GENETIC SEQUENCING IN HEALTHY POPULATIONS

BY

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LIST OF ABBREVIATIONS

ACMG: American College of Medical Genetics and Genomics

CLIA: Clinical Laboratory Improvement Amendments

DTC: Direct-to-consumer

FDA: United States Food and Drug Administration

GINA: Genetic Information Nondiscrimination Act

HIPAA: Health Insurance Portability and Accountability Act

UNESCO: The United Nations Educational, Scientific, and Cultural Organization

WGS: Whole genome sequencing

ABSTRACT

After the success of the Human Genome Project, genetic sequencing technology has improved exponentially. Consumers can now have parts of their genome sequenced for under $100. Genetic sequencing in this direct-to-consumer (DTC) setting comes with many ethical problems that, despite being brought to national attention almost ten years ago, still have not been addressed. Significant regulation is needed in DTC genetic sequencing. As genetic sequencing becomes more widely available, Whole Genome Sequencing (WGS) will move into the clinical space, providing massive amounts of information about patients. Many have suggested using this technology in the standard screening of healthy populations. This brings ethical dilemmas as well, particularly when considering the use of WGS in fetuses, infants, and children. While WGS may be acceptable for use in adults if adequate safeguards are put into place, parents have a moral duty, based on the child's right to future autonomy and right not to know genetic information, not to permit WGS to be performed on their children.

INTRODUCTION

After the success of the Human Genome Project, genetic sequencing technology has improved exponentially. As this technology has gotten faster and less expensive, a fundamental shift has occurred in the way that genetic sequencing is conducted, and genetic information is used. Genetic sequencing has traditionally been exclusively in the hands of researchers and medical providers. Publicly available genetic tests traditionally focused on one or a few gene variants, tested to diagnose or study one or a specific handful of diseases or differences or to spot rare but treatable conditions in newborns and infants. This is no longer the case. Genetic testing has become genetic screening: more widespread, more frequently used, more commercial, and less targeted. Health risk and treatability are no longer the main factors in determining whether an individual should undergo genetic sequencing. This shift from testing to screening has brought about a host of new ethical and legal questions in relation to genetic sequencing of healthy populations.

When discussing this topic, it is important to clarify what is meant by the terms "sequencing," "testing," and "screening." These terms are often used interchangeably in the literature, but each term has a different connotation. Throughout this thesis, "genetic sequencing" will refer to the process of determining the order of the base pairs in the entire genome or large portion of it to find many or all an individual's genotypes. "Genetic testing" will refer to either sequencing or the determining of single genotypes when there is some medical indication or desire to diagnose or treat a condition. "Genetic screening" will refer to either sequencing or the determining of single genotypes in healthy populations when there is no medical indication for doing so.

This thesis explores the ethical and legal dilemmas that accompany the rapid technological development occurring in the field of genetic sequencing by considering three paradigmatic examples of the new situations that genetic screening and whole genome sequencing (WGS) in various healthy populations present to ethicists. As costs to perform genetic sequencing have decreased, direct-to-consumer (DTC) genetic sequencing has become widespread. In the first chapter, the history and legal and ethical implications of this commercial gene sequencing are discussed. DTC genetic sequencing occurs outside of the medical setting and often without the oversight or even knowledge of a healthcare professional. As costs continue to drop, widespread genetic sequencing may become a part of public health policy, used for sequencing entire populations. In the second chapter, ethical issues involved in screening healthy populations using WGS are considered. As WGS becomes more prevalent, it will eventually move into neonatal and pediatric care. In the third chapter, the legal and ethical implications of the use of whole-genome sequencing in fetuses, newborns, and children are considered.

There has been an explosion of companies providing DTC genetic sequencing for markers of increased risk of developing certain diseases. While genetic sequencing used to be solely at the discretion of researchers, healthcare providers and genetic counselors, it is now available to anyone willing to spit into a test tube and pay a few hundred dollars or less for their results. The FDA has responded to this form of sequencing by temporarily banning some commercial companies from providing information about results that may affect health. This ban has been lifted in the United States for some conditions, but full "health reports" are still commercially available in other countries and may soon be available in the US again as well.

Chapter 1 considers the history of commercial genetic health sequencing both in the United States and abroad, using 23andMe, the most popular company currently operating and the company that has received the most attention from the FDA, as the primary example. This raises a number of these ethical issues. First, reliability of sequencing is somewhat questionable, as the labs involved are often not regulated by the FDA and make claims of certainty far beyond the currently available technology. Second, privacy of genetic information is also a concern, with potential reporting requirements, insurance impacts, and employment discrimination. Third, excess anxiety may also be caused by sequencing, as consumers wait for their results and try to understand esoteric percentages of risk, particularly of untreatable conditions like Alzheimer's. Fourth, results received may also be beyond the average consumer's ability to understand and accurately process. Fifth, the information available to consumers as they try to decide about whether to undergo genetic sequencing is varied at best and misleading at worst. True informed consent is problematic absent substantial effort. Sixth, the way that direct-to-consumer genetic sequencing is advertised can also present problems. Within healthcare settings, there is less incentive to hide risks from patients. Companies like 23andMe, on the other hand, are selling a product to make a profit, creating motive to hide or distort risks. Finally, healthcare providers are notably absent from the DTC process, and many of those providers have expressed concerns. Without consulting with someone trained in interpreting genetic results, the results that consumers receive could be missing important considerations, like family history or lifestyle issues. Doctors with little experience in genetics also fear having their practice and their available time swamped by patients who do wish to discuss their commercial genetic results with a healthcare professional.

Commercial genetic health sequencing, unlike the other two examples discussed, has already become a widespread reality. As such, researchers have been able to consider and gather data pertaining to the ethical issues involved in this use of novel gene sequencing technology. After considering the ethical issues involved in DTC genetic sequencing, I will discuss the available empirical data. Studies have shown that many of these concerns about consumer well-being have been overblown, particularly regarding potential large-scale consumer anxiety. More qualitative research has demonstrated, however, that while these concerns may not impact the large numbers of people that bioethicists feared, those that are adversely affected may face major personal and emotional challenges and concerns. These concerns are important, despite the findings of quantitative research, and need to be addressed.

As the cost to sequence a whole genome has decreased, the use of WGS to screen large populations has become more feasible. Currently, genetic sequencing in the healthcare setting is only performed when there is some indication that the patient may have a condition, usually either the presentation of symptoms or a concerning family history. Screening for any disease, genetic or pathological, in a healthy population is rare. In healthy adults, it is almost exclusively done in groups with a higher risk of catching or spreading disease. Tuberculosis screening, for instance, is usually only performed on those traveling to certain parts of the world or planning to work with the sick. With the decreasing costs of sequencing technology, however, some in public health are beginning to consider using WGS to screen entire healthy adult populations for a huge number of conditions, a possibility discussed in Chapter 2.

WGS screening of healthy adult populations would bring up new ethical issues that must be considered before the implementation of any sort of large-scale program. Genetic sequencing takes time and waiting for test results could create high levels of unnecessary anxiety. Many genetic results present uncertainty in meaning, either because of mistakes in sequencing or because of the unknowns inherent in current genetic knowledge. Results indicating the likelihood of developing future conditions that cannot be prevented or treated, for example Alzheimer's, may help people likely to contract the condition plan their lives, but may also cause them pain and suffering in the meantime. The results of genetic sequencing could cause genetic discrimination, particularly in disability insurance claims. Genetic information is unique because it provides information that can affect entire families, creating dilemmas for healthcare providers. The benefits of performing WGS in healthy adult populations may not be worth the costs, and the ratio of the two must be carefully considered.

There have been calls for WGS to be used for screening in healthy fetuses and children. Many have even suggested that this sequencing someday be included in standard newborn or prenatal screening procedures. This would create a host of ethical issues, and these issues are discussed in Chapter 3. Those in the disability rights community fear the impact of WGS in fetuses on the public perception of disability. Because of the uncertainty of benefit to the infant, WGS may not justifiably fit in with the current mandatory nature of newborn screening. Data acquired from mandatory newborn WGS would create privacy risks as well. When considering children, it is difficult to get true informed decisions from parents for WGS due to several complications. Parents may not even have the moral right to give permission for WGS to be performed on their children, as it may violate the child's

right not to know. Parental knowledge of genetics may contribute to genetic determinism, hindering the child's right to an open future. Adoption may also present special concerns when considering WGS in children.

There are a huge number of potential ethical quandaries that may accompany the decreasing cost and increasing ease of genetic sequencing and screening. Despite this, however, there are huge benefits that can come from this increased access to technology for both diagnostic and life planning purposes. The dilemmas presented in this thesis must be considered and addressed if society is to reap these benefits without major upheaval, scandal, and harm. Chapter 4 focuses on ways that these ethical concerns can be addressed and mitigated, particularly through reconsideration of the use of WGS for general screening purposes, education for those who chose to receive WGS, the expansion of the Genetic Information Nondiscrimination Act (GINA) protections, and the prohibition of WGS in fetuses, newborns, and children.

CHAPTER 1: DIRECT-TO-CONSUMER GENETIC SEQUENCING

Introduction

Technology allowing genetic sequencing has become less expensive and more widely available over the past decade, leading to an explosion of companies providing direct-to-consumer (DTC) genetic sequencing for markers of increased risk of developing particular diseases. The most well-known of these companies is 23andMe, a genetic screening service for ancestry that has expanded into also providing health information. While genetic sequencing used to be solely at the discretion of healthcare providers and genetic counselors, it is now available to anyone willing to spit into a test tube and pay a few hundred dollars or less for their results. This has raised significant ethical concerns among bioethicists, the FDA, and the general public. The FDA responded to these concerns by temporarily suspending 23&Me's operation as a health testing provider, although this suspension has been recently partially lifted. 23andMe often refers to their services as genetic testing, but under the definitions established in this thesis, they are actually performing genetic screening by sequencing large parts of the genomes of healthy people.

In an attempt to find solutions to the challenges presented by DTC genetic screening, bioethicists have begun to research the impacts of this testing on consumers, on health providers, and on society as a whole. Empirical studies have shown that many of these concerns about consumer well-being have been overblown, particularly regarding potential large-scale consumer anxiety. More qualitative research has demonstrated, however, that while these concerns may not affect the large numbers of people that bioethicists feared, those who are adversely impacted may face major personal and

emotional challenges and concerns. These concerns are important, despite the quantitative data, and need to be addressed.

This chapter looks at the history of 23andMe as an emblematic example of the growth of the DTC genetic testing industry. It then turns to several of the major ethical concerns raised by this testing, including reliability of the testing, privacy of genetic information, consumer anxiety caused by testing, consumers' ability to understand the results they receive, the information available to consumers online and its impact on informed consent, advertising issues, and the role and concerns of healthcare providers in DTC genetic screening.[1]

History

23andMe is one of the more popular and well-known DTC genetic screening services. In 2008, the company launched as a companion service to Ancestry.com, offering genetic sequencing to provide customers with information about their heritage, their relatives, and their health.[2] In June of 2010, the FDA released a letter warning 23andMe, as well as four other similar companies, that FDA approval would be required for the health-related sequencing these companies were performing, despite the tests' being performed only in a single lab owned by each company and not distributed to other labs, a practice generally outside the FDA's purview.[3] The company responded by filing for approval with the FDA in July of 2012, submitting some follow up material that September,

[1] The storage of this genetic information for use in research is beyond the scope of this chapter.
[2] Samuel Gibbs, "DNA-Screening Test 23andMe Launches in UK after US Ban," *The Guardian*, December 1, 2014, sec. Technology, https://www.theguardian.com/technology/2014/dec/02/google-genetic-testing-23andme-uk-launch.
[3] Andrew Pollack, "F.D.A. Faults 5 Companies on Genetic Tests," *The New York Times*, June 11, 2010, http://www.nytimes.com/2010/06/12/health/12genome.html.

but failed to communicate with the FDA after their first follow up submission.[4] After more than a year without response, the FDA ordered that all health information testing cease in a letter published in November, 2013. The FDA letter cited a lack of adequate evidence that the methods used by 23andMe provided accurate health results and frustration with the company's lack of communication.[5] 23andMe complied the next month, providing only ancestry information to its American customers.[6]

Around this time, a class action lawsuit was filed against the company, alleging that the advertising misled customers, that the test results provided were "meaningless," and that there was "no analytical or clinical validation for the [genetic testing] for its advertised uses."[7] This suit was dismissed to compel arbitration in 2016 after the Ninth Circuit Court determined that the arbitration clause in the service agreement provided to the customers was valid and enforceable.[8]

In June 2014, 23andMe submitted paperwork to the FDA in an attempt to receive approval for the determination of one specific genotype, a marker for Bloom syndrome, a rare condition found mainly in Ashkenazi Jews. After studies were submitted showing an excellent concordance with conventional DNA sequencing methods and relatively high

[4] Anna Edney, "FDA Tells Google-Backed 23andMe to Halt DNA Test Service," *Bloomberg.com*, November 25, 2013, http://www.bloomberg.com/news/articles/2013-11-25/fda-tells-google-backed-23andme-to-halt-dna-test-service.
[5] Andrew Pollack, "F.D.A. Orders Genetic Testing Firm to Stop Selling DNA Analysis Service," *The New York Times*, November 25, 2013, http://www.nytimes.com/2013/11/26/business/fda-demands-a-halt-to-a-dna-test-kits-marketing.html.
[6] Brian Fung, "Bowing Again to the FDA, 23andMe Stops Issuing Health-Related Genetic Reports," *Washington Post*, December 6, 2013, https://www.washingtonpost.com/news/the-switch/wp/2013/12/06/bowing-again-to-the-fda-23andme-stops-issuing-health-related-genetic-reports/.
[7] Dan Munro, "Class Action Law Suit Filed Against 23andMe," *Forbes*, December 2, 2013, http://www.forbes.com/sites/danmunro/2013/12/02/class-action-law-suit-filed-against-23andme/.
[8] Erica Teichert, "23andMe Escapes California Class Action," Modern Healthcare, August 24, 2016, http://www.modernhealthcare.com/article/20160824/NEWS/160829974.

user comprehension of results, the FDA approved the screening, re-opening the door for DTC genetic screening in the United States.[9] In October of 2015, that door was opened wider, with information about an individual's carrier status for thirty-six conditions, including cystic fibrosis, sickle cell anemia, and Tay-Sachs disease, becoming available.[10] On April 6, 2017, the FDA approved 23andMe to provide screening for genotypes related to ten health conditions, including late-onset Alzheimer's and Parkinson's Disease, finding that studies indicate that "23andMe GHR tests correctly and consistently identified variants associated with the 10 indicated conditions or diseases from a saliva sample" and " people using the tests understood more than 90 percent of the information presented in the reports."[11] While this is a major step forward for DTC genetic testing companies, it is still a far cry from the 240 health conditions, including breast cancer, that the company offered risk percentages for prior to the 2013 FDA shutdown.[12]

