Science and Technology Committee
House of Commons
London
SW1A 0AA

January 14, 2020

To whom it may concern

I was privileged to be invited to attend and give evidence to the House of Commons Science and Technology Committee in October 2019, during the previous committee's inquiry into Commercial Genomics. Your predecessors requested some additional information in relation to questions 72 and 103 of the oral evidence session[1], specifically:

- Where external researchers can access the clinical evidence behind the genetic variants that 23andMe searches for
- The methodology of the consumer comprehension testing, including the number and profiles of consumers involved, whether the testing was run by 23andMe or an independent organisation, and how comprehension was gauged
- The results of this testing, and whether such testing covers all tests offered by 23andMe in the UK, and if it is repeated to ensure the results are up to date

Enclosed in this letter is additional information in relation to each of these points. An appendix, with further information pertaining to the user comprehension studies, is also attached. If you would like any further information or wish to find out more about 23andMe and commercial genomics as you begin to think about future work of the Committee, I would welcome the opportunity to meet.

Yours faithfully,

Kathy Hibbs,
Chief Legal and Regulatory Officer
23andMe

[1] Science and Technology Committee (2019), *Oral Evidence: commercial genomics, HC 33*

Additional Information requested by the Science and Technology Committee

Access to clinical evidence

The 23andMe Personal Genome Service (PGS) is the world's only consumer genetic test which offers health reports that have the US FDA's independent assurance of validity and clear results. Competitor products require a prescription from a physician, they have not undergone FDA or any other similar regulatory agency review and also do not meet the FDA's robust post market quality system requirements.

23andMe reports are not intended to diagnose any disease, tell users anything about their current state of health, or to be used to make medical decisions, including whether or not users should take a medication or how much of a medication users should take. When users purchase a 23andMe testing kit, they are provided with a package insert which provides details on intended use, important warnings and limitations, test performance, user studies and specific test information.[2]

Further information is provided to customers when they receive their results. Each health report provides users with an overview of the condition (for example age-related macular degeneration) which contains information on the genetic variants tested for, the limitations and intended uses of the report, and the other factors that influence the chance of developing the condition. The scientific details section provides further detail and includes references to relevant scientific publications which provide the peer reviewed, published clinical evidence behind the genetic variants tested.

Medical professionals can access information and report examples for all of 23andMe's genetic reports[3] to better understand the types of information that their patients may receive and wish to share with them.

Scientific standards for 23andMe's Health reports[4]

For a genetic association to be included in a curated Health report, there must be multiple sources of scientific evidence supporting the link between the genetic variant and the underlying phenotype. 23andMe also look for functional and

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[2] 23andMe, *Genetic Health Risk Reports V5 Package Insert*, available at: https://permalinks.23andme.com/pdf/PN-20-0279.pdf

[3] 23andMe, Explore 23andMe genetic reports, available at: https://medical.23andme.com/reports/

[4] Nhan, Chubb and Wu (2017), 23andMe White Paper 23-15 Scientific Standards for 23andMe's Health and Trait Reports, available at: https://permalinks.23andme.com/pdf/23-15_scientific_standards_for_curated_reports.pdf

biological evidence supporting a causative role for the variant's effect on the condition or trait. There must also be no compelling contradictory evidence refuting the genetic association. Taken together, the evidence should establish a consensus that the variant has a meaningful and real effect on the condition of interest.

The evidence supporting the genetic associations underlying the curated reports is drawn from two sources: clinical guidelines and peer-reviewed scientific publications. Clinical guidelines summarize entire bodies of evidence and thus are considered sufficient on their own in the absence of more recent contradictory evidence. The two types of studies 23andMe look for in peer-reviewed literature are clinical and functional studies. Clinical studies demonstrate an association between a variant and a specific phenotype observed in certain populations. Functional studies demonstrate the functional effects of the variant in pathologically relevant cell lines, animal models, or human subjects. Literature evidence can also include consensus statements or review articles supporting the effect of the variant or the class of variants to which it belongs.

