Direct-to-Consumer (DTC) Genetic Testing

ARE YOU THE PRODUCT?

Thomas R. Curran, Jr., M.D.

Mapping the Human Genome

- The vast majority of the human genome was sequenced by the year 2000. It marked the end of the beginning
- 99.9% of human DNA sequences are identical to each other
- The other 0.1% of variation is expected to provide many of the clues to the genetic risk for common illnesses
- This information comes with vast ethical, legal, and social implications

Old School Screening=Newborn Screening

Designed for pre-symptomatic identification of serious conditions for which there are effective treatments

The 4 primary considerations for conditions to be screened:

1) The condition represents a significant public health problem

2) There is an accurate and low-cost screening test

3) Treatments exist with proven efficacy

4) States are capable with screening and follow-up

Traditional Reasons for Genetic Testing

- To confirm a disease diagnosis (Alpha-1-Antitrypsin Deficiency)
- To screen for carriers of genetic mutations (Tay-Sachs disease)
- To screen newborns for inborn metabolic diseases (PKU)
- To predict susceptibility to future disease (BRCA1&2)
- To predict how an individual may respond to a particular drug therapy (pharmacogenomics)

The Pros of the Medical Model

- Clinically indicated genetic testing is ordered and interpreted by medical genetic providers
- The health care system is the mediator of genetic information, responsible for its quality, creation, interpretation, delivery, protection, and implications
- In particular, the medical model is committed to protecting the privacy of health information, including genetic information

The Cons of the Medical Model

- The private sector complains that the medical model innovates too slowly because of regulation and professional resistance to new practices
- Some contend that the resistance stems from the desire to preserve medical professional autonomy
- There is a shortage of skilled medical genetics practitioners
- Many see medical genetics as having failed to live up to the hype surrounding human genetics and genomics research

The Big DTC Player: 23andMe

- 23andMe for health and ancestry data
  - The health reports tell you about physical traits, wellness, carrier status for certain genetic mutations, and genetic risk for certain diseases
  - The ancestry report tells you about your ancestry composition and has an opt-in DNA relatives tool
  - 5 million customers and counting

23andMe Marketing

Background music… Getting to Know You

A woman participating in various activities all over the world

Embedded text

-There are parts of you yet to be discovered

-And through our DNA

-We are all connected

23andMe Health and Trait Reports

- Wellness and Trait report
- Carrier Status report
- Genetic Health Risk report

Wellness and Trait Report

- Tells you the version of each trait you are most likely to have based on your genetics
- Compares your genetic results to 23andMe research participants (mostly European ethnicities)
- Most traits aren't passed down in a strictly Mendelian fashion
- Examples in the report include: dry/wet ear wax, flushing after alcohol consumption, and the ability to smell asparagus in your urine

“Carrier” Status Report

- Report on 40+ inherited, autosomal recessive diseases such as cystic fibrosis, sickle cell anemia, and PKU
- Many of the conditions in this report can be caused by hundreds to thousands of genetic variants and the report doesn’t include all possible variants.
- This means the test can’t detect all carriers
- Some Carrier Status tests are more relevant for certain ethnicities than others

Genetic Health Risk Report

- The test genotypes a limited set of variants associated with potential risk for a grab bag of 10 conditions. It includes Parkinson's disease and late-onset Alzheimer's disease
- Although the included mutations increase the risk for these conditions, they account for a fraction of those genetic variants contributing to the diseases
- The test's positive predictive value is low because most of the mutations are incompletely penetrant or are modified by other factors

The 2 Opt-In Genetic Reports (so far)

- Parkinson's disease
  - ~ 1 million cases in the US
- Late-Onset Alzheimer's disease
  - ~ 5 million cases in the US

- Both diseases are debilitating, unpredictable, and have no cure.
- The FDA says that these tests are intended to provide genetic risk information to consumers but they cannot determine a person's overall risk of developing the disease

Parkinson's disease

- It is estimated that 5% of Parkinson's disease is inherited, meaning a genetic test will only have limited use
- The genetics of Parkinson's disease are extremely complex, even if you do carry a gene linked to the condition, it does not mean you will go on to develop it
- Appropriate access to counseling and advice is critically important

Late-onset Alzheimer's disease

- 23andMe's website states, "'Genetic testing for late-onset Alzheimer's disease is not currently recommended by any healthcare professionals."
- The website also states, "there is currently no known prevention or cure for Alzheimer's disease."
- The genetics of Alzheimer's disease are extremely complex, even if you do carry a gene linked to the condition it does not mean you will go on to develop it

23andMe fine print

- Your ethnicity may affect the relevance of each report
- The test is not intended to tell you anything about your current state of health, or be used to make medical decisions
- Each report describes if a person has variants associated with a higher risk of developing a disease, but does not describe a person's overall risk of developing the disease

Is Ignorance Bliss?

- Should I tell my partner they might have to be my caretaker one day?
- What do I tell my siblings/children?
- Should I be scared?
- What does “genetic risk” even mean?
- What if I’m part of an ethnic or racial group for which these results are less valid because most of the testing was done on people of a different descent?