Even these limited health data were prohibited by state law in some places. New York had laws that prohibited residents from sending saliva samples out of the state. Maryland had taken their prohibition further, barring DTC genetic testing in any form. In December 2015, however, these laws were challenged in federal court, where it was

[9] Robert Hof, "Seven Months After FDA Slapdown, 23andMe Returns with New Health Report Submission," Forbes, June 20, 2014, http://www.forbes.com/sites/roberthof/2014/06/20/seven-months-after-fda-slapdown-23andme-returns-with-new-health-report-submission/; John Gever, "2015 Recap: FDA Approves First 23andMe Genetic Test," MedPage Today, December 28, 2015, http://www.medpagetoday.com/Genetics/GeneticTesting/55438.
[10] Pollack, "23andMe Will Resume Giving Users Health Data."
[11] FDA Office of the Commissioner, "Press Announcements - FDA Allows Marketing of First Direct-to-Consumer Tests That Provide Genetic Risk Information for Certain Conditions," April 6, 2017, https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm551185.htm.
[12] Erika Check Hayden, "Out of Regulatory Limbo, 23andMe Resumes Some Health Tests and Hopes to Offer More," *Nature News*, October 27, 2015, https://doi.org/10.1038/nature.2015.18641.

determined that the FDA's designation of 23andMe's test kits as over-the-counter superseded the state laws prohibiting their use.[13]

Despite the limitations placed on 23andMe in the United States by the FDA, the company continued to expand and offer its health-related testing services internationally. Full genetic screening with the accompanying health information became available in the United Kingdom in December of 2014[14] and in Canada in October of 2015[15] and continues to be available today. The health agencies in both Canada and the UK require only that the method of collection, collecting saliva in a tube, be safe, a far lower standard that the FDA's requirements that the screening be reliably accurate, and the results and their implications be fully understood by customers.[16]

Ethical Concerns

Many in the medical community have expressed concern over the ethical issues posed by the DTC genetic screening offered by 23andMe and similar companies. Questions of reliability, privacy, consumer anxiety, the ability of consumers to understand results, the ability of consumers to give informed consent, the role of healthcare providers in a DTC environment, and the impact of DTC genetic screening advertisement all arise and must be addressed. Researchers have been working since the advent of DTC genetic screening to

[13] Mark Huffman, "New York and Maryland Prohibitions against 23andMe Fall," December 4, 2015, https://www.consumeraffairs.com/news/new-york-and-maryland-prohibitions-against-23andme-fall-120415.html.
[14] Gibbs, "DNA-Screening Test 23andMe Launches in UK after US Ban."
[15] Andre Picard, "Controversial Genetic Self-Testing Kits Coming to Canada," The Globe and Mail, October 2, 2014, http://www.theglobeandmail.com/life/health-and-fitness/health/genetic-self-testing-kits-to-come-to-canada/article20885678/.
[16] Peter Whoriskey, "Wondering If You Have the Gene Linked to Alzheimer's? You May Have to Leave the U.S. to Find Out," *Washington Post*, December 7, 2015, https://www.washingtonpost.com/news/wonk/wp/2015/12/07/wondering-if-you-have-the-gene-linked-to-alzheimers-you-may-have-to-leave-the-u-s-to-find-out/.

empirically study the impacts of these different concerns. While much of this research indicates that many of these ethical concerns are somewhat overblown, it is important to note the limitations of this research and to continue discussing DTC genetic screening's ethical implications. In 2010, the Secretary's Advisory Committee on Genetics, Health, and Society released a report on the ethical and legal issues in DTC genetic sequencing. This report outline many of the ethical issues discussed below, including a lack of federal oversight, uncertainty in results, privacy difficulties, and a lack of consumer understanding, and outlined several recommendations for bridging gaps in reliability, advertising regulation, and consumer education.[17] The Government Accountability Office conducted a study of DTC companies later the same year, using donor samples sent to different companies with both true and false information. They discovered problems with reliability, consistency between companies, and egregiously misleading advertising.[18] Despite these early reports, however, very little has been done to address the ethical implications of DTC genetic screening, and the concerns elucidated then remain relevant today.[19]

Reliability

The reliability of DTC genetic screening is incredibly important. Unreliable results can increase anxiety and cause unnecessary use of health services in those whose reported probabilities of disease are skewed high by misunderstanding and mistake, while at the

[17] Secretary's Advisory Committee on Genetics, Health, and Society, "Direct-to-Consumer Genetic Testing" (Department of Health and Human Services, April 2010), http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_DTC_report_2010.pdf.
[18] Gregory Kutz, "Direct-to-Consumer Genetic Tests: Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices," Testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives (United States Government Accountability Office, July 22, 2010), https://www.gao.gov/assets/130/125079.pdf.
[19] Muin J. Khoury, "Direct to Consumer Genetic Testing," Centers for Disease Control and Prevention, *Genomics and Health Impact Blog* (blog), April 18, 2017, https://blogs.cdc.gov/genomics/2017/04/18/direct-to-consumer-2/.

same time preventing those whose results are skewed in the other direction from seeking further testing and care that could benefit their health. The accuracy of the actual sequencing procedure used by DTC testing companies have been shown to be high, with one study finding the concordance rates between three of the major services available to be above 99.6%.[20] 99.6%, however, is not 100%. One case study found several examples of mistaken findings in DTC reports on the presence of genetic variations that relate to a person's tolerance of a particular drug that is used to treat leukemia, as well as genes used to predict breast cancer.[21]

Even with 100% accuracy in the genetic sequencing itself, however, there are still reliability concerns present. Among different companies, the percentages presented for the likelihood of developing certain diseases tends to vary greatly. Despite the fact that these companies have the same genome in front of them, differences in reference populations, methods of calculating risk percentages, and which genes are considered can result in very different predictions.[22] One medical researcher reported having her genome sequenced with four different companies, each of whom returned different risk assessments. These assessments were based on the same genetic code and the same background research, but the companies had calculated the risks presented by these genes completely differently, leading to confusion and a lack of trust in the results.[23]

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[20] Kenta Imai, Larry J. Kricka, and Paolo Fortina, "Concordance Study of 3 Direct-to-Consumer Genetic-Testing Services," Clinical Chemistry 57, no. 3 (March 2011): 518–21.
[21] C A Brownstein, D M Margulies, and S F Manzi, "Misinterpretation of TPMT by a DTC Genetic Testing Company," Clinical Pharmacology & Therapeutics 95, no. 6 (June 1, 2014): 598–600, doi:10.1038/clpt.2014.60.
[22] Kenta Imai, Larry J. Kricka, and Paolo Fortina, "Concordance Study of 3 Direct-to-Consumer Genetic-Testing Services," Clinical Chemistry 57, no. 3 (March 2011): 518–21.
[23] James M. DuBois, "Genetic Testing: Understanding the Personal Stories," Narrative Inquiry in Bioethics 5, no. 3 (January 8, 2016): 201–3, doi:10.1353/nib.2015.0061.

Reliability must be considered not only in terms of the concordance or accuracy of the genetic tests themselves, but also in terms of how risk is calculated and reported. Increases in FDA oversight of the methods used by DTC gene screening companies could help alleviate some of these issues. As the science of genomics progresses, the reliability of interpretations will also progress, as much of the current confusion is due to our lack of knowledge about the exact ways certain genes influence disease. In the meantime, however, DTC genetic screening companies must be careful to conduct their calculations in a transparent way and make clear to their consumers the inherent uncertainty in the information they are providing.

Privacy

After testing has been completed, there are ethical implications for consumers' privacy, something the consumer may or may not realize. The first of these issues involves insurance. While the Genetic Information Nondiscrimination Act of 2008 (GINA) does prevent health insurance providers or employers from considering a person's genetic information or genetic predispositions when making hiring or insurance decisions, GINA's insurance protections only extend to health insurance. Companies offering other types of insurance, particularly life insurance, disability insurance, or long-term care insurance, are not covered.[24] These companies legally can and frequently do ask those attempting to procure these types of insurance for any genetic testing information they may have. Failure to answer these questions honestly, if it is discovered, can lead to breach of contract actions, a termination of coverage, and in the case of life insurance, no payout whatsoever.[25] This

[24] "Genetic Information Nondiscrimination Act of 2008," Pub. L. No. 110–233, 122 Stat. 881 (2008).
[25] Jody Allard, "How Gene Testing Forced Me to Reveal My Private Health Information," VICE, May 27, 2016, http://www.vice.com/read/how-gene-testing-forced-me-to-reveal-my-private-health-information.

concern could be addressed by updating the GINA legislation to include all providers of insurance relating to health and disability.

Another privacy concern involves the use of stored genetic information by law enforcement. The privacy policies available on 23andMe's website say that the company will comply with court orders to turn over individual genetic information. The company will inform the consumer if this happens, unless disclosing this information violates the court order or the law.[26] While this initially seems like a major issue, the legal protections already in place in the criminal justice system prevent the abuse of this power by law enforcement. Court orders are only issued with probable cause, and a law enforcement officer with probable cause to retrieve your DNA from a gene testing company would also have probable cause to just take a sample of your DNA and sequence it themselves. Therefore, having your genetic material stored by the company will not change whether law enforcement gets your DNA for comparison.

Consumer Anxiety

Consumer anxiety is one of the most frequently cited concerns about the direct-to-consumer nature of DTC genetic screening. Without having the assistance of a health care professional in deciding on whether to test, what to test, and how to interpret results, consumers may have increases in anxiety due to their test results, particularly results that show an increased chance of incurable and unpreventable diseases like Alzheimer's or Parkinson's. Fears of creating this anxiety for consumers have led 23andMe to offer results

[26] Kashmir Hill, "Cops Are Asking Ancestry.Com and 23andMe for Their Customers' DNA," Fusion (blog), October 16, 2015, http://fusion.net/story/215204/law-enforcement-agencies-are-asking-ancestry-com-and-23andme-for-their-customers-dna/.

relating to Alzheimer's or Parkinson's only after it has been specifically requested by the consumer.[27] Misunderstandings of results can also create excess anxiety in consumers.

Because of the frequent concern expressed about increased consumer anxiety, there have been a number of empirical studies on the impact of DTC genetic screening on consumer anxiety. These studies have generally found that there is no statistically significant relationship between the use of DTC genetic screening and increases in anxiety. One study published in the New England Journal of Medicine found no significant difference in anxiety, with 90.3% of consumers having no test-related distress.[28] An online survey found that only 24.6% of those who responded claimed a change in health anxiety, with most of those people reporting a decrease in anxiety.[29] Longitudinal studies have had similar findings. An in-depth study of twenty patients published in the Journal of Community Genetics found, after following the patients for a year, that most either felt no emotional impact or were relieved after receiving their DTC results.[30] A larger yearlong study of 2240 DTC genetic screening consumers found no test-related distress in 96.8% of the participants.[31] A randomized study at the Mayo Clinic found that anxiety levels in DTC

[27] Gina Kolata, "F.D.A. Will Allow 23andMe to Sell Genetic Tests for Disease Risk to Consumers," *The New York Times*, April 6, 2017, sec. Health, https://www.nytimes.com/2017/04/06/health/fda-genetic-tests-23andme.html.
[28] Cinnamon S. Bloss, Nicholas J. Schork, and Eric J. Topol, "Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk," *New England Journal of Medicine* 364, no. 6 (February 10, 2011): 524–34, doi:10.1056/NEJMoa1011893.
[29] Corin Egglestone, Anne Morris, and Ann O'Brien, "Effect of Direct-to-Consumer Genetic Tests on Health Behaviour and Anxiety: A Survey of Consumers and Potential Consumers," *Journal of Genetic Counseling* 22, no. 5 (April 3, 2013): 565–75, doi:10.1007/s10897-013-9582-6.
[30] Katherine Wasson et al., "Primary Care Patients' Views and Decisions About, Experience of and Reactions to Direct-to-Consumer Genetic Testing: A Longitudinal Study," *Journal of Community Genetics* 4, no. 4 (July 7, 2013): 495–505, doi:10.1007/s12687-013-0156-y.
[31] Cinnamon S. Bloss et al., "Impact of Direct-to-Consumer Genomic Testing at Long Term Follow-Up," *Journal of Medical Genetics*, April 4, 2013, jmedgenet-2012-101207, doi:10.1136/jmedgenet-2012-101207.

consumers were only modestly elevated a week after receiving results, and no significant difference in anxiety after a year.[32]

Concerns over the usefulness of these sorts of empirical studies on consumer anxiety have been raised. The terms "anxiety" and "worry" are rarely defined in these types of studies. Anxiety is also usually self-reported, instead of measured using scientifically designed and tested scales. Anxiety itself is not a reliable or predictive measure for assessing the psychological or behavior impacts of DTC genetic screening. Notably, anxiety is generally not correlated with changes in health behavior or other expected responses to genetic results.[33] Predictive health information of all types are going to create some form of anxiety, either when waiting on results or after receiving them. This does not mean that these results aren't still beneficial to patients. The empirical studies that have been conducted so far may also not have typical sample populations. While DTC genetic screening is growing, it is still in its early stages and those who have utilized it are primarily early adopters. These early adopters are more likely to be educated, experienced in health care or genetics, or more prepared to handle their results. This difference may be skewing the empirical data and preventing studies from revealing the true risks to the average consumer.

