Published in final edited form as:

J Clin Oncol. 2020 January 20; 38(3): 284. doi:10.1200/JCO.19.02347.

Reply to Patel and McLeod

Madison K. Kilbride, PhD, Susan M. Domchek, MD, Angela R. Bradbury, MD

Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA

We thank Patel and McLeod¹ for their thoughtful engagement with our recent Commentary in *Journal of Clinical Oncology*.² In their correspondence, Patel and McLeod echo our concerns about the regulatory language of the US Food and Drug Administration (FDA) as it pertains to direct-to-consumer (DTC) genetic testing.¹ In particular, they argue that greater clarity is needed for DTC pharmacogenetic tests, including the pharmacogenetic test from 23andMe. To our knowledge, this test is not yet being offered as part of the Health and Ancestry Service of 23andMe. The company did, however, receive FDA authorization in October 2018 to market its Personal Genome Service Pharmacogenetic Reports.³ This test, which may become available to consumers in the near future, genotypes 33 variants in 8 genes related to drug metabolism.³

Although we chose to focus on the *BRCA* test from 23andMe as a case study, we agree with Patel and McLeod¹ that many of the concerns that we raised extend to DTC pharmacogenetic testing. We also agree that there are some important differences between the *BRCA* test from 23andMe and the company's potential pharmacogenetic offering.

Close reading of the FDA's Decision Summary for pharmacogenetic reports from 23andMe suggests that the issue of confirmatory testing may be even more complicated for DTC pharmacogenetic testing than it is for DTC *BRCA* testing.³ In considering why the FDA stresses confirmatory testing for DTC pharmacogenetic results, Patel and McLeod suggest that "the agency is not confident in the application or actionability of the DTC results."¹ Yet there may be another reason for promoting confirmatory pharmacogenetic testing that is upstream of actionability and concerns the analytic validity of the test (ie, how well the test identifies the presence or absence of a particular genetic change). We believe this interpretation finds support in the FDA's Decision Summary for the pharmacogenetic

Corresponding author: Madison K. Kilbride, PhD, Department of Medical Ethics and Health Policy, Perelman School of Medicine at the University of Pennsylvania, 423 Guardian Dr, Blockley Hall, 14th Floor, Philadelphia, PA 19104-4884; madisonk@upenn.edu.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

Disclosures provided by the authors and data availability statement (if applicable) are available with this article at DOI <https://doi.org/10.1200/JCO.19.02347>.

Reply to Patel and McLeod

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated unless otherwise noted. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Open Payments is a public database containing information reported by companies about payments made to US-licensed physicians (Open Payments).

No potential conflicts of interest were reported.

reports from 23andMe, which states that “results should be confirmed by an independent pharmacogenetic test before making any medical decisions since there is residual uncertainty associated with the analytical validation data.” As the Decision Summary explains, the uncertainty is “[d]ue to the large margin of error (ie, wide CIs), and selection bias (ie, samples were chosen from a biobank based on the variants already detected by the candidate assay).”

The discussion by Patel and McLeod¹ of pharmacogenetic testing and the need for greater clarity regarding clinical confirmatory testing aptly illustrates the complexity of this growing market. As new DTC offerings with potentially significant health implications become available, it is essential that consumers and providers understand that confirmatory testing may be needed for different reasons, depending on the nature of a test.

ACKNOWLEDGMENT

Supported by T32 training Grant No. HG009496 from the National Human Genome Research Institute (M.K.K.).

REFERENCES

1. Patel J, McLeod HL: Clarity also needed for direct-to-consumer pharmacogenetic tests. *J Clin Oncol* doi: 10.1200/JCO.19.01917
2. Kilbride MK, Domchek SM, Bradbury AR: How should patients and providers interpret the US Food and Drug Administration’s regulatory language for direct-to-consumer genetic tests? *J Clin Oncol* 10.1200/JCO.18.01418 [epub ahead of print on June 7, 2019]
3. US Food and Drug Administration: Evaluation of automatic Class III designation for the 23andMe Personal Genome Service (PGS) Pharmacogenetic Reports: Decision summary. https://www.accessdata.fda.gov/cdrh_docs/reviews/DEN180028.pdf