23andMe scientists and medical professionals evaluate these published studies to make sure the findings are supported by strong study designs and appropriate methods. Some of the factors considered include:

- The study population - Is the population studied large enough to give a meaningful interpretation of the study results, and can the results be generalized to 23andMe customers?
- Methodology - Did the study use an appropriate study design to address the hypothesis? Did the authors adjust for covariates and account for possible confounding factors?
- Clinical and statistical significance - What is the strength of the statistical evidence supporting the researchers' conclusions? Did they correct for multiple hypotheses? What is the magnitude of the effect?

The 23andMe laboratory is also accredited by the College of American Pathologists (CAP), which has served as a model for various federal, state, and private laboratory accreditation programs throughout the world.

Carrier status reports

23andMe Carrier Status reports identify whether a person carries specific genetic variants known to cause autosomal recessive conditions. Carriers do not typically have the condition themselves, but they can pass the genetic variant down to their children. 23andMe Carrier Status reports are regulated by the U.S. Food and Drug

Administration (FDA) and meet FDA requirements for being clinically and analytically valid.

The 23andMe PGS test uses qualitative genotyping to detect clinically relevant variants in the genomic DNA of adults, from saliva collected using an FDA-cleared collection device (Oragene·DX model OGD-500.001) for the purpose of reporting carrier status, and reporting and interpreting genetic health risks. The relevance of each report varies based on ethnicity. The carrier status reports can be used to determine carrier status but cannot determine if you have two copies of any genetic variant. These carrier reports are not intended to tell you anything about your risk for developing a disease in the future or anything about the health of your foetus, or your newborn child's risk of developing a particular disease later in life. For Gaucher Disease Type 1, 23andMe provide a single report that includes information on both carrier status and genetic health risk.

Genetic variants must meet one of the following criteria to be included in a Carrier Status report:

- Clinical guidelines recommend carrier screening for the variant for the given recessive condition
- At least two independent published clinical studies demonstrate a genotype-phenotype correlation and at least one study provides functional evidence supporting a causative role for the variant

Genetic Health Risk Reports

23andMe Genetic Health Risk reports identify whether a person has specific genetic variants associated with various health conditions and provide information about the risk for these conditions. In some cases, a single copy of a variant is associated with increased risk; in other cases, two copies or a combination of variants may be necessary. Many of these conditions are also influenced by non-genetic factors and genetic variants not covered by the reports. Thus, having a variant or combination of variants associated with increased risk does not mean a person will definitely develop the disease or condition, and vice versa.

The relevance of each report varies based on ethnicity. The genetic health risk reports describe if a person has variants associated with a higher risk of developing a disease, but do not describe a person’s overall risk of developing the disease. The reports are not intended to diagnose any disease, tell you anything about your current state of health, or to make medical decisions, including whether or not you should take a medication or how much of a medication you should take.

Although these reports include some conditions that are inherited in an autosomal recessive manner, they are distinct from Carrier Status reports in that the conditions described by Genetic Health Risk to the carrier, are lower penetrance, tend to be adult-onset or have milder symptoms, or are not typically considered relevant for reproductive decision-making.

As with our Carrier Reports, genetic variants must meet one of the following criteria to be included in a Genetic Health Risk report:

- Clinical guidelines recommend screening for the variant for the given condition
- At least two independent published peer reviewed clinical studies demonstrate a genotype-phenotype correlation and at least one study provides functional evidence supporting a causative role for the variant. In addition, the risk associated with at least one combination of genotypes that includes the variant is substantial or clinically significant

When reporting quantitative measures of risk in these reports, preference is given to absolute risk over relative risk and to larger and more recent studies when available. Likelihood ratios may also be provided when data is available to derive these estimates. The populations to which risk estimates apply are always reported, as these risk estimates may not be accurate across populations.

Sharing research with the scientific community is key to 23andMe's mission. All scientific publications, white papers and conference presentations are publicly available on the 23andMe website[5], with over 235,000 visits recorded to these pages in the year to date.

Through 23andMe's Research Innovation Collaborations Program[6], external academic researchers can work with 23andMe scientists to study the de-identified, aggregated data provided by the 23andMe Research Cohort of millions of participants with the goal of discovering new genetic associations and developing new methods and tools with the collaborators.