There is also a major difference in reactions between those who receive expected or negative results, meaning no adverse results were found, and those who receive surprising or positive results. This can make looking at the anxiety of a group of DTC

[32] "Emotional Toll of DTC Genetic Testing," *Medical Ethics Advisor*, December 1, 2011.
[33] Serena Oliveri et al., "Anxiety Delivered Direct-to-Consumer: Are We Asking the Right Questions about the Impacts of DTC Genetic Testing?," *Journal of Medical Genetics* 53, no. 12 (December 1, 2016): 798–99, https://doi.org/10.1136/jmedgenet-2016-104184.

genetic screening consumers as a whole and drawing conclusions based on percentages and statistical averages misleading. If a majority of those who receive their test results do not feel anxious because their results were negative, and their disease risks are low or average, those who have positive results or high risks and feel very anxious will get lost in the statistical analysis. While those who have a catastrophic reaction to their results may be very rare[34] and those with increased anxiety may make up a small percentage of DTC consumers, these people's difficulties and concerns are still important. The personal stories of those who have received DTC genetic screening show that despite the small impact claimed by empirical studies, anxiety caused by the results can be very real and very concerning. Case studies show patients who receive genetic information, particularly those undergoing commercial BRCA mutation testing for breast cancer risk, going to genetic counselors with severe anxiety, distress, and a lack of knowledge and understanding.[35] Other personal stories of DTC genetic screening consumers tell of severe personal anxiety caused by confusion over the meaning of risk percentages, by the discovery of a predisposition to Alzheimer's thanks to testing of one's parents or children, and other major concerns.[36]

This sort of anxiety needs to be addressed to prevent DTC genetic screening from causing unnecessary harm to consumers. By addressing the other ethical issues discussed here, however, much of this anxiety can be alleviated. Increased healthcare professional

[34] J. Scott Roberts and Jenny Ostergren, "Direct-to-Consumer Genetic Testing and Personal Genomics Services: A Review of Recent Empirical Studies," *Current Genetic Medicine Reports* 1, no. 3 (July 12, 2013): 182–200, doi:10.1007/s40142-013-0018-2.
[35] Lindsay Dohany et al., "Psychological Distress with Direct-to-Consumer Genetic Testing: A Case Report of an Unexpected BRCA Positive Test Result," *Journal of Genetic Counseling* 21, no. 3 (January 21, 2012): 399–401, doi:10.1007/s10897-011-9475-5.
[36] DuBois, "Genetic Testing."

involvement and information presented in a more understandable format will help alleviate anxiety created by confusion or the misinterpretation of the meanings of risks. Providing greater information in a more easily accessibly format during the purchase and consent process can help prevent nasty surprises and help consumers prepare themselves for the information they are going to receive. While consumer anxiety can be a major issue, it is a symptom of the other issues with DTC genetic screening and will decrease as these other issues are addressed.

Consumer Understanding

One of the major differences between genetic testing done in a health care setting and DTC genetic screening is the way in which results are delivered. In a healthcare setting, test results come from a doctor or genetic counselor, who can relay information in a way that's tailored to the individual's needs, wants, and health literacy level. DTC results, however, are not. Consumers often receive over one hundred different health-based reports, and these results are accompanied by hundreds of pages of reading and supplementary information, which are written on a grade level higher than the average American adult is capable of truly comprehending and may not truly represent a person's health risks.[37]

One concern critics of DTC screening point out is a fear that without the guidance of healthcare professionals, the average consumer won't be able to understand the inherent uncertainty of disease risks presented as percentages. Genetics, after all, are only part of what determines a person's health and overall risk of developing a disease. Type 2 diabetes,

[37] Christina R. Lachance et al., "Informational Content, Literacy Demands, and Usability of Websites Offering Health-Related Genetic Tests Directly to Consumers," *Genetics in Medicine* 12, no. 5 (May 2010): 304–12, doi:10.1097/GIM.0b013e3181dbd8b2.

for example, is often one of the diseases that risk levels are given for, but genetics only determine about a quarter of a person's actual risk of developing the condition over the course of their lifetime.[38] Studies show that this particular risk may be overblown. The majority of people in western populations understand that health is a complicated combination of inheritance and behavioral factors.[39] DTC consumers were also found to be unlikely to interpret genetic results as deterministic of health outcomes, although those with lower education levels were more likely to interpret results deterministically.[40]

More general understanding is still a valid concern, however. When average people are given either real or sample test results from 23andMe and other DTC genetic screening companies, confusion seems to be the norm. One online survey gave the same sample results to potential consumers and to genetic counselors. Most of the consumers believed that the results were easy to interpret, but few of them actually interpreted them correctly. Consumer interpretations were very different from the interpretations given by genetic counselors, particularly with regard to the usefulness of the results.[41] When customers of 23andMe were given two mock results, only 23.8% were able to interpret both of the reports correctly. There was a major income gap between those who were able to understand and those who weren't, with those making more than $50,000 a year 3.289

[38] Rachael Rettner, "23andMe: What's Really Wrong with Personal Genetic Tests," Live Science, November 26, 2013, http://www.livescience.com/41534-23andme-direct-to-consumer-genetic-test-shortcomings.html.
[39] Colleen M. McBride, Christopher H. Wade, and Kimberly A. Kaphingst, "Consumers' Views of Direct-to-Consumer Genetic Information," *Annual Review of Genomics and Human Genetics* 11, no. 1 (2010): 427–46, doi:10.1146/annurev-genom-082509-141604.
[40] Kimberly A. Kaphingst et al., "Patients' Understanding of and Responses to Multiplex Genetic Susceptibility Test Results," *Genetics in Medicine* 14, no. 7 (July 2012): 681–87, doi:10.1038/gim.2012.22.
[41] J. W. Leighton, K. Valverde, and B. A. Bernhardt, "The General Public's Understanding and Perception of Direct-to-Consumer Genetic Test Results," *Public Health Genomics* 15, no. 1 (June 30, 2011): 11–21, doi:10.1159/000327159.

times more likely to interpret both results correctly.[42] Personal narratives seem to support these findings. A British reporter who received 107 health-based reports described them as "cryptic" and extremely confusing.[43] One tale of confusion came from a medical researcher, showing that understanding problems in DTC genetic testing are widespread and serious, regardless of education level.[44]

This widespread confusion must be addressed for DTC genetic screening to be provided in an ethical way. While making large amounts of supplemental information is an admirable attempt to foster self-education among consumers, it can be confusing. Genetic health results are inherently complicated, but genetic counselors manage to convey this information to their patients in an understandable way. DTC companies should involve healthcare providers and genetic counselors in a revamping of the way they present health information to their consumers, perhaps by recommending that all positive findings be confirmed in a clinical setting. Simple key facts and clear language should be used to convey results in a way that minimizes confusion, thereby minimizing the anxiety associated with confusion and uncertainty.

Available Information and Informed Consent

Confusion can be an issue in DTC genetic screening even before consumers receive results. Having adequate information available in an understandable format is a necessity for consumers to be truly informed when they give their consent to having their genes

[42] Scott McGrath and Dhundy (Kiran) Bastola, "DTC Genetic Testing and Consumer Comprehension," in *Proceedings of the 5th ACM Conference on Bioinformatics, Computational Biology, and Health Informatics*, BCB '14 (New York, NY, USA: ACM, 2014), 582–583, doi:10.1145/2649387.2660559.
[43] Oliver Smith, "23andMe Analyzed My DNA, but Is It a Good Idea?," The Memo, April 25, 2016, http://www.thememo.com/2016/04/25/23andme-scientists-dna-genetics-analysed-ethics-scientist/.
[44] DuBois, "Genetic Testing."

sequenced for health information. Consumers' primary sources of this information are the websites run by the companies. It is important that the websites for companies offering DTC screening give consumers an accurate picture of the results they will be receiving, including the risks and potential benefits of having this information, the limitations of current genetic health results, the potential impacts on family members, and the policies of the companies regarding privacy. The quality and availability of this information varies wildly from company to company, but, in general, there are serious deficits in this area. Benefit statements presented on these websites outnumber risk and limitation statements six to one. These statements are often contradictory. One company, for example, claimed that benefits included potential disease prevention, but also claimed that their products were not intended to diagnose, treat, cure, or prevent any disease.[45]

One study evaluated twenty-nine health-related DTC genetic screening websites for informational content, health literacy required for understanding, and usability. The findings showed major deficiencies in available information. These sites on average required a grade fifteen reading level, greater than the education of the average person. Only 7% of sites used mostly common language and, when technical terms were required, explained their meanings consistently. Less than half provided a glossary or tutorial to help consumers understand the information. Only one-third of sites provided the scientific evidence that supported testing particular genetic markers and only one-fifth explained how they used the genetic markers to calculate consumer's health risk. Information about the limitations of genetic health results was generally difficult to find and privacy information

[45] Amanda Singleton et al., "Informed Choice in Direct-to-Consumer Genetic Testing (DTCGT) Websites: A Content Analysis of Benefits, Risks, and Limitations," *Journal of Genetic Counseling* 21, no. 3 (December 23, 2011): 433–39, doi:10.1007/s10897-011-9474-6.

and risks were easily accessible on only half of the sites, but 90% of sites provided benefits in prominent and easily accessible locations. Healthcare provider involvement was also generally unavailable on most sites. Only 14% provided consumers with an opportunity to consult with a healthcare provider before testing and only 28% offered consultation post-testing. Only 21% of sites offered information for healthcare providers looking for assistance in interpreting their patients' DTC genetic results.[46]

Professional associations like the American College of Medical Genetics and Genomics have provided guidelines and suggestions about what should be made available to consumers prior to their purchase and prior to receiving their results. These guidelines recommend providing information on test validity, the current limitations of the science of genetic testing, and the risks and benefits of testing. They also suggest using Clinical Laboratory Improvement Amendments (CLIA)-certified labs to ensure reliable results without contamination, maintaining consumer's privacy, providing clinical evidence for behavioral change recommendations, and involving a health professional in the presentation of results.[47] These guidelines are a good start to providing consumers with the information they need to give informed consent. They are currently not mandatory, however. As the FDA takes greater control over the DTC genetic testing industry, they will be in a position to make these guidelines mandatory as a condition of approval, helping ensure that consumers know what they're getting into.

Receiving results for unpreventable or untreatable diseases like Alzheimer's or Parkinson's carries a higher risk of anxiety and distress, and therefore consumers need

[46] Lachance et al., "Informational Content, Literacy Demands, and Usability of Websites Offering Health-Related Genetic Tests Directly to Consumers."
[47] Ibid.

more protection in these areas. 23andMe provides additional information about the risks involved before this kind of information is "unlocked" for the consumer in an attempt to make sure that people have considered the implications of this knowledge, but this may not be enough. Personal stories demonstrate that many consumers just click through these warnings without reading or digesting the additional information.[48] Additional measures like quizzing on information may help prevent consumers from skipping over this important information without understanding the implications of what they are doing.

The moral responsibility of health care providers to receive informed consent before any testing or treatment of a patient is founded on the fiduciary duty of the healthcare provider to the patient, the asymmetry on knowledge between the patient and the provider, and the general right to bodily autonomy. While there is no fiduciary duty that exists between a DTC genetics company and their consumer, the company still has a moral responsibility to gain informed consent. A knowledge asymmetry is still present in a commercial setting, as is the consumers' right to bodily autonomy. Despite a lack of fiduciary duty owed by the company, DTC genetic companies do have a duty not to harm their customers. By respecting the autonomy of consumers and ensuring they are properly informed and making autonomous decisions, companies can increase the likelihood of benefit and decrease the risk to their customers.

Advertising

Advertising also helps to provide information to the public about the risks and benefits of DTC genetic screening. This advertising can be helpful and informative, but, if

[48] DuBois, "Genetic Testing."

poorly done, can cause anxiety and spread misinformation. It is important that this advertising be done responsibly.

An example of the problems of irresponsible DTC genetic screening advertisement can be found in the US marketing campaign undertaken in Denver and Atlanta to encourage female consumers to get screened for the presence of BRCA, a serious risk factor for breast and uterine cancer. Those who were at low risk for possessing the BRCA genes, those without a family history of breast cancer, had little increase in anxiety due to exposure to the advertising campaign. Those with a higher risk as indicated by family history, however, had an increase in anxiety.[49] Of those exposed to the ad campaign, 10% reported increased worry about breast cancer and the BRCA gene. Many of those exposed also overestimated the benefits and appropriateness of screening, with many women considering screening that would not generally be suggested by a genetic counselor or other healthcare provider.[50] While the gene in this instance was specific, advertising screening for a broader selection of health risks could have similar effects on the general population.

The advertising produced by DTC genetic screening companies has the potential to greatly influence the public's perception of the risks, benefits, and appropriateness of genetic screening. Advertising must be accurate about the potential benefits of screening, without making exaggerated or unsubstantiated claims. It should also provide information about the risks of screening similar to the list of potential side effects listed at the end of every prescription drug advertisement. With the extension of FDA authority to cover DTC genetic testing in recent years, advertising issues could be safeguarded against through

[49] McBride, Wade, and Kaphingst, "Consumers' Views of Direct-to-Consumer Genetic Information."
[50] Bloss et al., "Impact of Direct-to-Consumer Genomic Testing at Long Term Follow-Up."

regulation similar to that used to control prescription drug advertisement, something the FDA should consider implementing.

The Role of Healthcare Providers

Healthcare providers and genetic counselors have three major concerns about DTC genetic screening.[51] Providers, particularly primary care physicians, do not feel informed or prepared enough to answer questions and effectively counsel their patients who come to them with DTC results. They also fear that an increase in DTC genetic screening will lead to an overutilization of healthcare services and diagnostic testing, as well as take up significant amounts of provider time that could be more productively spent elsewhere. On the other hand, there are concerns about patients' reliance on DTC results without assistance from a healthcare provider or genetic counselor, particularly considering the lack of lifestyle information included in the percentage risks that DTC companies provide.

Surveys of health professionals show that most do not feel confident in their ability to assist patients who come to them with DTC genetic results. Levels of experience with these results are low, and healthcare providers' awareness of the details of DTC genetic screening is inconsistent.[52] This problem is particularly evident when talking to primary care physicians. When surveyed, only about 15% of family and internal medical providers felt that they were prepared to answer patients' questions about their results.[53] This knowledge deficiency leads directly to an increased use of the healthcare system. Many

[51] Lesley Goldsmith et al., "Direct-to-Consumer Genomic Testing from the Perspective of the Health Professional: A Systematic Review of the Literature," *Journal of Community Genetics* 4, no. 2 (January 16, 2013): 169–80, doi:10.1007/s12687-012-0135-8.
[52] Ibid.
[53] Karen P. Powell et al., "Primary Care Physicians' Awareness, Experience and Opinions of Direct-to-Consumer Genetic Testing," *Journal of Genetic Counseling* 21, no. 1 (July 16, 2011): 113–26, doi:10.1007/s10897-011-9390-9.

genetic counselors have seen an increase in referral of DTC patients to them from primary care physicians, both those who feel in over their head, and those who think the results show something serious. While only about half of genetic professionals surveyed believed that DTC genetic results were useful to them in helping their patients, these results led to suggestions of downstream care and confirmatory testing costing anywhere from $40 to $20,604.[54] Although there is currently little statistical evidence that DTC genetic screening prompts notable changes in healthcare utilization, numbers of doctor visits, or the use of screening tests and other medical procedures,[55] these surveys of genetic counselors indicate that this is likely to change as the costs of DTC genetic screening go down and awareness and utilization of these services rise.

