worry for individuals with no real increased risk. Too high a cutoff and the false negatives increase, creating needless complacency for individuals with a real risk. The discriminatory ability of a test, to thread the needle between too many false positives and negatives is described by a measure called the area under the curve or AUC. (1 is a perfect test no false positive or negatives, .5 is the same as tossing a coin)

Clinically, being overweight contributes to the risk of type 2 diabetes and 23andMe used this accepted clinical risk factor in determining the cutoff for their polygenic score. Under the best of conditions, e.g., white Europeans, the polygenic score’s AUC or discrimination is about .68 - better than a coin toss, but certainly not diagnostic. The PGS’s performance is worst for African Americans, at .59, with the other racial groups lying between the two values. To give you some comparative value, the AUC for mammography is .91, so it would be fair to characterize this new report as a rough screening tool, more medical edutainment.

When 23andMe indicates that you have a genetic “increased likelihood” of Type 2 diabetes, it is going to be correct roughly 68% of the time, and that risk is greater than you might have if you were merely overweight. Now if that sentence leaves you confused as to what to do, imagine how it would read to the general public or to physicians who trained long before GWAS was a concept let alone an acronym.

What’s a patient to do?

Whether you have or have not an “increased likelihood” of Type 2 diabetes requires some explanation, some context. And 23andMe is to be congratulated for spending the time to try and get that explanation right; making use of input from the scientific literature, care providers, researchers, and user testing sessions. It is far more informative than the copies of medical tests that doctors often provide.

For those at “increased likelihood” they report the remaining lifetime risk for developing diabetes, a risk that diminishes with increasing age; for forty-somethings “increased likelihood” means a 37% risk in the remainder of your life, for a seventy-year-old, the risk is 11%.

23andMe freely acknowledges that type 2 diabetes is not purely genetic; GWAS derived polygenic scores, in general, reflect about 30% of the risk, lifestyle, the “dog whistle” for diet and exercise make a significant contribution. And while you are stuck with your genes, you can modify your diet and exercise. To begin a discussion, they provide a “prevalence explorer” tool that allows one to see the impact of altering these lifestyle factors on their risk; providing an answer to the question of whether losing weight, eating differently and exercise will make a difference. This is perhaps the report’s real value; to the extent that this is a personalized motivational tool rather than a clinical

screening test 23andMe is providing a real service.

What's a physician to do?

You would suspect that those individuals paying for this additional information are motivated to lead healthy lives and while that may be the case, only about a third of 23andMe's customers share the reports with their physicians. And in many cases, physicians are unprepared to answer questions and discuss the meaning of the report. For many of us, it was not covered in medical school. [1]

An "increased likelihood" is not a reason or indication to proceed with more definitive testing for type 2 diabetes or "pre-diabetes." The physician's visceral response to reach for a confirming lab test, to do something, is in my mind, the most significant concern. It is just not a screening tool and if used in that way will create considerable expense with little value.

It is an engagement tool, creating an opportunity for discussion with a motivated patient; they ordered the report, paid for it and brought the results to their physician – it doesn't get much more motivated in the walking well. There are two approaches to guiding population health. You can nudge and regulate the population by taxing sugary beverages and labeling everything, or you can help one individual at a time to adjust their life based on what their genes might be telling them. Personalized medicine is about the latter, and we should make use of the opening that 23andMe provides.

[1] A webinar and other educational outreach by 23andMe to its physician community is planned for the next month or so.

Sources: In addition to the whitepaper I had an opportunity to discuss the report and its underlying science with a team from 23andMe, Liza Crenshaw, Esther Kim, Pharm. D, and Altovise Ewing, Ph.D.

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Links

[1] <https://www.flickr.com/photos/keepthebyte/2231596646>

[2] <https://theconversation.com/can-a-genetic-test-predict-if-you-will-develop-type-2-diabetes-113343>

[3] https://permalinks.23andme.com/pdf/23_19-Type2Diabetes_March2019.pdf