23andMe's research and collaborations have been featured in more than one hundred publications, and the Publication Dataset Access Program[7] supports sharing of the de-identified GWAS summary statistics. Access is provided through a Data Transfer Agreement to protect the privacy of participants' data.

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[5] 23andMe, Research publications, available at: https://research.23andme.com/publications/
[6] 23andMe, Research Innovation Collaborations Programme, available at: https://research.23andme.com/research-innovation-collaborations/
[7] 23andMe, Publication Dataset Access, available at: https://research.23andme.com/dataset-access/

23andMe's Genotyping Services for Research[8] can also be used as a service for genotyping participants. In particular, through the Populations Collaborations Program, 23andMe aims to support genotyping of populations from around the world that are under-represented in genetic studies.

The 23andMe PGS test has a high level of analytical validity – it has demonstrated 99% concordance with Sanger sequencing, which is considered the clinical "gold standard," and 99% precision.[9]

User comprehension

All 23andMe Health test results are returned to users in an easy-to-understand format which has been shown to be comprehensible by average consumers at a rate of at least 90% per report concept in multiple studies.[10] In addition each Health report category includes an educational module which is intended to further support the safe and effective use of the 23andMe test results.

As set out in more detail in Appendix A (attached hereto), six user comprehension studies were performed to assess how well people understand the PGS Carrier Status test reports. Studies are performed by an independent firm with expertise in recruiting for and performing general population studies using quota-based sampling to ensure that participants represented a wide range of demographic characteristics and were not current or prior customers of 23andMe. 23andMe has conducted six separate user comprehension studies, covering all key concepts in its health reports. In the six studies there were 2,239 demographically diverse participants: by gender (1,251 female and 988 male); by race (1,332 Caucasian, 329 African, 167 Asian, 351 Hispanic and 60 mixed race), by age (716 between the ages of 18-34, 795 between the ages of 35-54 and 728 who were 55 or older) and by level of education (732 having completed secondary education or less, 640 having attended some college and 867 having completed college and/or post graduate studies). User comprehension does not vary in any significant way between participants in any of the above demographics.

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[8] 23andMe, Genotyping services for research, available at: https://research.23andme.com/genotyping-services-research/

[9] ScienceDirect, *Sequencing*, available at: https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/sequencing

[10] 23andMe Personal Genomics Service, *Genetic Health Risk package insert*, available at: https://permalinks.23andme.com/pdf/PN-20-0279.pdf

Comprehension was tested through a two-step process. First, participants' understanding of genetics was tested prior to viewing the educational module and test reports. Second, participants were shown the educational module and the test reports. Participants then completed the test report comprehension survey. The User Studies are moderated in person in order to use trained moderators to collect observational, qualitative data on participants' overall experience with the survey and with the test reports and labelling. Participants are randomly assigned to a study arm, pursuant to which they will receive reports reflecting one of the potential results for the test report included in the study, i.e. Carrier, Genetic Health Risk, etc, being assessed. For example, to assess user comprehension of the Carrier results both the single genetic variant Bloom Syndrome test report and multivariant Cystic Fibrosis test report were studied. Overall comprehension rates per test report concept averaged 92% across all concepts in both studies. Importantly, the studies also demonstrated that comprehension of three out of five concepts tested was significantly improved following participants completing the 23andMe Carrier testing education module which is provided to customers as part of the 23andMe experience. As shown in detail on Appendix A the User Comprehension studies for Genetic Health Risk and Pharmacogenetic also demonstrate the same high levels of user comprehension and the benefit to user of the 23andMe education modules for those reports.

In addition to the studies of test report concepts, the ability of consumers to read and use the 23andMe collection saliva kit was also assessed. The overall comprehension rate on the collection kit instructions was 92.1% and more than 97% of samples returned by users in the collection study met all laboratory quality criteria, demonstrating that users from diverse backgrounds can understand the collection kit instructions and provide adequate saliva samples.

Conclusion

23andMe welcomes the Science and Technology Committee's inquiry into commercial genomics and the continued focus on genomics by the UK Government.