Despite this fear of overutilization, there is an opposite, but equally concerning, problem. Healthcare providers fear that consumers who receive genetic results and choose not to discuss them with their healthcare providers might face issues caused by misunderstanding or over-valuing results. According to a comprehensive 2012 survey, only about 28% of DTC genetic screening consumers actually follow up with a health professional, and only 9% follow up with confirmatory testing.[56] Those who receive reports of low risk may feel a false sense of security, despite the possibility of other risk factors that the reports do not consider like lifestyle choices or family history. Those with a higher risk for certain diseases would possibly be better served by going through confirmatory clinical testing, which is more reliable, can be tailored to specific patients and their personal

[54] Monica A. Giovanni et al., "Health-Care Referrals from Direct-to-Consumer Genetic Testing," *Genetic Testing and Molecular Biomarkers* 14, no. 6 (October 28, 2010): 817–19, doi:10.1089/gtmb.2010.0051.
[55] Roberts and Ostergren, "Direct-to-Consumer Genetic Testing and Personal Genomics Services."
[56] David J. Kaufman et al., "Risky Business: Risk Perception and the Use of Medical Services among Customers of DTC Personal Genetic Testing," *Journal of Genetic Counseling* 21, no. 3 (January 26, 2012): 413–22, doi:10.1007/s10897-012-9483-0.

risk factors and family history, and is presented to genetic counselors in a form that they are prepared to interpret quickly and accurately.[57] Genetic counselors are also usually in a better position to know when confirmatory testing is indicated, preventing overutilization of medical services.

These important concerns about DTC genetic testing must be addressed, particularly as use increases. Consumers should be strongly encouraged to share their results with their primary care physician and told that positive results require confirmatory testing in a clinical setting. If DTC companies provide results in a way that is understandable to health professionals and provide information to help them in counseling their patients, problems of both over and underutilization of health services could be remedied. Armed with the knowledge necessary to interpret test results during routine preventive care, they will be able to perform gatekeeping functions to the use of medical services based on these tests, discouraging overutilization while still ensuring those with higher disease risk get the care and additional screening indicated.

[57] Pim Suwannarat, MD, "Why You Should Think Twice About At-Home Genetic Testing," *US News & World Report*, July 11, 2016, http://health.usnews.com/health-news/patient-advice/articles/2016-07-11/why-you-should-think-twice-about-at-home-genetic-testing.

CHAPTER 2: WHOLE GENOME SEQUENCING IN HEALTHY ADULTS

Introduction

As genetic sequencing becomes more common and commercialized, attitudes toward whole genome sequencing (WGS) are beginning to change as well. Now that genetic testing is not just for those in the process of diagnosis, many healthy adults may begin to expect WGS as a part of their standard preventive healthcare, possibly even part of their standard health insurance coverage. WGS is different from DTC genetic sequencing in two major ways. WGS takes place in a clinical setting and is done by healthcare providers. WGS also provides patients with significantly more information than DTC results, as WGS sequences the entire active genome while DTC sequencing focuses on sequencing certain genes. While WGS creates many issues similar to those raised by DTC genetic screening, this different setting and mass of available information create unique concerns as well. Patient anxiety, uncertainty about results, difficult issues surrounding non-treatable conditions, and the possibility of genetic discrimination are raised in both contexts, although the implications differ. New ethical concerns raised include the obligations patients and their healthcare providers might owe to patients' families and the benefits of including WGS in standard healthcare for the healthy compared to the costs involved.

Anxiety

Patients who receive WGS will face potential anxiety much like those who receive genetic results through commercial companies. Finding that one has a genetic propensity for a disease or some other negative condition can color a person's view of their life and

the world. Like anxiety in DTC consumers, however, concerns about this anxiety may be somewhat overblown.

In addition to creating personal difficulties, high levels of anxiety can prevent positive life changes in patients receiving results. Lifestyle changes are most likely to occur right after results are received, but these changes only occur when there is a balance of an awareness of danger and a feeling of control over their ultimate health outcomes.[58] Those who make healthy changes tend to be those who feel that there is a personalized threat to their health, but aren't so overwhelmed by fear that they feel as though they have no agency over their health outcomes. Some people will see genetic results as dispositive of their eventual outcome and believe that any lifestyle changes would have no impact and therefore wouldn't be worth the trouble.[59]

As WGS is still relatively expensive to do for a single individual and is not offered clinically, there has been little opportunity to study the actual impacts on patient anxiety levels. Limited evidence from clinical genetic screening of healthy populations shows that even when positive results are received, while anxiety does increase somewhat initially, it returned to almost baseline level in a fairly short period of time.[60] One study on this issue considered healthy patients who had received genetic testing diagnosing them with Lynch Syndrome three or more years previously. Lynch Syndrome is a genetic mutation that raises a person's chance of colorectal cancer by fifty to eighty percent and greatly increases

[58] Helle Vendel Petersen et al., "Balancing Life with an Increased Risk of Cancer: Lived Experiences in Healthy Individuals with Lynch Syndrome," *Journal of Genetic Counseling* 23, no. 5 (October 1, 2014): 778–84, 783, https://doi.org/10.1007/s10897-013-9682-3.
[59] H. L. Hietaranta-Luoma et al., "Using ApoE Genotyping to Promote Healthy Lifestyles in Finland – Psychological Impacts: Randomized Controlled Trial," *Journal of Genetic Counseling* 24, no. 6 (December 1, 2015): 908–21, https://doi.org/10.1007/s10897-015-9826-8.
[60] Ibid.

the chances of having other cancers as well.[61] Anxiety and worry in this population was found to have returned to baseline levels in six to twelve months after receiving results.[62] These healthy patients engaged in a balancing of their anxiety with the control that they felt over their health outcomes.[63] This balance was significantly helped by the knowledge that being aware of their condition and having regular scans conducted decreases morbidity and mortality by up to sixty percent.[64] This study emphasized the importance of actionability, the ability of information to be put to use in a clinical setting for treatment or preventive purposes, to resulting anxiety after receiving genetic results. Given the amount of information that comes from WGS, most patients who undergo WGS will receive actionable results of some sort, like those in the Lynch Syndrome study, but will also receive non-actionable results. Results that cannot be acted on may create a much higher level of anxiety in patients, as they do in consumers of DTC genetic testing, and, likewise, the experience of those patients should not be discounted.

Uncertainty

In addition to the anxiety created by receiving results, anxiety can be created by the uncertainty inherent in genetic sequencing. As in DTC sequencing, there are two major sources of uncertainty in WGS: a potential lack of accuracy of results and a lack of understanding of accurate results. Accuracy in testing results is a major concern, despite the amazing technological advances in genomic sequencing that have been made in the past decade. High quality WGS can identify base pairs at 99.9% accuracy. However, there

[61] Petersen et al., "Balancing Life with an Increased Risk of Cancer." at 778.
[62] Ibid at 782.
[63] Ibid at 783.
[64] Ibid at 779.

are six billion base pairs in a human genome, and even if only .1% of those base pairs are sequenced incorrectly, six million base pairs could be incorrect.[65] Those incorrect base pairs could result in giving bad information about health predictors being given to patients, causing unnecessary anxiety and potentially influencing patients' life choices.

The magnitude of information provided by WGS for each patient can be a source of uncertainty as well. The sheer volume of information available means that almost everyone will have abnormal findings of some sort.[66] The meaning of these findings may be uncertain; moreover, as more is learned, their interpretation may change, and could become more significant, less significant, or even more uncertain over time. There is significant uncertainty in the meaning of many, if not most, genetic results. While some genetic conditions are well understood, others confound scientists. In diseases that are caused partially by genetics and partially by environment, the ratio of influence is at best an educated guess. Many with a similar genotype will also have different phenotypical expressions, depending on environment or on interactions with other genes. As in DTC gene testing, trying to assign specific risk percentages for disease to the presence of particular genes will be difficult, even in a clinical environment. Many findings will not be actionable, and many people have no social framework for dealing with these findings, particularly if the spread of WGS is not also accompanied by the growth of pre-screening

[65] Christopher H. Wade, Beth A. Tarini, and Benjamin S. Wilfond, "Growing Up in the Genomic Era: Implications of Whole-Genome Sequencing for Children, Families, and Pediatric Practice," *Annual Review of Genomics and Human Genetics* 14, no. 1 (August 31, 2013): 535–55, 541, https://doi.org/10.1146/annurev-genom-091212-153425.
[66] Mark A. Rothstein, "The Case against Precipitous, Population Wide, Whole-Genome Sequencing," *The Journal of Law, Medicine & Ethics* 40, no. 3 (September 2012): 682–89, 682, https://doi.org/10.1111/j.1748-720X.2012.00699.x.

counseling.[67] Results that lack specificity when indicating late-onset, untreatable conditions can be particularly harmful. When a genotype does not provide specific information like degree of impairment or age of onset, these uncertainties will undoubtedly cause significant increases in anxiety. Without some certainty, patients will not be able to use the information in any positive way. When there is certainty, patients can at least plan a lifestyle that will be minimally impeded by their future disease, but uncertainty makes this benefit more speculative and increases the risk that patients might limit their lives unnecessarily because of their genetic code.

As science progresses, the significance of genetic findings may also become more evident. These new findings may ethically necessitate recontacting those who were tested previously, but this would be a resource-intensive activity that would have to be weighed carefully against the benefits of the new information obtained.

Genetic Discrimination

Like those who undergo DTC genetic screening, those who receive WGS as a part of their ordinary preventive care may face damage and discrimination based on their results. GINA prohibits the use of genetic information when making decisions about employment or private health insurance coverage.[68] Many states also have their own legal protections, with twenty-six states prohibiting health insurers from requiring genetic tests or information, forty-three states prohibiting health insurers from basing eligibility decisions on genetic information, and forty-one states prohibiting health insurers from

[67] R H Sijmons, "A Clinical Perspective on Ethical Issues in Genetic Testing," *Accountability in Research* 18, no. 3 (2011): 148–62.
[68] Note 24 supra.

using genetic information for risk classification in underwriting.[69] However, many areas of work and health are still susceptible to genetic discrimination and many argue against the protections for genetic information will lead to adverse selection, with those with known genetic conditions being more likely to seek insurance, raising the cost.[70] Companies may also try to skirt GINA and state regulations, leading to well-founded fears that genetic testing may be detrimental.[71] Fortunately, employers who have attempted to go around GINA have begun facing serious repercussions. In a 2015 case, the first to go to trial under GINA, an employer was forced to pay $2.25 million because of GINA violations. The employer had requested that two employees undergo genetic testing to help determine who was defecating on the warehouse floor. Despite the non-medical nature of the testing, the employees were granted summary judgement of the case.[72] These fears may create a wealth divide in the availability of WGS, as many fear that billing their insurance for WGS could lead to discrimination and only those wealthy enough to pay out of pocket feel comfortable agreeing to this type of screening.[73]

While, legally, health insurance is protected from genetic discrimination, disability and life insurance are not. Some states limit how disability insurers can use genetic information, but do not limit access to genetic information by disability insurers. There are no federal limitations on genetic discrimination in disability insurance.[74] This can have

[69] Susan M. Wolf and Jeffrey P. Kahn, "Genetic Testing and the Future of Disability Insurance: Ethics, Law & Policy," *The Journal of Law, Medicine & Ethics* 35 (June 1, 2007): 6–32, 12, https://doi.org/10.1111/j.1748-720X.2007.00148.x.
[70] Ibid.
[71] K. G. Fulda and K. Lykens, "Ethical Issues in Predictive Genetic Testing: A Public Health Perspective," *Journal of Medical Ethics* 32, no. 3 (2006): 143–47, 144.
[72] Lowe v. Atlas Logistics Group Retail Servs. Atlanta, LLC, 102 F. Supp. 3d 1360 (US District Court for the Northern District of Georgia 2015).
[73] Fulda and Lykens, "Ethical Issues in Predictive Genetic Testing," at 144.
[74] Wolf and Kahn, "Genetic Testing and the Future of Disability Insurance," at 7, 13.

major impacts of the desirability of WGS for ordinary patient care. Higher costs for disability insurance can create an incentive for employers to not hire people with certain genotypes, despite the illegality of the employer requiring genetic results.[75] While the ADA and GINA prohibit making hiring decisions based solely on genetic information as discrimination, genetic information can be used for other decisions.[76] Employers can legally use genetic information to decide not to hire an individual if the genetic code in question means the job would adversely affect the person's health, for instance if that person has a particular genetic susceptibility to some substance used on the job site.[77]

WGS can also affect an individual's ability to obtain public disability insurance, including Worker's Compensation, Supplemental Security Income, and Social Security Disability Insurance. All applicants for SSDI and SSI are required to disclose all genetic testing that has been done. Administrators for the Social Security Administration can even require applicants to get genetic testing done when making determinations of eligibility.[78] When Worker's Compensation eligibility is determined, prior WGS can create problems with causation and pre-existing conditions. A successful Worker's Compensation claim requires proof of causation by something workplace-related and fails if the condition pre-existed the claimant's employment.[79] WGS can show a pre-disposition to a particular condition or injury, causing a question of whether the true cause of the condition or injury was actually in the workplace.[80] Genetic testing that occurs after a claim can diagnose

[75] Ibid at 16.
[76] Ibid.
[77] Ibid.
[78] Ibid at 22.
[79] Ibid at 19.
[80] Ibid.

conditions that explain previously undiagnosable symptoms, allowing argument that the condition was pre-existing.[81]

Provider Obligations to Patients' Families

WGS can create family-based ethical dilemmas for the healthcare professionals providing the results of testing. Genetic information is unique medical information in that it can often provide important medical information about the patient's family members as well as the patient. This raises ethical questions of whether healthcare providers have an obligation to pass this information on to the affected family members. There are several ways to consider this ethical obligation. Some, particularly those with a libertarian focus, believe that personal autonomy and choice is the most important consideration when facing this dilemma. If patients' personal autonomy takes precedence, they have a right to choose whether to share. On the other hand, members of the patient's family may feel that they are entitled to the information so that they have all available information with which to make their own autonomous choices.[82] Others with a more justice-based or utilitarian may agree, arguing that the most good and beneficence would be produced by sharing relevant knowledge with the family so that they are able to seek treatment, reduce uncertainty, and plan and prepare for future impacts such as pain or reproductive issues.[83] The answer to this dilemma is far from clear, and should be made in a deliberate manner, not ad-hoc in hospitals and doctors' offices across the country without discussion and the inclusion of ethicists, family advocates, and other interested parties. One recommended solution is to

[81] Ibid at 15.
[82] Fulda and Lykens, "Ethical Issues in Predictive Genetic Testing," at 145.
[83] Ibid.

educate patients about the impact of the genetic information on their family members and encourage them to share that information.

Cost Versus Benefit

When considering whether WGS is an appropriate and ethical intervention in healthy populations, the ratio of cost to benefit must be carefully considered. The resources available for healthcare are limited, and to spend money on one intervention inevitably requires a trade-off in some other area. To justify this trade-off, the benefits of WGS in healthy populations must outweigh the costs. While this may seem like simple math, it is far from an easy calculation.