23andMe 'Research Participants'

- In 2010, all customers of 23andMe were recruited for an ongoing research project entitled 23andWe
- Participation entailed the customers electively providing personal phenotypic data that would be added to their genotypic data
- Approximately 90% of customers consented to participate
- The average 'research participant' contributed additional phenotypic data on 11 topic specific research questionnaires

Demographics of Research Participants

- Men slightly outnumber women
- Age distribution is bimodal centering around 30 and 60 years
- Most have a college education and income of at least $100,000/year
- The vast majority were of European descent

The 23andMe Business Model

- Front End- the direct to consumer genetic/ancestry business

- Back End- involves pairing clients genetic data with their actual physical conditions, aggregating and anonymizing the data, and selling this information
  - Third party companies (Pfizer, Genentech)
  - Research institutions (Stanford)
  - Nonprofits (Michael J. Fox Foundation)

23andMe's Aggregate Data

- The data is generated by the individual clients, and ~ 80% of the clients are of European descent
- The genetic database has noticeable gaps, especially among Africans, Middle Easterners, Central Asians, Southeast Asians, and indigenous Americans
- 2018 23andMe initiatives:
  - Populations Collaborations Program: allows U.S. based scientists already studying underrepresented groups to apply for free spit kits and DNA analysis
  - Global Genetics Project: free tests to people who can trace all 4 grandparents to one of 61 underrepresented countries

23andMe and Genentech

- In 2016, Genentech, a leading biotechnology company, and 23andMe entered into a $60 million deal to perform whole-genome sequencing on DNA samples collected by 23andMe from patients with Parkinson's disease
- 23andMe's terms of service states that genetic information and self-reported health information may be shared with 'research partners' including commercial partners.

Genotyping versus Sequencing

- Genotyping- the process of determining which genetic variants an individual possesses. For looking at many different variants at once, genotyping chips are an efficient and accurate method. Cost-effective.

- Sequencing- a method used to determine the exact sequence of a certain length of DNA. Sequencing can be used to genotype someone for known variants as well as identify variants that mat be unique to that person. Expensive.

Ethical Issues with Sequencing

- Adequacy of consumers' informed consent
- Transparency of companies' research activities
- Variants of uncertain significance
- Incidental findings
- Ramifications for blood relatives
- The risk of re-identification

Concerns about the Genentech Business Deal

- Will participants be offered the option of receiving results and appropriate genetic counseling?
- How will informed consent be obtained for whole genome sequencing?
- Will the genomic/phenotypic data collected from this project be made available to other researchers?
- What about the possibility of unauthorized re-identification of an individual from “de-identified” DNA sequence data?

De-anonymizing genetic samples

- New lab techniques can unearth genetic markers tied to specific physical traits
- Using this process, one MIT scientist was able to identify the people behind five supposedly anonymous genetic samples randomly selected from a public research database
- It took him less than a day

The Privacy Delusion

- HIPAA, a 1996 federal law, allows medical companies to share and sell patient data if it has been anonymized
- This loophole has proven to be a cash cow
- Once genetic data has been linked to a specific person, the potential for abuse is vast
- Linda Avey, a cofounder of 23andMe, has admitted that “it’s a fallacy to think that genomic data can be fully anonymized.”

Genetic Information Nondiscrimination Act

- In 2008, GINA was passed to address the need to regulate how genetic information is used, most notably protecting against discrimination in health insurance and employment.
- GINA has serious limitations:
  - Its lack of application to life insurance, long-term care insurance, and to employers of < 15 employees
  - GINA places the burden on victims of genetic discrimination to prove that their information was misused

23andMe and Sharing/Selling Your Data

- 23andMe pledges it won't share identifiable test results unless the consumer signs a 2,700 word "research consent document"
- The 22-page privacy policy states that anonymized information can be shared without consent
- The policy goes on to say: "it is possible that a third party that has obtained some of your genetic data could compare that partial data to the published results and infer some of your other personal information"

Informed Consent Process

- Medical/Academic Institutions
  - Often have someone to walk through documents with potential study participants
  - Attempt to make sure they understand all of the risks/benefits
- 23andMe
  - User clicks I DO GIVE CONSENT
  - As a result, their genetic profile plus any information they enter into surveys can be used for research in de-identified/aggregated form

23andMe Privacy Policy

- Can unilaterally change the terms and conditions of its privacy policies at any time
- As a commercial enterprise, it is not bound by the same obligations as medical professionals
- Tension exists between the way 23andMe portrays itself as a health company and simultaneously wants to be treated like every other tech company that makes its money from big data

Phenotypic and Genomic Data

- There are many sources of genomic data
- Linking phenotypic data to genomic data is much more difficult
- 23andMe acquires this linked health and behavioral data by continuously pushing out surveys to the 80% of its users that clicked the research box
- The average user answers 300 phenotypic/behavioral questions

The Golden State Killer

- In April 2018, local investigators used a DNA-comparison service to track down a man police believed to be the Golden State Killer
- Investigators identified the suspect using a decades old DNA sample obtained from the crime scene
- The sample was uploaded to GEDmatch, a crowdsourced database of ~ a million distinct DNA sets shared by volunteers
- Investigators contended they did not need a court order before using GEDmatch

Privacy Best Practices for Consumer Genetic Testing

- In July of 2018, 23andMe partnered with a Washington, DC nonprofit named The Future of Privacy Forum
- They created new, voluntary guidelines in which DTC companies would obtain consumers separate express consent before turning over their individual genetic data and personal information to third parties

GlaxoSmithKline and 23andMe

- Also in July of 2018, 23andMe announced it was partnering with pharmaceutical behemoth GSK
- In the $300 million/4 year deal, 23andMe will give GSK access to it's users aggregated, de-identified genetic data

Empowered Consumers or Suckers?

- Altruists could contend that the customer's know what they're doing and see their participation as a way to make a difference

- Sceptics could make the case that the customers have been hoodwinked into contributing their genetic data, suckered by a fun service into giving more than expected

GATTACA

- “ There is no gene for fate.”
- Quote from the 1997 film that portrayed a dystopian vision of a world divided between the “valids” and the “in-valids”
- Genomics is best viewed as a complex and probabilistic science, in which a constellation of genetic variations makes the odds, but many other factors, environmental as well as biological, decide the outcome


SCIENCE
HEY!
WAIT
UP!!!
ETHICS