APPENDIX

23andMe performed six user comprehension studies to establish that average consumers could understand and appropriately use the 23andMe Personal Genome Service (PGS) health reports. All of these studies were performed by an independent firm with expertise in recruiting for and performing general population studies using quota-based sampling to ensure that participants represented a wide range of demographic characteristics and were not current or prior customers of 23andMe. The User Studies were moderated in person in order to use trained moderators to collect observational, qualitative data on participants' overall experience with the survey and with the test reports and labelling. Participants are randomly assigned to a study arm, pursuant to which they will receive reports reflecting one of the potential results for the test report included in the study, i.e. Carrier, Genetic Health Risk, etc., being assessed.

The table below summarizes the combined demographic make up of the participants in the six user comprehension studies.

Summary of total Demographics from all Report Concepts User Comprehension Studies

Demographic Category	Count	Total
Sex	1251	2,239
	988	
Ethnicity	1332	2,239
	329	
	167	
	351	
	60	
Age	716	2,239
	795	
	728	
Education	732	2,239
	640	
	867	

The tables below reflect the summary results by demographic factors for each of the six user comprehension studies by report type.

Carrier Status Reports- User Comprehension Studies

Below are selected tables from two studies of report concepts used in 23andMe Carrier Status test reports. The first study tested comprehension where a single variant is involved in determination of carrier status. The second study tests comprehension where there are multiple variants associated with carrier status.

1. Carrier Status User Comprehension - Single Variant - Bloom Syndrome

Table 1 - Comprehension Rates by Study Arm and Concept - Bloom Syndrome

Comprehension concept	Comprehension rates (%) within each study arm					Overall comprehension rates (%)
	Full Match Variant Absent	Full Match Variant Present	Full Match Not Determined	Partial Match Variant Absent	No Match Variant Absent	
Purpose of test	90.4	95.5	94.8	91.7	89.2	92.4
Test results		95.5	94.8			95.2
Limitations of test	88.9	91.8	94.1	93.2	90.0	91.6
Ethnicity relevance	96.3		95.6	91.7	94.6	94.6
Meaning of results	89.6	97.8		94.0	87.7	92.3
Appropriate follow-up	94.1	95.5	94.1	92.5	92.3	93.7

Table 2 - Demographic characteristics of study participants - Bloom Syndrome

	Number (Percent of Total) per Study Arm					Overall Percent of Total
Age	Full Match Variant Absent	Full Match Variant Present	Full Match Not Determined	Partial Match Variant Absent	No Match Variant Absent	
18-34	41 (30.4%)	40 (29.9%)	47 (34.8%)	48 (36.1%)	37 (28.5%)	31.9%
35-54	46 (34.1%)	52 (38.8%)	41 (30.4%)	50 (37.6%)	51 (39.2%)	36.0%
55+	48 (35.6%)	42 (31.3%)	47 (34.8%)	35 (26.3%)	42 (32.3%)	32.1%
Ethnicity/Race						
White only, Non-Hispanic	77 (57.0%)	75 (56.0%)	79 (58.5%)	71 (53.4%)	70 (53.8%)	55.8%
Black only, Non-Hispanic	20 (14.8%)	25 (18.7%)	19 (14.1%)	22 (16.5%)	23 (17.7%)	16.3%
Asian only, Non-Hispanic	13 (9.6%)	14 (10.4%)	13 (9.6%)	11 (8.3%)	11 (8.5%)	9.3%
Mixed or Other*	3 (2.2%)	3 (2.2%)	8 (5.9%)	1 (0.8%)	4 (3.1%)	2.8%
Hispanic	22 (16.3%)	17 (12.7%)	16 (11.9%)	28 (21.1%)	22 (16.9%)	15.7%
Education						
High School or Less	50 (37.0%)	40 (29.9%)	33 (24.4%)	46 (34.6%)	43 (33.1%)	31.8%
Some College	36 (26.7%)	35 (26.1%)	30 (22.2%)	37 (27.8%)	33 (25.4%)	25.6%
College Graduate	49 (36.3%)	59 (44.0%)	72 (53.3%)	50 (37.6%)	54 (41.5%)	42.6%
Sex						
Male	56 (41.5%)	48 (35.8%)	57 (42.2%)	54 (40.6%)	53 (40.8%)	40.2%
Female	79 (58.5%)	86 (64.2%)	78 (57.8%)	79 (59.4%)	77 (59.2%)	59.8%

* For recruitment purposes "other" included "non-white" participants. For data analysis purposes, participants from this category were re-categorized by self-reported race/ethnicity.