When considering the cost-benefit ratio of an intervention, some consider only the cost of one screening test compared to the benefits that accrue to those who test positive for the condition being screened. This leaves many costs and benefits unaccounted for. Depending on the prevalence of the condition, many of those screened will not have the conditions in question and will cost significant amounts to test while receiving little medical benefit.[84] Another cost often left out of the consideration is the cost of informing the public and managing anxiety in those screened before results are received. As mentioned earlier, even with high reliability, false positives that will require expensive confirmatory testing are possible. A low penetrance, or likelihood that a gene causes a particular disease, combined with the current uncertainty of the meanings of specific genes, can also create significant amounts of unwarranted, life-long anxiety in patients who have

[84] Anya Prince et al., "Genomic Screening of the General Adult Population: Key Concepts for Assessing Net Benefit with Systematic Evidence Reviews," *Genetics in Medicine; Chapel Hill* 17, no. 6 (June 2015): 441–43, 442, http://dx.doi.org/10.1038/gim.2014.129.

a particular genotype but will never develop the diseased phenotype.[85] Any well-run screening program also entails costs for monitoring and the quality and validity of the tests used.[86] WGS also creates costs associated with storing the large amounts of data produced and re-contacting patients about incidental findings or findings of little clinical utility that become treatable or better understood with time.

Determining the benefits of a screening program like WGS in healthy populations is also more complicated that it may appear. Those who are found to have serious conditions are the obvious beneficiaries of screening. The significance of these benefits, however, depends on the conditions being screened for. The availability of treatment and the risks involved in the different available interventions to prevent or forestall a discovered risk of developing a condition are a major limitation on benefit.[87] The magnitude of the conditions diagnosed also affects the level of benefits provided, with more benefits accruing from the discovery of a more serious condition.[88] The efficacy of early, pre-symptomatic treatment compared to treatment after a condition is discovered by normal diagnostics is also important to the benefit level of a screening program.[89] Benefits must also be conferred in a just way, with care taken to ensure equality in access to both the screening programs and the related interventions, something determined far too often by the resources and socioeconomic status of the patient, instead of the medical need.[90] Benefits must also be conferred in a way that allows the maximum possible autonomy of

[85] Ibid.
[86] S. D. Grosse et al., "Population Screening for Genetic Disorders in the 21st Century: Evidence, Economics, and Ethics," *Public Health Genomics* 13, no. 2 (December 2009): 106–15, 107, http://dx.doi.org/10.1159/000226594.
[87] Prince et al., "Genomic Screening of the General Adult Population," at 442.
[88] Ibid.
[89] Ibid.
[90] Grosse et al., "Population Screening for Genetic Disorders in the 21st Century," at 107.

those involved, with informed consent and consideration of patients' rights to the privacy of their information always of paramount concern.[91]

Decisions on the use of WGS in the standard care of healthy patients as a screening measure should be made based on a thorough analysis of cost, both to society and to the patients, compared to the accrued benefit. Unfortunately, this has not always been the case for prior decisions made about genetic screening programs. Decisions about genetic screening of healthy populations have instead often been "determined by technological capability, advocacy, and medical opinion rather than through a rigorous, objective, evidence-based review process."[92] What ratio of cost to benefit should be considered as sufficient has not been discussed in any official or systematic way in the United States.[93] Most screening decisions are made on a state-by-state basis, with little in common between the states and insufficiently careful consideration of those decisions.[94] Internationally, similarly situated countries like those in the European Union have major policy differences in regard to genetic screening of healthy populations. Were these decisions truly evidence-based, presumably similar decisions would be reached in similar countries.[95]

At a national level in the United States, however, evidenced-based and well-considered recommendations for genetic testing have fared somewhat better. The American College of Medical Genetics and Genomics has endorsed fifty-nine medically actionable genes that clinical laboratories should generally analyze and report whenever

[91] Ibid.
[92] Ibid at 112.
[93] Ibid at 109.
[94] Ibid at 108.
[95] Ibid at 109.

genetic sequencing is performed on a patient.[96] While these recommendations, which have been adopted by all states, did take into account the availability of treatment and prevention and the penetrance of the genes in question when creating these recommendations, the first published list was released with little input from either ethicists or experts in evidence-based medicine.[97] Without these fields represented, it is unlikely that justice, autonomy, or the appropriate ratio of total cost to total benefit was considered sufficiently. However, when the update of the list was released in 2016, more parties were included. For example, bioethicists insisted that autonomy be given significant new protections, ensuring that the update included a robust consent requirement that included informing patients of the right to opt out of any or all of the suggested tests. This provides hope for the future of rationality, ethics, and evidence-based medicine in genetic screening policy.[98]

[96] Sarah S. Kalia et al., "Recommendations for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing, 2016 Update (ACMG SF v2.0): A Policy Statement of the American College of Medical Genetics and Genomics," *Genetics in Medicine* 19, no. 2 (February 2017): 249–55, https://doi.org/10.1038/gim.2016.190.
[97] Grosse et al., "Population Screening for Genetic Disorders in the 21st Century," at 108.
[98] Kalia et al., "Recommendations for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing, 2016 Update (ACMG SF v2.0)."

CHAPTER 3: WHOLE GENOME SEQUENCING IN FETAL, INFANT, AND CHILD SCREENING

Introduction

While WGS presents ethical considerations when used in any healthy population, the use of WGS in fetuses, infants, or children presents special ethical considerations. When considering the performance of WGS on presumably healthy fetuses, disability rights activists have significant concerns about the impact should this procedure become a standard. These activists argue that this would lead to a devaluation of the lives of the disabled and create a new practice of eugenics aimed at wiping out disabled fetuses. There have also been proposals to include WGS in the mandatory newborn screening programs that exist across the United States. However, there has been insufficient consideration of the special costs created by including WGS in these programs. Issues of privacy and data storage also arise when considering implementing such significant screening on newborns. Beyond newborn screening and into childhood, infants and children are also not able to give effective consent, as they lack the capacity to truly understand all the implications of WGS. Because of this lack of capacity and understanding, they are not able to express or enforce their right not to know information about themselves. Providing the non-medical results that WGS can provide can lock children out of an open future, with genetic determinism creating barriers that a child may not be able to surmount. WGS may also erect barriers in the adoption setting, harming the open future of some children by preventing them from being adopted and creating a genetic underclass of children in the state's care.

Pre-natal Genetic Screening

Public Perception of Disability and Impacts on the Disabled Community

Many fear that the use of genetic testing in screening fetuses will lead to eugenic efforts against the disabled.[99] Prenatal diagnosis of disabling conditions has led to more negative attitudes about disability in general.[100] According to disability advocates, pre-natal screening for disabling conditions will lead to the abortion of disabled fetuses. This leads to the expressivist argument against any prenatal diagnosis of disabilities, including WGS.[101] The expressivist argument states that aborting disabled fetuses sends a public message that it is ethical and acceptable to abort for disability, which in turn sends the message that disabled lives are worth less. These messages that can be very damaging for disabled individuals living lives they consider worthy.[102] WGS as a prenatal screening tool could expand these concerns, with more risks of conditions able to be diagnosed. As genetic knowledge increases, it will be easier and more common to find disabilities in fetuses using genetic screening. Fetuses that would be considered healthy today might be considered disabled in the future because of this new information, and this may lead to an increase in abortion due to this classification.

[99] K. G. Fulda and K. Lykens, "Ethical Issues in Predictive Genetic Testing: A Public Health Perspective," *Journal of Medical Ethics* 32, no. 3 (2006): 143–47, 143

[100] Grace Li, Subhashini Chandrasekharan, and Megan Allyse, "'The Top Priority Is a Healthy Baby': Narratives of Health, Disability, and Abortion in Online Pregnancy Forum Discussions in the US and China," *Journal of Genetic Counseling* 26, no. 1 (February 1, 2017): 32–39, 32, https://doi.org/10.1007/s10897-016-9976-3.

[101] Erik Parens and Adriene Asch, "The Disability Rights Critique of Prenatal Genetic Testing," *The Hastings Center Report; Hastings-on-Hudson* 29, no. 5 (October 1999): S1-22.

[102] Antina de Jong and Guido M.W.R. de Wert, "Prenatal Screening: An Ethical Agenda for the Near Future," *Bioethics* 29, no. 1 (January 1, 2015): 46–55, 48, https://doi.org/10.1111/bioe.12122.

There are three main justifications often provided for genetic prenatal screening for non-treatable disabling conditions: avoiding of increased healthcare costs, avoiding pain and suffering in affected children, and promoting autonomous reproductive decisions for families.[103] The first of these two justifications lead to a rhetoric that would create the harm to the disabled community that advocates fear. To put these justifications forward implies that having disabled children in a society is bad for and costly to society, which in turn implies that only the healthiest children should be chosen and are more wanted.[104] Many disabled individuals lead lives that they consider fulfilling and worth having.[105] These justifications also imply that disability is the problem that must be solved. Disability advocates insist that this is not the case. Were social stigma and lack of access adequately addressed, disabled individuals would be able to lead lives every bit as full and meaningful as their non-disabled counterparts.[106] By looking at disability as the problem, society is allowing a single trait, the disability, to overshadow the importance of the whole individual.[107] The Deaf Community, in particular, subscribes to this view. They resent the medicalization of deafness and see it as just a different lifestyle than the hearing community, not a worse one. Many Deaf parents welcome the birth of Deaf children, as they believe it will be easier for the children to fit into the Deaf Community.[108]

If prenatal genetic screening is to be used, it must be framed and justified as promoting informed reproductive choices for parents in their unique circumstance about

[103] Ibid.
[104] Ibid at 49.
[105] Parens and Asch, "The Disability Rights Critique of Prenatal Genetic Testing."
[106] Ibid.
[107] Ibid.
[108] S. J. Stern et al., "Attitudes of Deaf and Hard of Hearing Subjects towards Genetic Testing and Prenatal Diagnosis of Hearing Loss," *Journal of Medical Genetics; London* 39, no. 6 (June 2002): 449, http://dx.doi.org/10.1136/jmg.39.6.449.

both the fetus at issue and any future reproductive decisions. This frame emphasizes personal decisions based on individual circumstances without implying that there is an overall value judgement on the worth of a certain type of people.[109] The deliberation that goes into the decision whether to terminate a pregnancy is highly individual, and promoting autonomous reproductive decision-making respects parents' autonomy and allows them to decide what would best benefit their family and their situation.[110] Termination decisions are based on social structure and family interconnectivity, religious belief, the narrative of parental unconditional love, the availability of support for and lack of stigma against disabled individuals, availability of monetary resources, and the politicization of issues of healthy birth and abortion, factors that will vary widely between different parents and situations.[111] Parents may also wish to know disability status not to terminate, but instead to adequately prepare to care for the disabled child.

In addition to conditions that are traditionally thought of as disabilities, WGS would provide information about many non-medical traits such as coloring, height, athletic ability, and intelligence. This information could give parents the ability to selectively terminate in order to have children with more desirable traits, creating major eugenics fears. If only those that are above average are selected for and born, the average begins to shift, and those whose parents couldn't afford such selection could become significantly genetically burdened compared to those who come from financial resources, an affront to justice.

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[109] De Jong and de Wert, "Prenatal Screening." at 50.
[110] Greer Donley, Sara Chandros Hull, and Benjamin E. Berkman, "Prenatal Whole Genome Sequencing: Just Because We Can, Should We?," *The Hastings Center Report* 42, no. 4 (2012): 28–40, 31, https://doi.org/10.2307/23882773.
[111] Li, Chandrasekharan, and Allyse, "'The Top Priority Is a Healthy Baby,'" at 35.

WGS in Newborn Screening

The Mandatory Nature of Newborn Screening

Current newborn screening processes in the United States, for instance testing for PKU, a condition that leads to mental and physical impairment but can be entirely mitigated by placing the infant on a specific diet, are done automatically at birth, without the consent of the parents.[112] Newborn screening is considered mandatory, meaning no formal consent is required. Parents can opt out of newborn screening, but most do not know that this option is even available to them.[113] The mandatory nature of newborn screening is justified because the diagnosis of the included conditions is of significant and immediate benefit to the child and thus the child would be harmed without the screening.[114] To include WGS in mandatory newborn screening and exempt it from parental permission generally, as many have proposed, it would have to fall under similar justifications. However, much, if not most, of the medical information provided by WGS is not related to conditions that will manifest or can be treated in childhood, and therefore WGS does not fit the current model of justification for mandatory screening programs. Even if WGS were to be included in these programs, information would still have to be provided to parents, both to inform them of their right to refuse the screening and to clear up the many misconceptions about genetics

[112] S. D. Grosse et al., "Population Screening for Genetic Disorders in the 21st Century: Evidence, Economics, and Ethics," *Public Health Genomics*; Basel 13, no. 2 (December 2009): 106–15, 110, http://dx.doi.org/10.1159/000226594.
[113] Beth A. Tarini and Aaron J. Goldenberg, "Ethical Issues with Newborn Screening in the Genomics Era," *Annual Review of Genomics and Human Genetics* 13, no. 1 (September 12, 2012): 381–93, 384, https://doi.org/10.1146/annurev-genom-090711-163741.
[114] Ibid.

that are held by the general population and providing that information would have significant costs.[115]

The cost of adding WGS to newborn screening has greater significance than the cost of WGS screening in adult population. The costs of one-third of births are covered by Medicaid.[116] Adding WGS to mandatory newborn screening will increase the costs of this screening, taking up already severely limited Medicaid funding. This will take funding away from other programs, such as prenatal care or education for new mothers. These types of programs have significantly more immediate benefit to newborns than WGS information about future diseases that may or may not come pass.

Privacy and Data Storage

Conducting WGS as part of newborn screening would also create logistical hurdles involving privacy and data storage. WGS creates massive amounts of data about every individual. If all newborns were screened, eventually the space to store six billion base pairs for each of the three hundred million people in the United States would be needed. No system is foolproof, and no matter what system was used to store this information, it would entail some risk of private genetic information being leaked to the public, thus potentially violating the Health Insurance Portability and Accountability Act of 1996, popularly known as HIPAA.[117] There is also a risk that the storage of the genetic information of every newborn as part of a state-run program like newborn screening would

[115] Mary Ann Baily and Thomas H. Murray, "Ethics, Evidence, and Cost in Newborn Screening," *The Hastings Center Report* 38, no. 3 (2008): 23–31, 26.
[116] Ibid at 25.
[117] Heidi Carmen Howard et al., "Whole-Genome Sequencing in Newborn Screening? A Statement on the Continued Importance of Targeted Approaches in Newborn Screening Programmes," *European Journal of Human Genetics*, Leiden 23, no. 12 (December 2015): 1593–1600, 1595, http://dx.doi.org/10.1038/ejhg.2014.289.

create the perception of government overreach and possibly even government tracking, alienating sections of the public from both government health programs and hospital births.[118]

Having this data in storage could have benefits, but each of the benefits comes with its own set of risks. Some have proposed that one benefit of newborn screening is that the genome would be sequenced once and could then be used in the future at a low cost. However, with the rapid advances in sequencing technology, it is likely that it would be both cheaper and more accurate to conduct genetic testing when it was indicated for some specific purpose.[119] Others have suggested that whatever database WGS results are stored in could create a major research resource, but the use of the fruits of a mandatory program to conduct research violates the principle of autonomy and is likely to create mistrust in the public.[120]

WGS in Children

Informed Permission

The use of WGS to screen healthy fetuses and children will present unique challenges in obtaining this permission from parents in a truly informed way, assuming consent will be sought. While informed consent is at the center of most medical practice, infants and children are not competent to give consent, as they are unable to fully grasp the implications of any medical procedure or test. Because children must be treated nonetheless, parental permission is either combined with or substituted for the assent of the

[118] Tarini and Goldenberg, "Ethical Issues with Newborn Screening in the Genomics Era," at 386.
[119] Howard et al., "Whole-Genome Sequencing in Newborn Screening?" at 1595.
[120] Tarini and Goldenberg, "Ethical Issues with Newborn Screening in the Genomics Era."

child, the actual patient. Obtaining informed permission from parents regarding WGS is complicated by several issues.

Given the large number of popular misconceptions about genetics, significant information and education are needed to make most parents sufficiently informed about what they are agreeing to when they agree to have their child undergo WGS.[121] Even with significant information available, many parents do not take the time to deliberate on the long-term impacts of genetic screening for their child.[122] They are often swayed primarily by the "inflicted ought," the feeling of obligation that they ought to find out everything that is knowable about their child. This is particularly true when testing is done for diagnostic purposes and parents are asked if they wish to know information about adult onset conditions as well, as would be the case in WGS.[123] A deliberative process is required for parents to see around these pressures, one that is unfortunately not always taken. The recent advent of a relative easy way to conduct genetic screening in fetuses may make consent more difficult to obtain in prenatal cases, as well. Cell-free fetal DNA is a new procedure that allows the sequencing of a fetus' genotype using only a sample of the mother's blood, instead of the invasive amniocentesis that used to be required.[124] The perceived simplicity

[121] Christopher H. Wade, Beth A. Tarini, and Benjamin S. Wilfond, "Growing Up in the Genomic Era: Implications of Whole-Genome Sequencing for Children, Families, and Pediatric Practice," *Annual Review of Genomics and Human Genetics* 14, no. 1 (August 31, 2013): 535–55, 542, https://doi.org/10.1146/annurev-genom-091212-153425.
[122] Ainsley J. Newson, "Whole Genome Sequencing in Children: Ethics, Choice and Deliberation," *Journal of Medical Ethics* 43, no. 8 (August 1, 2017): 540–42, https://doi.org/10.1136/medethics-2016-103943.
[123] Ibid.
[124] Bernard M. Dickens, "Ethical and Legal Aspects of Noninvasive Prenatal Genetic Diagnosis," *International Journal of Gynecology & Obstetrics* 124, no. 2 (February 1, 2014): 181–84, 181, https://doi.org/10.1016/j.ijgo.2013.11.001.

of this procedure may cause mothers to give permission for fetal WGS without adequate consideration, since it would, after all, only be a normal blood draw.[125]

Considering issues of informed consent for WGS in fetuses and children presumes, however, that parents have the right to give permission for this screening before their children are able to make the decision on their own. Many do not agree that this is the case.

The Right Not to Know

Children may have a right not to know their genetic information until they reach majority and are able to choose whether to know that information, something that allowing parents to give permission for WGS could take away. Parents have a moral duty not to know that stems from the child's right to an open future, the right to not have choices made on their behalf that would unnecessarily undermine their future ability to make fundamental life choices as an adult with as little limitation as possible.[126] These rights are based in respect for the autonomy of the child as a future rational being entitled to make independent and personal decisions. Adults have the right not to know their genetic information, and if genetic information is forced upon a child, it is impossible to unknow that information in the future. This right has been recognized internationally. Article 5c of the UNESCO Universal Declaration on the Human Genome and Human Rights proclaims: "The right of every individual to decide whether or not to be informed of the results of genetic examination and the resulting consequences should be respected."[127] Article 10(2) of the European Convention on Human Rights and Biomedicine comes to a similar

[125] Ibid at 182.
[126] Pascal Borry, Mahsa Shabani, and Heidi Carmen Howard, "Is There a Right Time to Know? The Right Not to Know and Genetic Testing in Children," *The Journal of Law, Medicine & Ethics* 42, no. 1 (March 1, 2014): 19–27, 21, https://doi.org/10.1111/jlme.12115.
[127] Ibid at 20.

conclusion, stating: "Everyone is entitled to know any information collected about his or her health. However, the wishes of individuals not to be so informed shall be observed."[128]

Several organizations have published recommendations that respect the right of children not to know their genetic information in the future. The American Academy of Pediatrics recommends, "Unless there is anticipated benefit to the child, pediatricians should decline requests from parents or guardians to obtain predispositional genetic testing until the child has the capacity to make the choice."[129] The American Society of Human Genetics recommendations say: "Providers caring for children may discourage actions that may be adverse to the interest or the well-being of the child."[130] Most clinical ethics guides give similar advice, discouraging genetic screening for any non-actionable conditions until the child reaches majority and can exercise the right not to know.[131]

Genetic results that will be actionable before the child reaches majority are generally considered exempt from the right not to know. The accepted standard of decision-making on behalf of children is the child's best interest. Testing that will provide a real medical benefit to the child will provide a child direct benefits that other, non-actionable genetic information will not.[132]

Genetic Determinism

[128] Ibid.
[129] John D. Lantos, Michael Artman, and Stephen F. Kingsmore, "Ethical Considerations Associated with Clinical Use of Next-Generation Sequencing in Children," *The Journal of Pediatrics* 159, no. 6 (December 2011): 879–880, https://doi.org/10.1016/j.jpeds.2011.07.035.
[130] Ibid at 880.
[131] Borry, Shabani, and Howard, "Is There a Right Time to Know?" at 20.
[132] Ibid at 22.

Parents' knowledge about their child's genetics can influence the way a child is raise, possibly creating limitations for the child that could deprive the child of the right to an open future. Information about susceptibility, late-onset conditions, or non-medical traits will challenge the idea of a baby as a healthy, blank slate and could shape a child's upbringing and change the course of the child's life in a way that the child has no capacity to consent to.[133]

Parents who discover that their children are susceptible to certain conditions or will have an untreatable disease later in life may shelter their children in non-beneficial ways. Case studies of parents who have received information about genetic markers for late-onset Pompe disease in their children found that stigmatization and guilt created tensions in the parents' relationship with their children. Anxiety and stigmatization created issues of overprotectiveness, which can hinder a child's development.[134] Anxiety about susceptibility to a condition can even contribute to the condition in question, as a lack of exposure to germs at a young age can actually weaken a child's immune system and make genetic susceptibility more dangerous.[135]

The massive amount of information about an individual that WGS provides is not limited to medical data. There is currently significant uncertainty and lack of knowledge about non-medical genotypes and the way those genotypes interact with the environment to present particular phenotypes. Eventually WGS will be able to provide information about an individual's current and future height, hair and eye color, personality, intelligence,

[133] Donley, Hull, and Berkman, "Prenatal Whole Genome Sequencing," at 32.
[134] K. Golden-Grant, J. L. Merritt, and C. R. Scott, "Ethical Considerations of Population Screening for Late-Onset Genetic Disease," *Clinical Genetics* 88, no. 6 (December 1, 2015): 589–92, https://doi.org/10.1111/cge.12566.
[135] Donley, Hull, and Berkman, "Prenatal Whole Genome Sequencing," at 37.

athletic ability, and other talents. Parents who have this information about their child's genetic potential may push the child in a specific direction or attribute the child's successes and failings to the child's genome. For example, a parent who knows that a child is genetically predisposed to a low IQ may tolerate low grades from the child and fail to provide him or her with the expectations and support that children need to reach their full potential and have the most open future.[136]

Issues in the Context of Adoption

Adoption presents many difficult issues in medical treatment. The lucky few children in the foster care system who are adopted often have no known family history. These children have also almost always gone through substantial hardship in their lives, leading to psychological and behavioral difficulties that can mask other symptoms. This can leave children struggling to find parents and care and adoptive parents struggling to do what is best for their new child.

Prospective adoptive parents usually want to know all they can about a child they are looking to adopt. Some have proposed conducting WGS on children in the foster care system who are up for adoption to try to "match" children to adoptive parents that would be best prepared to raise that child.[137] This type of matching, however, serves the interest of the prospective parents instead of the benefit of the child. While both interests are important, those who look to adopt have already decided that they have a place in their life for a child who is potentially unknown or struggling. On the other hand, a child's interest

[136] Ibid at 36.
[137] Kimberly J. Leighton, "Accepting Adoption's Uncertainty: The Limited Ethics of Pre-Adoption Genetic Testing," *Journal of Bioethical Inquiry* 11, no. 2 (June 1, 2014): 245–60, https://doi.org/10.1007/s11673-014-9519-2.

in finding a home and a family is far more urgent. A child who has genetic issues faces the serious risk of being marginalized by WGS, since given the option and the number of children up for adoption, few prospective parents are going to seriously consider adopting a child with known genetic challenges.[138]

Genetic testing post-adoption for the medical benefit of the child is a different matter. Newborn screening and genetic testing in the case of symptoms, as would be done for any other child, are necessary for children up for adoption to receive adequate healthcare.[139] Once a child is adopted, adoptive parents may wish to know some genetic information to substitute for a lack of family history. The lack of available family history may shift the risk-benefit ratio for adoptive children compared to biological children, so some genetic testing that is not appropriate for other children may be appropriate for adopted children due to this greater benefit. However, this should be considered in each individual case by the family, the child, and the healthcare professionals and undertaken with great care to ensure that the child's right not to know is not violated.[140] Adopted children can then choose what information they want to receive when they reach majority, something many do choose to pursue using DTC genetic testing.[141]

[138] Ibid.
[139] Julia Crouch et al., "'We Don't Know Her History, Her Background': Adoptive Parents' Perspectives on Whole Genome Sequencing Results," *Journal of Genetic Counseling; New York* 24, no. 1 (February 2015): 67–77, 70, http://dx.doi.org/10.1007/s10897-014-9738-z.
[140] Ibid at 75.
[141] Ibid at 68.

CHAPTER 4: RECOMMENDATIONS FOR THE USE OF GENETIC SEQUENCING IN HEALTHY POPULATIONS

Introduction

Based on the ethical discussions in Chapters 2 and 3, the following recommendations will best uphold and protect the values of beneficence, autonomy, and justice. WGS should not be used generally in screening healthy adults and should only be conducted in those who request it after precautions have been taken. GINA should be expanded to protect employment benefits and disability insurance. WGS should not be used in fetuses, but genetic screening of fetuses for information that is medically relevant to reproductive choices should be not only offered, but subsidized. WGS should not be permitted in newborns and children, even with the permission of parents, and DTC companies should not be permitted to sequence the genes of minors.

Recommendations for DTC Genetic Screening

There are many ethical concerns raised by the growth of the DTC genetic testing industry. With careful oversight and regulation, however, DTC genetic testing can continue in a safe and ethical way. Regulation in this area is increasing, with the FDA taking the lead. As this regulation is developed, it is important that the experiences of those who are not the average consumer be considered. While empirical research might suggest that many fears about DTC genetic testing are not as dangerous as they seem, those who may suffer from more extreme reactions and issues must not be ignored. The availability and readability of information should be the first priority for regulators, with consideration for the content and wording of online resources, the legibility of results, and the content of advertising. Increasing the knowledge and understanding of both consumers and the

healthcare professionals who will be treating these consumers will help to combat many of the major causes of consumer anxiety and distress. DTC companies should be required to recommend confirmatory testing of positive results in the healthcare setting. The recommendation would increase the involvement of healthcare professionals and move consumers into the clinical space, where better and more robust information would be provided to them. Privacy of genetic information should be the second priority of regulators. Those who receive DTC genetic testing results must be protected from misuse of their genetic information or discrimination based on the results they receive. While GINA is a good step in this direction, it does not go far enough and needs to be expanded. With careful, well-considered expansion of the regulation of DTC genetic testing, consumers can be protected from unnecessary anxiety, misunderstanding, and rising healthcare costs associated with increased utilization without preventing them from accessing the genetic health information they desire.

Recommendations for Whole Genome Sequencing in Healthy Adults

In adults with the ability to consent to genetic testing, WGS should not be suggested as a screening measure for those who are healthy. For screening for a condition in a healthy population to be beneficial and worth the cost to the healthcare system, experts should consider if the disease is serious, if it has a high detectable prevalence in the screened population, if there are few false positives in the test, if the test is accurate, if it detects disease early enough that intervention improves outcomes, if it is not too risky and is affordable and available, and, if a treatment does exist, if it is more effective when applied

before symptoms begin and is not too risky or toxic.[142] Most of the information provided by WGS does not meet one or more of those criteria. Instead, healthy adults should be offered screening for only the 59 conditions suggested by the ACMG, as these genetic results have been considered carefully and found to be actionable and reliable. Conditions should only be added to this screening panel after the same or similar careful consideration, including whether there is preventive treatment and whether screening can prevent uncertainty during later diagnostic testing or allow planning of a lifestyle that will be less arduously affected by the condition.[143] Providing information on conditions with no treatment or with great uncertainty in specifics like degree or age of onset can cause substantial patient anxiety and should be done only when there is substantial other benefit, for instance aiding in reproductive choice.[144]

If a competent adult specifically requests WGS, healthcare providers should only provide it after significant genetic counseling and education. Receiving genetic results has not been shown to make people more likely to make healthy lifestyle choices like controlling soda intake or exercising daily, so this testing should not be covered by public funding, as WGS has an insufficient ratio of costs to benefits.[145] To help control the anxiety that potentially comes with many of the results given in WGS, providers need to provide follow-up contact and ongoing information to help patients balance their anxiety with

[142] Mark A. Rothstein, "The Case against Precipitous, Population Wide, Whole-Genome Sequencing," *The Journal of Law, Medicine & Ethics* 40, no. 3 (September 2012): 682–89, 683, https://doi.org/10.1111/j.1748-720X.2012.00699.x.
[143] K. Golden-Grant, J. L. Merritt, and C. R. Scott, "Ethical Considerations of Population Screening for Late-Onset Genetic Disease," *Clinical Genetics* 88, no. 6 (December 1, 2015): 589–92, 591, https://doi.org/10.1111/cge.12566.
[144] Ibid.
[145] John M. Quillin, "Lifestyle Risk Factors Among People Who Have Had Cancer Genetic Testing," *Journal of Genetic Counseling* 25, no. 5 (October 1, 2016): 957–64, https://doi.org/10.1007/s10897-015-9925-6.

control, particularly if the patient may have passed the condition on to his or her children.[146] WGS may provide results that have implications for the patient's family. The patient should be educated on the importance of those implications and highly encouraged to pass that information along to affected family members so that they can make autonomous decisions. To require healthcare providers themselves to pass this information on to family members without the patient's consent is not practical, however; the provider may have no way of contacting the family. Moreover, to reveal the information– both the genotype itself and even the fact that the patient chose to receive WGS -- without the patient's consent would constitute a breach of confidentiality, which must be balanced against the importance of the information on a case-by-case basis.