Table 3 - Post-test usability survey response rates per theme - Bloom Syndrome

Post-test survey theme	% Positive or neutral answers
Clarity of survey instructions	97%
Ability to find information	99%
Overall survey interest	99%
Survey duration	99%

2. Carrier Status User Comprehension - Multi-Variant - Cystic Fibrosis

Below are selected tables from the Cystic Fibrosis user study.

Table 4 - Comprehension Rates by Study Arm and Concept - Cystic Fibrosis

	Comprehension rates (%)				
	Cystic Fibrosis Test within each study arm		Overall for the Cystic Fibrosis Test	Overall for the Bloom Syndrome Test*	Overall for Carrier Status Tests in General#
Comprehension concept	Ethnicity Match, Zero Variants Present, One Not Determined	Two Variants Present			
Purpose of test	84.3	78.3	81.3	92.4	89.2
Limitations of test	90.2	82.1	86.2	91.6	90.0
Test results	90.2	93.4	91.8	95.2	93.5
Meaning of results	92.2	100.0	96.1	92.3	93.5
Ethnicity relevance	93.1	N/A	93.1	94.6	94.3
Appropriate follow-up	94.1	97.2	95.6	93.7	94.2

*From Table 4 PN-50-0026 *23andMe Bloom Syndrome Test Report Moderated User Comprehension Study Report*
#Average across 5 Bloom Syndrome Test study arms and 2 Cystic Fibrosis Test study arms

Table 5 - Demographic characteristics of study participants - Cystic Fibrosis

	Number (Percent of Total) per Study Arm		
Age	Ethnicity Match, Zero Variants Present, One Not Determined	Two Variants Present	**Overall Percent of Total**
18-34	29 (28.4%)	38 (35.8%)	67 (32.2%)
35-54	41 (40.2%)	32 (30.2%)	73 (35.1%)
55+	32 (31.4)	36 (34.0%)	68 (32.7%)
Ethnicity/Race			
White only, Non-Hispanic	69 (67.6%)	71 (67.0%)	140 (67.3%)
Black only, Non-Hispanic	11 (10.8%)	15 (14.2%)	26 (12.5%)
Asian only, Non-Hispanic	3 (2.9%)	6 (5.7%)	9 (4.3%)
Hispanic	16 (15.7%)	13 (12.3%)	29 (13.9%)
Other or Mixed	3 (2.9%)	1 (0.9%)	4 (1.9%)
Education			
High School or Less	33 (32.4%)	37 (34.9%)	70 (33.7%)
Some College	28 (27.5)	34 (32.1%)	62 (29.8%)
College Graduate	41 (40.2%)	35 (33.0%)	76 (36.5%)
Sex			
Male	43 (42.1%)	45 (42.5%)	88 (42.3%)
Female	59 (57.8%)	61 (57.5%)	120 (57.7%)

Table 6 - Post-test usability survey response rates per theme - Cystic Fibrosis

Post-test survey theme	**% Positive or neutral answers**
Clarity of survey instructions	97.6
Ability to find information	99.0
Text easy to read	97.1
Helpful illustrations and colors	97.6
Overall survey interest	99.0
Appropriate survey duration	99.5

Genetic Health Risk Reports- User Comprehension Studies

Below are selected tables from two studies of report concepts used in 23andMe Genetic Health risk test reports. The first study tested comprehension for the Hereditary Thrombophilia (VTE) test report. The second study tested user comprehension for Alpha-1 Antitrypsin Deficiency (AATD) test report. The concepts tested in these studies apply to all PGS Genetic Health Risk reports, including cancer reports.