To protect those who do receive genetic screening and to prevent genetic testing from becoming limited to the economically elite, GINA should be expanded to protect employment benefits and both public and private disability insurance. Disability insurance is as socially important and necessary as health insurance, as evidenced by the existence of state and federal programs like Worker's Compensation in a country as safety-net adverse as the United States, and that insurance deserves equal protection under the law.

Recommendations for Whole Genome Sequencing in Fetuses

WGS should not be performed in fetuses because it violates a child's rights to an open future and the resulting moral duty of parents not to know genetic information. Genetic information tested for and given to parents should be limited to actionable

[146] Helle Vendel Petersen et al., "Balancing Life with an Increased Risk of Cancer: Lived Experiences in Healthy Individuals with Lynch Syndrome," *Journal of Genetic Counseling* 23, no. 5 (October 1, 2014): 778–84, 783, https://doi.org/10.1007/s10897-013-9682-3.

information that will assist the parents in making informed reproductive choices. The rhetoric surrounding any genetic testing in fetuses should be clearly and carefully framed to reduce the likelihood of damage to the disabled community. The purpose of testing must be framed as allowing parents to make informed reproductive choices for themselves, their child, and their family. Implying that genetic screening programs in fetuses is meant to ensure the healthiest children, decrease healthcare costs, or promote the public good sends a message that disabled children are not wanted and disabled lives are not worth their cost, a message that must be carefully avoided. Health care professionals should instead be trained to counsel parents with a focus on personal circumstance, without directly or forcefully advocating the termination of a disabled fetus.

Justice must be ensured when providing appropriate, non-WGS fetal genetic testing. All people of child-bearing age should be given information about the types of genetic testing available to them; limited genetic screening for carrier status should be publicly funded for those who want it but are unable to afford it. To do otherwise would put those with more economic resources in a better position to have genetic testing done while excluding the poor, possibly shifting the costs of caring for disabled children disproportionately to the poor and exacerbating inequality.[147]

Recommendations for Whole Genome Sequencing in Newborns and Children

WGS should not be permitted for newborns and children, even with parental consent. Allowing WGS in children violates their rights to an open future and to not know

[147] Di Zhang et al., "Eugenics and Mandatory Informed Prenatal Genetic Testing: A Unique Perspective from China," *Developing World Bioethics* 16, no. 2 (August 1, 2016): 107–15, https://doi.org/10.1111/dewb.12088; Antina de Jong and Guido M.W.R. de Wert, "Prenatal Screening: An Ethical Agenda for the Near Future," *Bioethics* 29, no. 1 (January 1, 2015): 46–55, https://doi.org/10.1111/bioe.12122.

their genetic information. Parents should only be permitted to give permission for genetic testing that is actionable for children before they reach the age of majority. WGS should also not be performed on children with actionable results returned and all other results stored away for future use, as some have suggested.[148] This stored information is still a risk to the child without their consent or benefit, as no system is completely secure and the temptation to use such a database for research purposes would be almost irresistible.[149] The likelihood that holding such information would be beneficial in the future is small, as technology is likely to make genetic sequencing far cheaper and more accurate by the time the genetic information might be needed.

DTC companies should not be permitted to conduct genetic screening on minors under any circumstances. DTC genetic testing is currently often marketed to parents and most companies will currently process DNA from minors with only parental permission.[150] Parental permission for WGS is not sufficient to over-ride a child's right not to know even in the clinical setting, where such information can be monitored, and accurate information can be provided. To allow parents to go around their healthcare provider and receive such information from a private company is unacceptable.

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[148] Christopher H. Wade, Beth A. Tarini, and Benjamin S. Wilfond, "Growing Up in the Genomic Era: Implications of Whole-Genome Sequencing for Children, Families, and Pediatric Practice," *Annual Review of Genomics and Human Genetics* 14, no. 1 (August 31, 2013): 535–55, 542, https://doi.org/10.1146/annurev-genom-091212-153425.

[149] Heidi Carmen Howard et al., "Whole-Genome Sequencing in Newborn Screening? A Statement on the Continued Importance of Targeted Approaches in Newborn Screening Programmes," *European Journal of Human Genetics* Leiden 23, no. 12 (December 2015): 1593–1600, 1595, http://dx.doi.org/10.1038/ejhg.2014.289.

[150] Pascal Borry, Mahsa Shabani, and Heidi Carmen Howard, "Is There a Right Time to Know? The Right Not to Know and Genetic Testing in Children," *The Journal of Law, Medicine & Ethics* 42, no. 1 (March 1, 2014): 19–27, 23, https://doi.org/10.1111/jlme.12115.

Mandatory newborn genetic screening must be kept to those conditions for which diagnosis would have an immediate benefit for the infant to maintain the justification for the mandatory nature of the newborn screening program.

When considering genetic testing for adopted children or those awaiting adoption, special concern must be taken to not burden the child without providing sufficient direct benefit. Children who are awaiting adoption should only be genetically screened for the conditions that professional organizations suggest all newborns be screened for at birth. Further genetic testing should only be conducted if there are specific symptoms or a clinical indication due to family history. Any testing beyond this could put an unjustifiable burden on those children waiting to be adopted. Some genetic testing that is inappropriate for biological children may be appropriate for children who have already been adopted because the lack of family history may change the ratio of risk to benefit for certain genetic tests. Each of these situations must be considered carefully and individually by the parents, the healthcare provider, and, if mature enough, the child, and should only be undertaken when adoptive parents have committed to continued care for the child, regardless of results. However, these children still have the right not to know and WGS should still not be performed.

Conclusion

As science races toward a future where WGS can be performed on anyone at relatively low cost, care must be taken to ensure that WGS is provided in an ethical, beneficial way, without harming the rights of any of those involved. Genetic information increasingly pervades medical records and influences the way patients are treated. This information is unique from other medical information because it is uniquely individual and

identifiable in a way other medical information is not and can potentially have meaning for family members of the patient in question. These differences warrant special protections for genetic sequencing. Genetic sequencing has the power to provide new information about disease origins and mechanisms, knowledge that could lead to new treatments and cures, and many see only the projected benefits and want to dive head-first into this new technology. It is important, however, that the scientific and medical community take the time to consider all of the risks and drawbacks before jumping in.

REFERENCES

Allard, Jody. "How Gene Testing Forced Me to Reveal My Private Health Information." VICE, May 27, 2016. http://www.vice.com/read/how-gene-testing-forced-me-to-reveal-my-private-health-information.

Baily, Mary Ann, and Thomas H. Murray. "Ethics, Evidence, and Cost in Newborn Screening." *The Hastings Center Report* 38, no. 3 (2008): 23–31.

Bloss, Cinnamon S., Nicholas J. Schork, and Eric J. Topol. "Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk." *New England Journal of Medicine* 364, no. 6 (February 10, 2011): 524–34. https://doi.org/10.1056/NEJMoa1011893.

Bloss, Cinnamon S., Nathan E. Wineinger, Burcu F. Darst, Nicholas J. Schork, and Eric J. Topol. "Impact of Direct-to-Consumer Genomic Testing at Long Term Follow-Up." *Journal of Medical Genetics* 50, no. 6 (June 1, 2013): 393–400. https://doi.org/10.1136/jmedgenet-2012-101207.

Borry, Pascal, Mahsa Shabani, and Heidi Carmen Howard. "Is There a Right Time to Know? The Right Not to Know and Genetic Testing in Children." *The Journal of Law, Medicine & Ethics* 42, no. 1 (March 1, 2014): 19–27. https://doi.org/10.1111/jlme.12115.

Brownstein, C A, D M Margulies, and S F Manzi. "Misinterpretation of TPMT by a DTC Genetic Testing Company." *Clinical Pharmacology & Therapeutics* 95, no. 6 (June 1, 2014): 598–600. https://doi.org/10.1038/clpt.2014.60.

Check Hayden, Erika. “Out of Regulatory Limbo, 23andMe Resumes Some Health Tests and Hopes to Offer More.” *Nature News*, October 27, 2015. https://doi.org/10.1038/nature.2015.18641.

Crouch, Julia, Joon-ho Yu, Aditi G. Shankar, and Holly K. Tabor. “‘We Don’t Know Her History, Her Background’: Adoptive Parents’ Perspectives on Whole Genome Sequencing Results.” *Journal of Genetic Counseling; New York* 24, no. 1 (February 2015): 67–77. http://dx.doi.org/10.1007/s10897-014-9738-z.

Dickens, Bernard M. “Ethical and Legal Aspects of Noninvasive Prenatal Genetic Diagnosis.” *International Journal of Gynecology & Obstetrics* 124, no. 2 (February 1, 2014): 181–84. https://doi.org/10.1016/j.ijgo.2013.11.001.

Dohany, Lindsay, Shanna Gustafson, Whitney Ducaine, and Dana Zakalik. “Psychological Distress with Direct-to-Consumer Genetic Testing: A Case Report of an Unexpected BRCA Positive Test Result.” *Journal of Genetic Counseling* 21, no. 3 (January 21, 2012): 399–401. https://doi.org/10.1007/s10897-011-9475-5.

Donley, Greer, Sara Chandros Hull, and Benjamin E. Berkman. “Prenatal Whole Genome Sequencing: Just Because We Can, Should We?” *The Hastings Center Report* 42, no. 4 (2012): 28–40. https://doi.org/10.2307/23882773.

DuBois, James M. “Genetic Testing: Understanding the Personal Stories.” *Narrative Inquiry in Bioethics* 5, no. 3 (January 8, 2016): 201–3. https://doi.org/10.1353/nib.2015.0061.

Edney, Anna. “FDA Tells Google-Backed 23andMe to Halt DNA Test Service.” *Bloomberg.Com*, November 25, 2013.

http://www.bloomberg.com/news/articles/2013-11-25/fda-tells-google-backed-23andme-to-halt-dna-test-service.

Egglestone, Corin, Anne Morris, and Ann O'Brien. "Effect of Direct-to-Consumer Genetic Tests on Health Behaviour and Anxiety: A Survey of Consumers and Potential Consumers." *Journal of Genetic Counseling* 22, no. 5 (April 3, 2013): 565–75. https://doi.org/10.1007/s10897-013-9582-6.

"Emotional Toll of DTC Genetic Testing." *Medical Ethics Advisor*, December 1, 2011.

FDA Office of the Commissioner. "Press Announcements - FDA Allows Marketing of First Direct-to-Consumer Tests That Provide Genetic Risk Information for Certain Conditions," April 6, 2017. https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm551185.htm.

Fulda, K. G., and K. Lykens. "Ethical Issues in Predictive Genetic Testing: A Public Health Perspective." *Journal of Medical Ethics* 32, no. 3 (2006): 143–47.

Fung, Brian. "Bowing Again to the FDA, 23andMe Stops Issuing Health-Related Genetic Reports." Washington Post, December 6, 2013. https://www.washingtonpost.com/news/the-switch/wp/2013/12/06/bowing-again-to-the-fda-23andme-stops-issuing-health-related-genetic-reports/.

Genetic Information Nondiscrimination Act of 2008, Pub. L. No. 110–233, 122 Stat. 881 (2008).

Gever, John. “2015 Recap: FDA Approves First 23andMe Genetic Test.” MedPage Today, December 28, 2015. http://www.medpagetoday.com/Genetics/GeneticTesting/55438.

Gibbs, Samuel. “DNA-Screening Test 23andMe Launches in UK after US Ban.” *The Guardian*, December 1, 2014, sec. Technology. https://www.theguardian.com/technology/2014/dec/02/google-genetic-testing-23andme-uk-launch.

Giovanni, Monica A., Matthew R. Fickie, Lisa S. Lehmann, Robert C. Green, Lisa M. Meckley, David Veenstra, and Michael F. Murray. “Health-Care Referrals from Direct-to-Consumer Genetic Testing.” *Genetic Testing and Molecular Biomarkers* 14, no. 6 (October 28, 2010): 817–19. https://doi.org/10.1089/gtmb.2010.0051.

Golden-Grant, K., J. L. Merritt, and C. R. Scott. “Ethical Considerations of Population Screening for Late-Onset Genetic Disease.” *Clinical Genetics* 88, no. 6 (December 1, 2015): 589–92. https://doi.org/10.1111/cge.12566.

Goldsmith, Lesley, Leigh Jackson, Anita O’Connor, and Heather Skirton. “Direct-to-Consumer Genomic Testing from the Perspective of the Health Professional: A Systematic Review of the Literature.” *Journal of Community Genetics* 4, no. 2 (January 16, 2013): 169–80. https://doi.org/10.1007/s12687-012-0135-8.

Grosse, S. D., W. H. Rogowski, L. F. Ross, M. C. Cornel, W. J. Dondorp, and M. J. Khoury. “Population Screening for Genetic Disorders in the 21st Century: Evidence, Economics, and Ethics.” *Public Health Genomics; Basel* 13, no. 2 (December 2009): 106–15. http://dx.doi.org/10.1159/000226594.

Hietaranta-Luoma, H. L., H. T. Luomala, H. Puolijoki, and A. Hopia. "Using ApoE Genotyping to Promote Healthy Lifestyles in Finland – Psychological Impacts: Randomized Controlled Trial." *Journal of Genetic Counseling* 24, no. 6 (December 1, 2015): 908–21. https://doi.org/10.1007/s10897-015-9826-8.

Hill, Kashmir. "Cops Are Asking Ancestry.Com and 23andMe for Their Customers' DNA." *Fusion* (blog), October 16, 2015. http://fusion.net/story/215204/law-enforcement-agencies-are-asking-ancestry-com-and-23andme-for-their-customers-dna/.