1. Genetic Health Risk Report User Comprehension - Hereditary Thrombophilia

Table 7 - Comprehension Rates by Study Arm and Concept - VTE

Comprehension concept	Comprehension rates (%) within each study arm					Overall comprehension rates (%)
	0 Variants Detected	1 Variant Detected- Slightly Increased Risk	2 Variants Detected - Increased Risk	Result Not Determined	1 Variant Not Detected and 1 Variant Not Determined	
Test results	90.3	90.7	92.4	91.7	93.3	91.7
Purpose of test	92.0	84.1	92.4	87.0	90.5	89.2
Limitations of test	90.3	87.9	93.3	92.6	88.6	90.5
Ethnicity relevance	92.9	89.7	94.3	89.8	87.6	90.9
Meaning of results	99.1	90.7	94.3	97.2	98.1	95.9
Other risk factors	95.6	86.0	93.3	94.4	90.5	92.0
Appropriate follow-up	95.6	85.0	93.3	93.5	91.4	91.8

Table 8 - Demographic characteristics of study participants - VTE

	Number (Percent of Total) per Study Arm					Overall Percent of Total
Age	0 Variants Detected	1 Variant Detected- Slightly Increased Risk	2 Variants Detected - Increased Risk	Result Not Determined	1 Variant Not Detected and 1 Variant Not Determined	
18-34	40 (35.4%)	36 (33.6%)	33 (31.4%)	37 (35.2%)	28 (25.9%)	32.3%
35-54	30 (26.5%)	38 (35.5%)	41 (39.0%)	42 (40.0%)	39 (36.1%)	35.5%
55+	43 (38.1%)	33 (30.8%)	31 (29.5%)	26 (24.8%)	41 (38.0%)	32.3%
Ethnicity/Race						
White only, Non-Hispanic	70 (61.9%)	68 (63.6%)	64 (61.0%)	63 (60.0%)	69 (63.9%)	62.1%
Black only, Non-Hispanic	18 (15.9%)	16 (15.0%)	14 (13.3%)	12 (11.4%)	13 (12.0%)	13.6%
Asian only, Non-Hispanic	5 (4.4%)	5 (4.7%)	4 (3.8%)	7 (6.7%)	13 (12.0%)	6.3%
Hispanic	19 (16.8%)	15 (14.0%)	20 (19.0%)	20 (19.0%)	12 (11.1%)	16.0%
Other or Mixed	1 (0.9%)	3 (2.8%)	3 (2.9%)	3 (2.9%)	1 (0.9%)	2.0%
Education						
High School or Less	42 (37.2%)	41 (38.8%)	29 (27.6%)	38 (36.2%)	36 (33.3%)	34.6%
Some College	27 (23.9%)	28 (26.2%)	38 (36.2%)	37 (35.2%)	32 (29.6%)	30.1%
College Graduate	44 (38.9%)	38 (35.5%)	38 (36.2%)	30 (28.6%)	40 (37.0%)	35.3%
Sex						
Male	50 (44.2%)	51 (47.7%)	47 (44.8%)	47 (44.8%)	45 (41.7%)	44.6%
Female	63 (55.8%)	56 (52.3%)	58 (55.2%)	58 (55.2%)	63 (58.3%)	55.4%

Table 9 - Post-test usability survey response rates per theme - VTE

Post-test survey theme	% Positive or neutral answers
Clarity of survey instructions	95.9
Ability to find information	97.8
Text easy to read	95.4
Helpful illustrations and colors	97.2
Overall survey interest	99.3
Appropriate survey duration	99.6

2. Genetic Health Risk Report - Alpha-1 Antitrypsin Deficiency (AATD)

Table 10 - Comprehension Rates by Study Arm and Concept - AATD

Comprehension concept	Comprehension rates (%)		
	AAT Deficiency Novel Concept: 2 Variants Detected – Not at Risk (N = 112)	Previously Tested Representative Genetic Health Risk reports (N = 538)	Average for all Representative Genetic Health Risk reports (N = 650)
Test results	NA	91.7	91.7
Purpose of test	87.5	89.2	88.9
Limitations of test	91.1	90.5	90.6
Ethnicity relevance	NA	90.9	90.9
Meaning of results	92.9	95.9	95.4
Inheritance	92.9	NA	92.9
Other risk factors	NA	92.0	92.0
Appropriate follow-up	89.3	91.8	91.4