Hof, Robert. "Seven Months After FDA Slapdown, 23andMe Returns with New Health Report Submission." Forbes, June 20, 2014. http://www.forbes.com/sites/roberthof/2014/06/20/seven-months-after-fda-slapdown-23andme-returns-with-new-health-report-submission/.

Howard, Heidi Carmen, Bartha Maria Knoppers, Martina C. Cornel, Ellen Wright Clayton, Karine Sénécal, and Pascal Borry. "Whole-Genome Sequencing in Newborn Screening? A Statement on the Continued Importance of Targeted Approaches in Newborn Screening Programmes." *European Journal of Human Genetics : EJHG; Leiden* 23, no. 12 (December 2015): 1593–1600. http://dx.doi.org/10.1038/ejhg.2014.289.

Huffman, Mark. "New York and Maryland Prohibitions against 23andMe Fall," December 4, 2015. https://www.consumeraffairs.com/news/new-york-and-maryland-prohibitions-against-23andme-fall-120415.html.

Imai, Kenta, Larry J. Kricka, and Paolo Fortina. “Concordance Study of 3 Direct-to-Consumer Genetic-Testing Services.” *Clinical Chemistry* 57, no. 3 (March 2011): 518–21.

Jong, Antina de, and Guido M.W.R. de Wert. “Prenatal Screening: An Ethical Agenda for the Near Future.” *Bioethics* 29, no. 1 (January 1, 2015): 46–55. https://doi.org/10.1111/bioe.12122.

Kalia, Sarah S., Kathy Adelman, Sherri J. Bale, Wendy K. Chung, Christine Eng, James P. Evans, Gail E. Herman, et al. “Recommendations for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing, 2016 Update (ACMG SF v2.0): A Policy Statement of the American College of Medical Genetics and Genomics.” *Genetics in Medicine* 19, no. 2 (February 2017): 249–55. https://doi.org/10.1038/gim.2016.190.

Kaphingst, Kimberly A., Colleen M. McBride, Christopher Wade, Sharon Hensley Alford, Robert Reid, Eric Larson, Andreas D. Baxevanis, and Lawrence C. Brody. “Patients’ Understanding of and Responses to Multiplex Genetic Susceptibility Test Results.” *Genetics in Medicine* 14, no. 7 (July 2012): 681–87. https://doi.org/10.1038/gim.2012.22.

Kaufman, David J., Juli M. Bollinger, Rachel L. Dvoskin, and Joan A. Scott. “Risky Business: Risk Perception and the Use of Medical Services among Customers of DTC Personal Genetic Testing.” *Journal of Genetic Counseling* 21, no. 3 (January 26, 2012): 413–22. https://doi.org/10.1007/s10897-012-9483-0.

Khoury, Muin J. “Direct to Consumer Genetic Testing.” Centers for Disease Control and Prevention. *Genomics and Health Impact Blog* (blog), April 18, 2017. https://blogs.cdc.gov/genomics/2017/04/18/direct-to-consumer-2/.

Kolata, Gina. “F.D.A. Will Allow 23andMe to Sell Genetic Tests for Disease Risk to Consumers.” *The New York Times*, April 6, 2017, sec. Health. https://www.nytimes.com/2017/04/06/health/fda-genetic-tests-23andme.html.

Kutz, Gregory. “Direct-to-Consumer Genetic Tests: Misleading Test Results Are Further Complicated by Deceptive Marketing and Other Questionable Practices.” Testimony before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives. United States Government Accountability Office, July 22, 2010, https://www.gao.gov/assets/130/125079.pdf.

Lachance, Christina R., Lori A. H. Erby, Beth M. Ford, Vincent C. Allen, and Kimberly A. Kaphingst. “Informational Content, Literacy Demands, and Usability of Websites Offering Health-Related Genetic Tests Directly to Consumers.” *Genetics in Medicine* 12, no. 5 (May 2010): 304–12. https://doi.org/10.1097/GIM.0b013e3181dbd8b2.

Lantos, John D., Michael Artman, and Stephen F. Kingsmore. “Ethical Considerations Associated with Clinical Use of Next-Generation Sequencing in Children.” *The Journal of Pediatrics* 159, no. 6 (December 2011): 879-880.e1. https://doi.org/10.1016/j.jpeds.2011.07.035.

Leighton, J. W., K. Valverde, and B. A. Bernhardt. “The General Public’s Understanding and Perception of Direct-to-Consumer Genetic Test Results.” *Public Health Genomics* 15, no. 1 (June 30, 2011): 11–21. https://doi.org/10.1159/000327159.

Leighton, Kimberly J. “Accepting Adoption’s Uncertainty: The Limited Ethics of Pre-Adoption Genetic Testing.” *Journal of Bioethical Inquiry* 11, no. 2 (June 1, 2014): 245–60. https://doi.org/10.1007/s11673-014-9519-2.

Li, Grace, Subhashini Chandrasekharan, and Megan Allyse. “‘The Top Priority Is a Healthy Baby’: Narratives of Health, Disability, and Abortion in Online Pregnancy Forum Discussions in the US and China.” *Journal of Genetic Counseling* 26, no. 1 (February 1, 2017): 32–39. https://doi.org/10.1007/s10897-016-9976-3.

Lowe v. Atlas Logistics Group Retail Servs. Atlanta, LLC, 102 F. Supp. 3d 1360 (US District Court for the Northern District of Georgia 2015).

McBride, Colleen M., Christopher H. Wade, and Kimberly A. Kaphingst. “Consumers’ Views of Direct-to-Consumer Genetic Information.” *Annual Review of Genomics and Human Genetics* 11, no. 1 (2010): 427–46. https://doi.org/10.1146/annurev-genom-082509-141604.

McGrath, Scott, and Dhundy (Kiran) Bastola. “DTC Genetic Testing and Consumer Comprehension.” In *Proceedings of the 5th ACM Conference on Bioinformatics, Computational Biology, and Health Informatics*, 582–583. BCB ’14. New York, NY, USA: ACM, 2014. https://doi.org/10.1145/2649387.2660559.

Munro, Dan. “Class Action Law Suit Filed Against 23andMe.” Forbes, December 2, 2013. http://www.forbes.com/sites/danmunro/2013/12/02/class-action-law-suit-filed-against-23andme/.

Newson, Ainsley J. “Whole Genome Sequencing in Children: Ethics, Choice and Deliberation.” *Journal of Medical Ethics* 43, no. 8 (August 1, 2017): 540–42. https://doi.org/10.1136/medethics-2016-103943.

Oliveri, Serena, Heidi C. Howard, Chiara Renzi, Mats G. Hansson, and Gabriella Pravettoni. “Anxiety Delivered Direct-to-Consumer: Are We Asking the Right Questions about the Impacts of DTC Genetic Testing?” *Journal of Medical Genetics* 53, no. 12 (December 1, 2016): 798–99. https://doi.org/10.1136/jmedgenet-2016-104184.

Parens, Erik, and Adriene Asch. “The Disability Rights Critique of Prenatal Genetic Testing.” *The Hastings Center Report; Hastings-on-Hudson* 29, no. 5 (October 1999): S1-22.

Petersen, Helle Vendel, Mef Nilbert, Inge Bernstein, and Christina Carlsson. “Balancing Life with an Increased Risk of Cancer: Lived Experiences in Healthy Individuals with Lynch Syndrome.” *Journal of Genetic Counseling* 23, no. 5 (October 1, 2014): 778–84. https://doi.org/10.1007/s10897-013-9682-3.

Picard, Andre. “Controversial Genetic Self-Testing Kits Coming to Canada.” The Globe and Mail, October 2, 2014. http://www.theglobeandmail.com/life/health-and-fitness/health/genetic-self-testing-kits-to-come-to-canada/article20885678/.

Pollack, Andrew. "23andMe Will Resume Giving Users Health Data." *The New York Times,* October 21, 2015. http://www.nytimes.com/2015/10/21/business/23andme-will-resume-giving-users-health-data.html.

———. "F.D.A. Faults 5 Companies on Genetic Tests." *The New York Times,* June 11, 2010. http://www.nytimes.com/2010/06/12/health/12genome.html.

———. "F.D.A. Orders Genetic Testing Firm to Stop Selling DNA Analysis Service." *The New York Times*, November 25, 2013. http://www.nytimes.com/2013/11/26/business/fda-demands-a-halt-to-a-dna-test-kits-marketing.html.

Powell, Karen P., Whitney A. Cogswell, Carol A. Christianson, Gaurav Dave, Amit Verma, Sonja Eubanks, and Vincent C. Henrich. "Primary Care Physicians' Awareness, Experience and Opinions of Direct-to-Consumer Genetic Testing." *Journal of Genetic Counseling* 21, no. 1 (July 16, 2011): 113–26. https://doi.org/10.1007/s10897-011-9390-9.

Prince, Anya, Jonathan S. Berg, James P. Evans, Daniel E. Jonas, and Gail Henderson. "Genomic Screening of the General Adult Population: Key Concepts for Assessing Net Benefit with Systematic Evidence Reviews." *Genetics in Medicine; Chapel Hill* 17, no. 6 (June 2015): 441–43. http://dx.doi.org/10.1038/gim.2014.129.

Quillin, John M. "Lifestyle Risk Factors Among People Who Have Had Cancer Genetic Testing." *Journal of Genetic Counseling* 25, no. 5 (October 1, 2016): 957–64. https://doi.org/10.1007/s10897-015-9925-6.

Rettner, Rachael. “23andMe: What’s Really Wrong with Personal Genetic Tests.” Live Science, November 26, 2013. http://www.livescience.com/41534-23andme-direct-to-consumer-genetic-test-shortcomings.html.

Roberts, J. Scott, and Jenny Ostergren. “Direct-to-Consumer Genetic Testing and Personal Genomics Services: A Review of Recent Empirical Studies.” *Current Genetic Medicine Reports* 1, no. 3 (July 12, 2013): 182–200. https://doi.org/10.1007/s40142-013-0018-2.

Robinson, Ann. “DNA-Testing Kit 23andme: Patient-Powered Healthcare or Just Confusing?” *The Guardian*, January 12, 2016, sec. Guardian Sustainable Business. https://www.theguardian.com/sustainable-business/2016/jan/12/dna-testing-kit-23andme-patient-powered-healthcare-genetics.

Rothstein, Mark A. “The Case against Precipitous, Population Wide, Whole-Genome Sequencing.” *The Journal of Law, Medicine & Ethics* 40, no. 3 (September 2012): 682–89. https://doi.org/10.1111/j.1748-720X.2012.00699.x.

Secretary’s Advisory Committee on Genetics, Health, and Society. “Direct-to-Consumer Genetic Testing.” Department of Health and Human Services, April 2010. http://oba.od.nih.gov/oba/SACGHS/reports/SACGHS_DTC_report_2010.pdf.

Shakespeare, Tom. “Choices and Rights: Eugenics, Genetics and Disability Equality.” *Disability & Society; Abingdon* 13, no. 5 (November 1998): 665.

Sijmons, R H. “A Clinical Perspective on Ethical Issues in Genetic Testing.” *Accountability in Research* 18, no. 3 (2011): 148–62.

Singleton, Amanda, Lori Hamby Erby, Kathryn V. Foisie, and Kimberly A. Kaphingst. "Informed Choice in Direct-to-Consumer Genetic Testing (DTCGT) Websites: A Content Analysis of Benefits, Risks, and Limitations." *Journal of Genetic Counseling* 21, no. 3 (December 23, 2011): 433–39. https://doi.org/10.1007/s10897-011-9474-6.

Smith, Oliver. "23andMe Analyzed My DNA, but Is It a Good Idea?" The Memo, April 25, 2016. http://www.thememo.com/2016/04/25/23andme-scientists-dna-genetics-analysed-ethics-scientist/.

Stern, S. J., K. S. Arnos, L. Murrelle, K. Oelrich Welch, W. E. Nance, and A. Pandya. "Attitudes of Deaf and Hard of Hearing Subjects towards Genetic Testing and Prenatal Diagnosis of Hearing Loss." *Journal of Medical Genetics; London* 39, no. 6 (June 2002): 449. http://dx.doi.org/10.1136/jmg.39.6.449.

Suwannarat, MD, Pim. "Why You Should Think Twice About At-Home Genetic Testing." US News & World Report, July 11, 2016. http://health.usnews.com/health-news/patient-advice/articles/2016-07-11/why-you-should-think-twice-about-at-home-genetic-testing.

Tarini, Beth A., and Aaron J. Goldenberg. "Ethical Issues with Newborn Screening in the Genomics Era." *Annual Review of Genomics and Human Genetics* 13, no. 1 (September 12, 2012): 381–93. https://doi.org/10.1146/annurev-genom-090711-163741.

Teichert, Erica. "23andMe Escapes California Class Action." Modern Healthcare, August 24, 2016. http://www.modernhealthcare.com/article/20160824/NEWS/160829974.

Wade, Christopher H., Beth A. Tarini, and Benjamin S. Wilfond. "Growing Up in the Genomic Era: Implications of Whole-Genome Sequencing for Children, Families, and Pediatric Practice." *Annual Review of Genomics and Human Genetics* 14, no. 1 (August 31, 2013): 535–55. https://doi.org/10.1146/annurev-genom-091212-153425.

Wasson, Katherine, Tonya Nashay Sanders, Nancy S. Hogan, Sara Cherny, and Kathy J. Helzlsouer. "Primary Care Patients' Views and Decisions about, Experience of and Reactions to Direct-to-Consumer Genetic Testing: A Longitudinal Study." *Journal of Community Genetics* 4, no. 4 (July 7, 2013): 495–505. https://doi.org/10.1007/s12687-013-0156-y.

Whoriskey, Peter. "Wondering If You Have the Gene Linked to Alzheimer's? You May Have to Leave the U.S. to Find Out." Washington Post, December 7, 2015. https://www.washingtonpost.com/news/wonk/wp/2015/12/07/wondering-if-you-have-the-gene-linked-to-alzheimers-you-may-have-to-leave-the-u-s-to-find-out/.

Wolf, Susan M., and Jeffrey P. Kahn. "Genetic Testing and the Future of Disability Insurance: Ethics, Law & Policy." *The Journal of Law, Medicine & Ethics* 35 (June 1, 2007): 6–32. https://doi.org/10.1111/j.1748-720X.2007.00148.x.

Zhang, Di, Vincent H. Ng, Zhaochen Wang, Xiaomei Zhai, and Reidar K. Lie. "Eugenics and Mandatory Informed Prenatal Genetic Testing: A Unique Perspective from China." *Developing World Bioethics* 16, no. 2 (August 1, 2016): 107–15. https://doi.org/10.1111/dewb.12088.

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