Table 11 - Demographic characteristics of study participants - AATD

	Number (Percent of Total)		
	AAT Deficiency Novel Concept: 2 Variants Detected – Not at Risk (N = 112)	Previously Tested Representative Genetic Health Risk reports (N = 538)	Average for all Representative Genetic Health Risk reports (N = 650)
Age			
18-34	31 (27.7%)	174 (32.3%)	205 (31.5%)
35-54	40 (35.7%)	190 (35.3%)	230 (35.4%)
55+	41 (36.6%)	174 (32.3%)	215 (33.1%)
Ethnicity/Race			
White only, Non-Hispanic	70 (62.5%)	334 (62.1%)	404 (62.2%)
Black only, Non-Hispanic	14 (12.5%)	73 (13.6%)	87 (13.4%)
Asian only, Non-Hispanic	3 (2.7%)	34 (6.3%)	37 (5.7%)
Hispanic	20 (17.9%)	86 (16.0%)	106 (16.3%)
Other or Mixed	5 (4.5%)	11 (2.0%)	16 (2.5%)
Education			
High School or Less	38 (33.9%)	186 (34.6%)	224 (34.5%)
Some College	30 (26.8%)	162 (30.1%)	192 (29.5%)
College Graduate	44 (39.3%)	190 (35.3%)	234 (36.0%)
Sex			
Male	48 (42.9%)	240 (44.6%)	288 (44.3%)
Female	64 (57.1%)	298 (55.4%)	362 (55.7%)

Table 12 - Post-test usability survey response rates per theme - AATD

Post-test survey theme	**% Positive or neutral answers**
Clarity of survey instructions	97.3
Ability to find information	100.0
Text easy to read	96.4
Helpful illustrations and colors	94.6
Overall survey interest	100.0
Appropriate survey duration	100.0

Pharmacogenetic Reports User Comprehension Studies

Below are selected tables from two studies of report concepts used in 23andMe Pharmacogenetic reports. The first study tested comprehension for the SSRI drug response. The second study tested user comprehension for Phenytoin drug response.

The concepts tested in these studies apply to all PGS Pharmacogenetic reports.

1. Pharmacogenetic Report for SSRI drug response.

Table 13 - Comprehension Rates by Study Arm and Concept - SSRI drug response

Comprehension Concept	**Comprehension rates (%) within each study arm**					**Overall Comprehension Rates (%)**
	Increased Chance of Side Effects	Result Not Determined	Cannot Interpret Result	Likely Typical Response	May be Less Effective	
Purpose of the Test	89.3%	86.7%	89.8%	91.2%	92.5%	89.9%
Result and Meaning	87.7%	90.0%	94.1%	92.1%	85.8%	89.9%
Limitations of Variant Coverage	91.0%	91.7%	94.9%	93.9%	94.2%	93.1%
Limitations of Medication Coverage	94.3%	95.8%	95.8%	92.1%	95.8%	94.8%
Appropriate Actions	91.8%	86.7%	94.1%	93.9%	95.0%	92.3%
Treatment Adherence	95.1%	96.7%	98.3%	96.5%	98.3%	97.0%
Other Risk Factors	94.3%	93.3%	95.8%	96.5%	95.0%	95.0%

Table 14 - Demographic characteristics of study participants - SSRI drug response

	Number (Percent of Total) Per Study Arm					Overall Number (Percent)
Age	Increased Chance of Side Effects	Result Not Determined	Cannot Interpret Result	Likely Typical Response	May be Less Effective	
18 - 34	39 (32.0%)	33 (27.5%)	42 (35.6%)	35 (30.7%)	39 (32.5%)	**188 (31.7%)**
35 - 54	46 (37.7%)	45 (37.5%)	46 (39.0%)	36 (31.6%)	42 (35.0%)	**215 (36.2%)**
55+	37 (30.3%)	42 (35.0%)	30 (25.4%)	43 (37.7%)	39 (32.5%)	**191 (32.1%)**
Ethnicity / Race						
White only, Non-Hispanic	75 (61.5%)	70 (58.3%)	69 (58.5%)	64 (56.1%)	71 (59.2%)	**349 (58.8%)**
Black only, Non-Hispanic	13 (10.7%)	18 (15.0%)	22 (15.3%)	18 (19.3%)	17 (16.7%)	**88 (14.8%)**
Asian only, Non-Hispanic	9 (7.4%)	12 (10.0%)	7 (5.9%)	8 (7.0%)	7 (5.8%)	**43 (7.2%)**
Hispanic	19 (15.6%)	18 (15.0%)	18 (15.3%)	22 (19.3%)	20 (16.7%)	**97 (16.3%)**
Other or mixed	6 (4.9%)	2 (1.7%)	2 (1.7%)	2 (1.8%)	5 (4.2%)	**17 (2.9%)**
Education						
High School or Less	43 (35.2%)	40 (33.3%)	37 (31.4%)	36 (31.6%)	34 (28.3%)	**190 (32.0%)**
Some College	33 (27.0%)	38 (31.7%)	36 (30.5%)	38 (33.3%)	42 (35.0%)	**187 (31.5%)**
College Graduate	46 (37.7%)	42 (35.0%)	45 (38.1%)	40 (35.1%)	44 (36.7%)	**217 (36.5%)**
Sex						
Male	68 (55.7%)	61 (50.8%)	52 (44.1%)	56 (49.1%)	49 (40.8%)	**286 (48.2%)**
Female	54 (44.3%)	59 (49.2%)	66 (55.9%)	58 (50.9%)	71 (59.2%)	**308 (51.8%)**
Total	**122**	**120**	**118**	**114**	**120**	**594**

Table 15 - Post-test usability survey response rates per theme - SSRI drug response

Post-test survey theme	% Positive or Neutral Answers
Length of the report	94.3%
Helpful illustrations and colors	97.0%
Information is easy to find	98.3%
Text size is easy to read	97.5%
Overall report is easy to read	97.1%

2. Pharmacogenetic Report for Phenytoin drug response.

Table 16 - Comprehension Rates by Study Arm and Concept - Phenytoin drug response

Comprehension Concept	Comprehension rates (%)		Overall Comprehension Rates (%) (N = 714)
	Phenytoin Arm (N=120)	All Previously Tested Arms (N=594)	
Purpose of the Test	89.2%	89.9%	89.8%
Result and Meaning	89.2%	89.9%	89.8%
Limitations of Variant Coverage	90.0%	93.1%	92.6%
Limitations of Medication Coverage	95.0%	94.8%	94.8%
Appropriate Actions	91.7%	92.3%	92.2%
Treatment Adherence	95.8%	97.0%	96.8%
Other Risk Factors	95.8%	95.0%	95.1%
Ethnicity Relevance	93.3%	NA	93.3%

Table 17 - Demographic characteristics of study participants - Phenytoin drug response

	Number (Percent of Total)		Overall Number (Percent)
Age	**Phenytoin Arm**	**All Previously Tested Drug Response Arms**	
18 - 34	43 (35.8%)	188 (31.7%)	231 (32.4%)
35 - 54	37 (30.8%)	215 (36.2%)	252 (35.3%)
55+	40 (33.3%)	191 (32.1%)	231 (32.4%)
Ethnicity / Race			
White only, Non-Hispanic	67 (55.8%)	349 (58.8%)	416 (58.3%)
Black only, Non-Hispanic	19 (15.8%)	88 (14.8%)	107 (15.0%)
Asian only, Non-Hispanic	16 (13.3%)	43 (7.2%)	59 (8.3%)
Hispanic	14 (11.7%)	97 (16.3%)	111 (15.6%)
Other or mixed	4 (3.3%)	17 (2.9%)	21 (2.9%)
Education			
High School or Less	36 (30.0%)	190 (32.0%)	226 (31.7%)
Some College	28 (23.3%)	187 (31.5%)	215 (30.1%)
College Graduate	56 (46.7%)	217 (36.5%)	273 (38.2%)
Sex			
Male	58 (48.3%)	286 (48.2%)	344 (48.2%)
Female	62 (51.7%)	308 (51.8%)	370 (51.8%)
Total	**120**	**594**	**714**

Table 18 - Post-test usability survey response rates per theme - Phenytoin drug response

Post-test survey theme	% Positive or Neutral Answers
Length of the report	91.7%
Helpful illustrations and colors	91.7%
Information is easy to find	99.2%
Text size is easy to read	97.5%
Overall report is easy to read	96.7%